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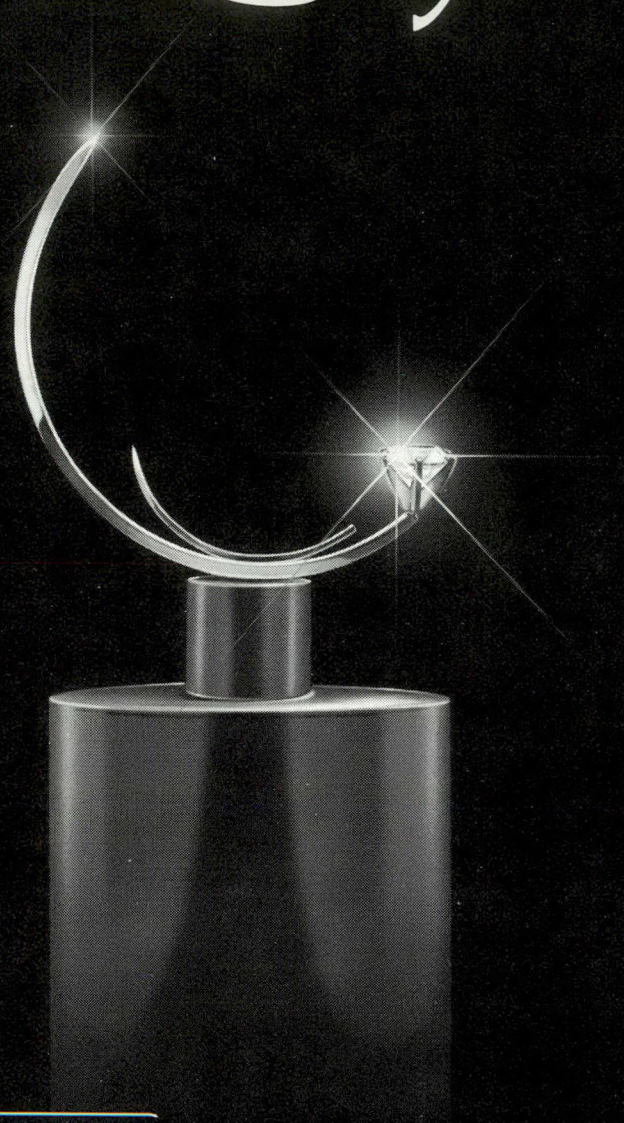

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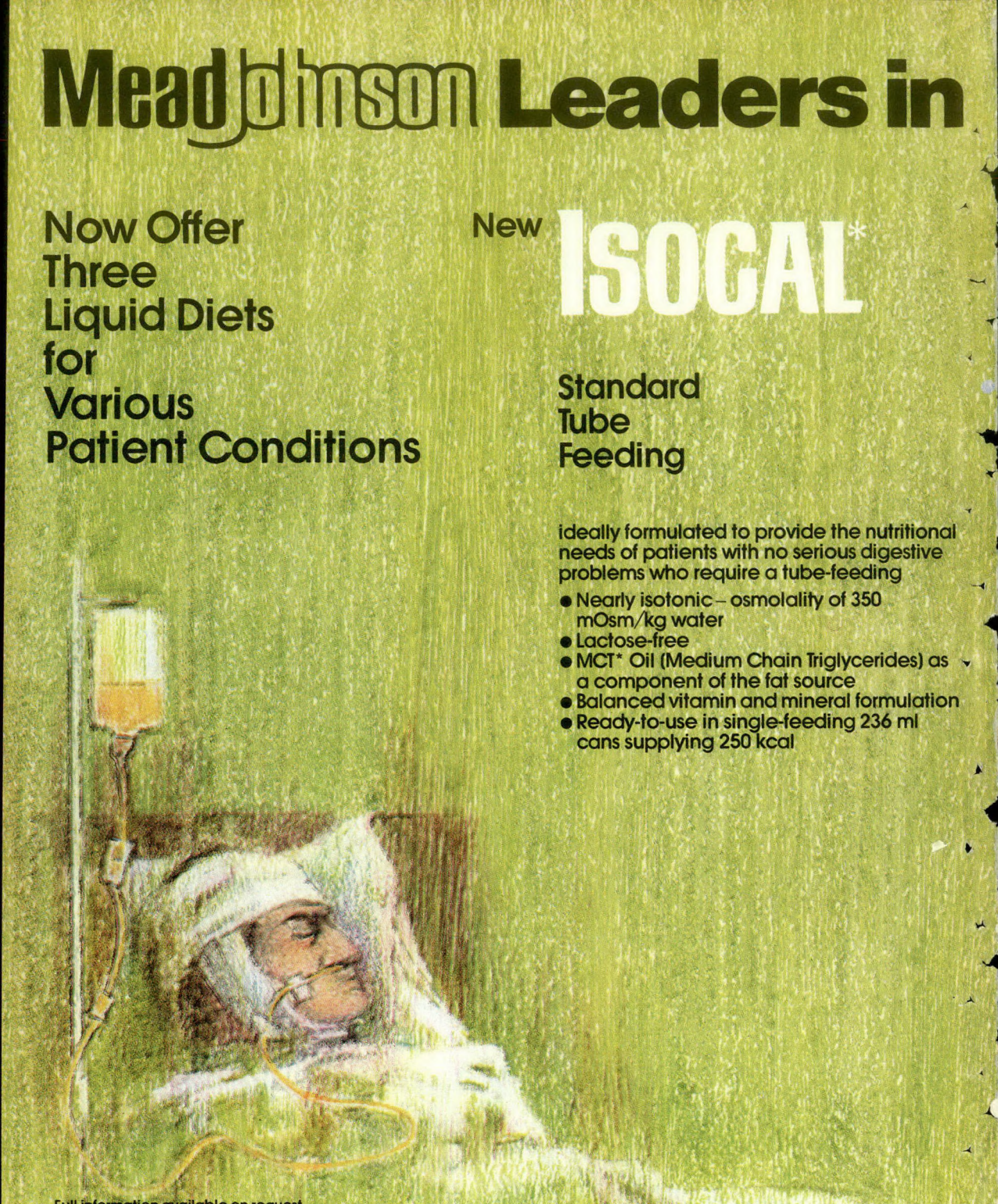

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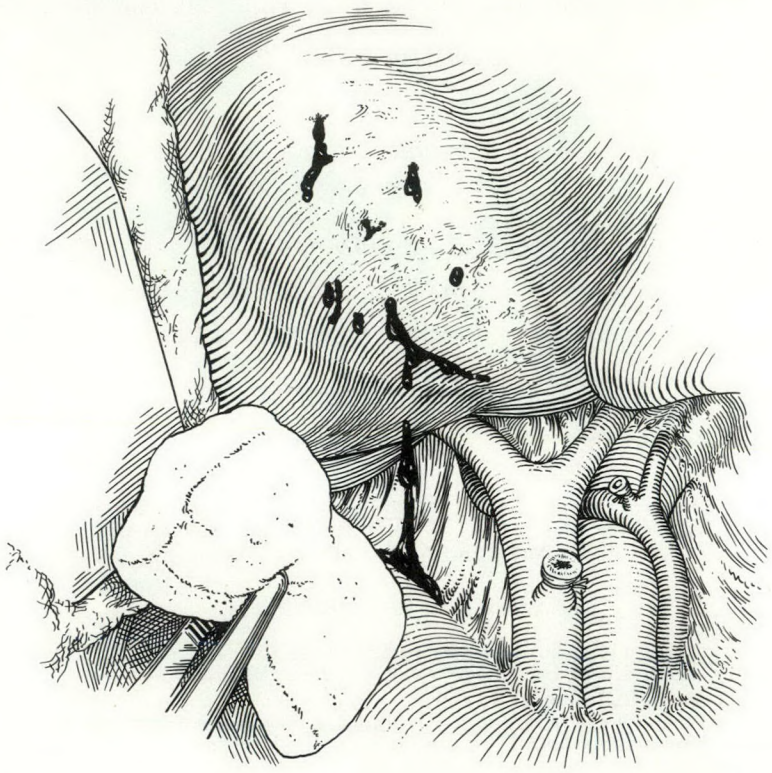

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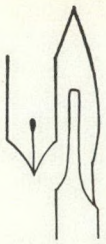

QUILL ON SCALPEL This section provides a medium through which Canadian surgeons can declare themselves, briefly and informally, on the day-to-day affairs of surgery.

ROUTINE OPERATIVE CHOLANGIOGRAPHY DURING CHOLECYSTECTOMY

During the past 15 years, operative cholangiography has been used increasingly in detecting stones in the common bile duct during cholecystectomy. Although most surgeons agree on the need for an operative cholangiogram after exploration of the common bile duct, not all have considered the procedure to be necessary during cholecystectomy. Some have strongly advocated the routine use of operative cholangiography—that is, for every cholecystectomy. On page 449 of the Journal, Nanson makes just such a plea and provides data to support his contention. The data were obtained from a retrospective study of 151 patients who underwent biliary tract surgery, 18 for secondary common bile duct exploration and 133 for cholecystectomy. Nanson describes eight benefits of operative cholangiography and concludes that the technique has taken the guess-work out of biliary tract surgery.

Nanson's arguments are for the most part unassailable. None would question the value of operative cholangiography in the diagnosis of anatomic abnormalities, for tumours involving the bile ducts, and as a check after choledochotomy. But debate will continue on the first two of the benefits Nanson describes; that is, the diagnosis of unsuspected stones and the avoidance of negative common bile duct exploration. Is routine use of cholangiography required to achieve these benefits? Many authors would agree with Nanson's affirmative answer and, moreover, point out the simplicity and safety of the procedure. In fact, many surgeons have adopted it as a routine procedure and would hold that without it cholecystectomy is incomplete. Can there be any argument to support the surgeon who does not use cholangiography routinely? For those who have carefully sifted the literature on the subject, a few disquieting facts remain that might still ruffle the enthusiasts. One concerns the yield rate of common duct stones from patients undergoing cholecystectomy. The American College of Surgeons study, which reviewed 28 621 cholecystectomies, disclosed that common bile duct stones were found in approximately 7% of patients.[1] Colcock and Perey[2] in 1964 reported common bile duct stones in 7.9% of 1754 patients undergoing cholecystectomy and Colcock and McManus[3] in 1955 gave an incidence of 10.4% of 1104 patients. In the Hampson and Petrie[4] series of 2090 cholectomies reported in 1964, stones were found in the common bile duct in 7.4% of patients. It is of interest that the use of operative cholangiography with cholecystectomy in 25% of patients in the American College study did not increase the yield of common bile duct stones compared with the other series in which a cholangiogram was seldom done with cholecystectomy. In other words, not enough unsuspected stones were found in this study to increase the recovery rate of common duct stones over other series. Further, Bartlett[5] was able to achieve a greater harvest of common bile duct stones without the aid of cholangiography. He found them in 16% of patients undergoing cholecystectomy; admittedly this accomplishment required a common duct exploration rate of 43%. It might be anticipated that routine operative cholangiography would result in a high yield rate of common bile duct stones without so many common bile duct explorations. But enthusiasts for routine cholangiography such as Schulenburg,[6] Mehn,[7] and Hermann and Hoerr[8] have strongly recommended its use without showing a higher yield rate of common bile duct stones. The latter benefit, though not the only one, is surely a major one.

Nanson does in fact report a commendably high yield rate of common duct stones (14.3%), which he believes is due to frequent and careful use of operative cholangiography. Interpretation of Nanson's data reveals that 88% of patients undergoing cholecystectomy had an operative cholangiogram, at least 20% of the patients had common bile duct exploration, and the yield rate of common bile duct stones was 14.3%. Thus, he has justified his first two claims for cholangiography: the discovery of unsuspected stones and the avoidance of unnecessary choledochotomy.

But even granting that the procedure will yield more common duct stones there remains the question of follow-up. Do patients having a cholangiogram with cholecystectomy fare better in the long run than patients having a cholecystectomy alone? Nanson's study suggests they should. But Madsen,[9] who studied two series of cholecystectomies—237 with operative cholangiography in 86%, and 237 with cholangiography in 25%—was unable to find enough evidence from a 5-year follow-up study to justify routine use of the procedure. The patients who did not have cholangiography fared surprisingly well.

Finally, one might expect a decrease in the incidence of secondary common bile duct exploration if operative cholangiography was performed more frequently. A recent study has shown only a slight decrease in the incidence (from 2.2 to 1.6%) of secondary common bile duct exploration as the frequency of operative cholangiography rose from zero to 36%.[10]

Operative cholangiography is clearly safe and has many advantages. Nanson's paper should encourage its use during cholecystectomy if there is the slightest doubt concerning the presence of stones in the common bile duct. Dogmatic insistence that it be done with every cholecystectomy is a position that is still debatable.

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REFERENCES

1. ARNOLD DJ: 28,621 cholecystectomies in Ohio. Results of survey in Ohio hospitals by Gallbladder Survey Committee, Ohio Chapter, American College of Surgeons. *Am J Surg* 119: 714, 1970
2. COLCOCK BP, PEREY B: Exploration of common bile duct. *Surg Gynecol Obstet* 118: 20, 1964
3. COLCOCK BP, MCMANUS JE: Experiences with 1,356 cases of cholecystitis and cholelithiasis. *Surg Gynecol Obstet* 101: 161, 1955
4. HAMPSON LG, PETRIE EA: Problem of stones in common bile duct with particular reference to retained stones. *Can J Surg* 7: 361, 1964
5. BARTLETT MK, QUINBY WC: Surgery of biliary tract; mortality and complications of cholecystectomy and choledochostomy for chronic cholecystitis. *N Engl J Med* 254: 154, 1956
6. SCHULENBERG CA: Operative cholangiography: 1,000 cases. *Surgery* 65: 723, 1969
7. MEHN WH: Operating room cholangiography. *Surg Clin North Am* 34: 151, 1954
8. HERMANN RE, HOERR SO: Value of routine use of operative cholangiography. *Surg Gynecol Obstet* 121: 1015, 1965
9. MADSEN CM: Routine or elective cholangiography during cholecystectomy? *Acta Chir Scand* suppl 283: 247, 1961
10. DUFF JH, SALVIAN AG, FINLEY RJ: Incidence of secondary common bile duct exploration. *Surg Gynecol Obstet* 139: 723, 1974.

CURRENT CONCEPTS

FRACTURE HEALING*

RICHARD L. CRUESS, MD, FRCS[C] and JACQUES DUMONT, MD, FRCS[C]

Summary: The sequence of events occurring after a fracture is now relatively well understood. Healing takes place in three phases—inflammatory, reparative and remodelling. In each phase certain cells predominate and specific histologic and biochemical events are characteristic. Factors that influence fracture healing are both local and systemic; the former include particularly the degree of local trauma and bone loss, the type of bone affected, the degree of immobilization and local pathologic conditions; the latter include age, hormones, local stress and electric currents. Natural processes of healing should be allowed to take their usual course and interference should be attempted only when there is demonstrable need or substantial advantages for the patient.

Résumé: Aujourd'hui, nous connaissons relativement bien la succession d'événements qui surviennent après une fracture. La guérison s'opère en trois phases: une phase inflammatoire, une phase de réparation et la dernière de remodelage. Dans chacune de ces phases, certaines cellules prédominent et les modifications histologiques et biochimiques spécifiques sont caractéristiques. Les facteurs qui jouent un rôle dans la guérison des fractures sont à la fois locaux et généraux. Parmi les premiers, figurent particulièrement le degré du trauma local et la perte de substance osseuse, le type d'os qui a été lésé, le degré de l'immobilisation et les conditions pathologiques locales. Dans les derniers, on trouve l'âge du blessé, son état hormonal, le stress local et les courants électriques. Il faut laisser à la nature le soin de suivre son évolution normale vers la guérison et on ne devra tenter d'intervenir dans cette évolution que si on peut mettre en évidence un besoin particulier ou des avantages considérables pour un malade donné.

*From the orthopaedic and accident services, Royal Victoria Hospital and McGill University, Montréal, Qué.

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The material contained in this article formed portion of a chapter (The Healing of Mesenchymal Tissues) of a book entitled "Fractures", edited by Charles A. Rockwood, Jr. and David P. Green, published by J. B. Lippincott, Co., Philadelphia, 1975.

Reprint requests to: Dr. R. L. Cruess, Orthopedic surgeon-in-chief, Royal Victoria Hospital, 687 Pine Ave. W., Montréal, Qué. H3A 1A1.

THE musculoskeletal system is a complex and important portion of the human body and damage to it is seldom simple. The structures injured include bones and soft tissues, joints, muscles, tendons, ligaments and blood vessels. Other organ systems also may be injured, making repair complex. Throughout human evolution, repair processes have developed that are predictable and ensure survival of the species because its individual members are able to return to a useful, functional existence; a knowledge of these active repair processes is essential for any surgeon who undertakes to treat injuries of the musculoskeletal system. It appears reasonable that, wherever possible, the natural processes should be allowed to take their usual course and that interference with them should only be attempted where there is demonstrable need or substantial advantages for the individual patient.

BASIC ELEMENTS OF FRACTURE HEALING

The sequence of events following a break in continuity of a bone has gradually become more clearly understood, and the cellular responses involved are now known to be quite complex. Fracture healing can conveniently be divided into a number of phases but events described in one phase persist into the next and events apparent in a subsequent phase begin before this particular phase predominates (Fig. 1). Thus, the division into phases is arbitrary, but this does make the overall picture clearer. These events have been described through the years in investigative reports and review articles.[1, 2]

Inflammatory Phase

A fracture results in damage to the bone itself (Fig. 2). The soft-tissue envelope including the periosteum and surrounding muscles tears and numerous blood vessels crossing the fracture line rupture. A hematoma accumulates within the medullary canal, between the fracture ends, and be-

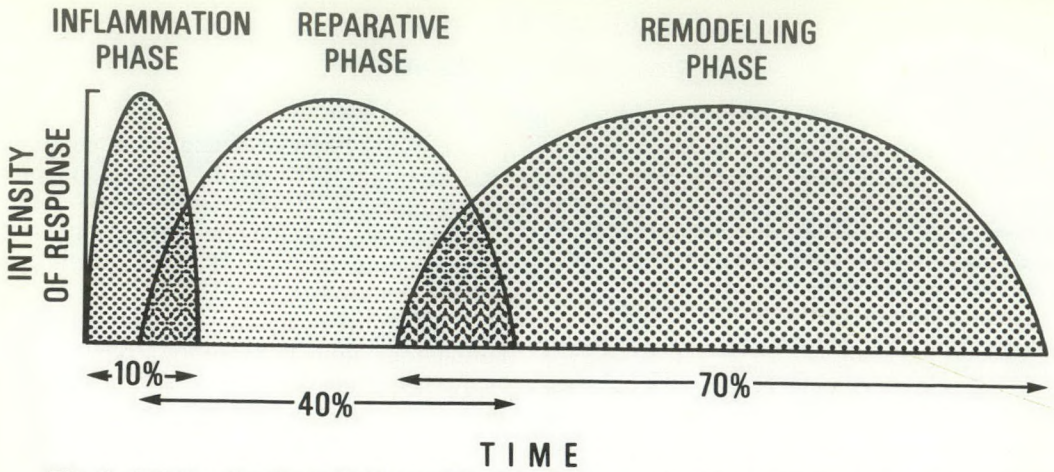

Fig. 1.—Relative durations of phases of inflammation, repair and remodelling in fracture healing.

neath any elevated periosteum; this blood rapidly forms a clot. Damage to the blood vessels has important effects. Osteocytes are deprived of their nutrition; they die as far back as the junction of collateral channels. Thus, the immediate ends of a fracture are dead as they contain no living cells. Severely damaged periosteum and marrow, as well as other surrounding soft tissues, may also add necrotic material to the region.[1]

The large amount of necrotic material elicits an immediate and intense acute inflammatory response. Widespread vasodilatation and exudation of plasma lead to the

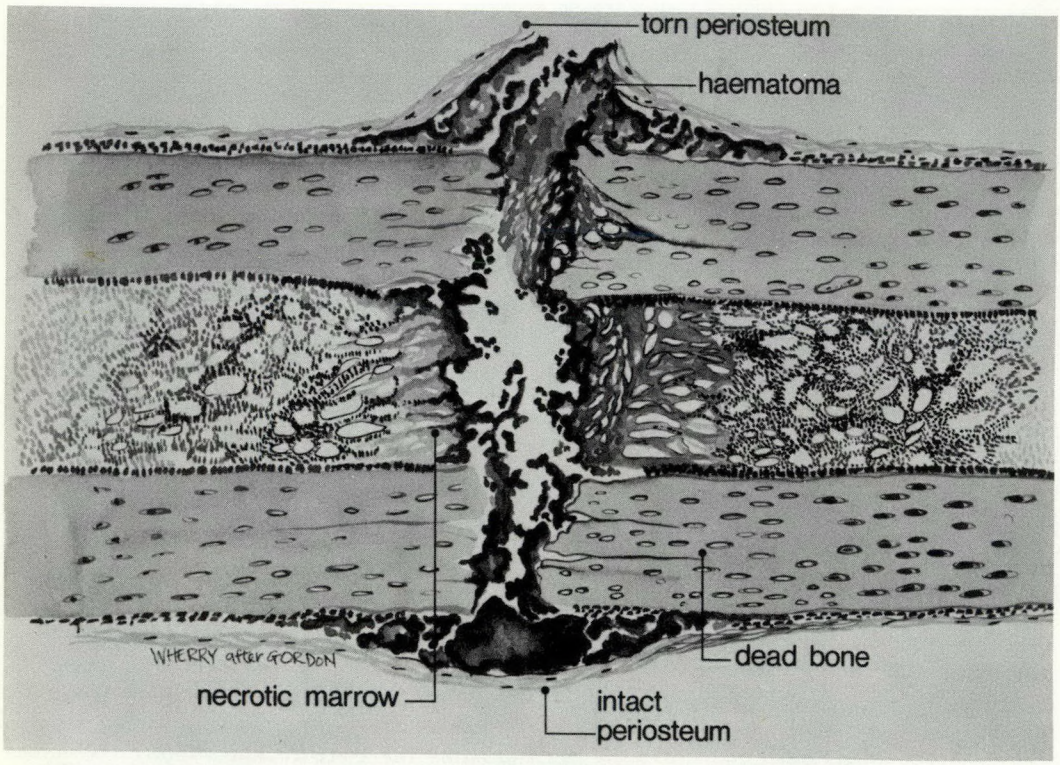

Fig. 2.—Initial events in fracture healing of long bone. Note torn periosteum opposite point of impact with, in many instances, intact periosteum on other side; development of hematoma beneath periosteum and between fracture ends; and necrotic marrow and dead bone close to fracture line.

acute edema seen in the region of a fresh fracture. Acute inflammatory cells migrate to the region, as do polymorphonuclear leukocytes and then macrophages. As the acute inflammatory response becomes less intense, the second phase begins and gradually becomes predominant.

Reparative Phase

The first step in the reparative phase is identical to the process seen in other tissues. The hematoma is organized (Fig. 3) and, though there is some controversy as to the necessity of this step, it appears that it is inevitable in the natural process of repair.[3] The hematoma, which probably has a small mechanical role in immobilizing the fracture, serves primarily as a fibrin scaffold over which reparative cells act.[4] The microenvironment at this stage about the fracture is known to be acid,[5] and this may well provide an additional stimulus to cellular behaviour during the early phases of repair. During the reparative process, the tissue pH gradually returns first to neutral and then becomes slightly alkaline.

The cells participating directly in the repair of fractures are of mesenchymal origin and are pluripotential. During fracture healing, cells, probably of common origin, form collagen, cartilage and bone. Small variations in their microenvironment and in the stresses to which they are subjected probably account for the function that predominates.[6] Some cells are derived from the cambium layer of the periosteum and form the earliest bone, particularly in children in whom this layer is active and important. Endosteal cells also participate. Surviving osteocytes do not take part in the repair process as they are destroyed during resorption.[7] However, the majority of cells directly taking part in fracture healing enter the fracture site with the granulation tissue that is seen to invade the region from surrounding vessels.[8] Whether these reparative cells are derived directly from endothelium,[8] are "wandering cells",[9] or are derived from nucleated red cells[10] seems of less importance than the fact that repair is indivisibly linked with the ingress of capillary buds.

The entire vascular bed of an extremity

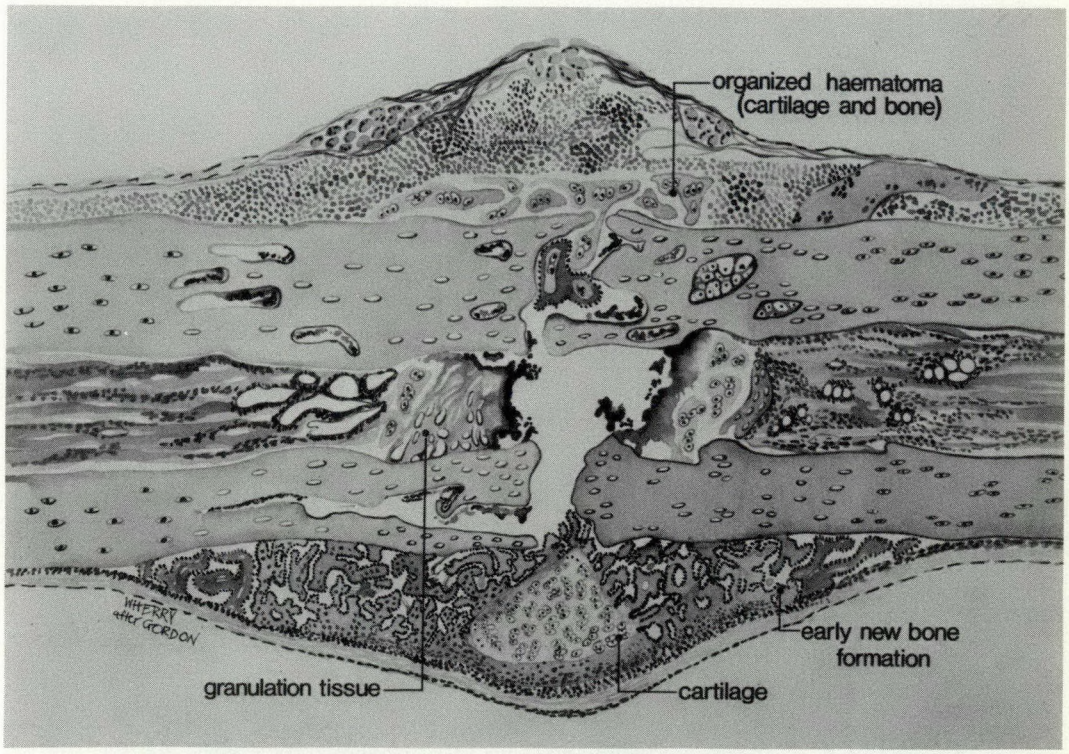

Fig. 3.—Early stage of repair at fracture site, with organization of hematoma, early primary new bone formation in subperiosteal regions and cartilage formation elsewhere.

enlarges shortly after the fracture has occurred but the osteogenic response is limited largely to the zones surrounding the fracture itself.[11] The principal origin of the blood vessels has been the subject of controversy but it appears that, ordinarily,[12, 13] the periosteal vessels contribute the majority of capillary buds early in normal bone healing, the nutrient medullary artery becoming more important later. When the surgeon interferes with this natural process, either by excessive stripping of the periosteum or by destroying the intramedullary system through the use of medullary nails, repair must proceed through the participation of vessels derived from the surviving system.[14]

The cells that invade the hematoma and rapidly begin to produce the tissue known as callus—made up of fibrous tissue, cartilage, and young, immature fibre bone—rapidly envelop the ends of the bone, with a resulting gradual increase in stability of the fracture fragments. The mechanisms controlling the behaviour of each individual cell at this stage of the repair process probably derive from the microenvironment in which the cell finds itself. Compression or the absence of tension discourages the formation of fibrous tissue. Variations in oxygen tension undoubtedly lead to the formation of either bone or cartilage; cartilage is formed where oxygen tensions are relatively low,[6] presumably because of the distance of the cell from its blood supply.[12]

Cartilage, thus formed, will eventually be resorbed by a process that is indistinguishable except for its lack of organization from endochondral bone formation. Bone will be formed *per primum* by those cells that have an adequate oxygen supply and are subjected to the proper mechanical stimuli. Early in the repair process, cartilage formation predominates and glycosaminoglycans are found in high concentrations. Later, bone formation is more obvious (Fig. 4).

Biochemically, events follow a sequential pattern: a high concentration of glycosaminoglycans early in the reparative process is followed by a gradual increase in the concentration of collagen, and an accumu-

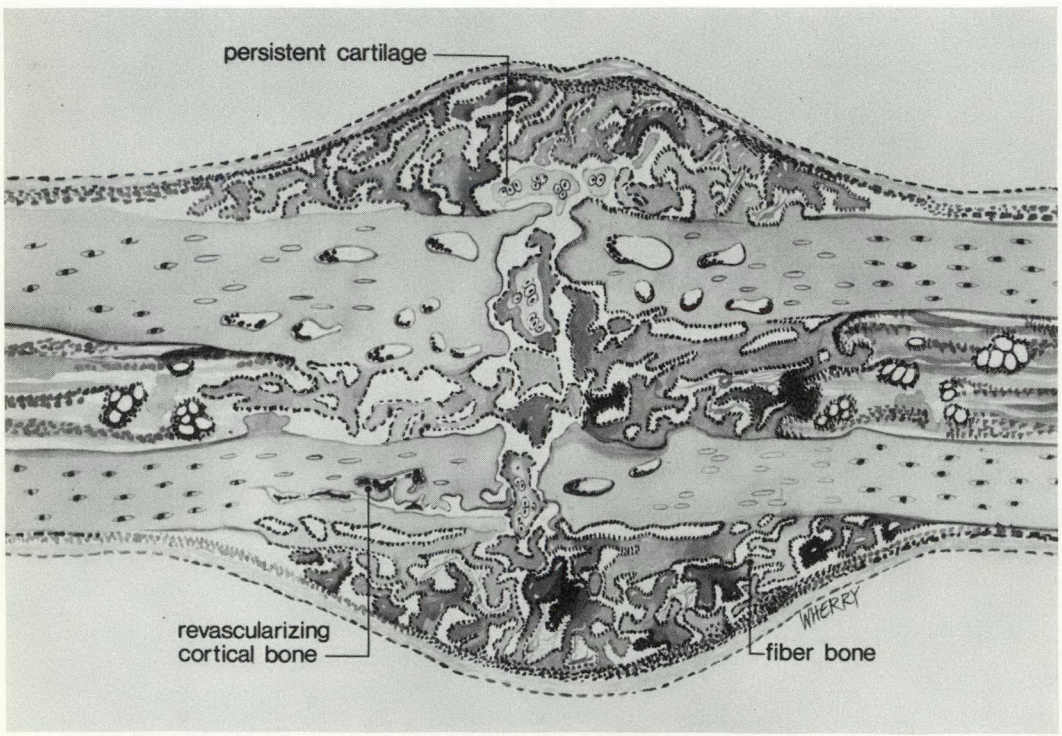

Fig. 4.—Later stage of repair at fracture site, with early immature fibre bone bridging fracture gap; persistent cartilage seen at points most distant from ingrowing capillary buds, which, in many areas, are surrounded by young new bone.

lation of calcium hydroxyapatite crystals constitutes a third stage (Fig. 5). The collagen content (on a weight basis) tends to return to normal after mineralization has occurred.[15]

Mineralized tissues are highly organized in their internal structure, this organization resulting from cellular activity. The initial step is the formation by osteoblasts of tropocollagen, which moves from an intracellular to an extracellular location and polymerizes to form collagen fibrils.[16]

Collagen fibrils have their own internal organization, and within the substance of the fibrils are spaces.[17] The spacing of these "hole zones" is quite regular and is related to the internal structure of the collagen molecules (Fig. 6).

The initial appearance of mineral in this region[18] is the consequence of an interaction between metastable solutions of calcium and phosphate and the groups of specific amino acid side-chains within the holes.[19] A series of organized collagen fibrils develop, within and around which are clustered crystals of calcium hydroxyapatite.

As this phase of repair takes place, the bone ends gradually become enveloped in a fusiform mass of callus containing increasing amounts of bone. Immobilization of the fragments becomes more rigid because of this internal and external callus formation, and clinical "union" eventually is said to have occurred. But union as an end point does not exist, because in the middle of the reparative phase the remodelling phase begins, with resorption of unneeded or inefficient portions of the callus and the laying down of trabecular bone along lines of stress.

Remodelling Phase

In 1892, Wolff[20] recognized that the architecture of the skeletal system corresponded to the mechanical need of this system and postulated his law. Remodelling about a fracture occurs over a prolonged period. Radioisotope studies have shown that increased activity in a fracture bone takes place for many more months than had previously been realized.[21]

Osteoclastic resorption of superfluous or poorly placed trabeculae occurs, and new struts of bone are laid down corresponding to lines of force. The control mechanism modulating this cellular behaviour is now

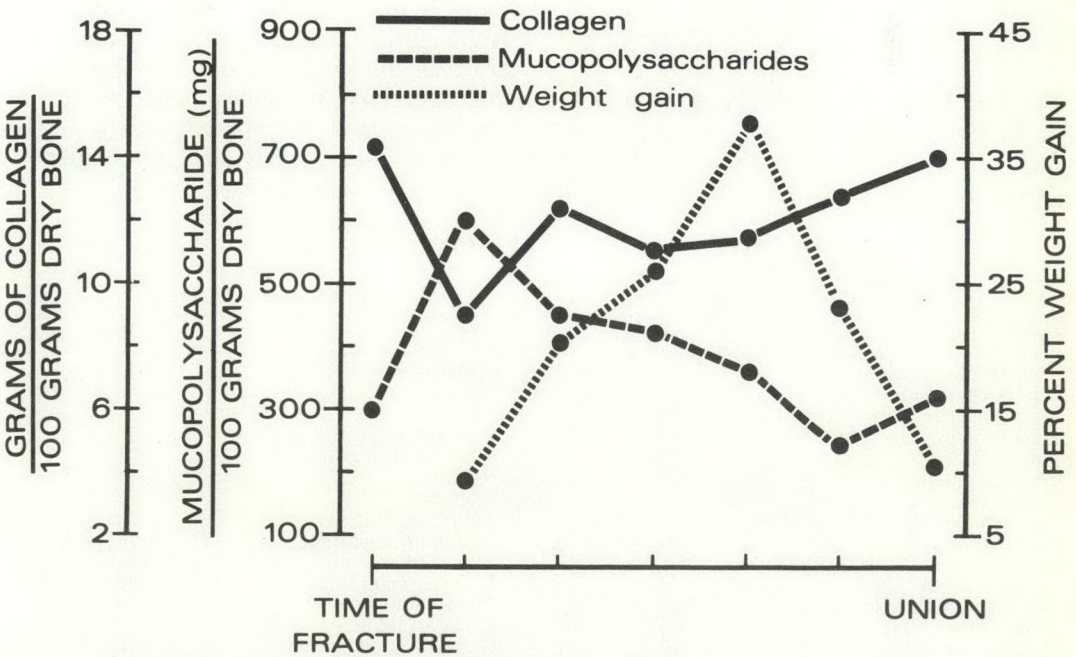

Fig. 5.—Summary of biochemical events following fracture. Collagen formation precedes accumulation of mineral, and mucopolysaccharide concentration decreases gradually as fracture healing progresses after initial rise.

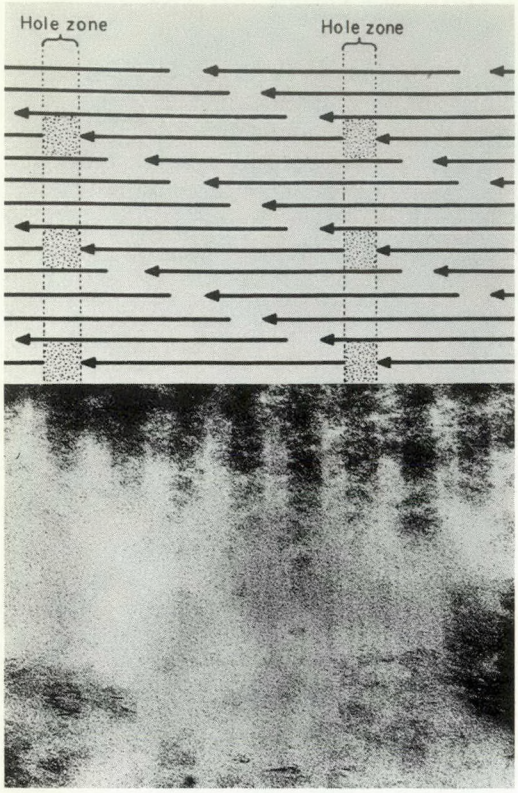

Fig. 6.—Mineralization in collagen at fracture site, the first mineral appearing in "hole zone". (Reproduced by permission from GLIMCHER MJ: Basic architectural principle in organization of mineralized tissues. *Clin Orthop* 61: 16, 1969.)

believed to be electrical. In stressing of a bone, electropositivity occurs on the convex surface and electronegativity on the concave, the current having been produced by a piezoelectric effect.[22] Circumstantial evidence indicates that regions of electropositivity are associated with osteoclastic activity and that regions of electronegativity are associated with osteoblastic activity.[23] Although the biophysical principles affecting bone structure are complex, their importance is established; moreover, Wolff's law is explainable in terms of alterations in the electric currents generated by crystalline structures within the bone that have a direct effect on cellular behaviour. The cellular module that controls remodelling is the resorption unit; this consists of osteoclasts that resorb bone and osteoblasts that lay down new haversian systems later.[24] The end result of the remodelling process is a bone that, if it has not returned to its original form, has been altered so that it may best perform the function demanded of it.

Conditions Influencing and Affecting Fracture Healing

Healing of a fracture is a consequence of cellular behaviour in a living organism and, as such, can be modified by almost all endogenous or exogenous factors that affect the metabolic function of cells. The literature abounds in reports of factors that can either promote or retard bone healing (Table I).[25] Although most of these factors probably do exert an influence that can be measured in the laboratory, in clinical practice fracture healing appears to proceed with a certain degree of predictability and is modified by relatively few influences.

TABLE I.—Factors Influencing Bone Healing

Claimed to promote healing		*Claimed to retard healing*	
Factor	*References*	*Factor*	*References*
Growth hormone	32, 49 - 52	Corticosteroids	46, 52, 60
Triiodothyronine	53	Alloxan diabetes	69, 70
Thyroxin	54	Castration	54
Thyrotropin	50	Vitamin A, high dose	58
Calcitonin	55, 56	Vitamin D, high dose	71
Insulin	57	Rachitis	71
Vitamin A	58	Anemia	72
Vitamin D	59	Aminoacetonitrile	73
Anabolic steroids	60	β-aminopropionitrile	74
Chondroitin sulfate	61, 62	Bone wax	75
Hyaluronidase	63	Delayed manipulation	36
Anticoagulants (dicumarol)	64	Denervation	76
Ultrasonics	65	X-ray irradiation	77
Electric currents	10	Hyperbaric oxygen (6 h, 2 atmospheres daily)	78
Hyperbaric oxygen (2 h, 3 atmospheres daily)	66, 67	Anticoagulants (dicumarol)	79
Physical exercise	68		

Local Factors

Degree of local trauma.—Fracture healing has been described as involving differentiation of cells from a mesenchymal pool. Fractures associated with more local trauma or trauma to the soft tissues surrounding the bone are well known to heal slowly, undoubtedly because the mesenchymal cells are relatively few and differentiate relatively slowly. The soft-tissue envelope around the fracture, in addition to providing mesenchymal cells for fracture healing, must here aid healing of the soft tissues themselves. Also, the hematoma escapes into the soft tissues, leading to a diffusion of mesenchymal cell effort. Finally, in simpler fractures a soft-tissue envelope is intact, at least on the concave side of a fracture, and this provides both a ready source of mesenchymal cells and a tube that directs the reparative efforts of these cells in the proper direction early.[26] This tube, of course, also helps to immobilize the fragments. The differences in the repair process between undisplaced and displaced fractures are well documented[12, 13] and concern a retardation of the rate, an increase in the amount of cartilage formed and a decrease in the amount of primary bone formation between fracture ends.

Open reduction itself increases the degree of local trauma and thus will ultimately retard healing. Introduction of metallic implants, no matter how inert, also will elicit tissue reaction[27] that makes use of reparative processes that otherwise would be directed exclusively to fracture healing. Therefore, some degree of interference with the normal reparative process is inevitable when it becomes necessary or desirable to carry out internal fixation of fractures—not a condemnation of internal fixation but a recognition of fact.

Degree of bone loss.—The end result of any metabolic function depends on the ability of the local cells to perform a given function. If the function exceeds their capacity, it will be performed either slowly or not at all. Loss of bone substance or excessive distraction of the fragments will lead to a condition in which the cells' ability to bridge the gap will be compromised.

Type of bone affected.—Cortical and cancellous bone respond to fractures somewhat differently. Cancellous bone unites rapidly, but only at points of direct contact. Where cancellous bone is not in contact, the gap will be filled by the spread of new bone from points of contact.[26, 28] Repair in cancellous bone is rapid because there are many points of bony contact rich in cells and blood supply. Charnley has commented on the lack of callus about fractures, which are primarily in cancellous regions.[26, 28]

Cortical bone unites by two mechanisms, depending on the local conditions. If apposition of cortical bone is exact and if immobilization is rigid, healing takes place end-to-end from the cortical surfaces, with very little external callus.[25, 29-40] If, on the other hand, the fragments are widely displaced, or if immobilization is not rigid, the standard process of repair involving external callus is seen.

Degree of immobilization.—This factor, together with the amount of soft-tissue trauma, probably is of paramount importance. Every clinician is aware that inadequate immobilization leads to delayed or nonunion. Experimentally, repeated manipulation retards fracture healing. It is probable that the initial fibrin scaffolding, which is formed as the first step in fracture repair, is disrupted if immobilization is not adequate and the bony bridge of external callus fails to form properly. If immobilization continues to be inadequate throughout the repair process, a cleft forms between the fracture ends and a false joint develops; the classical pseudarthrosis results.

Infections.—For fracture healing to proceed at a satisfactory rate, the local resources must be devoted primarily to healing the break in bony continuity. If infection is superimposed on a fracture or if the fracture occurs as a result of the infection, the local defences will be mobilized, either all or in part, to attempt to wall off and eliminate the infection. Healing will be retarded or may not occur at all.[41]

Local malignancy.—Unless the malignancy itself is treated, fractures through bone affected by a primary or secondary neoplasm usually will not heal. Subperiosteal new bone formation and callus can be seen microscopically but the presence of malig-

nant cells precludes effective immobilization of the fracture. This is particularly true if the malignant lesion is an expanding one, in which there is actually extension of the deposit into the areas from which healing must take place.

Other local pathologic conditions.—Fractures through bones affected by nonmalignant lesions may heal in some instances[30] but many conditions[31] such as Paget's disease or fibrous dysplasia heal slowly or not at all. Once more, the cause is a failure of normal differentiation of mesenchymal cells, and of ingrowth of capillaries from the surrounding tissues.

Radiation necrosis of bone.—Irradiated bone heals at a greatly retarded rate and, in many instances, nonunion results.[42] This is attributed to the patchy death of cells in the local region, to thrombosis of vessels and to the fibrosis of the marrow that interferes with the ingrowth of capillaries.

Avascular necrosis.—Under ordinary circumstances, healing proceeds from both sides of a fracture, differentiation of healing cells occurring approximately equally on both sides. When one fracture fragment has been rendered avascular, the healing process depends entirely on ingrowth of capillaries from the living side. Fractures associated with avascular necrosis of one fragment will heal but the rate is slower and the incidence is lower than in situations where this does not occur.[43] If both fragments are avascular, the chance of union occurring is very poor indeed.[26]

Intra-articular fractures.—Intra-articular fractures pose a more difficult problem. Synovial fluid contains fibrinolysins,[44] which are capable of lysing the initial clot and thus retarding the first stage in fracture healing. As with avascular necrosis, these fractures will heal, but the difficulties encountered are greater than those in cases of extra-articular fractures.

Systemic Factors

Age.—Fractures in the young heal rapidly, and the older the child the more the rate of healing resembles that of an adult. Also, the rapid remodelling that accompanies growth allows the young to correct greater degrees of deformity. Experimental work[45] with tritiated thymidine reveals a more rapid differentiation of cells from the mesenchymal pool in the young, so that more are available for the reparative process. In animals, fractures in elderly adults heal more slowly than those in younger ones; in clinical practice, this is difficult to document.

Hormones.—1. Corticosteroids: Both experimentally and clinically, corticosteroids greatly retard fracture healing.[46] They inhibit the differentiation of osteoblasts from mesenchymal cells[47] and decrease the rates of synthesis of the major components of bone matrix[48] necessary for repair.

2. Growth hormone: Although alterations in the concentration of circulating growth hormone probably have little effect on fracture healing clinically, experimental work has shown that the rate of repair can be profoundly influenced by this substance.[32, 49-51] Growth hormone is a potent stimulator of fracture healing.

3. Other hormones: Thyroid hormone, calcitonin, insulin, vitamins A and D in physiologic dosages, and anabolic steroids have been reported in experimental situations to enhance the rate of fracture healing (Table I[10, 32, 36, 46, 49-79]). Diabetes, castration, hypervitaminosis D, hypervitaminosis A, as well as the rachitic state, have been shown to retard fracture healing in experimental situations (Table I). Rarely in clinical practice do these substances or situations pose a serious problem.

Exercise and local stress about the fracture.—Denervation retards fracture healing, probably by diminishing the stress across the fracture site.[76] Exercise increases the rate of repair.[68] Clinicians have known that use of a fractured extremity promotes repair, and the recent development of weight-bearing techniques have confirmed this conviction. It is probable that bone formation is stimulated by forces acting across the fracture site, perhaps by initiating piezoelectric effects, which leads to accelerated rates of bone formation.

Electric currents.—The application of local electric current can stimulate healing in a fracture that has previously failed to respond to adequate treatment.[80, 81] This represents a clinical application of experimental work[22, 82] and may prove to be an important factor in the future.

REFERENCES

1. HAM AW: Repair of simple fracture, in *Histology,* sixth ed, Philadelphia, Lippincott, 1969, p 441
2. URIST MR, JOHNSON RW: Calcification and ossification; healing of fractures in man under clinical conditions. *J Bone Joint Surg* 25: 375, 1943
3. AEGERTER EE, KIRKPATRICK JA: Repair of fractures, in *Orthopedic Diseases: Physiology, Pathology, Radiology,* third ed, Philadelphia, Saunders, 1968, p 258
4. POTTS WJ: Role of hematoma in fracture healing. *Surg Gynecol Obstet* 57: 318, 1933
5. STIRLING RI: Report of investigation into process of healing of fractured bones, with some clinical applications. *Trans R Med Chir Soc Edinb* 46: 203, 1931
6. BASSETT CA: Current concepts of bone formation. *J Bone Joint Surg [Am]* 44: 1217, 1962
7. TONNA EA: Electron microscopic study of osteocyte release during osteoclasis in mice of different ages. *Clin Orthop* 87: 311, 1972
8. TRUETA J: Role of vessels in osteogenesis. *J Bone Joint Surg [Br]* 45: 402, 1963
9. YOUNG RW: Specialization of bone cells, in *Bone Dynamics. Henry Ford Hospital Symposium,* edited by FROST HM, Boston, Little, Brown, 1964, p 117
10. BECKER RO, MURRAY DG: Electrical control system regulating fracture healing in amphibians. *Clin Orthop* 73: 169, 1970
11. WRAY JB: Vascular regeneration in healing fracture. Experimental study. *Angiology* 14: 134, 1963
12. RHINELANDER FW, BARAGRY RA: Microangiography in bone healing. I. Undisplaced closed fractures. *J Bone Joint Surg [Am]* 44: 1273, 1962
13. RHINELANDER FW, PHILLIPS RS, STEEL WM, et al: Microangiography and bone healing. II. Displaced closed fractures. *J Bone Joint Surg [Am]* 50: 643, 1968
14. COTHMAN L: Vascular reaction in experimental fractures, microangiographic and radio-isotopic studies. *Acta Chir Scand* suppl 284: 1, 1961
15. UDUPA KN, PRASAD JC: Chemical and histochemical studies in organic constituents in fracture repair in rats. *J Bone Joint Surg [Br]* 45: 770, 1963
16. GRANT ME, PROCKOP DJ: Biosynthesis of collagen. 3. *N Engl J Med* 286: 291, 1972
17. HODGE DE, PETURSKA JA: Recent studies with electron microscope on ordered aggregates of tropocollagen macromolecule, in *Aspects of Protein Structure. Proceedings, International Symposium on Protein Structure, University of Madras, India,* edited by RAMACHANDRAN GN, New York, Academic Press, 1963, p 289
18. JACKSON SF: Fine structure of developing bone in embryonic fowl. *Proc R Soc Lond [Biol]* 146: 270, 1957
19. GLIMCHER MJ: Basic architectural principle in organization of mineralized tissues. *Clin Orthop* 61: 16, 1968
20. WOLFF J: *Das Gesetz der Transformation der Knochen,* Berlin, Hirschwald, 1892, p 199
21. WENDEBERG B: Mineral metabolism of fractures of tibia in man studied with external counting of Sr^{85}. *Acta Orthop Scand* 31 (suppl 52): 1, 1961
22. BASSETT CA, BECKER RO: Generation of electric potentials by bone in response to mechanical stress. *Science* 137: 1063, 1962
23. BASSETT CA: Biophysical principles affecting bone structure in, *Biochemistry and Physiology of Bone,* v 3, second ed, edited by BOURNE G, New York, Academic Press, 1971, p 28
24. FROST HM: *Laws of Bone Structure,* Springfield, Ill, Thomas, 1964, p 18
25. PENTTINEN R: Biochemical studies on fracture healing in rat. *Acta Chir Scand* (suppl 432): 1, 1965
26. CHARNLEY J: *Closed Treatment of Common Fractures,* third ed, Edinburgh, Livingstone, 1968, p 25
27. LAING PG, FERGUSON AB, HODGE ES: Tissue reaction in rabbit muscle exposed to metallic implants. *J Biomed Mater Res* 1: 135, 1967
28. CHARNLEY J, BAKER SL: Compression arthrodesis to knee: clinical and histological study. *J Bone Joint Surg [Br]* 34: 187, 1952
29. MÜLLER ME, ALLGOWER M, WILLENEGGER H: *Technique of Internal Fixation of Fractures,* New York, Springer, 1965
30. NEER CS, FRANCIS KC, MARCOVE RC, et al: Treatment of unicameral bone cyst. Follow-up study of one hundred seventy-five cases. *J Bone Joint Surg [Am]* 48: 731, 1966.
31. NICHOLAS JA, KILLORAN P: Fracture of femur in patients with Paget's disease; results of treatment in twenty-three cases. *J Bone Joint Surg [Am]* 47: 450, 1965
32. NICHOLS JT, TOTO PD, CHOUKAS NC: Proliferative capacity and DNA synthesis of osteoblasts during fracture repair in normal and hypophysectomized animals. *Oral Surg* 25: 418, 1968
33. O'DONOGHUE DH: Surgical treatment of fresh injuries to major ligaments of knee. *J Bone Joint Surg [Am]* 32: 721, 1950
34. IDEM: Analysis of end results of surgical treatment of major injuries to ligaments of knee. *J Bone Joint Surg [Am]* 37: 1, 1955
35. O'DONOGHUE DH, ROCKWOOD CA, ZARICZNYJ B, et al: Repair of knee ligaments in dogs. I. Lateral collateral ligament. *J Bone Joint Surg [Am]* 43: 1167, 1961
36. PAPPAS AN, RADIN E: Effect of delayed manipulation on rate of fracture healing. *Surg Gynecol Obstet,* 126: 1287, 1968
37. PEACOCK EE: Study of circulation in normal tendons and healing grafts. *Ann Surg* 149: 415, 1959
38. IDEM: Biological principles in healing of long tendons. *Surg Clin North Am* 45: 461, 1965
39. PEACOCK EE, VAN WINKLE W: *Surgery and Biology of Wound Repair,* Philadelphia, Saunders, 1970
40. PERREN SM, HUGGLER A, RUSSENBERGER S: Cortical bone healing. *Acta Orthop Scand* suppl 125: 1, 1965
41. ANDRIOLE VT, NAGELL DA, SOUTHWICK WO: Paradigm for human chronic osteomyelitis. *J Bone Joint Surg [Am]* 55: 1151, 1973
42. GOODMAN AH, SHERMAN MS: Postirradiation fractures of femoral neck. *J Bone Joint Surg [Am]* 45: 723, 1963

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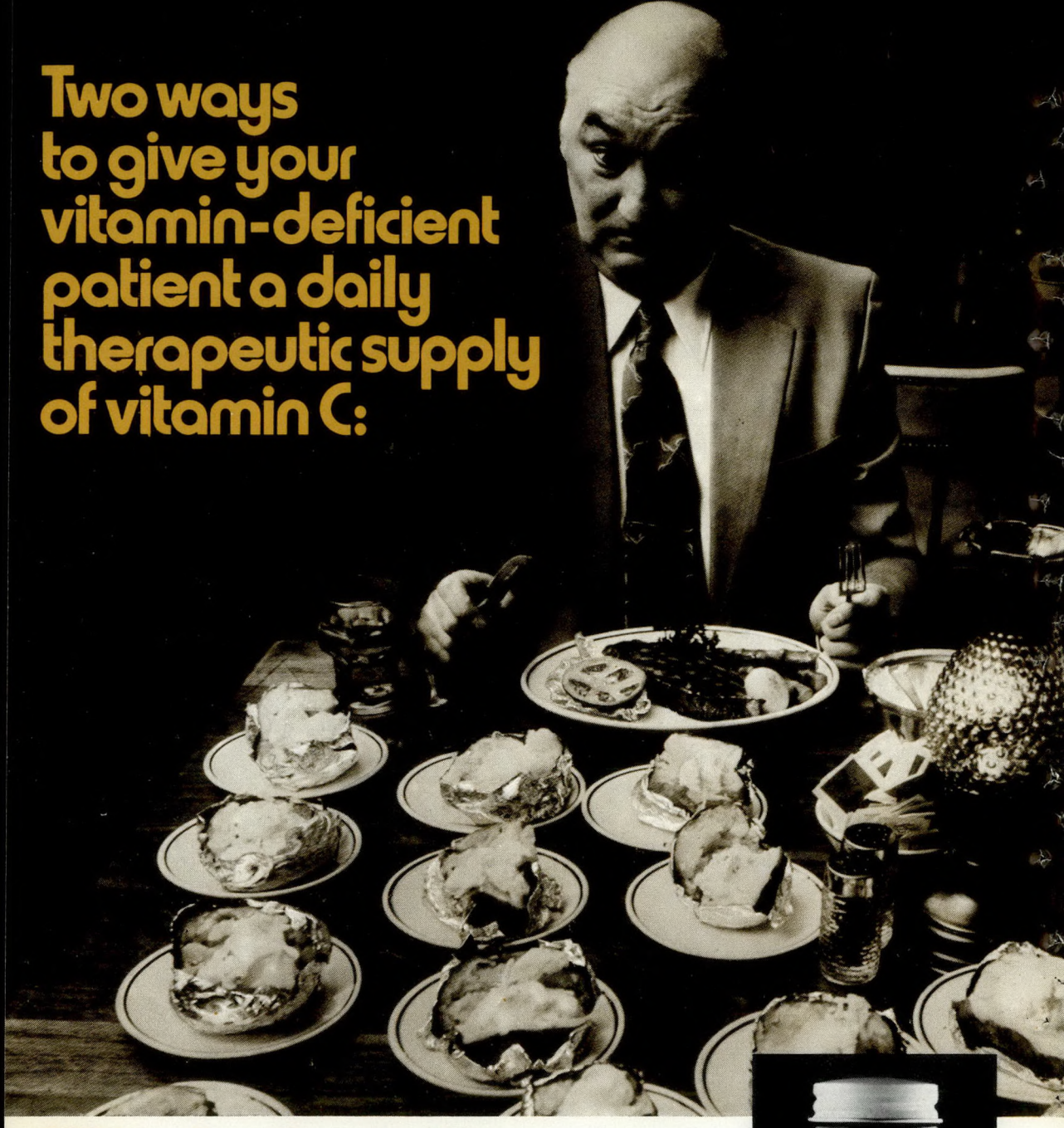

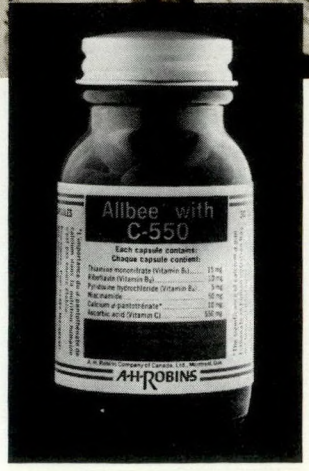

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43. BOYD HB, SALVATORE JE: Acute fracture of femoral neck: internal fixation or prosthesis? *J Bone Joint Surg [Am]* 46: 1066, 1964
44. LACK CH: Proteolytic activity and connective tissue. *Br Med Bull* 20: 217, 1964
45. TONNA EA, CRONKITE EP: Periosteum; autoradiographic studies on cellular proliferation and transformation utilising tritiated thymidine. *Clin Orthop* 30: 218, 1963
46. DUTHIE RB, BARKER AN: Histochemistry of preosseous stage of bone repair studied by autoradiography; effect of cortisone. *J Bone Joint Surg [Br]* 37: 691, 1955
47. SIMMONS DJ, KUNIN AA: Autoradiographic and biochemical investigations of effects of cortisone on bones of rat. *Clin Orthop* 55: 201, 1967
48. CRUESS RL, SAKAI T: Effect of cortisone upon synthesis rates of some components of rat bone matrix. *Clin Orthop* 86: 253, 1972
49. HSU JD, ROBINSON RA: Studies on healing of long-bone fractures in hereditary pituitary insufficient mice. *J Surg Res* 9: 535, 1969
50. KOSKINEN EV, RYOPPY I, LINDHOLM TS: Bone formation by induction under influence of growth hormone and cortisone. *Isr J Med Sci* 7: 378, 1971
51. MISOL S, SAMAAN N, PONSETTI IV: Growth hormone in delayed fracture healing. *Clin Orthop* 74: 206, 1971
52. KOSKINEN EV: Repair of experimental fractures under action of growth hormone, thyrotropin and cortisone. Tissue analytic, roentgenologic and autoradiographic study. *Ann Chir Gynaecol Fenn* 48 (suppl 90): 1, 1959
53. TARSOLY E, HÁJER G, URBÁN I: Uber die Heilung von Knochenfrakturen bei hypo- bzw. hyperthyreotischen Tieren. *Acta Chir Acad Sci Hung* 6: 435, 1965
54. KOSKINEN EV: Effect of endocrine factors on callus development in experimental fractures. *Symp Biol Hung* 7: 315, 1967
55. EWALD F, TACHDJIAN MO: Effect of thyrocalcitonin on fractured humeri. *Surg Gynecol Obstet* 125: 1075, 1967
56. ZIEGLER R, DELLING G: Effect of calcitonin on regeneration of circumscribed bone defect (bored hole in rat tibia). *Acta Endocrinol (Kbh)* 69: 497, 1972
57. SINGH RH, UDUPA KN: Some investigations on effect of insulin in healing of fractures. *Indian J Med Res* 54: 1071, 1966
58. UDUPA KN, GUPTA LP: Role of vitamin A in repair of fractures. *Ibid,* p 1122
59. STEIER A, GEDALIE I, SCHWARZ A, et al: Effect of vitamin D_2 and fluoride on experimental bone fracture healing in rats. *J Dent Res* 46: 675, 1967
60. KOWALEWSKI K, GORT J: Anabolic androgen as stimulant of bone healing in rats treated with cortisone. *Acta Endocrinol (Kbh)* 30: 273, 1959
61. BURGER M, SHERMAN BS, SOBEL AE: Observations on influence of chondroitin sulphate on rate of bone repair. *J Bone Joint Surg [Br]* 44: 675, 1962
62. HERBSMAN H, KWON K, SHAFTAN GW, et al: Influence of systemic factors on fracture healing. *J Trauma* 6: 75, 1966
63. BONI M, LENZI L, SILVA E, et al: Action of testicular hyaluronidase administered in vivo on mineralization of fracture callus in rats. *Calcif Tissue Res* 2 (suppl 30-30a): 1, 1968
64. ROKKANEN P, SLÄTIS P: Repair of experimental fractures during long-term anticoagulant treatment. *Acta Orthop Scand* 35: 21, 1964
65. KNOCH HG: Der Einfluss von Nieder- und Hochfrequenzschwingungen auf das Kallusgewebe im Tierexperiment. *Zentralbl Chir* 92 (suppl): 1784, 1967
66. COULSON DB, FERGUSON AB, DIEHL RC: Effect of hyperbaric oxygen on healing femur of rat. *Surg Forum* 17: 449, 1966
67. YABLON IG, CRUESS RL: Effect of hyperbaric oxygen on fracture healing in rats. *J Trauma* 8: 186, 1968
68. HEIKKINEN E, VIHERSAARI P, PENTTINEN R: Effect of previous exercise on development of experimental fractures callus. *Scand J Clin Lab Invest* 25 (suppl 113): 32, 1970
69. HERBSMAN H, POWERS JC, HIRSCHMAN A, et al: Retardation of fracture healing in experimental diabetes. *J Surg Res* 8: 424, 1968
70. HEROLD HZ, TADMOR A: Chondroitin sulphate in treatment of experimental bone defects. *Isr J Med Sci* 5: 425, 1969
71. COPP DH, GREENBERG DM: Studies on bone fracture healing. 1. Effect of vitamins A and D. *J Nutr* 29: 261, 1945
72. ROTHMAN RH: Effect of anemia on fracture healing. *Surg Forum* 19: 452, 1968
73. KOWALEWSKI K, COUVES CM, LANG A: Protective action of 17-ethyl-19-nortestosterone against inhibition of bone repair in lathyrus-fed rat. *Acta Endocrinol (Kbh)* 30: 268, 1959
74. WIANKO KB, KOWALEWSKI K: Strength of callus in fractured humerus of rat treated with anti-anabolic and anabolic compounds. *Acta Endocrinol* 36: 310, 1961
75. HOWARD TC, KELLEY RR: Effect of bone wax on healing of experimental rat tibial lesions. *Clin Orthop* 63: 226, 1969
76. RETIEF DH, DREYER CJ: Effects of neural damage on repair of bony defects in rat. *Arch Oral Biol* 12: 1035, 1967
77. ARIPOW UA, LIEMANOWA GI, SAATOW CI, et al: Zu den Besonderheiten des Verlaufs der Reparationsprozesse bei der Einwirkung einiger physikalischer Faktoren auf den Organismus. *Zentralbl Chir* 92: 1097, 1962
78. WRAY JB, ROGERS LS: Effect of hyperbaric oxygenation upon fracture healing in rat. *J Surg Res* 8: 373, 1968
79. CRENSHAW AH, editor: *Campbell's Operative Orthopaedics,* 2 v, fifth ed, St Louis Mosby, 1971
80. FRIEDENBERG ZB, HARLOW MC, BRIGHTON CT: Healing of nonunion of medial malleolus by means of direct current. Case report. *J Trauma* 11: 883, 1971
81. LAVINE LS, SHAMOS MH: Electric enhancement of bone healing. *Science* 175: 118, 1972
82. BECHTOL CO, FERGUSON AB, LAING PG: *Metals and Engineering in Bone and Joint Surgery,* Baltimore, Williams & Wilkins, 1959

REVIEW ARTICLE

CHOICE OF GASTRIC DRAINAGE PROCEDURES*

MAX M. COHEN, MB, ChB, FRCS(Edin), FRCS[C]†

Summary: The need for drainage after truncal or selective vagotomy is well accepted, but there is no agreement on the most suitable type of drainage procedure. A review of the literature, particularly of papers published in the last 3 years, suggests that whereas vagotomy with gastroenterostomy is followed by a relatively high incidence of bile vomiting, vagotomy with pyloroplasty carries a significantly higher risk of recurrent ulceration. The surgeon, therefore, should not hesitate to perform gastroenterostomy if the pyloroduodenum is severely scarred. As pyloroplasty is irreversible, gastroenterostomy is probably the drainage procedure of choice.

Résumé: On admet généralement le besoin de recourir à un drainage après une vagotomie sélective ou tronculaire, mais l'accord n'est pas fait sur la méthode de drainage la plus convenable. Après une revue de la littérature pertinente, surtout des articles publiées depuis les 3 dernières années, on peut conclure que, dans les cas où la vagotomie avec gastroentérostomie est suivie d'une fréquence relativement élevée de vomissement biliaire, la vagotomie avec pyloroplastie comporte un risque assez considérable d'ulcération récidivante. Le chirurgien ne devra donc pas hésiter à pratiquer une gastroentérostomie si la région pyloro-duodénale est le siège de lésions cicatricielles sévères. Comme la pyloroplastie est irréversible, la gastroentérostomie est probablement la méthode de drainage par excellence.

THE introduction of vagotomy in the treatment of duodenal ulcer, by Dragstedt and Owens in 1943,[1] led rapidly to the realization that unless the stomach was drained simultaneously many patients would develop prolonged gastric stasis and require reoperation. The need for drainage after truncal or selective vagotomy is not questioned, and in this paper I shall discuss the choice of drainage procedures available.

DEVELOPMENT OF PROCEDURES FOR DRAINAGE

The first *pyloroplasty* was performed by Heineke in 1886 and was popularized by Mikulicz.[2] The original Heineke-Mikulicz incision (length, 5 cm) was closed with several rows of interrupted cotton. This caused too much inversion and, as a result, pyloric obstruction, recurrent ulceration and leaks were common. The operation was condemned and forgotten until 1956, when Weinberg modified the original procedure by lengthening the incision slightly and suturing it transversely with a single layer of interrupted cotton sutures (Fig. 1).[3] Weinberg emphasized using nonabsorbable suture material, not incorporating the mucosa in the suture, and making no attempt to invert the inevitable dog-ears produced at each end of the sutured pyloroplasty. This technique of pyloroplasty is probably now the most widely practised, although many surgeons use absorbable sutures. I have seen several patients with recurrent ulceration after pyloroplasty at the site of silk sutures and for this reason I now use exclusively a single layer of interrupted polyglycolic acid sutures.

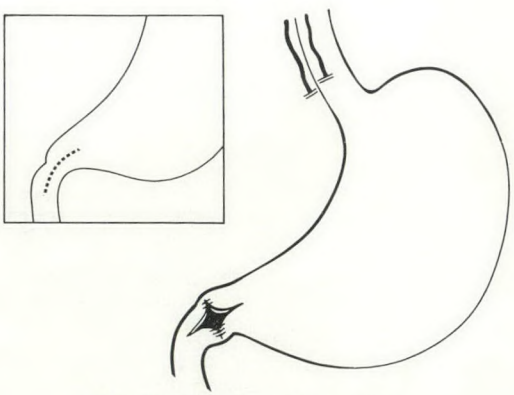

Fig. 1.—Weinberg pyloroplasty.

*Presented at the annual meeting of the Royal College of Physicians and Surgeons of Canada, Winnipeg, Man., January 1975.

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Judd[4] recommended excising the anterior two-thirds of the pyloric sphincter, including any anterior ulcer that may be present, before closing the pyloroplasty in the usual manner. Like the Heineke-Mikulicz pyloroplasty, this *pylorectomy* was originally introduced as the sole treatment for peptic ulcer, but this also fell into disrepute. It has recently been revived as an adjuvant to vagotomy.

The *gastroduodenostomy* is a compromise between pyloroplasty and gastroenterostomy. There are two main types of gastroduodenostomy: that described by Finney,[5] in which the incision passes through the pylorus, and that described by Jaboulay,[6] in which the anastomosis is subpyloric.

The Finney gastroduodenostomy (Fig. 2), if properly done, is more than a simple pyloroplasty. It requires complete mobilization of the duodenum, which is incised beyond the ampulla of Vater. If, for any reason, complete mobilization proves impossible, an alternative drainage procedure should be performed. The Finney operation provides a wide stoma between stomach and duodenum; the stoma extends from the pylorus to the full extent of the second part of the duodenum. The anastomosis is usually performed in two layers as for gastroenterostomy.

The Jaboulay gastroduodenostomy (Fig. 3) is similar to the Finney operation and also requires mobilization of the duodenum, but the incision does not pass through the pylorus, which is bypassed rather than incorporated in the stoma. It requires less mobilization than the Finney procedure, and Finney himself advocated its use when mobilization was difficult.[7]

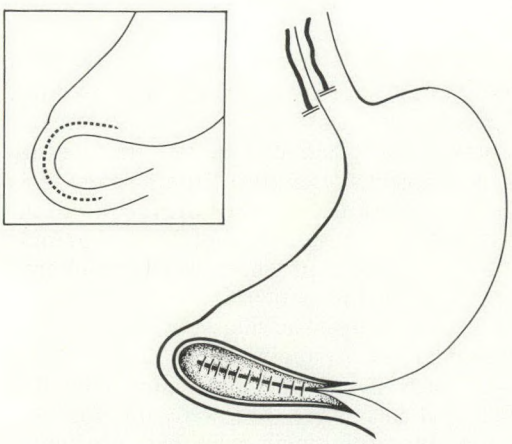

Fig. 2.—Finney gastroduodenostomy.

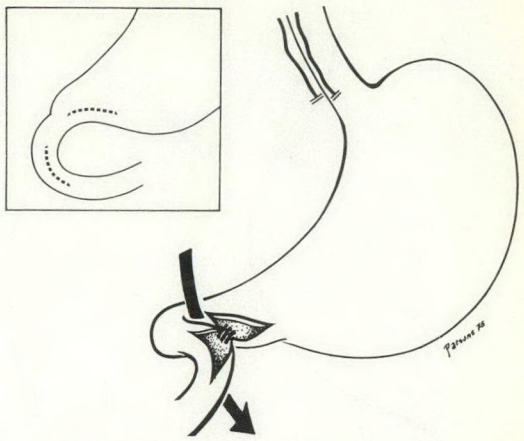

Fig. 3.—Jaboulay gastroduodenostomy.

The only prospective study of these various drainage procedures was reported by Thompson and Read.[8] In a randomized prospective study of 100 male patients with peptic ulcer in whom vagotomy plus either Heineke-Mikulicz or Finney drainage were carried out, no difference was found either in the rate of recurrent ulceration (12% and 11%, respectively) or in the incidence of dumping or diarrhea.

Gastroenterostomy was introduced in 1881 by Wölfler,[9] who used an anterior antiperistaltic gastrojejunostomy. Numerous variations have since been proposed but essentially the operation is antecolic (mainly as palliation for cancer) or retrocolic, and the stoma is fashioned in an antiperistaltic or isoperistaltic manner (Figs. 4 and 5).

Of all these procedures the pyloroplasty has been widely adopted since its reintroduction by Weinberg and is now probably the most common; it can be performed somewhat more rapidly than a gastrojejunostomy and is seemingly the more anatomic and physiologic choice. These considerations have outweighed for most surgeons the irreversible destruction of the pyloric sphincter that results.

Review of the Literature

Until recently no good data were available on which to base the choice of gastric drainage procedure. The literature pub-

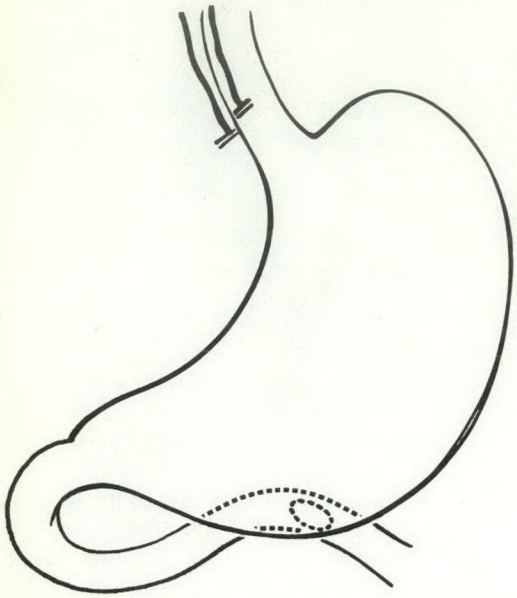

Fig. 4.—Posterior antiperistaltic gastroenterostomy.

lished up to 1967, collected by Cox,[10] consisted of retrospective reviews, and these revealed no difference in mortality or incidence of recurrent ulceration, but a slight increase in the incidence of bile vomiting after gastroenterostomy (Table I). However, more recently a number of studies have been reported that provide more information.

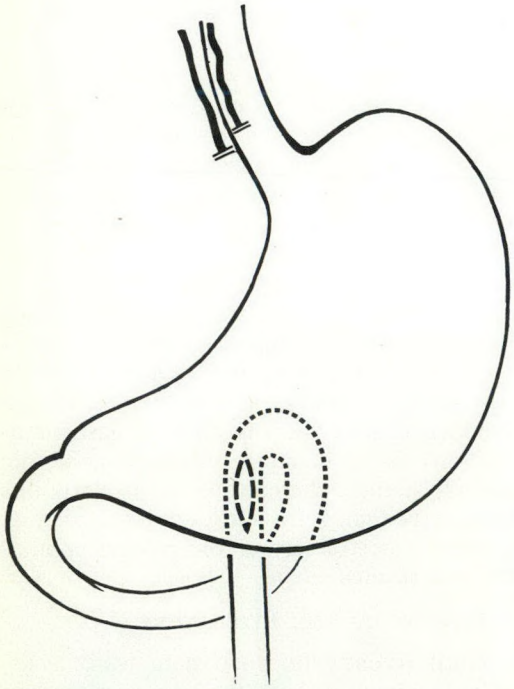

Fig. 5.—Posterior isoperistaltic vertical gastroenterostomy.

TABLE I.—COMPARISON OF RESULTS OF VAGOTOMY PLUS PYLOROPLASTY OR GASTROENTEROSTOMY FROM RETROSPECTIVE STUDIES REPORTED UP TO 1967

	Vagotomy and pyloroplasty (%)	*Vagotomy and gastro-enterostomy* (%)
Operative mortality	0.6	1.0
Recurrence rate	5.5	5.6
Dumping	12.0	9.0
Bile vomiting	6.0	14.0
"Good" results	89.0	90.0

In 1973, two British papers[11, 12] reported the results of prospective randomized trials of pyloroplasty versus gastroenterostomy. Both groups selected included only patients with duodenal ulcer in whom, at laparotomy, either procedure was considered feasible, thus excluding from the trials any patient with a severely scarred duodenum. The overall results of these two trials, from Glasgow and Belfast, are presented in Table II.

The Glasgow and Belfast trials were different in certain details. These differences were as follows:

1. Numbers of patients. The Glasgow series comprised 200 and 204 patients in the operative subgroups over a 6-year period whereas the Belfast series included only 50 in each in a 2-year period.

2. Types of operations. The Glasgow surgeons used truncal vagotomy and a Heineke-Mikulicz, single-layer, catgut closure, but the Belfast surgeons performed a modified Finney pyloroplasty with the gastroenterostomy being positioned nearer the pylorus.

3. Surgeons' expertise. In Glasgow, most of the 45 surgeons who operated on the patients were residents, but in Belfast only 2 surgeons, both of whom were consultants, operated on the patients.

4. Follow-up. The Glasgow patients were observed for a minimum of 2 years and were seen at a peptic ulcer clinic; the Belfast patients were followed up for 3½ years, by a physician who had no knowledge of the operation performed.

The Glasgow authors reported that recurrent ulceration was more common after pyloroplasty, though the difference was not significant. The incidence of dumping and of results that were good or excellent was similar in both subgroups, but there was a significantly higher incidence ($P < 0.001$) of bile vomiting following gastroenterostomy. The Glasgow group concluded from this study that the choice of drainage procedure should be determined at exploration and that "the surgeon should not hesitate to select the more easy gastrojejunostomy in circumstances when a pyloroplasty seems likely to be more difficult and, therefore, more hazardous to the patient". They pointed out that an anastomotic leak is a much more serious complication than bile vomiting.

The Belfast authors found no significant difference between the two groups with respect to recurrent ulceration or other disability, although there was a marginal advantage on the clinical grading in those patients who received gastroenterostomy. The authors concluded that as gastroenterostomy is reversible it is the drainage procedure of choice.

The results of both the Glasgow and Belfast trials combined with respect to the two procedures (vagotomy and pyloroplasty, and vagotomy and gastroenterostomy) are summarized in Table III. Though dumping and recurrent ulceration are more common after pyloroplasty, even with the combined data these factors do not achieve statistical significance.

There have been two other major studies of gastric drainage procedures, neither of which was truly a randomized, prospective study. Goligher and associates from Leeds[13] reported the findings in 164 patients followed up for 5 to 8 years after vagotomy (truncal type) and pyloroplasty (Heineke-Mikulicz). The results have been compared with those following truncal vagotomy and gastroenterostomy, the latter being performed as part of a well-known, prospective, controlled trial of elective surgery for duodenal ulcer by the same group. They found that while recurrent ulceration and overall poor results were more common after vagotomy and pyloroplasty than any other operation, there was no statistically significant difference compared with vagotomy and gastroenterostomy. Table IV

TABLE II.—DETAILS OF GLASGOW AND BELFAST TRIALS

	Glasgow trial				*Belfast trial*			
	Vagotomy and pyloroplasty		*Vagotomy and gastroenterostomy*		*Vagotomy and pyloroplasty*		*Vagotomy and gastroenterostomy*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
No. of patients	204		200		50		50	
No. of patients followed up* (and %)	166	81	166	83	46	92	48	96
Operative deaths	0		1		0		0	
Recurrent ulcer	8	5	5	3	2	4	1	2
Dumping	45	25	36	22	18	39	12	25
Bile vomiting	9	6†	25	16†	4	9	5	10
"Good" results	146	88	143	86	40	87	44	92

*Glasgow trial, > 2 yr; Belfast trial, 3½ yr.
†Difference significant, $P < 0.01$.

TABLE III.—COMBINED GLASGOW AND BELFAST TRIALS

	Vagotomy and pyloroplasty		*Vagotomy and gastroenterostomy*	
	No.	*%*	*No.*	*%*
Total no. of patients followed up	212		214	
Proven recurrence	10	5	6	3
Dumping	63	30	48	22
Bile vomiting*	13	6	30	14

*$P < 0.01$.

TABLE IV.—GLASGOW, BELFAST AND LEEDS TRIALS COMBINED

	Vagotomy and pyloroplasty		*Vagotomy and gastroenterostomy*	
	No.	*%*	*No.*	*%*
No. of patients	466		376	
No. of patients followed up	376		333	
Recurrent ulcer	21	6	9	3
Dumping	86	23	77	23
Bile vomiting*	29	8	48	14

*P < 0.01.

shows the combined results from the Glasgow, Belfast and Leeds studies. The incidence of dumping and the good-to-excellent results are identical following the two operations and, as expected, there was a highly significant increase in the incidence of bile vomiting after vagotomy and gastroenterostomy.

The final study that merits comment is the multihospital veterans' administration study reported by Postlethwait.[14] A total of 1357 men were randomly allocated to four treatment groups, one of which was vagotomy and drainage. The surgeon was free to choose the drainage procedure he preferred. On this basis, 135 pyloroplasties and 106 gastroenterostomies were performed, and 85% of patients were followed up for 5 years. Unfortunately, the only comparative data given for these operations is the recurrent ulceration rate, which was 8.9% for pyloroplasty and 5.7% for gastroenterostomy. Once again the rate of recurrent ulceration was higher after vagotomy and pyloroplasty, but the difference was not statistically significant. If, however, the results from this study are combined with those from the three British centres, it is apparent that recurrent ulcer is almost twice as common after pyloroplasty as after gastroenterostomy (Table V). If we assume that the patients in all these studies are sufficiently similar to permit combined statistical analysis, then the difference in the rate of recurrent ulceration is significant. To prove this point conclusively, a single prospective study of about 1000 patients would be required.

CONCLUSION

A review of the recent literature suggests that whereas vagotomy with gastroenterostomy is followed by a relatively high incidence of bile vomiting, vagotomy with pyloroplasty carries a significantly higher risk of recurrent ulceration. The surgeon, therefore, should not hesitate to perform gastroenterostomy if the pyloroduodenum is severely scarred. As pyloroplasty is irreversible, gastroenterostomy is probably the drainage procedure of choice.

I am indebted to Miss Patricia Parsons, department of medical illustration, University of British Columbia, for the illustrations.

REFERENCES

1. DRAGSTEDT LR, OWENS FM: Supradiaphragmatic section of vagus nerves in treatment of duodenal ulcer. *Proc Soc Exp Biol Med* 53: 152, 1943
2. MIKULICZ J: Zur operativen Behandlung des stenosirenden Mageneschwüres. *Arch Klin Chir* 37: 79, 1888
3. WEINBERG JA, STEMPIEN SJ, MOVIUS HJ, et al: Vagotomy and pyloroplasty in treatment of duodenal ulcer. *Am J Surg* 92: 202, 1956
4. JUDD ES: Excision of ulcer of duodenum. *Journal-Lancet* 42: 381, 1922
5. FINNEY JM: New method of pyloroplasty. *Bull Johns Hopkins Hosp* 13: 155, 1902
6. JABOULAY M: La gastro-entérostomie; la jéjunoduodénostomie; la résection du pylore. *Arch Prov Chir* 1: 1, 1892

TABLE V.—ALL STUDIES COMBINED

	Vagotomy and pyloroplasty		*Vagotomy and gastroenterostomy*	
	No.	*%*	*No.*	*%*
No. of patients followed up	491		413	
Proven recurrence*	34	7	15	4

*P < 0.5.

7. FINNEY JM: Finney pyloroplasty. *Surg Gynecol Obstet* 43: 508, 1926
8. THOMPSON BW, READ RC: Long-term randomized prospective comparison of Finney and Heineke-Mikulicz pyloroplasty in patients having vagotomy for peptic ulceration. *Am J Surg* 129: 78, 1975
9. WÖLFLER A: La gastro-entérostomie. *Zentralbl Chir* 8: 705, 1881
10. Cox AG: Vagotomy and drainage procedures. Present position. *Progr Surg* 8: 45, 1970
11. KENNEDY F, MACKAY C, BEDI BS, et al: Truncal vagotomy and drainage for chronic duodenal ulcer: controlled trial *Br Med J* 2: 71, 1973
12. KENNEDY T, JOHNSTON GW, LOVE AH, et al: Pyloroplasty versus gastrojejunostomy. Results of double-blind, randomized, controlled trial. *Br J Surg* 60: 949, 1973
13. GOLIGHER JC, PULVERTAFT CN, IRVIN TT, et al: Five- to eight-year results of truncal vagotomy and pyloroplasty for duodenal ulcer. *Br Med J* 1: 7, 1972
14. POSTLETHWAIT RW: Five year follow-up results of operations for duodenal ulcer. *Surg Gynecol Obstet* 137: 387, 1973

DAVIS & GECK SURGICAL ESSAY AWARD FOR RESIDENTS

The *Canadian Journal of Surgery* announces the institution of an award of $1000.00 for the best paper on a surgical topic submitted by a surgical resident. To be given annually by Davis & Geck, this award is intended to promote scientific and literary excellence among Canadian surgeons in training. The first award will be presented in 1976.

The conditions of entry for the award for 1976 are the following: —

1. Candidates shall be currently engaged in a recognized surgical residency program leading to eligibility for the Fellowship of the Royal College of Physicians and Surgeons of Canada in one of the surgical specialties (cardiovascular and thoracic surgery, general surgery, neurosurgery, obstetrics and gynecology, ophthalmology, orthopedic surgery, Otolaryngology, plastic surgery and urology).

2. The material to be submitted shall be in the form of a manuscript relating to work in which a surgical resident is or has been the prime or major investigator. Prior oral presentation at a Royal College meeting or a Surgical Forum meeting will not be a disqualification, but prior publication as a formal paper in a journal will. The paper should relate to any field of surgical interest. The manuscript must conform to the style requirements of the *Journal* and must not exceed 3000 words of text and six tables and/or six figures.
   Coauthors are permitted on the understanding that the candidate shall be the first author and that only the first author shall be eligible for the award.

3. Entries must be received in the office of the *Journal* no later than June 30, 1976. Each entry must be submitted to Dr. D. A. E. Shephard, MB, FRCP(C), Associate Editor, Canadian Journal of Surgery, P O Box 8650, Ottawa, Ontario, K1G 0G8, with a letter stating that the paper is being submitted as an entry for the Davis & Geck Essay Award.

4. The award-winning paper shall be published in the *Canadian Journal of Surgery* and shall be the property of the *Journal*.

All papers submitted will be judged by an independent committee comprising at least one member of the editorial board of the *Journal*, one Fellow of the Royal College of Physicians and Surgeons of Canada, and one representative of The Canadian Medical Association, together with other Fellows invited to serve at the discretion of the three permanent members of the committee. For the purpose of judging, the candidates will be anonymous. The judges' decision shall be final.

The name of the successful candidate and the title of the paper will be announced in the November 1976 issue of the *Journal*.

SELF-ASSESSMENT

SESAP II QUESTION

Beginning with this issue of the Journal, your coeditors institute a new feature—inclusion of a multiple-choice question related to one of the papers published in the Journal. The question has been taken, by permission of the American College of Surgeons, from "SESAP II Syllabus: Surgical Education and Self-assessment Program No. 2".

The American College of Surgeons, through its Committee on Continuing Education, during the past several years has constructed two self-assessment programs—SESAP I and SESAP II. The SESAP II program is accompanied by a volume devoted to an explanation or critique of each of the items. This critique discusses each of the choices, both right and wrong, as the choices relate to the item stem. The SESAP II program and the book of critiques are available in syllabus form on application to the American College of Surgeons.

Subscriptions to and enrolment in SESAP II will continue for approximately 2½ more years, and application may be obtained by writing to SESAP, American College of Surgeons, 55 East Erie St., Chicago, IL 60611, USA.

You are invited to participate by examining this item, which deals with issues raised by the paper entitled "Hyperparathyroidism: Evaluation of Four Decades of Parathyroid Surgery" by E. E. Mason, J. Hoines and J. B. Freeman on page 422 of this issue of the Journal. On page 447 you will find a critique of the item with a discussion of the correct answer as well as reasons for the incorrectness of the other answers.

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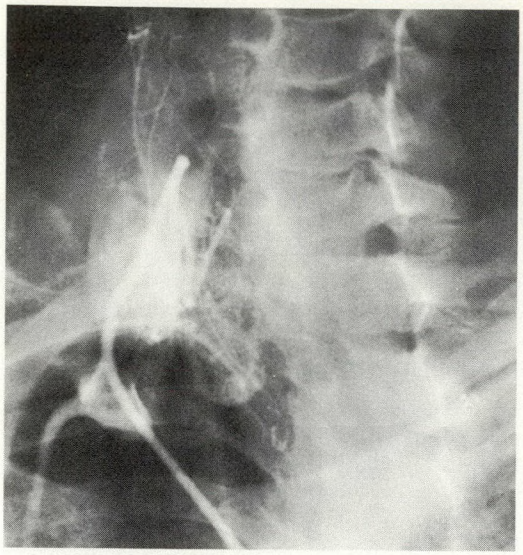
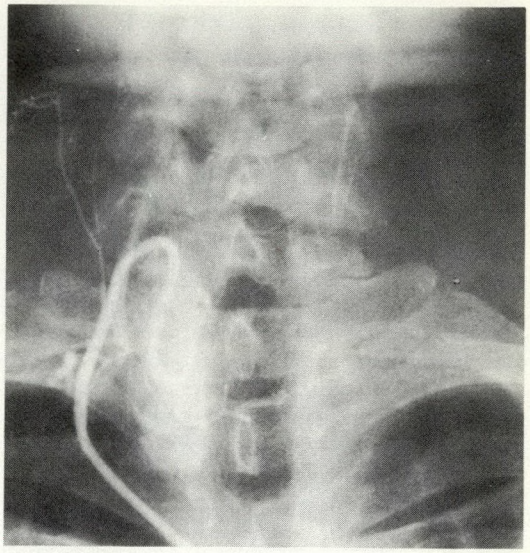
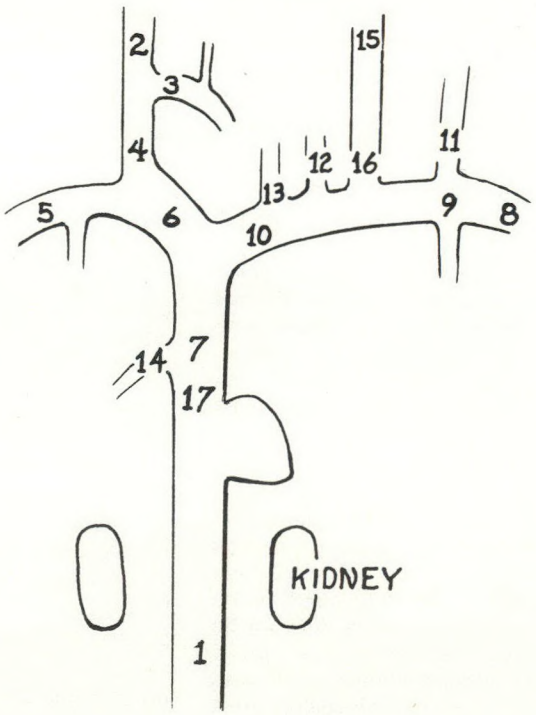
533. A 45-year-old man is referred for evaluation because of persistent hypercalcemia (calcium concentration 12.8 mg/100 ml) and hypophosphatemia (phosphorus concentration 1.5 mg/100 ml) developing after removal of a parathyroid adenoma which measured 6 by 2.5 by 1.5 cm and is said to have been located inferiorly in the prevertebral space in the left side of the neck. Arteriograms of the thyroid and the results of multiple selective venous parathyroid hormone assays are shown . . . At reexploration of the neck the most likely finding would be

(A) hyperplasia of three remaining parathyroids, the glands varying in size
(B) adenoma of the upper right parathyroid in an ectopic position without enlargement of the other two parathyroids
(C) adenoma of the thyroid with moderate enlargement of two parathyroids on the right and one on the left
(D) two small, apparently normal parathyroids adjacent to the lower pole of the thyroid bilaterally

(For the critique of Item 533 see page 447)







1—Inferior Vena Cava Below Renals	0.267 ng/ml	9—Subclavian Close to Left Internal Jugular	0.311
2—High Internal Jugular, Right	0.304	10—Middle Left Innominate	1.23
3—Superior Thyroid, Right	0.476	11—Left External Jugular	0.368
4—Low Internal Jugular, Right	0.248	12—Left Thyroid	0.296
5—Subclavian Lateral to Internal Mammary	0.259	13—Thyroid ima	3.98
6—Right Innominate	0.285	14—Azygous	0.284
7—Superior Vena Cava, Middle	0.35	15—High Internal Jugular, Left	0.316
8—Left Subclavian Lateral to Internal Mammary	0.316	16—Low Internal Jugular	0.290
		17—Low Superior Vena Cava	0.368

HYPERPARATHYROIDISM: EVALUATION OF FOUR DECADES OF PARATHYROID SURGERY*

E. E. MASON, MD, PhD, J. HOINES† and J. B. FREEMAN, MD, FRCS[C]

Summary: A review of 98 patients with hyperparathyroidism operated on at the University of Iowa during a 45-year period reveals a very great increase in the frequency of the clinical diagnosis. More patients are being operated on each year and more glands are being removed or biopsied. The proportion of patients in whom light microscopic examination of the parathyroid reveals hyperplasia remains less than 25%. Better methods are needed for identification of hyperplasia. Clinically, a few patients in whom the diagnosis of adenoma is made appear later to have more diffuse parathyroid disease. At present, however, when an adenoma is found, the decision to perform subtotal removal of apparently normal parathyroid tissue is made only reluctantly. The conclusion drawn from this review is that patients with hyperparathyroidism must be studied more intensively and followed for many years, whether or not an operation is performed. Although the diagnosis of hyperparathyroidism is now made readily and operative treatment seems to be more effective, much has yet to be learned about hyperparathyroidism.

Résumé: La revue des dossiers des 98 patients souffrant d'hyperparathyroïdisme qui ont été opérés à l'Université de l'Iowa durant une période de 45 ans révèle une énorme augmentation de la fréquence du diagnostic clinique. Chaque année, le nombre de malades opérés augmente et il en est de même des glandes excisées ou soumises à la biopsie. La proportion de malades où l'examen de la parathyroïde par microscope optique révèle un hyperplasie reste inférieure à 25%. Il faut recourir à des meilleures méthodes pour identifier l'hyperplasie. Quelques malades, chez lesquels on avait posé un diagnostic clinique d'adénome ont présenté ultérieurement une affection parathyroïdienne plus diffuse. Présentement toutefois, en présence d'un adénome, la décision de pratiquer une ablation subtotale d'un tissue parathyroïdien apparemment normal n'est prise qu'avec réticence. La conclusion qu'on peut tirer de cette revue est qu'il est impérieux d'étudier plus à fond les malades atteints d'hyperparathyroïdie et de les suivre pendant plusieurs années, qu'ils aient été opérés ou non. Même si le diagnostic d'hyperparathyroïdie est aujourd'hui plus aisé et le traitement chirurgical plus efficace, il faut admettre qu'il reste beaucoup à apprendre sur l'hyperparathyroïdie. ....

AN excellent illustration of serendipity, the prepared mind, and the dictum that what you know is what you find, is given by the history of hyperparathyroidism. The first adenoma detected at the University of Iowa was removed in 1929, only 4 years after Mandl's report,[1] and the case was the sixth reported in the literature.[2] In those days the disease was severe, with deforming bone disease and progressive destruction of the kidneys. It was also rare, but if the adenoma could be found and removed the disease was thought to be cured. Today, however, the disease appears to be decreasingly severe and, in addition, demands for operative treatment of hyperparathyroidism are increasingly frequent. These observations stimulated a review of 45 years' experience at the University of Iowa and a survey of evolving attitudes toward the etiology, pathology, management and prognosis of hyperparathyroidism.

CHANGES IN CLINICAL PATTERN

In 1934, Albright, Aub and Bauer[3] reported an astonishing series of hyperparathyroidism in 17 patients, in all of whom the disease was confirmed at operation. In eight of these patients the disease had been discovered through the deliberate investigation of patients with renal stones. The late Dr. F. R. Keating spent a year in Boston learning all he could about the activities, thoughts and organization that had led to the finding of such a relatively large number of patients with hyperparathyroidism, and he then returned to the Mayo Clinic where, by 1945, he and Cook[4] had recognized new cases of the disease in 24 patients in 2½ years—in contrast to its occurrence in only 14 patients in 14 years before this intensive interest.

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At the University of Iowa, where the experience has been similar to that of other centres, the increase in frequency of diagnosis was first noted in 1960. The type of disease that was discovered suggests that the increase was related to the intensive study of patients with renal stones, together with an occasional discovery because of the presence of peptic ulcer, pancreatitis, or multiple glandular disease. Notable was the occasional finding of the disease in a patient who had no bone or renal disease but who had vague symptoms; moreover, the vagueness made such a patient's case an enigma until some thoughtful medical student or physician considered the possibility of hyperparathyroidism and requested the appropriate laboratory tests. But recently, because of automated laboratory screening, an ever-increasing number of patients with suspected hyperparathyroidism is being seen. Since only *patients* are being screened we do not know, even now, the precise frequency of hyperparathyroidism.

Table I shows the University of Iowa experience divided into four nearly equal groups. The first 22 patients were seen in a period of 30 years, the second 22 were seen in a single decade, the third 26 patients were seen in a brief 4-year span, and the last 25 patients were operated on during 1974. During each of the first 3 decades, the numbers of patients operated on were 10, 7 and 5 patients respectively. This experience suggests that there were a few patients with long-standing, severe disease and that, when the disease was first recognized, all of these patients were treated, and that this was followed by a disappearance of those forms of the disease that were relatively severe and, clinically, most easily diagnosed. There followed a decade of treating patients with predominantly renal manifestations of the disease. Now, more patients are being treated with chemical abnormalities but with minimal evidence of bone or renal disease, as well as, increasingly, patients with no symptoms (Fig. 1).

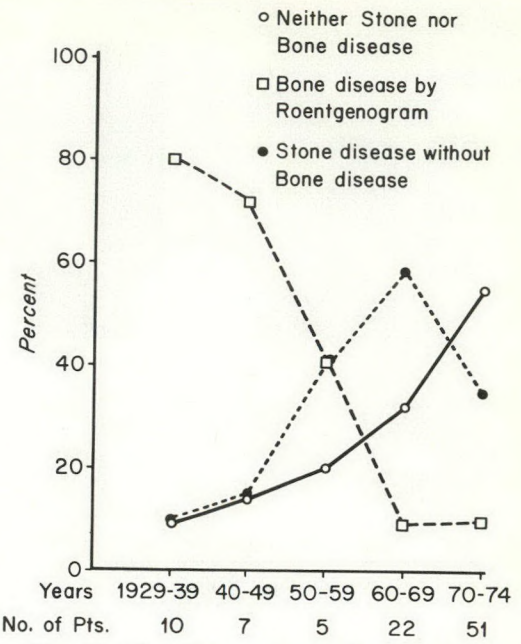

Fig. 1.—Changing pattern of hyperparathyroidism. Note early predominance of bone disease, then renal stone disease and more recently asymtomatic disease.

Etiology

Our understanding of the etiology remains little more than passive astonishment at the increase in number of patients. It is a disease with an insidious onset, progressing slowly in most patients, and symptoms are present for a long time before they require a diagnosis, though this duration is decreasing (Fig. 2).

Several differences between men and women could have a bearing on current

TABLE I.—Numbers of Patients Operated on for Hyperparathyroidism, and Serum Calcium Ranges, in Four Periods Between 1929 and 1974

Serum calcium (mg/dl)	*1929 to 1959*	*1960 to 1969*	*1970 to 1973*	*1974*	*1929 to 1974*
16	4	2	1	0	7
14.1 — 16	9	4	3	0	16
12.1 — 14	2	6	5	10	23
10.5 — 12	7	10	17	15	49
Total	22	22	26	25	95

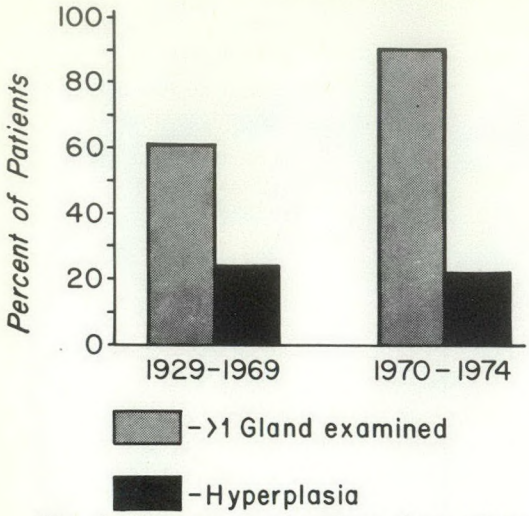

Fig. 2.—Proportions of patients from whom more than one gland was examined and from whom hyperplastic glands were found during periods 1929 to 1969 and 1970 to 1974.

differences in frequency and severity of the disease between the sexes (Table II). Keating reported a higher normal serum calcium concentration in men, especially in the first half of life.[5] It is possible that hyperparathyroidism in either sex is not a primary neoplasm but rather a disruption of normal calcium homeostasis. From studying the disease in the many patients with renal insufficiency and secondary hyperparathyroidism or tertiary hyperparathyroidism, we know that a disease very similar to so-called primary hyperparathyroidism can result from unusual demands on calcium regulatory organs.

Intrinsic defects in homeostasis, as in the families with multiple glandular syndrome, are rare. There are probably other instances of disturbed cell growth producing benign neoplasms, and these rarely give rise to a functioning carcinoma. The majority of patients with hyperparathyroidism, however, probably have a form of tertiary disease; but we have not yet made the necessary observations, such as have been made in patients with renal insufficiency, that would permit us to discern the sequence of events. In contrast to the situation with other endocrine organs, the feedback is a direct action of calcium on the parathyroid, with no hypothalamic or pituitary involvement. Yet control of calcium and phosphorus metabolism is far from simple. Parathormone is active in three major sites: the kidneys, bones and gastrointestinal tract. It is synergistic in its actions with vitamin D. Furthermore, parathormone is probably responsible for the conversion of 25-dihydroxyvitamin D_3 to its biologically active metabolite, 1,25-dihydroxyvitamin D_3, and the latter, in turn, acts as a feedback inhibitor of parathormone secretion. Thus, plasma levels of both calcium and vitamin D_3 are controlled by, and also inhibit, the secretion of serum parathormone. In bone, the effects of parathormone are offset by calcitonin, which tends to enhance osseous formation and to decrease resorption. Finally, both the serum albumin and the acid-base status affect serum calcium concentrations.

To determine the relationships between normal calcium metabolism and the disturbances that lead to hyperparathyroidism, it may be helpful to obtain information about calcium homeostasis in persons in whom the disease is developing under circumstances much less obvious than chronic renal failure. Studies of such patients once identified should be designed to reveal the cyclical and circadian rhythms for blood concentrations not only of calcium and phosphorus but also of parathyroid hormone and possibly calcitonin as well.

TABLE II.—Differences in Features of Hyperparathyroidism in Males and Females Treated Surgically During Periods 1929 to 1969 and 1970 to 1974

	Female		*Male*	
	1929-1969	*1970-1974*	*1929-1969*	*1970-1974*
No. of patients	23	37	20	18*
Average age (yr)	51	47	39	47
Duration of symptoms > 3 yr, %	57	35	85	50
Calcium > 14 mg/dl, %	43	5	45	11
Renal stones, %	57	38	55	56
Bone disease, %	43	8	35	11

*Includes 4 patients from Veterans' Administration Hospital, Iowa City.

Serum chloride concentrations tended to be high in our patients. Wills and McGowan[6] have contrasted the hyperchloremia of hyperparathyroidism with the hypochloremia commonly noted in patients with hypercalcemia from other causes. The serum chloride concentration in our patients ranged from 96 to 112 mmol (= meq)/*l*, the median and average both being 105 mmol/*l*—certainly not sufficiently abnormal to be of diagnostic assistance, though such a finding perhaps might constitute another avenue for study of the developmental course of the disease. Tubular phosphate reabsorption is inhibited by parathyroid hormone and, at the same time, phosphate excretion in its varying degrees of ionization is a factor in the regulation of acid-base balance. Hyperchloremic acidosis may be the consequence of impaired renal acid-base regulation in hyperparathyroidism, but such a conclusion does not indicate whether excess parathyroid hormone is the cause of abnormal acid-base balance or an effect.

Pathology

At first, hyperparathyroidism was always considered as resulting from the effects of a benign functioning neoplasm of which, once found and removed, the patient could be considered cured. This was the case in the first patient treated at the University of Iowa: This patient had such an adenoma, and when the adenoma was removed in 1929 the other parathyroid glands were inspected and declared to be normal. In 1943 a second adenoma was removed, and in 1947 this patient died from renal failure. In patients who do not have hyperplasia, removal of a single adenoma is usually curative. There is increasing evidence, however, that hyperparathyroidism, even in patients who appear to have adenomatous disease, may reflect hyperplasia of all parathyroid tissue.[7] Our inability to diagnose this form of the disease is accounted for by the great variability in glandular size in cases of parathyroid hyperplasia. Hence an "adenoma" may represent a rather large hyperplastic gland, whereas a "normal-sized gland" may represent a small hyperplastic gland. That there are patients who have no adenoma, but moderate and varying enlargement of several or all glands is unequivocal. There are also patients in whom all parathyroids appear normal grossly and by light microscopy but in whom there are subcellular abnormalities suggestive of functional overactivity by electron microscopy.[8] To add to the mystery, there are patients with renal insufficiency and secondary hyperparathyroidism in whom there develops what appear to be adenomas. Today, therefore, we see cases of a disease that is usually mild (or even totally asymptomatic) yet much more common—and much less well understood in terms of etiology and pathology.

Although our pathologists now examine many more glands and biopsies of glands (Fig. 2), the frequency of diagnosis of hyperplasia has not increased. At times, recurrent adenoma formation occurs whereas at other times an initial diagnosis of hyperplasia is followed by that of an adenoma later. Better microscopic diagnosis is necessary and, without this, operative treatment is likely to be inappropriate and the prognosis guarded. This raises the question regarding prolonged observation as an alternative form of management to early operation. When hyperparathyroidism was known only as a morbid and potentially lethal disease, there was no excuse for delay in treatment: every day a patient has severe hypercalcemia, the greater the number of nephrons destroyed and the greater the loss of bone minerals; also, the more he is predisposed toward peptic ulcer or pancreatitis and the more he is exposed to the risk hyperparathyroid crisis and death from this and from other complications of the disease.

Indications for Operation

For patients without symptoms and for those in whom the serum calcium concentration is less than 11.5 mg/dl, the question, "Is prolonged preoperative observation permissible?" must be asked. Conversely, one must ask, "Can we justify early operation for all patients with mild disease that, previously, never would have been discovered?" Obviously, because the asymptomatic patients include those with early but progressive and ultimately severe disease, all those patients must be followed, if not operated on. To say that the disease could be due to a malignant neoplasm does not appear to be justified. Only two patients with para-

thyroid cancer have been seen in 45 years at the University of Iowa.

Since every patient should be followed, even after a successful operation, more of the observation, in patients with mild disease, should be preoperative. We often follow patients with suspected hyperparathyroidism until enough repeated chemical analyses have been obtained to convince us that the disease is present. We can now make the diagnosis even when the serum calcium concentration is not appreciably elevated because of a serum parathyroid hormone that is too high for the simultaneously sampled level of serum calcium.[9] Although automated laboratory procedures have made diagnostic acumen relatively less important, the earlier and more frequent diagnosis in patients with mild disease makes clinical judgement more important in following up these patients, in withholding operation until there is some indication of increasing severity, or appearance of symptoms, and in ascertaining more exactly what it is that we are treating.

Ideally, prolonged observation without operation should be in accordance with a definite protocol and the data pooled so that we could learn as much as possible as quickly as possible. Purnell and colleagues[10] instituted one such study and it appears that in the majority of their patients the disease has not progressed and that avoidance of operation is not harmful. Of course, any patient in whom symptoms develop that are consistent with hypercalcemia or in whom the serum calcium concentration increases progressively, or remains above 11.5 mg/dl should be treated surgically. This, however, leaves an ever-increasing number of asymptomatic patients with serum calcium values below 11.5 mg/dl who must be followed and only operated on if their disease becomes more severe.

Operative Procedure

How much parathyroid tissue should be removed at operation? Paloyan, Lawrence and Straus[11] recommend subtotal parathyroidectomy, leaving only about 50 mg of the gland that appears most normal and accessible. These authors reported that the majority of the patients had had hyperplasia, though this was not known until the surgeons began removing most of the parathyroid tissue; moreover, the pathologists in that particular institution were more often able or willing to make a diagnosis of hyperplasia than are, for example, those at ours. It is certainly no longer acceptable to terminate the operation as soon as an adenoma has been found and removed.

With the more recent search for all of the parathyroid tissue, the greater use of biopsy and frozen section and the removal of more glands, serum calcium values seem to have been restored to normal in a greater proportion of patients (Fig. 3). At the same time, however, there are more patients in whom the disease is milder and in whom the period of postoperative observation is shorter, so that we cannot be sure that the more aggressive operative treatment is more effective. Furthermore, the risks of permanent hypoparathyroidism after subtotal parathryoidectomy are not insignificant.

We need improved methods of finding all parathyroid tissue at operation. A safe and effective stain or a radioactive tag that could be taken up by parathyroid tissue would help; and if the intensity of the uptake were related to the production of parathyroid hormone it would be even better. All the parathyroid glands should be located to rule out multiple adenomas or hyperpla-

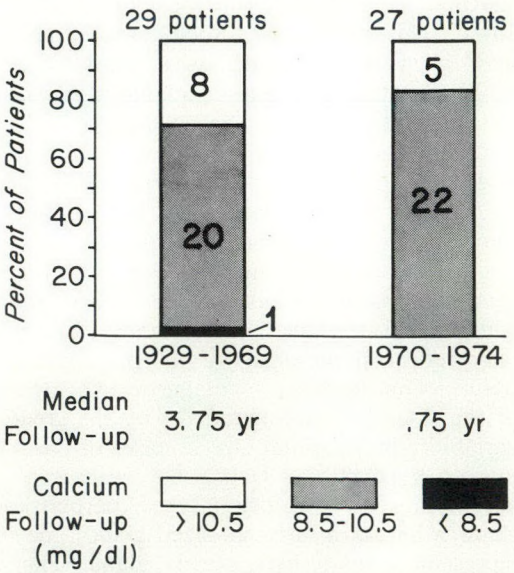

Fig. 3.—Frequency of normal serum calcium concentrations during 1970 to 1974 in comparison with concentrations recorded for 1929 to 1969.

sia. Obviously normal glands should be biopsied and marked with a metallic clip, or suture, taking care to preserve blood supply. Obvious adenomas should be removed.

If there is no single adenoma, if there is hyperplasia or if there is any likelihood of hyperplasia even with an apparent adenoma, subtotal parathyroidectomy is indicated. The tissue to be left then becomes of primary concern. No parathyroid tissue should be removed until an estimated 50 mg of the gland that appears most normal, well-vascularized and accessible has been selected, marked and established as the patient's probable lifetime solitary source of parathyroid hormone. To remove three or even two normal parathyroid glands from the neck during exploration and before all glands have been located is a frequent temptation, particularly during a prolonged, frustrating search. This temptation must be resisted if the development of hypoparathyroidism is to be prevented in some of those patients who present the more difficult diagnostic and therapeutic problems. If no abnormal tissue can be found, thyroid lobectomy should be performed on the side of the missing gland. Transcervical thymectomy and exploration of the superior mediastinum is a particularly important aspect of the operation when one or both inferior glands have not been located. If all glands appear normal, removal of 3 or 3½ glands is a reasonable procedure. Persistent hypercalcemia after such a procedure may result from the existence of an adenoma in a fifth parathyroid that was never located or from another lesion.

Need for Prolonged Observation After Operation

A final question concerns the length of follow-up of patients treated surgically. Despite the long period of interest in this disease, the patients at the University of Iowa have not been followed with the frequency and for the length of time that appears now to be indicated, and this is probably the experience throughout most of the country. Today there is really only one way of determining the correctness of diagnosis and treatment in a particular individual: each patient must be observed for the rest of his life. The course of the first patient with hyperparathyroidism seen at the University of Iowa exemplifies this point: he died at the relatively young age of 36 from recrudescence of hypercalcemia and its consequences 17 years after removal of an adenoma. His disease was severe when it was first diagnosed. By contrast, mild disease will probably remain mild. Unless we become as aggressive about observing our patients as we have thus far been in operating on them, we will never fully understand the disease.

Records of patients studied at the University of Iowa in the early decades are filled with data regarding urinary excretion of calcium and phosphorus.[2] We now have available investigative procedures that were not previously available yet we are not studying the patients with the intensity that those early patients stimulated. Maybe the diagnosis today is too easy.

Future Needs

We need much more information about the course of hyperparathyroidism both with and without operation. When an operation has been performed it might be of help to measure combined serum calcium and parathyroid hormone concentrations after the serum calcium and phosphorus concentrations have stabilized. We need more electron microscopic studies of parathyroid tissue that appears normal both grossly and by light microscopy, and that has been removed from patients diagnosed as having adenomas, to see if a prediction can be made from the microscopic findings as to whether overactive parathyroid tissue will cause a persistence or recurrence of hypercalcemia.[8] We need parathyroid hormone assay of adenomatous, hyperplastic and grossly normal tissue removed from these patients. We need tests of the parathyroid hormone levels at lowered serum calcium concentrations to determine the secretory capacity of remaining tissues. Such hypocalcemic stress tests should be done repeatedly in the same patient over many years.

Finally, our obligation to these patients, since we are so uninformed about all aspects of their disease, is to continue observing them at appropriate intervals for as

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long as possible, whether they undergo an operation or not. Hyperparathyroidism is commonly a mild disease that can be safely observed; it can also be a rapidly lethal disease or a debilitating chronic disease. If the patient remains asymptomatic and with a serum calcium concentration of below 11.5 mg/dl, observation is reasonable and, perhaps, the preferred course. We believe that neck exploration is indicated both in the patient with symptoms and in the patient with no symptoms in whom the serum calcium value is 11.5 mg/dl on three occasions or more over a period of 6 months.

References

1. Mandl F: Therapeutischer Versuch bei Ostitis fibrosa generalisata mittels Exstirpation eines Epithelkörperchentumors. *Wien Klin Wochenschr* 38: 1343, 1925
2. Boyd JD, Milgram JE, Stearns G: Clinical hyperparathyroidism. *JAMA* 93: 684, 1929
3. Albright FA, Aub JC, Bauer W: Hyperparathyroidism; common and polymorphic condition as illustrated by seventeen proved cases from one clinic. *JAMA* 102: 1276, 1934
4. Keating FR, Cook EN: Recognition of primary hyperparathyroidism; analysis of 24 cases. *JAMA* 129: 994, 1945
5. Keating FR: Clinical problem of primary hyperparathyroidism. *Med Clin North Am* 54: 511, 1970
6. Wills MR, McGowan GK: Hyperchloraemia as diagnostic feature in hyperparathyroidism. *J Bone Joint Surg* [*Br*] 45: 799, 1963
7. Paloyan E, Lawrence AM, Straus FH: *Hyperparathyroidism,* New York, Grune, 1973, p 82
8. Haff RC, Black WC, Ballinger WF: Primary hyperparathyroidism: changing clinical, surgical and pathologic aspects. *Ann Surg* 171: 85, 1970
9. Arnaud CD, Tsao HS, Littledike T: Radioimmunoassay of human parathyroid hormone in serum. *J Clin Invest* 50: 21, 1971
10. Purnell DC, Smith LH, Scholz DA, et al: Primary hyperparathyroidism: prospective clinical study. *Am J Med* 50: 670, 1971
11. Paloyan E, Lawrence AM, Straus FH: *Hyperparathyroidism,* New York, Grune, 1973, p 180

EFFECT OF SYMPATHETIC INHIBITION ON MAXIMAL MUSCLE BLOOD FLOW IN THE NORMAL AND ATHEROSCLEROTIC HUMAN LEG*

CHARLES J. WRIGHT, MB, FRCS, FRCS(Edin), FRCS[C]

Summary: The control of blood flow in skeletal muscle is incompletely understood, and for this reason the effect of sympathetic inhibition on muscle blood flow in the leg was studied. One group of patients selected for study comprised 20 patients without evidence of vascular disease; a second comprised 20 with peripheral occlusive arterial disease, in whom the site of occlusion varied from the aorta to the lower leg arteries. None had undergone previous vascular surgery or sympathectomy. Variables studied included resting muscle blood flow; maximal muscle blood flow; interval from tourniquet release to onset of peak flow; duration of peak blood flow; muscle blood flow after tourniquet release; and skin temperature in the foot. Muscle blood flow was calculated from xenon-133 clearance. The variables were studied before and after ischemia (thigh tourniquet) and before and after sympathetic inhibition (immersion of hands and wrists in water at 45°C). The significant differences between the two groups related to peak flow after ischemic exercise, the interval from tourniquet release to peak flow and duration of peak flow. Sympathetic inhibition was followed by no significant changes in maximal muscle blood flow, though there was a significant decrease in resting muscle blood flow. The results of the present study, in which noninvasive sympathetic blockade was used, confirm the findings of others that muscle blood flow does not change after operative sympathectomy.

Résumé: On ne comprend encore qu'imparfaitement le mécanisme de la circulation sanguine dans le muscle strié du squelette. C'est pourquoi nous avons étudié l'effet de l'inhibition du sympathique sur la circulation de la jambe. Cette étude a porté sur deux groupes de 20 malades: dans le premier, les sujets ne présentaient aucun signe de maladie vasculaire; le second comportait des malades souffrant d'occlusion artérielle, dont le siège variait de l'aorte aux artères inférieures de la jambe. Aucun de ces malades n'avait subi auparavant d'opération vasculaire ni la sympathectomie. Parmi les examens et les observations pratiqués, figuraient: la circulation du muscle au repos, la circulation musculaire maximale, l'intervalle séparant la libération du tourniquet et le début de la circulation de pointe, la durée de celle-ci, la circulation musculaire après l'abandon du tourniquet et la température cutanée du pied. Pour calculer la circulation musculaire, nous avons utilisé la clearance du xénon-133. Les variations ont été étudiées avant et après ischémie (tourniquet appliqué sur la cuisse), de même qu'avant et après inhibition du sympathique (immersion des mains et des poignets dans de l'eau à 45°C). Les différences marquées entre les deux groupes portaient sur la circulation de pointe après ischémie, l'intervalle entre l'abandon du tourniquet et de la circulation de pointe et la durée de celle-ci. L'inhibition du sympathique n'a entrainé aucune modification notable dans la circulation maximale du muscle, sauf une diminution significative dans la circulation du muscle au repos. Les résultats de la présente étude, au cours de laquelle le blocage du sympathique a été effectué sans aucun moyen de pénétration interne de l'organisme, confirment les recherches d'autres auteurs: la circulation sanguine du muscle ne change aucunement après une sympathectomie opératoire.

IT has been known since the work of Bernard in 1852[1] that sympathetic outflow to cutaneous vessels causes vasoconstriction. The control of blood flow in skeletal muscle, however, is complex and is not yet completely understood. Vasoconstrictor and vasodilator fibres have been identified in skeletal muscle blood vessels,[2, 3] but during exercise the effect of vasodilator metabolites produced locally is the predominant factor in the large increase in blood flow.[4, 5] Both lumbar sympathectomy and sympathetic blockade have been widely used in the treatment of peripheral arterial disease[6-8] and are still frequently performed when direct arterial reconstruction is either contraindicated or technically impossible. Although the main indication for sympathetic ablation is skin ischemia with rest pain, it is not unusual for patients in whom sympathetic ablation has been performed also to

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experience improvement in walking distance without claudication.

This study was designed to examine the effect of sympathetic inhibition on muscle blood flow in the leg.

Patients and Methods

Patients

Forty patients were studied, of whom 20 had no historical or clinical evidence of vascular disease (mean age, 59 ± 12 years) (group 1) and 20 had peripheral occlusive arterial disease (64 ± 12 years) (group 2). In the atherosclerotic group, the main site of occlusion varied from the aorta to the lower leg arteries. Some patients had presented with intermittent claudication and some with foot pain or paresthesias, but none had actual or impending gangrene. No patient who had undergone any previous vascular surgery or sympathectomy was included in the study. Three of the patients in group 2 had diabetes. Informed consent was obtained from each patient.

Experimental Procedure

The studies were conducted in an air-conditioned room (21°C). Patients were resting supine, and, after a wide sphygmomanometer cuff had been placed around the thigh, the leg to be studied was cradled in a foam mould. A thermistor probe was attached to the sole of the foot and wired to a telethermometer (Yellow Springs Instrument Co.). Temperature readings were taken at 5-minute intervals throughout the experiment. After a 30-minute rest period, capillary blood flow in the anterior tibial muscles was measured by the xenon-133 clearance technique. Then, 30 μCi of ^{133}Xe dissolved in 0.1 ml of sterile saline was injected directly into the muscle mass and the isotope clearance curve charted by a scintillation counter, rate meter and recorder. Muscle blood flow (ml/100 g·min) was calculated from the clearance curve by means of the formulas derived by Lassen, Lindbjerg and Munck.[9]

After the thigh tourniquet had been inflated to a pressure exceeding the systolic pressure in the arm, the patient exercised the ankle until forced to stop by pain. No patient exercised for less than 2 minutes. The tourniquet was then released and the following measurements were recorded: peak muscle blood flow; time elapse from release of the tourniquet to onset of peak flow; duration of peak blood flow; and muscle blood flow at 1-minute intervals for 5 minutes after tourniquet release.

To block sympathetic outflow to the legs, both of the patient's hands and wrists were then immersed in water at 45°C; with the patient lying supine the temperature of the foot was measured for further 5-minute intervals until no more increase in skin temperature was recorded. Then, all the measurements already described were repeated before and after reinflation of the tourniquet.

A typical pattern of clearance of ^{133}Xe is shown in Fig. 1. After injection of the bolus of ^{133}Xe into the muscle mass, resting blood flow is measured by drawing a line through the slope and applying the standard formula. As the records are made from a logarithmic output, the slope of ^{133}Xe clearance when the flow is stable is a straight line. When the thigh tourniquet is applied, blood flow ceases and the radioactivity in the muscle remains constant. On release of the tourniquet the blood flow increases rapidly; in this particular example it became maximal after about 30 seconds. The muscle blood flow at any moment may be determined by drawing the straight line tangent to the clearance curve at that point. In this example, the steepest slope and thus the maximal blood flow was found in the interval between B and C, and the low level of normal resting flow was reached after ap-

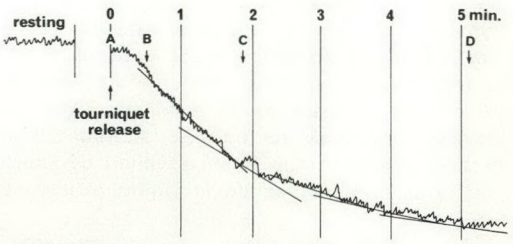


Fig. 1.—Clearance of ^{133}Xe from anterior tibial muscle after ischemic exercise. Blood flow is calculated at any point from the slope of the tangent to the curve. Tourniquet is released at point A; blood flow is maximal after 30 seconds (at B), reaching a maximum between B and C, and a low level or normal at D, at 5.1 minutes. Absolute radioactive counts are not relevant. (Pen moves across paper from left to right).

TABLE I.—MUSCLE BLOOD FLOW BEFORE AND AFTER SYMPATHETIC INHIBITION*

Variable	*Group 1 (Patients without atherosclerosis)*		*Group 2 (Patients with atherosclerosis)*	
	Before	*After*	*Before*	*After*
Resting blood flow (ml/100 g·min)	3.3 ± 1.2[a]	2.3 ± 1.3[a]	3.5 ± 1.8[b]	2.1 ± 1.2[b]
Peak flow (ml/100 g·min)	69.2 ± 22.8[c]	64.4 ± 18.3[d]	23.9 ± 12.6[c]	22.8 ± 12.1[d]
Interval to peak flow (s)	14.8 ± 11.9[e]	13.2 ± 10.9[f]	81.1 ± 59.0[e]	88.1 ± 62.2[f]
Duration of peak flow (s)	89.4 ± 37.2[g]	75.9 ± 26.9[h]	166.8 ± 67.8[g]	181.8 ± 75.1[h]

*Differences are significant for pairs of results as follows: a: $P < 0.005$, b: $P < 0.001$, c: $P < 0.01$, d: $P < 0.01$, e: $P < 0.01$, f: $P < 0.05$, g: $P < 0.01$, h: $P < 0.01$. Other differences within and between groups are not significant.

proximately 5.1 minutes. Blood flow was also measured in each experiment at 1-minute intervals from tourniquet release by drawing the tangents to the curve at the appropriate points (Fig. 1). In each patient, therefore, ^{133}Xe was injected only twice, once before and once after sympathetic inhibition.

For statistical analysis, the paired Student's *t* test was used in comparing results before and after sympathetic inhibition in each group, and the unpaired *t* test was used in comparing the results for the two groups with each other.

RESULTS

Comparison of Muscle Blood Flow in Atherosclerotic and Normal Limbs

An overall comparison of results is provided in Table I. Resting muscle blood flow was 3.3 ± 1.2 ml/100 g·min in the patients in group 1 (no vascular disease) and 3.5 ± 1.8 ml/100 mg·min in those in group 2 (atherosclerosis). Peak flows after ischemic exercise were 69.2 ± 22.8 and 23.9 ± 12.6 ml/100 g·min, respectively. The interval from tourniquet release to peak flow and the duration of peak flow were both significantly longer in the atherosclerotic group. Muscle blood flow measurements at 1-minute intervals after ischemic exercise are plotted in Fig. 2. Blood flow in the two groups after sympathetic inhibition shows little change except that resting flow is lower in both groups.

Effects of Sympathetic Inhibition on Muscle Blood Flow

Group 1.—Resting muscle blood flow decreased significantly ($P < 0.005$) from 3.3 ± 1.2 to 2.3 ± 1.3 ml/100 mg·min after sympathetic inhibition, but there was no change in peak muscle blood flow, time elapse to peak, duration of peak flow, or flow at 1-minute intervals following the tourniquet release (Table I, Fig. 3).

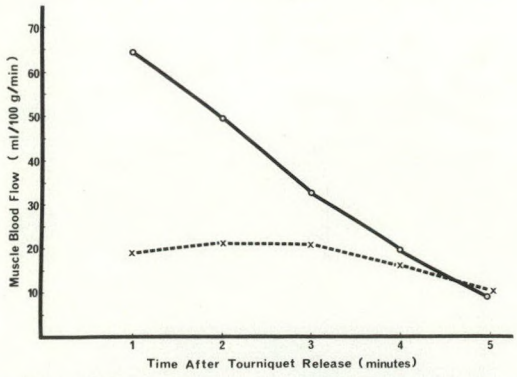


Fig. 2.—Muscle blood flow after ischemic exercise. Comparison of responses in normal and atherosclerotic limbs. (O = normal limbs [group 1]; X = atherosclerotic limbs [group 2]).

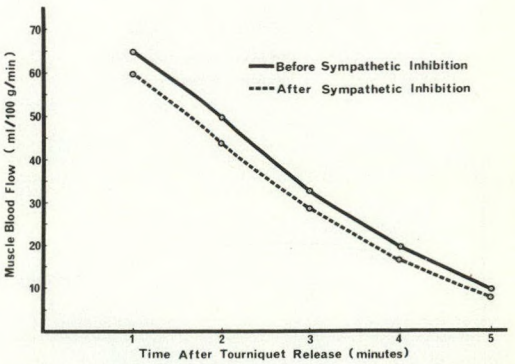


Fig. 3.—Muscle blood flow at 1-minute intervals after tourniquet release in patients with no vascular disease (group 1).

Group 2.—As in group 1, there was a highly significant decrease in resting muscle blood flow after sympathetic inhibition, from 3.5 ± 1.8 to 2.1 ± 1.2 ml/100 g·min ($P < 0.001$) and no change in the other variables (Table I, Fig. 4).

Temperature Change in Foot Skin

During sympathetic inhibition the mean increase in foot skin temperature was 4.94 ± 3.08°C in group 1 and significantly less ($P < 0.05$) at 1.65 ± 1.67°C in group 2 (Table II). There was no significant difference between the groups in the interval from commencement of upper limb heating to the recording of maximal foot skin temperature; no differences were noted among the diabetics. The chart of a typical experiment showing the sequence of events in relation to the foot skin temperature changes is presented in Fig. 5.

TABLE II.—TEMPERATURE INCREASES IN FOOT SKIN

	Group 1	Group 2
Temperature increase (°C)	4.94 ± 3.08*	1.65 ± 1.67*
Interval to peak temperature (min)	29.2 ± 9.6	35.5 ± 7.9

*Difference significant, $P < 0.05$.

DISCUSSION

The results of this study reveal that there is no change in maximal muscle blood flow after sympathetic inhibition. The method of blocking sympathetic outflow by heating the upper limbs[10] is known to depend on a central effect. The vasomotor centre is sensitive to a change in the temperature of its perfusate of as small as 0.1°C. The major effects of inhibition of the vasomotor centre are, of course, on the skin (Fig. 5) but skeletal muscle has a sympathetic supply also,[2, 3] even if its function has not yet been precisely defined. The consistent significant decrease in *resting* muscle blood flow after sympathetic blockade reported by Wright and Cousins[11] was demonstrated also in the present study. The recorded effects on resting muscle blood flow suggest that sympathetic inhibition is effectively produced by upper limb heating, and this has been confirmed by others.[12] One must conclude that the lack of response of *maximal* muscle blood flow to sympathetic inhibition in this study is because maximal muscle blood flow is entirely under the control of local factors; this does not mean that the method of achieving sympathetic inhibition was ineffective.

The extent of the increase in muscle blood flow caused by ischemic exercise was similar to that reported from other centres,[13-15] and the differences in response between normal and atherosclerotic limbs (Table I, Fig. 2) have also been documented. It is not surprising that the flow response to exercise in the normal legs (Fig. 3) was greater than that observed in patients with arterial disease (Fig. 4) and that the sympathetic blockade had no influence on the results in either group. Attempts have been made to correlate the site and severity of arterial disease and the exercising blood flow

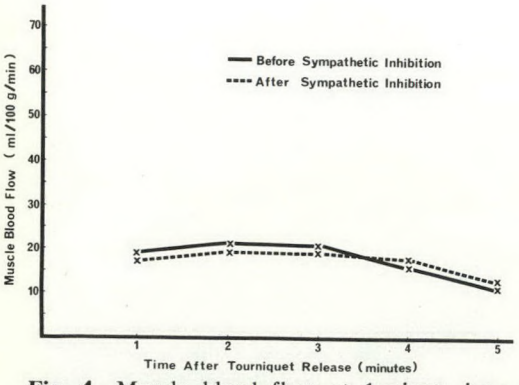


Fig. 4.—Muscle blood flow at 1-minute intervals after tourniquet release in patients with atherosclerosis (group 2).

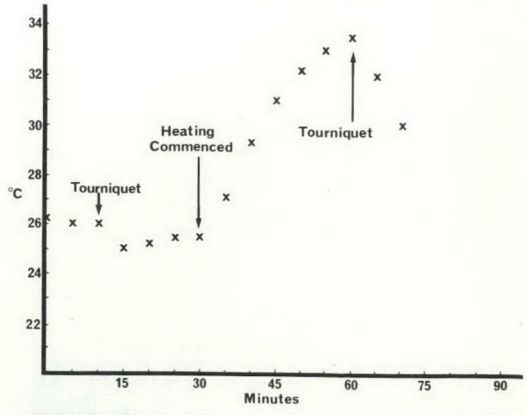


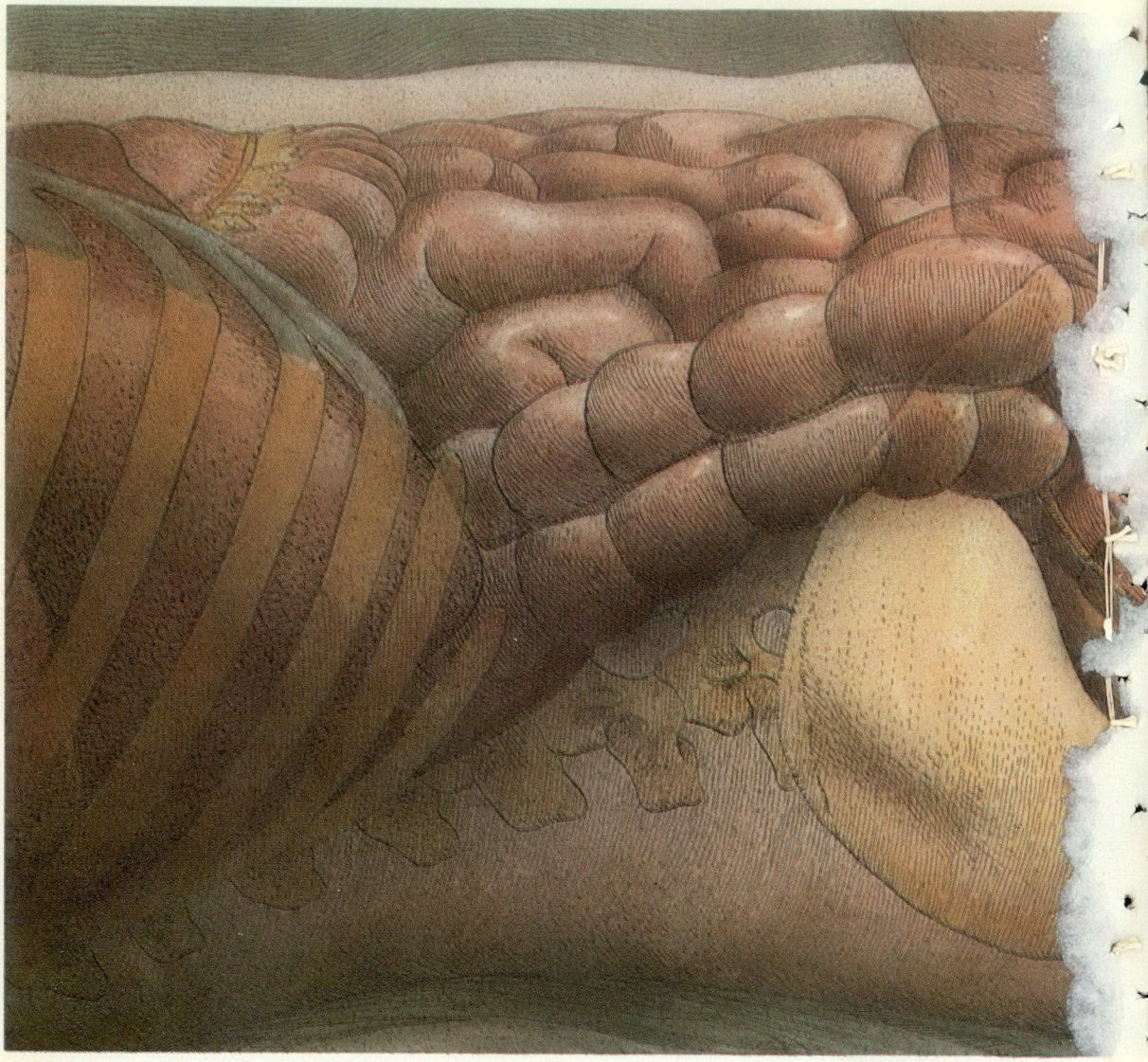
Fig. 5.—Foot skin temperature changes during one experiment.

changes,[13, 14] but the individual variation is too large for this to be clinically useful. Arteriographic findings in conjunction with the clinical and historical data remain the critical method of assessment when reconstructive arterial surgery is contemplated.

Others[16, 17] have reported the absence of any change in exercising muscle blood flow following operative sympathectomy, and the present study confirms these findings using a noninvasive technique of sympathetic blockade. The improvement in claudication distance that patients sometimes observe after sympathectomy or chemical sympathetic blockade requires some other explanation. It is notoriously difficult to standardize conditions for measuring claudication distance, and the improvement may be the result of a placebo effect. Another possibility is a disruption that sympathetic ablation causes of afferent neural pathways that are partially responsible for the ischemic muscle pain. On the other hand, the benefit of sympathetic ablation in patients with rest pain or paresthesias in the foot is well known. The increase in foot skin temperatures (Table II, Fig. 5) is due in part to the existence of superficial arteriovenous communications that carry increased flow after sympathectomy, but the large increase in total limb blood flow at rest in relation to the relatively small flow in skin arteriovenous communication[18, 19] suggests that nutritive blood flow in skin capillaries is also increased. The infrequent occurrence of "paradoxical gangrene" after sympathectomy[20] probably relates to a critical decrease in distal perfusion pressure in some cases.

References

1. Bernard C: Expérience sur les fonctions de la portion céphalique du grand sympathique. *C R Soc Biol (Paris)* 4: 155, 1853
2. Rosell S, Bolme P, Ngai SH: Interaction between cholinergic vasodilator and adrenergic vasoconstrictor nerves on canine skeletal muscle blood vessels, in *Circulation in Skeletal Muscle,* edited by Hudlicka EO, Oxford, Pergamon, 1968, p 43
3. Schramm LP, Honig CR, Bignall KE: Active muscle vasodilation in primates homologous with sympathetic vasodilation in carnivores. *Am J Physiol* 221: 768, 1971
4. Grant RT: Observations on blood circulation in voluntary muscle in man. *Clin Sci* 3: 157, 1938
5. Kjellmer I: On competition between metabolic vasodilatation and neurogenic vasoconstriction in skeletal muscle. *Acta Physiol Scand* 63: 450, 1965
6. Blain A, Zadeh AT, Teves ML, et al: Lumbar sympathectomy for arteriosclerosis obliterans. *Surgery* 53: 164, 1963
7. Strandness DE, Bell JW: Critical evaluation of results of lumbar sympathectomy. *Ann Surg* 160: 1021, 1964
8. Reid W, Watt JK, Gray TG: Phenol injection of sympathetic chain. *Br J Surg* 57: 45, 1970
9. Lassen NA, Lindbjerg IF, Munck O: Measurement of blood flow through skeletal muscle by intramuscular injection of xenon-133. *Lancet* 1: 686, 1964
10. Gibbon JH, Landis EM: Vasodilatation in lower extremities in response to immersing forearms in warm water. *J Clin Invest* 11: 1019, 1932
11. Wright CJ, Cousins MJ: Blood flow distribution in human leg following epidural sympathetic blockade. *Arch Surg* 105: 334, 1972
12. Rapaport SI, Saul AM, Hyman C, et al: Tissue clearance as measure of nutritive blood flow and effect of lumbar sympathetic block upon such measures in calf muscle. *Circulation* 5: 594, 1952
13. Lindbjerg IF: Diagnostic application of 133 xenon method in peripheral arterial disease. *Scand J Clin Lab Invest* 17: 589, 1965
14. Bell G, Short DW: Measurement of blood flow through muscle from clearance of radioactive xenon. *Surg Gynecol Obstet* 127: 61, 1968
15. Idem: Effect of thromboendarterectomy upon muscle blood flow as measured by clearance of 133 xenon. *Surgery* 70: 649, 1971
16. Hoffmann DC, Jepson RP: Muscle blood flow and sympathectomy. *Surg Gynecol Obstet* 127: 12, 1968
17. Smith RB, Dratz AF, Coberly JC, et al: Effect of lumbar sympathectomy on muscle blood flow in advanced occlusive vascular disease. *Am Surg* 37: 247, 1971
18. Cousins MJ, Wright CJ: Graft, muscle, skin blood flow after epidural block in vascular surgical procedures. *Surg Gynecol Obstet* 133: 59, 1971
19. Zanick DC, Delaney JP: Temperature influences on arteriovenous anastomoses. *Proc Soc Exp Biol Med* 144: 616, 1973
20. Balas P, Plessas S, Segditsas TH, et al: Post lumbar sympathectomy gangrene. *Angiology* 21: 552, 1970



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.J., p. 1177.

GLIMPSES OF SURGICAL HISTORY: E FOR EDISON, THE ELECTRIC LAMP AND ENDOSCOPY

D. A. E. SHEPHARD

Thomas Edison (1847-1931), like his contemporary Alexander Graham Bell, influenced medicine and surgery in many ways, both general and specific. In a general sense, Edison's invention of the electric lamp in 1879 altered the pattern of everyone's lives; for surgeons, electric illumination of the operating room and the operative field made surgical work easier, more accurate and safer. Edison's influence was profound because the introduction of the electric lamp initiated a new era and a new way of seeing things.

Physicians of all specialties could now look at the body in a new light. Not only could they illuminate the surface of the body reliably and brightly, but also they could examine the body's orifices—and even the cavities of the body. Physicians could literally look within (endoscopy = endon, *within;* skopein, *to examine).*

Electric endoscopy is an excellent example of a surgical technique that was influenced specifically by Edison's work. Endoscopy of the urethra and bladder developed in three periods. In 1805 Bozzini of Germany invented a light conductor, but the illumination provided was insufficient. The essential idea, however, caught on. During the next 50 years various people worked towards a practical endoscope, but it was Désormeaux of France who made the first practical endoscope. When he exhibited it in Paris in 1853 he ushered in the second period of endoscopy. Désormeaux' endoscope made use of an alcohol wick flame and a mirror, and his instrument was soon modified by others. But endoscopes of this period were unsatisfactory because they required the use of daylight or a burning flame as the source of illumination; even the diaphanoscope of Bruck, which opened the electric period of endoscopy, with its electrically heated platinum wire, was clumsy, requiring a large battery and a water cylinder for cooling.

The incorporation of a miniature electric lamp in the endoscope was a real advance. As a Lancet *editorial of 1892 put it, "The introduction of the electric light . . . gave a fresh impulse to invention, and marks an entirely new departure." The great advance, as noted in the* Canadian Medical Association Journal *for 1911, was that ". . . the lamp could be placed at the bottom of the tube instead of having the light reflected into it . . . it made possible the application of lenses to magnify the field and a window to dilate the canal with air".*

And so Edison's major invention, like so many others of surgeons' nonmedical confrères, was one of numerous technical developments that have advanced the art of surgery.

VOLVULUS OF THE GALLBLADDER: CASE REPORT AND REVIEW OF THE LITERATURE*

VINCENT ECHAVE, MD and LAWRENCE G. HAMPSON, MD, FRCS[C], FACS

Summary: Volvulus of the gallbladder is a rare abdominal emergency: only 250 cases have been reported. A correct preoperative diagnosis is rarely made. However, it is most common in elderly women, and acute volvulus should be considered in the differential diagnosis of upper abdominal pain, particularly in elderly women with right upper quadrant pain. The treatment is early cholecystectomy.

Résumé: Le volvulus de la vésicule biliaire est une rare urgence abdominale. On n'en trouve que 250 cas rapportés dans la littérature. On pose rarement un diagnostic préopératoire exact. Cette pathologie est cependant très fréquente chez les femmes âgées, de sorte qu'il faudrait songer à un volvulus aigu dans le diagnostic différentiel d'une douleur abdominale du quadrant supérieur droit, surtout si la malade est une femme âgée. Le traitement consiste à pratiquer rapidement une cholécystectomie.

VOLVULUS of the gallbladder is rare, only about 250 cases having been reported. Acute torsion of the gallbladder was first described by Wendel in 1898;[1] his patient was a young woman who had a mobile abdominal mass. The majority of cases reported since have occurred in elderly women. Its occurrence in children was first reported in 1939[2] but few cases have been reported in the young since.[3, 4] The reports in the world literature have been largely of isolated cases occurring in many countries, which is consistent with the rarity of this clinical entity. To our knowledge this condition has been reported only twice previously in the Canadian literature.[8, 5] This paper is the third report in the Canadian literature.

CASE REPORT

An 87-year-old woman was admitted to hospital because of the relatively sudden onset of severe colicky pain in the right upper abdominal quadrant. The abdominal pain began a few days before admission and was associated with nausea but no vomiting. There was no history of jaundice, but she was known to have had gallstones for the previous 20 years; these had produced no symptoms except postprandial pain occasionally. On the day of admission the pain had become more severe and she had vomited once.

She was thin and in moderate abdominal discomfort. Blood pressure and pulse were normal; her oral temperature was 37.1°C.

Examination revealed guarding in the upper abdomen, particularly in the right upper quadrant, and a positive Murphy's sign. No masses were palpable, bowel sounds were heard and there were no signs of peritoneal irritation.

Chest radiography revealed an elevated right hemidiaphragm, calcification of the aorta and degenerative changes in the spine; both lung fields were clear. Abdominal radiographs visualized a single calculus in the region of the gallbladder, and feces and air in the colon; there was no evidence of bowel obstruction and the retroperitoneal shadows were normal. The leukocyte count was $9.5 \times 10^9/l$ (differential, normal); the total serum bilirubin concentration was 1 mg/dl; and the results of other investigations (serum electrolytes, alkaline phosphatase, serum glutamic oxaloacetic transaminase and lactic dehydrogenase) were normal.

Initial treatment consisted of nasogastric suction and intravenous administration of fluids. Her condition during the following days did not change appreciably: a low-grade fever persisted, her pulse rate slowly increased, and the pain remained localized to the right upper quadrant. As no improvement was evident a laparotomy was performed on the 5th hospital day. The gallbladder was greatly distended and completely gangrenous; it was also excessively mobile with little surrounding inflammation. Careful inspection revealed a counterclockwise torsion of 270° at the level of the cystic duct; an elongated gallbladder mesentery arising from a short base in the liver bed had made torsion possible. Detorsion was effected and the gallbladder was removed easily. She recovered well and was discharged 10 days after operation.

Pathological examination showed evidence of gangrene of the gallbladder and cholelithiasis.

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Discussion

Three anatomic abnormalities may lead to volvulus of the gallbladder. The gallbladder may lie free in the peritoneal cavity, connected to the biliary tree by the cystic duct only; this anatomic variation is congenital and explains the rarity of cases of acute volvulus in children.[2, 4] As a true mesentery is congenital in less than 5% of the population, it is possible that in some cases acute torsion of the gallbladder is associated with an acquired mesentery, the second anatomic abnormality. This condition usually occurs late in life and it is therefore logical to presume that, with ageing, the supporting fatty tissue surrounding the abdominal viscera atrophies; the resulting visceroptosis favours excessive mobility and torsion. Spinal deformities producing changes in anatomic position of the abdominal organs also may predispose to torsion; indeed, many of the reported cases have occurred in elderly women with severe scoliosis.[7, 8]

If there is an anatomic predisposition to volvulus one must consider how the acute process might be initiated. Several different mechanisms have been suggested. Peristalsis of the surrounding organs, when sufficiently vigorous, might initiate torsion.[9] This is more likely if the gallbladder contains stones and so behaves more as a mobile solid organ.[10] According to other authors, a tortuous arteriosclerotic cystic artery may initiate torsion.[11] Falls or violent movements have also been suggested as initiating events.[12]

Although the condition affects normal gallbladders, cholelithiasis is frequently associated. One might expect the existence of cholelithiasis and chronic cholecystitis to result in chronic inflammation and fibrosis, which would tend to reduce the mobility of the gallbladder and thus lessen the likelihood of torsion.

Volvulus of the gallbladder is more common in females than in males; it is also more common in the old, the peak incidence occurring in persons in the 7th and 8th decades of life.[13]

A palpable abdominal mass is a variable finding, and in the patient whose case we report it was not possible to palpate the gallbladder despite its large size, possibly because of voluntary guarding in the upper abdomen. Features considered highly suggestive of acute volvulus of the gallbladder are acute pain and vomiting without jaundice in an elderly woman, and the appearance within a few hours of onset of an enlarged and palpable gallbladder.[14] The diagnosis of this condition is difficult but it should be included in the differential diagnosis of the acute abdomen, particularly in elderly women with right upper quadrant pain.[15]

The treatment is early cholecystectomy. Removal of the gallbladder is facilitated by the long mesentery, the great mobility of the gallbladder and the absence of inflammatory reaction. If the treatment is delayed, the natural course of the disease is perforation of the gangrenous wall with bile peritonitis, which has a high mortality in this group of elderly patients.[9]

References

1. Wendel AV: Case of floating gallbladder and kidney complicated by cholelithiasis with perforation of gallbladder, *Ann Surg* 27: 199, 1898
2. Cuervo S, Cuervo T: A propósito de dos casos de vólvulo biliar en niños de cinco y once años de edad respectivamente. *Arch Soc Est Clin Habana* 33: 295, 1939
3. Sattarov RK: Zavarot zhelechnogo puzyria u rebenka. *Vestn Khir* 107: 85, 1971
4. Rawson HD: Torsion of gall-bladder in child of 12 with review of literature. *Aust NZ J Surg* 22: 315, 1953
5. Gowland MM: Acute volvulus of gallbladder. *Can Med Assoc J* 54: 485, 1946
6. Moses P, Hick ES: Torsion of gallbladder with gangrene. *Can Med Assoc J* 58: 382, 1948
7. Mouzas GL: Torsion of gallbladder in kyphoscoliotic patient. *Postgrad Med J* 36: 686, 1960
8. Rais O, Thulin CA: Torsion of gallbladder; report of one case and review of literature. *Acta Chir Scand* 113: 289, 1957
9. Greenwood RK: Torsion of gall bladder. *Gut* 4: 27, 1963
10. Levene A: Acute torsion of gall-bladder; post-mortem findings in two cases. *Br J Surg* 45: 338, 1958
11. Caldwell KP: Torsion of gall-bladder. *Br Med J* 2: 1425, 1950
12. Berry WH: Torsion of gallbladder. *JAMA* 112: 1580, 1939
13. Maingot RH: *Abdominal Operations,* sixth ed, London, Lewis, 1974
14. Short AR, Paul RG: Torsion of gall-bladder. *Br J Surg* 22: 301, 1934
15. Bothra R: Torsion of gallbladder in aged *Br J Surg* 60: 359, 1973

BIBLIOGRAPHY

1. ADAMCZAK T: Acute torsion of gallbladder. *Pol Przegl Chir* 31: 1129, 1959
2. ANDROSOVA TP, GRACH ZI, SHESHINA NP: Torsion of gallbladder. *Vestn Khir* 97: 89, 1966
3. ARTHUR HR: Acute torsion of gallbladder. *Br Med J* 2: 265, 1937
4. ASHBY BS: Acute and recurrent torsion of gallbladder. *Br J Surg* 52: 182, 1965
5. AVANZI JJ, BIANCHI O: Volvulus of gallbladder. *Semin Med (Buenos Aires)* 122: 989, 1963
6. BABNIK C, SCHIFFER J, MAZOR A: Volvulus of gallbladder. *Harefuah* 82: 515, 1972
7. BALDI EM: Choleperitoneum caused by volvulus of gallbladder in pregnant woman. *Semin Med (Buenos Aires)* 121: 1000, 1962
8. BALDOE EA: Acute torsion of gallbladder. *West Afr Med J* 16: 128, 1967
9. BEAN LL, SYMOND DA: Acute torsion of gallbladder. *US Armed Forces Med J* 4: 411, 1953
10. BELL DM: Torsion of gall bladder. *Br Med J* 1: 29, 1955
11. BELTRAMI G: Volvulus of gallbladder. *Osp Maggiore* 50: 254, 1962
12. BREWER GE: Preliminary report on surgical anatomy of gallbladder and ducts from analysis of one hundred dissections. *Ann Surg* 29: 721, 1899
13. BOGLE JH: Gangrene of gallbladder due to torsion in 9-year-old child. *Am J Dig Dis* 89: 484, 1955
14. CANAZIO P: Acute abdomen caused by torsion of gallbladder. *G Ital Chir* 16: 81, 1960
15. CARTER R, THOMPSON RJ, BRENNAN LP, et al: Volvulus of gallbladder. *Surg Gynecol Obstet* 116: 105, 1963
16. CASE TC: Acute torsion of gallbladder. *Am J Surg* 82: 749, 1951
17. CHRISTENSEN E: Torsion of gall-bladder. *Br Med J* 2: 1160, 1956
18. DEYSINE M, PELLICIA O: Volvulus of gallbladder. *Am Surg* 32: 63, 1966
19. DUARI M: Two cases of acute torsion of gallbladder. *Gut* 7: 73, 1966
20. FISCHER A: Ueber torsion der Gallenblase *Zentralbl Chir* 52: 1527, 1925
21. FRANCILLON J, COGNAT M, JALON M: Gallbladder volvulus. *Lyon Chir* 64: 97, 1968
22. GILLETT DJ: Torsion of gall-bladder. *Aust NZ J Surg* 36: 50, 1966
23. GROSS RE: Congenital anomalies of gallbladder; review of 148 cases with report of double gallbladder. *Arch Surg* 32: 131, 1936
24. IDEM: *Surgery of Infancy and Childhood,* Philadelphia, Saunders, 1953
25. HENDRY DT: Torsion of gallbladder. Case report. *S Afr Med J* 3: 723, 1968
26. HORANSKY M: Volvulus of gallbladder. *Rozhl Chir* 42: 123, 1963
27. HOSNY SH: Torsion of gallbladder. *Ir J Med Sci* 6: 85, 1964
28. IMBERT P, ARGENSON C, MAMBRINI A: Volvulus de la vésicule biliaire. *Mar Chir* 17: 283, 1965
29. KETTNER G: Uber einen Fall kompletter Torsion der Gallenblase. *Zentralbl Chir* 57: 589, 1930
30. KOSIK I, PRIBYL R: Volvulus of gallbladder. *Rozhl Chir* 41: 127, 1962
31. KRABBEL M: Die Stieltorsion der Gallenblase. *Dtsch Z Chir* 154: 76, 1920
32. KRAMER D: Torsion of gallbladder. *Ned Tijdschr Geneeskd* 106: 376, 1972
33. KROPFF G, THUAUD J: Volvulus of gallbladder (some comments on case). *Sem Hop Paris* 36: 3048, 1960
34. KRUKENBERG H: Ueber Gallenblasenkoliken ohne Gallensteine. *Berl Klin Wochenschr* 40: 667, 1903
35. LAGON MG, CREEDON PJ: Torsion of gallbladder. Case report and discussion. *Ohio State Med J* 63: 68, 1967
36. LAL RB, PEPPER M, PUESTON CB: Torsion of gallbladder. *Arch Surg* 97: 750, 1968
37. LAMBERT-LECLER G, LOMBARD R, HOTERMANS JM: Une observation de volvulus de la vésicule biliaire. *Rev Med Liege* 19: 358, 1964
38. LEGER L, DEBEYRE J, MAZINGARBE A: Volvulus de la vésicule biliaire. *J Chir (Paris)* 61: 21, 1945
39. LIEN YH: Gallbladder torsion, report of two cases. *Zhong Waike Z* 10: 85, 1962
40. LIPATOV VN, MISNIK VI, KHOKHLOV AM: O zavorotakh zhelchnogo purzyria. *Khirurgiia (Mosk)* 49: 41, 1972
41. MARKS RM, SHEDD CG, LOCKE AW: Volvulus of gallbladder associated with myocardial infarction; report of case and review of literature. *N Engl J Med* 251: 95, 1954
42. MAY RE: Unusual case of torsion of gallbladder. *Br J Clin Pract* 21: 191, 1967
43. MELNIK LA: Torsion of gallbladder. *Vestn Khir* 84: 115, 1960
44. MERCIER R, BOLO R, FOUQUES P: Volvulus de la vésicule biliaire. *J Chir (Paris)* 88: 177, 1964
45. MUSAVI S, YEAGER GH: Torsion of gallbladder. *JAMA* 170: 670, 1959
46. PANECKA A, KURCZAB J: Skret pecherzyka zolciowego. *Pol Przegl Chir* 42: 1243, 1970
47. PINTO DJ: Volvulus of gall bladder. *East Afr Med J* 48: 667, 1971
48. PRZEDPELSKI S, CHWIALKOWSKI J: Skret pecherzyka zolciowego. *Pol Przegl Chir* 42: 497, 1970
49. RECHT W: Torsion of double gall-bladder; report of case and review of literature. *Br J Surg* 39: 342, 1952
50. RIETBERG M: Torsion of gall-bladder. *Arch Chir Neerl* 18: 195, 1966
51. ROSSOUW J: Torsion of gall bladder — case where gallbladder was firmly attached to liver. *S Afr Med J* 44: 47, 1970
52. ROYLE JP: Torsion of gallbladder. *Aust NZ J Surg* 34: 68, 1964
53. ROZSOS I: On gallbladder torsion *Orv Hetil* 107: 1213, 1966
54. SARRO PALÂU M, ARIS FERNÁNDEZ A: Vólvulo de la vesícula biliar. *Rev Esp Enferm Apar Dig* 32: 699, 1970
55. SHIROTA A, TOMITA K, TOMONO T: On vólvulus of gallbladder. *Clin Surg (Tokyo)* 19: 47, 1964
56. SKÁLA J, KORCÁK V: Vólvulus zlucniku. *Rozhl Chir* 50: 302, 1971
57. SOFINSKII NA: Case of torsion of gallbladder. *Khirurgiia (Mosk)* 38: 111, 1962

58. STIPA V, NEMETH A: Volvulus of gallbladder. (Etiopathogenetic and clinical considerations and case contribution). *Policlinico Chir* 69: 394, 1962
59. SYCINSKI Z, TATARZYNSKA A: Skret percherzyka zolciowego przyczyna "ostrego brzucha". *Wiad Lek* 26: 1435, 1973
60. TODUA SB: Torsion of gallbladder. *Khirurgiia (Mosk)* 37: 139, 1961
61. TREZZA CE, MONACO M: Su di un caso di volvolo della colecisti. *Minerva Chir* 28: 127, 1973
62. VAN DAN EYNDE P, BUISSERET E: Case of volvulus of gallbladder. *Acta Gastroenterol Belg* 22: 292, 1959
63. WILKS AE, ORSINI RA: Vólvulo de la vesícula biliar. *Prensa Med Argent* 52: 156, 1965
64. WILSON EA: Correspondence: torsion of gallbladder. *S Afr Med J* 42: 172, 1968
65. ZATRIC A: Akutna torzija holeciste (morbus Wendel). *Med Pregl* 25: 99, 1972

NEGATIVE CHOLECYSTOGRAMS IN GALLBLADDER DISEASE

According to D. R. K. Reid and I. M. Rogers (Br J Surg *62: 581, 1975), "There is a general assumption that the diagnosis of gallbladder disease should . . . rest on the cholecystogram." These authors tested the validity of this assumption by studying the clinical and radiographic features and the surgical findings in 17 patients with typical recurrent biliary colic and a* negative *cholecystogram in whom the pain was completely relieved after cholecystectomy.*

On at least one occasion for each patient the cholecystogram had been reported to be negative. All patients had complained before operation of typical biliary colic, some had had jaundice and some had stones in the gallbladder at the time of cholecystectomy (in one instance a small stone was found in the cystic duct); none had stones in the common duct. Positive histologic findings (minimal to mild cholecystitis) were noted in all patients but two. Follow-up examination (range of follow-up, 6 months to 10 years) indicated that all patients became free of pain after cholecystectomy.

Reid and Rogers believe that clinicians should be willing to make a diagnosis of gallbladder origin for pain and to recommend cholecystectomy in spite of a negative cholecystogram "when there is typical biliary colic, when all other causes have been excluded and the symptoms are severe". Clinical or biochemical evidence of obstructive jaundice would support such a recommendation but the period of observation should be "adequate", for "only then will the clinician become convinced of the need for operation".

PANCREATIC PSEUDOCYST AND POLYCYTHEMIA AFTER RENAL TRANSPLANTATION*

D. M. GRACE, MD and C. R. STILLER, MD

Summary: A 43-year-old man with chronic glomerulonephritis received a cadaver renal transplant in 1972, and pancreatitis developed postoperatively. A large pseudocyst was noted 1 year later, when polycythemia was noted, in spite of good renal and pulmonary function. The polycythemia resolved after cystogastrostomy and has not recurred during 18 months of follow-up.

Résumé: En 1972, chez un homme de 43 ans souffrant de glomérulonéphrite chronique, on avait pratiqué la transplantation d'un rein de cadavre. L'opération terminée, une pancréatite s'était développée. Un an plus tard, on avait noté la présence d'un volumineux pseudo-kyste et de polycythémie, malgré la bonne qualité des fonctions rénale et pulmonaire. Nous avons pu vaincre la polyglobulie par drainage du pseudo-kyste dans l'estomac. La polycythémie n'a pas réapparu durant la période de 18 mois qui a suivi.

ACUTE pancreatitis is a relatively frequent complication of renal transplantation and may be related to such factors as uremia, hyperparathyroidism, immunosuppression, corticosteroids, gallstones and operative trauma.[1] Pseudocyst may develop after an attack of pancreatitis, and polycythemia is a complication of renal disease that has been observed in renal transplant recipients.[2, 3] In this report we document the development of both a pancreatic pseudocyst and polycythemia after renal transplantation. The polycythemia regressed and did not recur after successful drainage of the pseudocyst.

CASE REPORT

A 43-year-old man was admitted to hospital in January 1973 because of epigastric pain and a mass. Chronic glomerulonephritis had been diagnosed in 1957 and renal transplantation from a cadaver donor was carried out in September 1971, when the hemoglobin value had been 7.2 g/dl and the hematocrit, 20%. Renal function after operation was good, and immunosuppression was maintained by prednisone and athazioprine; furosemide was required for control of moderate hypertension. Acute epigastric pain and distension in November 1971 suggested the diagnosis of acute pancreatitis, but a perforated ulcer could not be excluded and therefore laparotomy was performed. This showed extensive pancreatitis with fat necrosis; the abdomen was closed without further treatment. Renal function remained good (serum creatinine value range, 1 to 1.5 mg/dl). In June 1972 another attack of severe epigastric pain occurred after a meal of fried chicken and beer. The hemoglobin value at this time was 16.5 g/dl, the hematocrit was 53%, the serum creatinine value was 1.3 mg/dl and the blood urea nitrogen value, 31 mg/dl. The epigastric pain recurred, a weight loss of 22 kg was noted and, in December 1972, an epigastric mass was detected.

Examination in hospital revealed the presence of a tender mass (diameter, 10 cm) beneath the left costal margin. The patient weighed 50 kg and his blood pressure was 160/100 mm Hg. Results of laboratory investigations were as follows: hemoglobin concentration, 18.9 g/dl; hematocrit, 58.5%; leukocyte count, 12.0 x $10^9/l$, and the serum creatinine concentration, 1.2 mg/dl. Studies with ^{51}Cr and RISA indicated a total blood volume of 102 ml/kg (normal, 70 $\pm$ 10), a red blood cell mass of 57.5 ml/kg (normal, 28 $\pm$ 4) and a plasma volume of 44.5 ml/kg (normal, 45 $\pm$ 5). Gallbladder radiographs were normal, but barium radiographs of the stomach showed a large mass compressing the lesser curve. The cystic nature of the mass was confirmed by an ultrasound study. Results of liver function tests and of a complete coagulation survey were normal. Pulmonary function studies revealed some degree of restriction and obstruction; the arterial oxygen tension was 70 mm Hg.

A phlebotomy (volume, 500 ml) lowered the hemoglobin concentration to 17.3 g/dl and the hematocrit to 51%; after removal of another 500 ml of blood 2 days later these values were 16.4 g/dl and 49.7% respectively. Three days later the abdomen was opened through a left subcostal incision, and a pancreatic pseudocyst containing 800 ml of clear fluid was drained into the posterior wall of the stomach. A lock stitch of 2-0 silk was used for hemostasis around an opening that admitted three fingers. The operation was uneventful and no transfusion was required.

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Apart from hiccups, which gradually cleared, and some coffee-ground drainage, the postoperative course was uneventful. One week after operation the hemoglobin value was 12.9 g/dl. The hemoglobin value gradually rose to 13.7 g/dl in May 1973 and reached a maximum of 15.9 g/dl in July 1973. Thereafter, the hemoglobin concentration has not exceeded 15 g/dl.

In June 1974 he was admitted for assessment of epigastric pain. No mass was found clinically or radiographically. The total serum bilirubin value increased to 3.6 mg/dl and alkaline phosphatase was elevated also (163 U/*l*); the serum amylase value, however, was normal. Gastroscopy showed a persistent prepyloric opening at the site of pseudocyst drainage but no other abnormality. The attacks of pain resolved and the final diagnosis was chronic pancreatitis. The most recent hemoglobin value was 14.1 g/dl and the hematocrit, 40.5%; the serum creatinine value was 1.2 mg/dl. At this time the patient's weight was 7.5 kg more than when the pseudocyst was drained.

Comment

The occurrence of polycythemia after renal transplantation is unusual, but is more common with cadaver renal transplants than with living donor kidneys. The explanation for its development is not clear. Chronic rejection may be a factor, but erythropoietin values may not be elevated.[2] Hypertension is a commonly associated finding, as is thromboembolism, though the latter did not develop in the present case. Polycythemia may also occur in patients with renal disease, and erythropoietin-like activity has been described in fluid from renal cysts.[4] To our knowledge, polycythemia has not been described in association with a pancreatic pseudocyst. In our case polycythemia may have been related to renal transplantation alone, and this type of polycythemia may resolve spontaneously. However, the disappearance of the pseudocyst may have been its cause. Recurrent pancreatitis remained a problem in this patient and, in the absence of gallstones and alcoholism, this might have been related to therapy with corticosteroids or azathioprine.[5]

References

1. Penn I, Durst AL, Machado M, et al: Acute pancreatitis and hyperamylasemia in renal homograft recipients. *Arch Surg* 105: 167, 1972
2. Swales JD, Evans DB: Erythraemia in renal transplantation. *Br Med J* 2: 80, 1969
3. Wu KK, Gibson TP, Freeman RM, et al: Erythrocytosis after renal transplantation. Its occurrence in two recipients of kidneys from same cadaveric donor. *Arch Intern Med* 132: 898, 1973
4. Rosse WF, Waldmann TA, Cohen P: Renal cysts, erythropoietin and polycythemia. *Am J Med* 34: 76, 1963
5. Kawanishi H, Rudolph E, Bull FE: Azathioprine-induced acute pancreatitis. *N Engl J Med* 289: 357, 1973

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†*Recommended dosage guidelines for patients with normal renal function.*

Please see following page for additional prescribing information.

CRITIQUE OF ITEM 533 (SESAP II)

On the basis of the data presented, a state of hyperparathyroidism is definite. The diagnosis of parathyroid adenoma at the original operation must be questioned, for it is difficult to differentiate, from a single gland, adenoma from hyperplasia either grossly or microscopically. Whether a second parathyroid adenoma or hyperplasia of all three remaining parathyroid bodies will be found cannot be predicted without the special studies shown in the illustrations. The arteriograms taken after injection of the right inferior thyroid artery show a blush which could represent either an adenoma of the thyroid itself or a parathyroid adenoma lying just inferior and posterior to the inferior border of the thyroid. If the latter is true, it must represent an ectopic position of the right superior parathyroid since the inferior parathyroids migrate into the anterior mediastinum, while the superior glands, when ectopic, are found posteriorly in the neck or mediastinum.

The selective venous parathyroid hormone studies show normal levels for all but two samples, ie, thyroid ima vein and middle left innominate vein samples. Hyperplasia or hyperfunction of the three remaining parathyroids would be expected to show increased levels in the venous drainage bilaterally, though the rise in parathyroid hormone levels would undoubtedly be less striking.

Therefore, choice (B) is the correct answer. (A) and (C) are ruled out by the unilaterality of the elevated venous readings. The arteriographic shadow is only slightly below the level of the clavicle. Therefore, the tumor which it represents can be removed at reexploration of the neck without formal exploration of the posterior mediastinum. Choice (D) is incorrect in view of the unilateral blush seen in selective arteriography on the level of the clavicle.

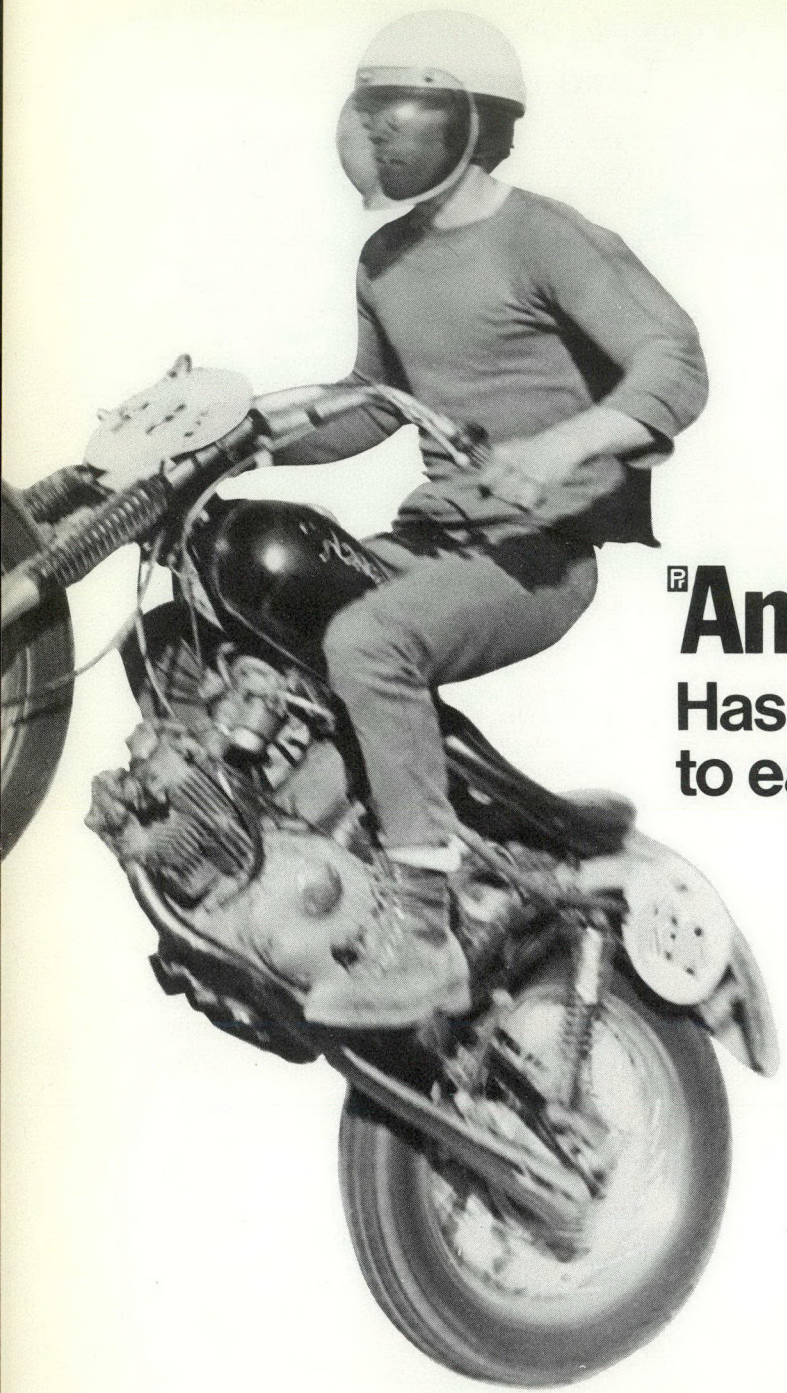
Special studies such as these should probably be reserved for unusual problems, particularly cases requiring reexploration. Both tests are expensive and carry added risk which seems unwarranted except in unusual circumstances. The diagnosis of hyperparathyroidism is not dependent on these sophisticated methods, and careful, thorough surgical exploration of the neck should suffice in the majority of cases.

B

References

533/1. POWELL D, SHIMKIN PM, DOPPMAN JL, et al: Primary hyperparathyroidism. Preoperative tumor localization and differentiation between adenoma and hyperplasia. *N Engl J Med* 286: 1169-1175, 1972

533/2. COPE O: Surgery of hyperparathyroidism; occurrence of parathyroids in the anterior mediastinum and the division of operation into 2 stages. *Ann Surg* 114: 706-733, 1941



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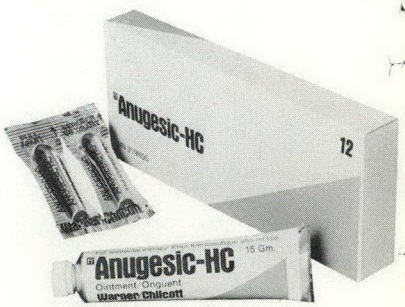

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Indications: Hemorrhoids, internal and external, pruritus ani, proctitis, cryptitis, fissures and incomplete fistulas and other congestive allergic and inflammatory conditions. May also be used prior to rectal examination to anaesthetize the area and for relief of pain and discomfort following anorectal surgery of all types. **Contraindication:** Should not be used in patients with sensitivity to any of the components. **Precautions:** Hydrocortisone-containing preparations should not be used until an adequate proctological examination is completed and diagnosis made. Specific measures against infection, allergy, and other causal factors must not be neglected. Prolonged use might produce systemic corticosteroid effects, although none have been noted to date. Discontinue medication if idiosyncratic reactions occur. **Adverse effects:** Occasionally patients may experience burning upon application, especially if the anoderm is not intact. Local sensitivity reactions have been rare. **Composition:** Suppositories contain Pramoxine HCl 25.0 mg, Hydrocortisone Acetate 5.0 mg, Zinc Oxide 316.0 mg, Oxyquinoline Sulphate 16.2 mg. Ointments contain Hydrocortisone Acetate 0.5%, Zinc Oxide 10.75%, Balsam Peru 1.87%, Bismuth Oxide 0.87%, Benzyl Benzoate 1.25%, Pramoxine HCl 1.0% and Bismuth Subgallate 2.25% in Cocoa Butter Base. **Supplied: Suppositories:** Boxes of 12. **Ointments:** 15 g tubes with applicator.

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OPERATIVE CHOLANGIOGRAPHY: EVALUATION AND A PLEA FOR ITS GENERAL USE*

ERIC M. NANSON, MB, FRCS, FRCS[C], FRACS, FACS

Summary: Operative cholangiography should be used routinely during operations on the gallbladder and biliary tree. The indications for operative cholangiography include demonstration of unsuspected stones, of abnormal biliary tree anatomy, and of tumour within intrahepatic branches of the biliary tree; determination of the nature of periampullary obstruction and of the best approach for removal of stones impacted low in the common bile duct; avoidance of unnecessary choledochotomy; assistance in diagnosis of stenosing cholangitis, cholangiolytic jaundice or choledochal cyst; and to ensure, postexploration, that the duct contains no stones. These indications were evaluated in a review of the records of 151 patients who underwent biliary tract operations. Operative cholangiography was performed in 133 of these patients. The review disclosed that 5.7% of common bile duct stones were totally unsuspected and that 30% of common bile ducts suspected to be abnormal were proven to be clear of stones, so that an unnecessary choledochotomy was avoided. The technique of operative cholangiography is simple, but successful use of it requires meticulous attention to detail and frequent use by a regular team.

Résumé: Selon nous, on devrait utiliser systématiquement la cholangiographique opération durant les interventions sur la vésicule biliaire et l'arbre biliaire. Parmi les indications de cette méthode figurent la découverte de calculs ignorés, d'anomalies anatomiques des voies biliaires et de tumeurs au sein de leurs ramifications intrahépatiques, la détermination de la nature d'une obstruction périampullaire et de la meilleure voie pour l'enlèvement de calculs qui seraient logés dans le cholédoque distal, la possibilité d'éviter une cholédochotomie inutile, l'aide au diagnostic d'une angiocholite sténosante, d'un ictère de stase ou d'un kyste du cholédoque, enfin, la possibilité de s'assurer, après exploration que le conduit ne contient pas de calculs. Nous avons évalué ces indications en passant en revue les dossiers de 151 malades qui avaient subi des opérations du tractus biliaire. L'angiocholégraphie opératoire a été pratiquée sur 131 de ces patients. Cette revue a permis de mettre à jour que 5% des calculs du cholédoque étaient entièrement ignorés et que 30% des cholédoques soupçonnés d'être anormaux étaient exempts de calculs, de sorte qu'on a évité dans tous ces cas une cholédochotomie absolument inutile. La technique de l'angiocholégraphie opératoire est simple mais, pour être couronnée de succès, elle doit être employée souvent par une même équipe bien entraînée et qui exige une attention méticuleuse.

THE need for operative cholangiography as an adjunct to operations on the biliary tree has been stressed by numerous authors,[1-4] beginning with Mirizzi in 1932.[5] Unless the surgeon uses it routinely he is unlikely to get good films, and he will not become skilled in interpreting them.[6] Furthermore, if the technique is used only sporadically, neither will radiographers become skilled in the technique required, nor will operating room nurses become accustomed to the meticulous attention to detail that is essential to obtain reproducible and reliable results. It should be routinely available and generally used during cholecystectomy.[7, 8]

Operative cholangiography permits the surgeon to do one or more of the following:

1. To reveal unsuspected stones in the common bile duct.
2. To avoid opening the common bile duct unnecessarily.
3. To demonstrate abnormal anatomy of the biliary tree.
4. To determine the nature of an obstruction in the region of the ampulla of Vater.
5. To demonstrate tumour within the intrahepatic branches of the biliary tree.
6. To aid in the diagnosis of stenosing cholangitis, cholangiolytic jaundice or choledochal cyst.
7. To reveal the best approach for removal of stones impacted at the lower end of the common bile duct.
8. To show, in the postexploration stage of the operation, that the duct contains no stones.

The usefulness of operative cholangiography is illustrated simply by the following case report.

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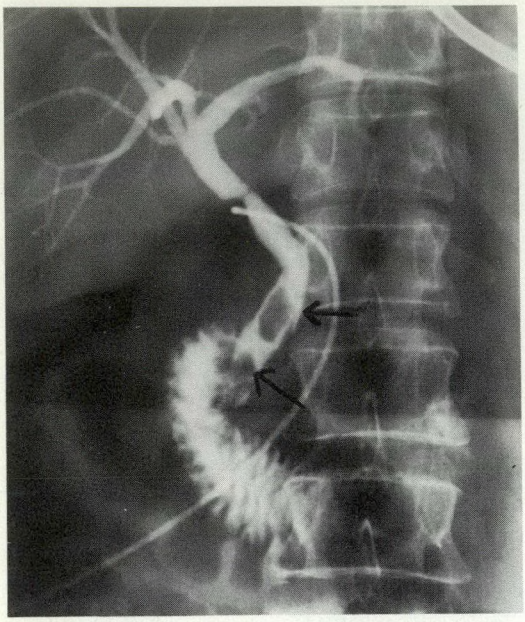

Fig. 1.—Two entirely unsuspected stones (arrows) in common bile duct demonstrated by operative cholangiogram.

A 64-year-old woman had had recurrent bouts of epigastric pain for 20 years and had also suffered from esophageal reflux. At no time had she been jaundiced. A cholecystogram had shown a nonfunctioning gallbladder. Operation revealed a small shrunken gallbladder, full of faceted stones. The common bile duct was normal in size, and the cystic duct was of small calibre. No stones were palpable in the common bile duct but operative cholangiography (Fig. 1) visualized two quite large stones (dimensions, 10 x 5 mm and 8 x 5 mm) in the retroduodenal portion of the common bile duct. These stones were entirely unsuspected and impalpable. Without operative cholangiography they would have been overlooked and left in situ to cause trouble later.

This paper provides an evaluation of operative cholangiography and a description of the technique, together with a recommendation for its wider use.

Evaluation of Indications for Operative Cholangiography

The indications for operative cholangiography have been evaluated in two ways: first, the records of 151 patients undergoing biliary tract surgery were analyzed, and second, the indications were reviewed in the light of these findings and those reported by others.

Analysis of Patient Records

To evaluate the usefulness of operative cholangiography, a retrospective analysis was made of the records of 151 patients who underwent biliary tract surgery over a 3-year period. The patients' ages ranged from 15 to 75 years (average, 47 years); there were 109 females and 42 males. Of the 151 patients, 133 were admitted for cholecystectomy and 18 were admitted for choledochostomy, having undergone cholecystectomy previously. Fig. 2 summarizes the dis-

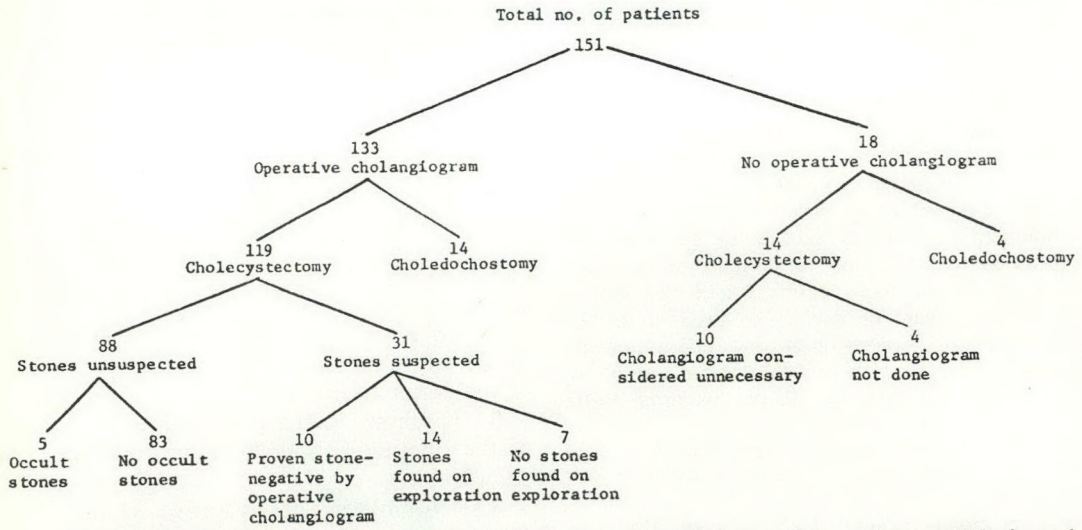

Fig. 2.—Distribution of 151 patients by radiologic and surgical procedure and by radiologic and surgical findings.

tribution of the 151 patients according to the radiologic and surgical procedures, together with the main findings.

Operative cholangiography was used in 133 of the 151 patients. Among the 18 in whom it was not performed, 14 underwent cholecystectomy and 4 underwent choledochostomy. In 10 of the 14 patients in this subgroup undergoing cholecystectomy a cholangiogram was considered unnecessary by the surgeons—a decision the wisdom of which can be questioned, because a surgeon never knows when a stone may lie undetected in the common bile duct. In the other four patients cholangiography was not done for specific reasons: in one use of x-rays was contraindicated because of pregnancy; in one stones were palpable in a dilated common bile duct, which was therefore explored; in one, percutaneous transhepatic cholangiography before operation had given sufficient detail; and in one patient cholangiography was unsuccessful for technical reasons. In the remaining 4 of the 18 patients in whom an operative cholangiogram was not done, a disorder of the common bile duct was found; in 2 of these patients a percutaneous transhepatic cholangiogram had already adequately delineated the common duct; in 1 a cholecystogram had visualized the common duct and had apparently demonstrated stones—yet at exploration no stones were found, so that, had operative cholangiography been done, this unnecessary choledochostomy could have been obviated; and in 1 cholangiography failed for technical reasons. In this subgroup of 18 patients who did not have operative cholangiography, then, it was not done in 3 for valid reasons: pregnancy in 1 and technical failure in 2. In the others, however, it is my opinion that operative cholangiography should have been performed. Those who had percutaneous transhepatic cholangiograms still required operative cholangiography after exploration to assure the surgeon that the duct had been completely cleared as far as a cholangiogram is able to do this.

Among the 133 patients in whom operative cholangiography was used, there were 119 who underwent cholecystectomy. In 88 of these patients there was no particular reason why the surgeon should suspect stones in the common bile duct. In the remaining 31 patients certain indications suggested the existence of possible stones in the common duct. In this subgroup of 119 patients the findings were as follows:

1. Of the 88 cholecystectomy patients in whom no abnormality of the common bile duct was suspected, 5 patients (6%) were found to have "occult" stones.

2. Of the 31 cholecystectomy patients in whom an abnormality in the common bile duct was suspected, 10 (30%) were proven by operative cholangiography to have no abnormality; therefore the common bile duct was not opened and a futile choledochotomy was avoided in these patients. Among the 21 patients whose common bile duct was explored, stones, gravel, or sludge was found in 14, and no abnormality was found in 7 in spite of a suspicious cholangiogram.

3. There were no false-negative results; that is, there were no patients in whom cholangiography was reported to be negative but in whom stones in the common bile duct were found subsequently.

Indications Based on Review of Present Study and of Literature

Indications for operative cholangiography may be summarized as follows:

1. Demonstration of unsuspected stones in the common bile duct. This is particularly important in patients undergoing cholecystectomy. Among our patients, 6% were found to have stones in the common bile duct that had not been suspected previously. Burnett and Bolton[1] reported a yield of 2.3% unsuspected stones, and Jolly and colleagues[2] found 6.3% of such "surprise" stones in 380 patients. For a relatively simple procedure, therefore, the yield of such stones is not insignificant.

2. Avoidance of unnecessary exploration of the common bile duct. The usually accepted indications for opening the common bile duct are these: (a) dilated extrahepatic ducts; (b) small stones in the gallbladder with a wide cystic duct; (c) palpable stones in the common duct; (d) a dilated common duct visualized by preoperative oral cholecystography or intravenous cholangiography; (e) a history of jaundice; and (f) repeated episodes of biliary colic, cho-

langitis or pancreatitis. Use of operative cholangiography helps the surgeon avoid opening the common duct unnecessarily in a certain proportion of patients ("avoidance rate").

In our study we found that there were 31 such patients with a "suspect" common bile duct and that an operative cholangiogram showed that 10 of these ducts in fact were free of stones. Burnett and Bolton[1] reported an avoidance rate of only 8.7% and Schulenburg[8] a rate of 5.5%.

In our series, a suspicious operative cholangiogram led to choledochotomy in 7 of 21 patients in none of whom were stones found—a false-positive rate of 33%. In these patients, however, there were clear indications for exploring the common bile duct, even in the absence of a "suspicious" cholangiogram.

3. Demonstration of abnormal anatomy. Periodically, an operative cholangiogram will demonstrate abnormal anatomy of the biliary tree and hence save the surgeon from seriously traumatizing the extrahepatic biliary system.[8] The types of anomaly thus demonstrated may be aberrant ducts, a gallbladder issuing directly from the common bile duct, a long tortuous cystic duct filled with stones and incorporated in the common duct wall, congenital stenosis of the common duct, a choledochal cyst, and, within the liver, a cholangiocele. Sandbloom[7] stressed this attribute of operative cholangiography. Fig. 3 is an operative cholangiogram that reveals a very dangerous situation; namely, an aberrant right hepatic duct running exactly parallel to and beside the cystic duct.

4. Demonstration of the nature of the obstruction of the ampulla of Vater. Not infrequently it is difficult to determine the cause of obstruction at the lower end of the common duct that produces jaundice. The cause is usually either stone or carcinoma of the head of the pancreas, but occasionally the cause is carcinoma of the common bile duct, carcinoma or papilloma of the ampulla of Vater, a stricture of the ampulla, or a diverticulum of the duodenum close to the termination of the common duct. Operative cholangiography is helpful in establishing this diagnosis, so that the appropriate operation may be done. Fig. 4 is an example of

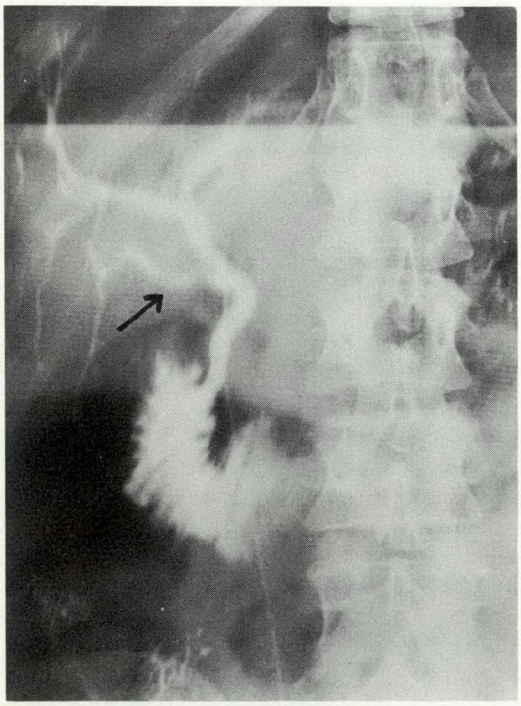

Fig. 3.—Accessory right hepatic duct (arrow) entering common bile duct beside cystic duct, visualized by operative cholangiogram.

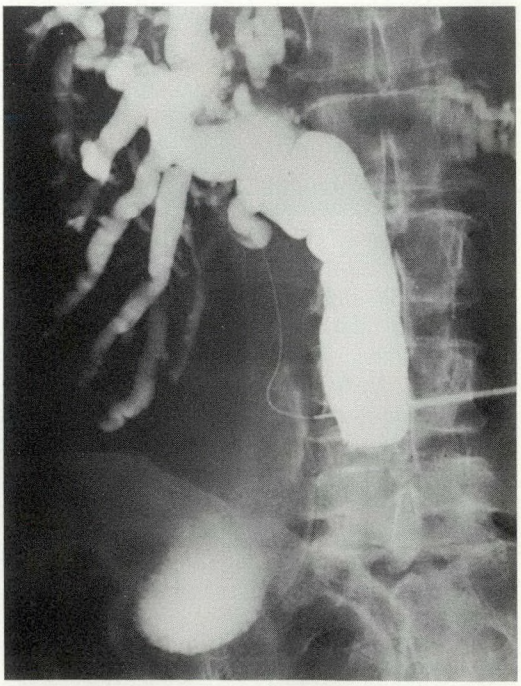

Fig. 4.—Obstruction of common bile duct by carcinoma of head of pancreas revealed by operative cholangiogram. Note sharp cut-off at lower end and gross dilatation of duct above.

an operative cholangiogram of a gross dilatation of a common duct caused by carcinoma of the head of the pancreas; the appearance of the termination of the common duct is typical.

5. Tumours of the intrahepatic biliary tree. The usual exploration of the biliary tree is remarkably ineffective in delineating tumours of the hepatic ducts and their radicles. Operative cholangiography is particularly useful in this respect and helps the surgeon plan an appropriate operative approach. Figs. 5 and 6 visualize a narrowing of the left hepatic duct, with dilatation of the left intrahepatic biliary ducts proximal to a malignant stricture.

6. Establishment of the diagnosis of stenosing cholangitis,[9] cholangiolytic jaundice, or choledochal cyst. Patients suffering from these conditions present with obstructive jaundice, the nature of which is often obscure. Because of the undilated state of the biliary tree in the first two conditions, percutaneous transhepatic cholangiography may be impossible. Laparotomy is necessary to prove the absence of any distal obstructing lesion in the biliary tree that may be amenable to surgery. Therefore, operative cholangiography is required by these patients.

7. Clarification of the approach to stones impacted at the lower end of the common bile duct. Stones may be impacted at the lower end of the common duct, or they may frequently be located in outpouchings or diverticula of the duct. They can be extremely difficult to remove by routine supraduodenal choledochostomy and are better approached by the transduodenal route. An operative cholangiogram is useful to indicate this.

8. Demonstration after exploration that the common bile duct contains no stones. This is essential when the common duct has contained stones, if the surgeon is to be certain that the presence of a stone is not overlooked and that the radiopaque contrast medium will flow freely into the duodenum. The fact that the common duct is clear is proven by the free flow of contrast medium into the duodenum and the outlining of the pancreatic duct. A pancreatic duct will not be visualized if there is residual distal block. However, this postexploration cholangiogram is difficult to perform and full of pitfalls. Grossly dilated in-

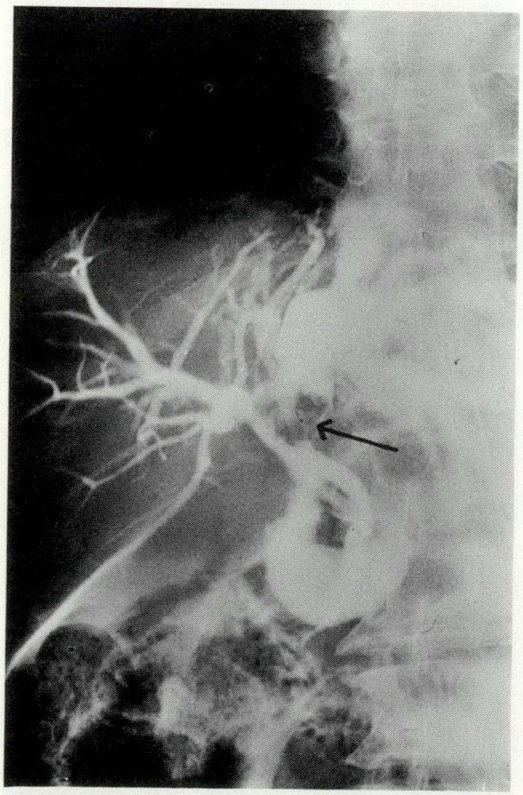

Fig. 5.—Narrowing of left hepatic duct (arrow) due to primary carcinoma of duct disclosed by operative cholangiogram.

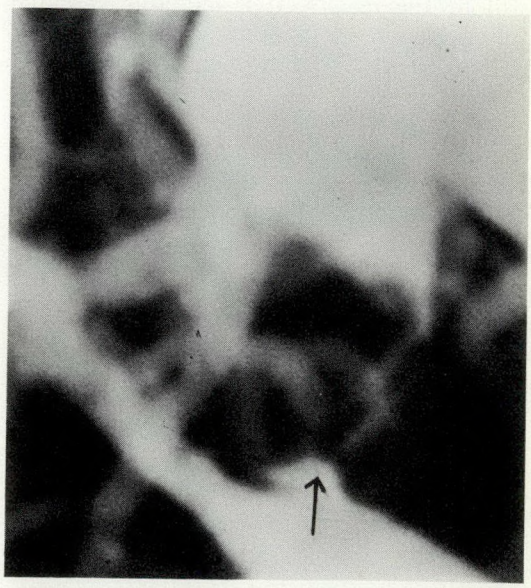

Fig. 6.—Magnified view of area of narrowing shown in Fig. 5.

trahepatic radicles cannot be proved to contain no stones, and such residual stones, undemonstrated at operation, will subsequently fall into the common bile duct when the patient is upright and ambulant, and hence cause further blockage. The only ways of obviating this are to perform either a large sphincteroplasty or a bypass procedure such as choledochoduodenostomy. Another difficulty is to exclude air bubbles when contrast medium is injected into a T-tube at operation. One way of accomplishing this is to inject the medium by way of the small plastic catheter that has been left in the cystic duct and to use the T-tube as an escape route for any trapped air bubbles. A third problem is that, after manipulation, the sphincter of Oddi may go into spasm, so that contrast medium does not flow freely into the duodenum; hence the surgeon cannot be sure that he has cleared the distal block. This problem can be overcome by administering atropine or hyoscine butylbromide or by instilling topical anesthetic down the catheter and waiting for pharmacologic relaxation of the sphincter.

Technique of Operative Cholangiography

Although operative cholangiography is not invariably successful, the more frequently it is used on a team basis the better will be the results. It is therefore essential to develop a meticulous technique and to adhere to it. The following points are important:

1. Positioning of the patient. Most modern operating tables have an x-ray cassette tunnel, either longitudinal or lateral. It is essential that the patient be positioned so that the area of the liver and biliary tree lies over this tunnel.

2. Positioning of diathermy body plate. The diathermy plate, or indifferent electrode, must be placed sufficiently caudad that the x-ray field is not obscured.

3. Removal of instruments from the x-ray field. Towel clips and other instruments and sponges with radiopaque markers must be removed before exposure so the essential structures of the common bile duct and duodenum are not obscured.

4. Opacification of duct systems. Figs. 7 to 9 illustrate equipment required for the two methods of opacifying the duct systems: catheterization and direct puncture. For *catheterization,* the catheter must be thin, readily introducible and secure. The disposable Cholangiocath (Edwards Laboratories, CA) is such a catheter. It has two useful features: a stopcock on its base and a flange on its top (Fig. 8). When introduced, the catheter must be carefully filled with saline to make sure that no air bubbles enter the biliary tree. The catheter can be left in place until the common duct has been explored; it can then be used for the postexploration cholangiogram. The catheter can also be left in

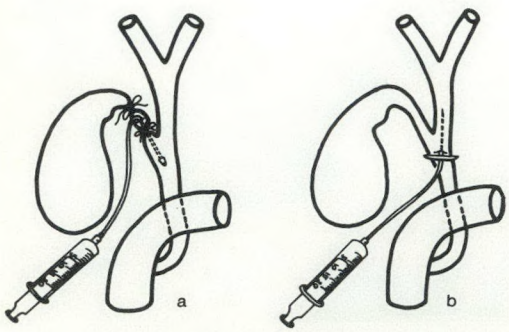

Fig. 7.—(a) Cholangiocath tied into cystic duct. (b) Scalp-vein needle in common bile duct.

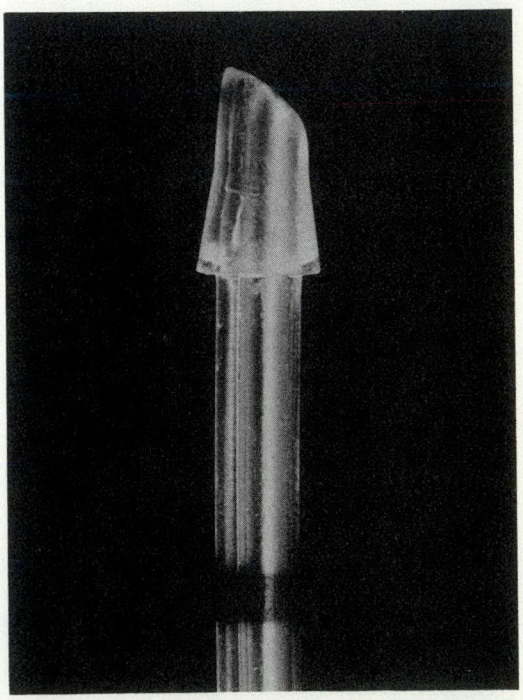

Fig. 8.—Tip of Cholangiocath. Note flange and radiopaque marker.

place to permit drainage of the common bile duct if only small-calibre catheters are required for drainage. If it is difficult to introduce the catheter, a silver probe passed down the cystic duct will break down the spiral valve of Heister. It is essential to pull the catheter back so that its flange impinges on the encircling ligature. This will prevent the catheter being pushed down too far so that its tip projects through the ampulla of Vater; it ensures that the cystic duct is outlined and that any stones in that duct are shown.

For *direct puncture,* which is necessary when the gallbladder has already been removed or when it is not possible to cannulate the cystic duct, a scalp-vein needle (Figs. 7 and 9) is useful. As in using the catheter, one must be careful to ensure that no bubbles lie within the needle or its tubing. This method has three disadvantages: (a) the cystic duct is not outlined well in patients in whom the gallbladder is still present; (b) the needle may slip out at a crucial stage; and (c) bile may occasionally leak from the puncture hole—a problem that can be dealt with by closing the hole with a fine purse-string suture.

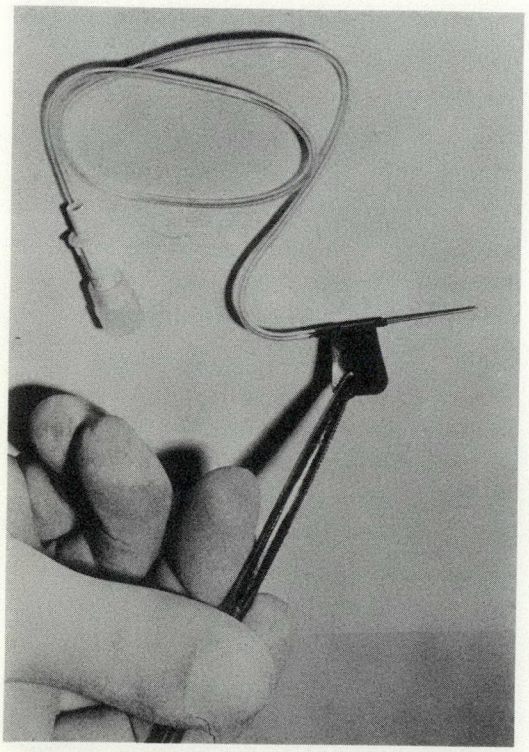

Fig. 9.—Scalp-vein needle and technique of holding it for insertion into common bile duct.

5. Scout film and radiographic technique. A preliminary scout film is frequently advisable to ensure that the position of the film is correct, that the exposure is appropriate allowing for the body build of the patient, and that the x-ray machine is functioning correctly.

6. Injections of contrast medium. The usual material is 30% Urografin (sodium and meglumine diatrizoate). This may be diluted to 15% with either normal saline or bile in the common duct. Two injections are made. First, 3 to 5 ml is injected, depending on the calibre of the common duct. This is instilled slowly and an exposure taken. This small volume of contrast medium is diluted by the bile and hence does not obliterate small stones; the main portion of the common bile duct will be delineated. Next, up to 15 to 20 ml of contrast medium is injected, again according to the calibre of the duct, and as the last 2 ml of dye is being injected the exposure is made. This gives a "functional" or "dynamic" cholangiogram and shows the dye flowing through the ampulla of Vater. For this last exposure the table is tilted 15° to the right so as to let the common duct and the ampulla of Vater fall away from the underlying spine. The films then are developed rapidly and inspected by the surgeon. If unsatisfactory more are taken, and a radiologist's opinion may be sought. Image intensifiers are now used for this work, but the definition is not as good as with x-ray film. There is no need to wait while the films are being processed because the surgeon can start to excise the gallbladder at this stage.

7. "Completion" cholangiogram. If the common duct has been explored and stones have been removed, a T-tube is usually placed in the duct through the exploration incision. Further cholangiography is wise to ensure that all stones have been removed and that contrast medium flows freely into the duodenum. The chief difficulty is to ensure that air, introduced during the exploration or trapped in the T-tube, is evacuated. To overcome this, a large volume of saline may be injected through the Cholangiocath in the cystic duct; this forces the air

bubbles out through the T-tube catheter. The radiopaque medium is then injected through a Cholangiocath, the T-tube being clamped. If dye does not flow freely into the duodenum there may be a residual stone in the ampulla of Vater or the sphincter of Oddi may be in spasm. An injection of atropine or hyoscine butylbromide intravenously will usually differentiate the two.

Discussion

Operative cholangiography has many applications. Its use before the common bile duct is opened may obviate the need for a choledochostomy because the duct is shown to be clear. More important, routine operative cholangiography may reveal unsuspected stones that would otherwise have been missed; a second, later operation is thereby obviated. By performing cholangiography early in the operation a dangerous anatomic situation may be revealed. Similarly, so that consequent damage to the common bile duct is avoided, the most appropriate approach to impacted stones may be indicated.

The postexploration cholangiogram is important in ensuring that no stones have been overlooked before the incision is closed. However, cholangiography at this stage is not infallible for two reasons: (a) when hepatic biliary radicles are grossly dilated, stones may lie hidden within the liver, only to reveal themselves subsequently when they fall into the common bile duct when the patient becomes ambulant; and (b) spasm of the sphincter of Oddi after instrumentation prevents contrast medium flowing freely into the duodenum, although clear radiographic detail of the lower end of the common bile duct will usually distinguish spasm from organic obstruction (especially if the sphincter has been freely passed with probes) and drugs such as atropine or local anesthetics may be used to induce relaxation.

It is always important to get a "functional" cholangiogram; that is, one in which the radiograph is taken while the contrast medium is actually flowing into the duodenum. Exposure made as the last 2 ml of contrast medium is being injected will ensure a good picture of the region of the ampulla; if the pancreatic duct is visualized, one can be sure the ampulla is clear. The fact that contrast medium enters the duct of Wirsung does not seem to predispose to postoperative pancreatitis.

Operative cholangiography lengthens the operation by about 15 to 20 minutes. Even so, time need not be wasted while the radiographs are being developed because the surgeon may proceed with cholecystectomy in the meantime; furthermore, the development time of x-ray film with modern radiographic techniques is short.

Closed-circuit television between the operating room and the radiology department permits immediate, skilled interpretation of the films by a radiologist and facilitates useful consultation between the surgeon and the radiologist.

The use of operative cholangiography has largely taken the guesswork out of biliary surgery. It carries no significant mortality or morbidity, and is an added safeguard to the patient.

References

1. Burnett W, Bolton PM: Operative cholangiography in surgery of gallstones: implementation of policy decision in consecutive series of 327 patients. *Aust NZ J Surg* 42: 14, 1972
2. Jolly PC, Baker JW, Schmidt HM, et al: Operative cholangiography: case for its routine use. *Ann Surg* 168: 551, 1968
3. Le Quesne LP: Discussion on cholangiography. *Proc R Soc Med* 53: 851, 1960
4. Mixter CG, Hermanson L, Segel AL: Operative cholangiography; evaluation of 406 cases. *Ann Surg* 134: 346, 1951
5. Mirizzi PL: La cholangiografia durante las operaciones de las vias biliares. *Bol Soc Crug Buenos Aires* 16: 1133, 1932
6. Nienhuis LI: Routine operative cholangiography. *Ann Surg* 154 (suppl): 192, 1961
7. Sandbloom P: In discussion of Jolly PC, Baker JW, Schmidt HM, et al: Operative cholangiography: case for its routine use. *Ann Surg* 168: 551, 1968
8. Schulenburg CA: Operative cholangiography: 1,000 cases. *Surgery* 65: 723, 1969

RESULTS OF CHOLECYSTECTOMY IN 1000 CONSECUTIVE PATIENTS*

LLOYD D. MacLEAN, MD, FRCS[C], MYRON GOLDSTEIN, MD, JENNIE E. MacDONALD, RN and ROBERT DEMERS, PhD

Summary: Analysis of the results of cholecystectomy in 1000 consecutive patients revealed an overall mortality of 0.6%; among patients who underwent cholecystectomy only, there were no deaths. Wound infection occurred in 3.4% of all patients but the rate exceeded 8% among those in whom another procedure was performed or there was acute cholecystitis. Cephaloridine given prophylactically was useful in decreasing the infection rate in the two latter groups.

Cystic duct cholangiography, used in 193 patients, increased the rate of stone retrieval from the bile ducts from 41 to 63%, but the incidence of both false-negative and false-positive cholangiograms was disturbingly high. Exploration was performed on clinical grounds despite a normal cholangiogram in 15 patients, with 5 positive results. Common duct exploration was productive 41% of the time when clinical judgement without cholangiography was used. While cystic duct cholangiography is useful, improvements in reliability are imperative and probably feasible, in view of the results achieved in the operating room and those in departments of radiology.

Résumé: L'analyse des résultats de 1000 patients consécutifs ayant subi une cholécystectomie montre un taux de mortalité de 0.6%. Nous ne rapportons aucun décès parmi les patients qui ont eu une cholécystectomie seulement. Une infection de plaie a présenté chez 3.4% de l'ensemble de patients, et ce taux excédait 8% si une autre opération était faite en même temps ou si le patient souffrait d'une cholécystite aiguë. Dans ces deux derniers groupes, la céphaloridine administrée de façon prophylactique a servi à diminuer le taux d'infection.

La cholangiographie peropératoire du canal cystique faite chez 193 patients a augmenté le taux de calculs enlevés du cholédoque de 41% à 63%. Toutefois l'incidence à la fois de taux négatifs et de faux positifs parmi les cholangiographies était très élevée.

Chez 15 patients, malgré une cholangiographie normale pour des raisons cliniques nous avons procédé à une exploration des voies biliaires et avons obtenu cinq résultats positifs. Lorsque nous avons procédé à une exploration du cholédoque sur un jugement clinique sans cholangiographie, les résultats se sont avérés positifs dans 41% des cas. Alors que la cholangiographie peropératoire est utile, des améliorations pour nous permettre de compter sur cet examen, s'imposent et sont probablement possibles d'après les résultats obtenus à la salle d'opération et en radiologie.

As part of a comprehensive assessment of the delivery of surgical care in the determination of areas for improvement or logical prospective trials, the results in 1000 consecutive patients undergoing cholecystectomy were scrutinized.

Materials and Methods

Variables Analyzed

The majority of the operations were performed by residents or interns during the 17-month period from January 1972 to May 1973. The 1000 cholecystectomies were performed in 724 females and 276 males (ratio, 2.6:1), whose ages ranged from 17 to 91 years (Fig. 1). Of these 1000 patients, 274 underwent at least one other operation in addition to cholecystectomy

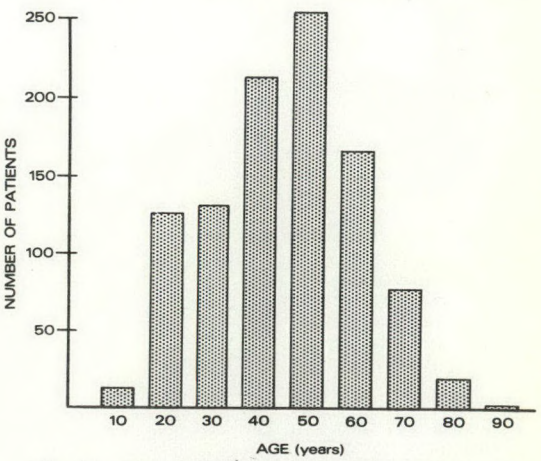

Fig. 1.—Age distribution of 1000 patients undergoing cholecystectomy.

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(Table I). The commonest associated procedures were common bile duct exploration and appendectomy. All patients were seen by one of us (J.E.M.), who recorded 37 variables that were transcribed to a central processing and storage computer for data processing by means of conventional Fortran language. The following variables were analyzed: mortality; incidence of wound infection (i.e., pus in the wound as opposed to transient nonsuppurating areas of redness or inflammation); incidence of wound infection complicating other operations done simultaneously; incidence of wound infection related to administration of cephaloridine prophylactically; pathologic diagnosis; culture of the bile and gallbladder wall; age of the patient and duration of operation; and the results achieved with intraoperative cholangiography.

The chi-square test was used in statistical analysis.

Culture Technique

Samples were taken of gallbladder bile and gallbladder wall and implanted immediately into Stuart medium[1] for transport and thereafter cultured appropriately for the detection of aerobic and anaerobic organisms. Preliminary tests indicated that this inexpensive transport medium was as effective as aerobic and anaerobic blood culture media in preserving organisms for culture.

TABLE I.—PROCEDURES ASSOCIATED WITH CHOLECYSTECTOMY

Procedure	*No. of procedures*
Common bile duct exploration	129*
Appendectomy	100
Repair of hiatus hernia	14
Vagotomy and pyloroplasty	7
Breast biopsy	6
Repair of ventral hernia	6
Splenectomy	6
Gastrojejunostomy	6*
Duodenotomy	5
Subtotal gastrectomy	5
Choledochoenterostomy	3*
Repair of umbilical hernia	3
Resection of ovarian cyst	3
Portacaval shunt	2*
Mitral valve replacement	2
Right nephrectomy	2
Intestinal bypass	2
Bilateral adrenalectomy	2
Lymph node biopsy	2*
Prostatic resection	1
Resection of Meckel's diverticulum	1
Closure of gastric perforation	1
Hemicolectomy	1
Resection of ureter	1
Cystogastrostomy	1*

*One death was associated with each of these procedures.

Radiologic Technique

Intraoperative cystic duct cholangiography was performed using standard techniques with a 100 mA mobile x-ray machine. The average exposure capability of the equipment was 80 mA at 0.3 s at 70 to 75 kVp. Two 10 x 12 grid cassettes with Radelin STF-2 intensifying screens loaded with Cronex 4 (par speed) film were used. Hypaque (60%), diluted by mixing three parts of dye with seven parts of normal saline, was injected through a long infant feeding tube into the cystic duct. Approximately 5 ml was injected for the first film and 10 to 30 ml, depending on duct size, for the second film.

The technique, standardized before the study, included availability of an experienced radiology technician assigned to the operating theatre, positioning of the patient to prevent overlap of the biliary tract and spine, and standard practices to prevent injection of air bubbles into the biliary tree.

Regimen for Prophylaxis with Cephaloridine

Cephaloridine, when used, was given according to the following regimen:[2] 1 g was injected intramuscularly before operation, on call; 1 mg was given 5 hours after operation and 1 g was given 12 hours after operation.

RESULTS

Mortality

There were no deaths among the 726 patients who underwent cholecystectomy alone, but among the entire group of 1000 there were 6 deaths (operative mortality, 0.6%) (Table II). The patients who died were three who underwent operation for extensive unresectable carcinoma in addition to incidental cholecystectomy, one who underwent emergency portacaval shunt, one in whom cystogastrostomy was performed for acute severe pancreatitis, and one with sup-

purative cholangitis in whom emergency cholecystectomy, common bile duct exploration and drainage were performed.

Pathologic Diagnosis

The pathologic diagnoses relating to the gallbladder are listed in Table III.

Wound Infection

Wound infections developed in hospital in 16 females and 18 males (rate, 3.4%). Development of wound infection in these 34 patients was related to various factors; the procedure performed, the use of cephaloridine prophylactically, the gallbladder lesion, the result of culture of operative site, the age of the patient and the duration of the operative procedure were important.

Influence of operative procedure, prophylactic cephaloridine therapy and abnormalities of gallbladder.—The influence on the incidence of wound infection of acute inflammation or gangrene of the gallbladder, and the risk of additional procedures and the control of these risks by use of prophylactic antibiotics, is summarized in Table IV.

When cholecystectomy alone was performed for chronic cholecystitis and the patient did not receive prophylactic cephaloridine (487 patients), the wound infection rate was 1.4%. Among the 129 patients in the same category who received cephaloridine prophylactically this rate was 0.7%; the difference was not significant. Performance of a procedure in addition to cholecystectomy in patients not receiving cephaloridine significantly increased the wound infection rate from 1.4 to 8.7% ($P < 0.001$). This increased risk of wound infection appeared to be prevented by the use of cephaloridine prophylactically (8.7 vs. 0%; $P < 0.05$).

Acute inflammation of the gallbladder also increased the risk of wound infection from 1.4 to 8.5% ($P < 0.001$). This category comprised the smallest number of patients, but prophylactic use of cephaloridine did not appear to decrease significantly the wound infection rate from this cause. If one compares the wound infection rates for cholecystectomy for acute cholecystitis and for cholecystectomy with an additional procedure, the infection rate was 8.4% in 283 patients not receiving cephaloridine. Patients undergoing similar procedures but who received prophylactic cephaloridine had a wound infection rate of 1.67%, and the difference is significant ($P < 0.05$).

Common bile duct exploration.—Because the performance of procedures in addition to cholecystectomy increases the incidence of wound infection, one might expect common duct exploration, the most frequently performed additional procedure to be associated with an increased rate of infection, which is in fact what we found. Among the 129 patients who underwent common bile duct exploration, wound infection occurred in 12 (9.3%). This procedure was done on 104 occasions for the 860 patients with chronic cholecystitis (12.1%), 23 times among the 125 patients with acute cholecys-

TABLE III.—PATHOLOGIC DIAGNOSES FOR 1000 PATIENTS UNDERGOING CHOLECYSTECTOMY

Diagnosis	*No. of patients*
Chronic cholecystitis	860
Acute or gangrenous cholecystitis	125
Adenocarcinoma of gallbladder	6
Adenocarcinoma of pancreas	2
Adenocarcinoma of common bile duct	2
No abnormality	3
No specimen	2

TABLE II.—DETAILS OF PATIENTS WHO DIED AFTER UNDERGOING CHOLECYSTECTOMY*

Age (yr)	*Sex*	*Diagnosis*	*Procedure in addition to cholecystectomy*	*Day of death (postoperative)*
62	M	Cancer of pancreas, with metastases	Gastrojejunostomy	24
57	F	Acute severe pancreatitis	Cystogastrostomy	10
79	M	Cancer of pancreas	Choledochoenterostomy	4
47	M	Cirrhosis of liver, esophageal varices	Portacaval shunt	4
71	M	Cholangitis, sepsis, shock, diabetes mellitus	Common bile duct exploration	4
83	F	Cancer of gallbladder	Lymph node biopsy	30

*For entire series, mortality was 0.6%; for patients undergoing cholecystectomy only, the mortality was zero.

TABLE IV.—Influence of Prophylactic Cephaloridine Related to Procedure and Pathology*

Group	Procedure	Pathology	Prophylactic cephaloridine	Wound infection: No. of patients with wound infection	Wound infection: Infection rate, %†
1	Cholecystectomy only (n = 487)	Chronic‡	No	7	1.4
2	Cholecystectomy only (n = 129)	Chronic	Yes	1	0.7
3	Cholecystectomy + another procedure (n = 206)	Chronic	No	18	8.7
4	Cholecystectomy + another procedure (n = 38)	Chronic	Yes	0	0
5	Cholecystectomy only (n = 77)	Acute§	No	6	8.5
6	Cholecystectomy only (n = 23)	Acute	Yes	1	4.5
7	Groups 3 + 5 (n = 283)		No	24	8.4
8	Groups 4 + 6 (n = 61)		Yes	1	1.6

*Does not include 15 patients with cancer or no abnormality of the gallbladder and 25 patients who had cholecystectomy + another procedure but in whom acute cholecystitis was the indication for operation in the first place.
†Differences are significant for the following groups, as follows: 1 and 3, $P < 0.001$; 1 and 5, $P < 0.001$; 3 and 4, $P < 0.05$; 7 and 8, $P < 0.05$.
‡Chronic cholecystitis.
§Acute cholecystitis.

titis (18.4%) and on 2 occasions for patients with intrahepatic biliary obstruction secondary to carcinoma (1.6%). Of these patients, 104 received no cephaloridine prophylactically and all 12 infections occurred in this group, an incidence of wound infection of 11.5%. However, 25 of the 129 patients had acute or chronic cholecystitis and they received cephaloridine prophylactically and among them were no wound infections; this difference is of borderline significance, probably because of the small sample size, but the overall rate of wound infection in this group therefore was 9.3%.

Culture of gallbladder wall and bile.—Cultures of the gallbladder wall of 235 patients yielded one or more species of organism in 67 (28.5%) (Table V). Cultures of the gallbladder bile from 419 patients grew one or more species in 119 (28.4%) (Table V).

With respect to the 27 patients with *acute* cholecystitis from whom cultures were obtained from the gallbladder wall, cultures in 11 (40.7%) were positive; and with respect to the 52 patients with acute cholecystitis from whom bile was cultured, a positive result was recorded in 21 (40.4%). For 194 patients with *chronic* cholecystitis, culture of the gallbladder wall was reported as being positive in 48 (24.7%) and culture

TABLE V.—Results of Cultures of Gallbladder Wall and Gallbladder Bile

Organism	Source of culture in gallbladder: Wall (n = 235)	Source of culture in gallbladder: Bile (n = 419)
E. coli	16	33
S. epidermidis	15	23
Enterobacter sp.	7	11
Klebsiella sp.	7	13
S. aureus	4	6
Enterococci sp.	4	3
Proteus mirabilis	3	1
α-hemolytic streptococcus	2	3
Hafnia sp.	2	2
Corynebacterium sp.	2	12
Aeromonas sp.	1	1
Staphylococcus albuf	1	0
Cl. welchii	1	0
Streptococcus sp.	1	4
β-hemolytic streptococcus	1	1
Salmonella sp.	0	2
Lactobacillus sp.	0	2
Cl. tetani	0	1
Achromobacter sp.	0	1
Total	67*	119†

*No growth was reported for 168 patients.
†No growth was reported for 300 patients.

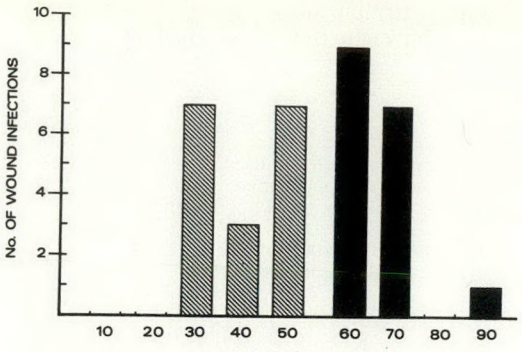

Fig. 2.—Incidence of wound infections related to age in 1000 patients who underwent cholecystectomy. Hatched bars: data relating to 737 patients under 60 years of age, among whom 17 (2.3%) had infection; solid bars: data relating to 263 patients over 60 years of age, among whom

of the gallbladder bile was positive in 90 of 349 (25.8%) so tested. The prominent organisms were *Escherichia coli* and *Staphylococcus epidermidis*.

Of the 34 patients in whom a wound infection developed, intraoperative culture either of the gallbladder wall or the bile was taken in 23. There was no growth in seven, but in six of these patients procedures in addition to cholecystectomy could have been the source of the infection. The organisms cultured from the infected wound were the same as those from the bile or gallbladder wall in 14 of the 16 remaining patients who had positive cultures at operation.

Patient age and length of operation.—In 737 patients under 60 years of age there were 17 wound infections (2.3%), whereas in 263 patients over 60 there were 17 (6.4%) (Fig 2). This is a highly significant difference ($P < 0.002$).

The median operating time was between 75 and 90 minutes. There were 13 wound infections in 569 patients whose operations took less than 90 minutes (2.3%) and there were 21 wound infections among 431 patients whose operations required more than 90 minutes (4.9%). This is also a significant difference ($P < 0.03$).

Intraoperative Cystic Duct Cholangiography and Common Bile Duct Exploration

Intraoperative cystic duct cholangiography was performed on 193 of the 1000 patients (Fig. 3). The cholangiogram was interpreted as normal in 155 and as positive or suggestive in 33; there were 5 technical failures. Of the 33 patients with positive cholangiograms, 27 underwent common bile duct exploration and stones were found in 17 (63%). The other six patients did not undergo common duct exploration despite a positive or suggestive cholangiogram, but the result in them was satisfactory on follow-up; none have recurrent symptoms that suggest retained stones in the common bile duct.

Among the 155 patients in whom cystic duct cholangiograms were normal, the common bile duct was explored in 15, despite

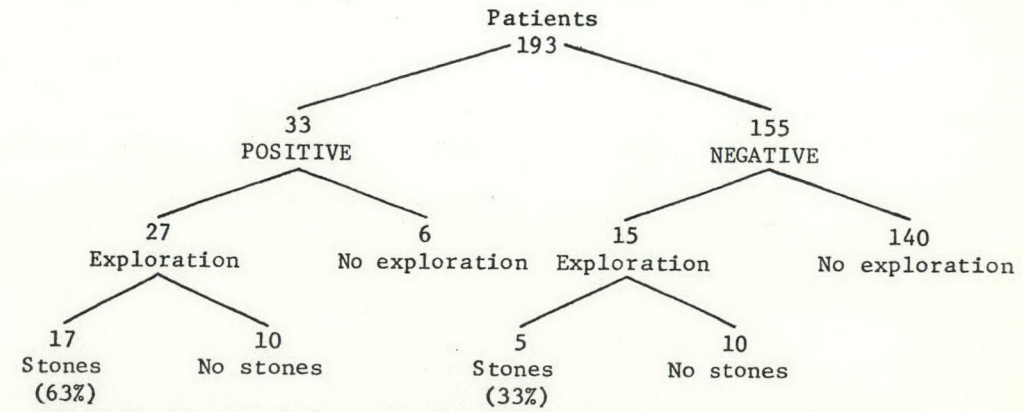

Fig. 3.—Results of cystic duct cholangiography in 193 patients. In 63% of patients with positive cholangiograms stones were found on duct exploration and the six patients not explored were asymptomatic: results in the latter therefore were false-positive. Note false-negative results in 33% of 15 patients in whom exploration was performed despite negative cholangiograms. Note also that cholangiograms were available in only 188 patients; in remaining 5 patients, cholangiography failed for technical reasons.

the normal radiographic findings, and, in 5 of these 15 patients, stones were found. The indications for cholangiography in these five patients were palpable stones in two and dilated bile ducts, pancreatitis, jaundice or multiple small stones in the gallbladder in varying combination in three.

There were 88 patients who did not have cystic duct cholangiography but who did appear to have a clinical indication for common bile duct exploration (Table VI). In these patients common duct exploration yielded positive findings in 36 patients and negative findings in 52. This high incidence of positive findings on exploration without cholangiography is related to the validity of the indications.

In this series 12 patients had proven retained stones in the common bile or hepatic ducts after cholecystectomy. In two of these patients there was associated malignant disease, both patients dying without further surgery; in three the stones were removed nonoperatively by a stone basket; in four the T-tube was removed, the patients remaining well clinically; in one the stone disappeared spontaneously; and in two patients the stones were removed at reoperation (Table VII).

No adverse effects of the prophylactic antibiotic used for three doses in this study were documented.

TABLE VII.—Results of 12 Patients with Retained Stones in Bile Ducts

Result	*No. of patients*
Re-exploration with removal	2
Spontaneous disappearance	1
Removal of T-tube with good clinical result	4
Nonoperative removal by basket	3
Died	2
Total	12

Discussion

The operative mortality for cholecystectomy has continued to decline since 1934, when Heuer published the first major report.[3] His review of 36 623 patients from 21 institutions in Europe and North America revealed an operative mortality of 6.6%. For the present series of 1000 patients, the overall mortality was 0.6%, with no deaths in patients who underwent cholecystectomy alone and only three deaths in patients with nonmalignant pancreatic or biliary disease. All six deaths occurred in patients in whom cholecystectomy was incidental and in whom operative procedures in addition to cholecystectomy were required.

Wound infection rates after cholecystectomy vary widely, from 2.5 to 15%.[4, 5] With respect only to those patients over 70, those with jaundice or common bile duct stone or those with acute cholecystitis, the infection rate reportedly is 27%.[6] This study confirms other reports in that age of the patient, duration of the operation and presence of acute inflammation of the gallbladder are all associated with higher wound infection rates, but it also suggests that additional procedures, including common bile duct exploration performed at the time of cholecystectomy, greatly increase the risk of infection. The present study has also shown that the prophylactic use of cephaloridine, starting before the procedure, appears to decrease the risk of infection associated with acute inflammation and additional procedures; this finding is consistent with that of Chetlin and Elliott,[6] who showed, in a pro-

TABLE VI.—Indications and Findings in 88 Patients Undergoing Common Bile Duct Exploration Without Cystic Duct Cholangiography

Positive indication	*No. of patients*	*Negative indication*	*No. of patients*
Palpable stones	10	Small stones	28
Dilated ducts	7	Dilated ducts	12
Jaundice	7	Jaundice	4
Positive transhepatic cholangiogram	6	Failed cholangiography	3
Small stones	4	Acute cholecystitis	2
Cancer(?)	1	Pancreatitis	1
Retained stone	1	No indication	2
Total	36		52

spective trial, that patients who are at high risk for infection after biliary duct surgery benefit from prophylactic use of an antibiotic. The wound infection rate associated with a regimen similar to that described herein was 4%, compared with 27% among similar but untreated controls.

We currently recommend, for prophylaxis, the use of cephaloridine, as advised by Polk and Lopez-Mayor,[2] for all patients over 60 years of age who are scheduled for cholecystectomy and in whom additional procedures are contemplated and for patients with acute cholecystitis. The value of prophylactic antibiotic therapy in patients with chronic cholecystitis in whom cholecystectomy only is performed is not established.

The importance of infected bile as a cause of wound infections is reaffirmed in this study.[4] Wound cultures might be a further guide in patients in whom additional procedures are performed at the time of cholecystectomy.[7]

We found no difference in the incidence of positive cultures between gallbladder wall or bile in the same patients. Quantitative cultures of bile might be the best guide to the potential risk of bile spillage at operation. In studies of the bile and gallbladder wall at the time of cholecystectomy, Robson, Bogart and Heggers[4] showed that organisms in a concentration of 10^5 per gram of tissue are almost always associated with subcutaneous invasion and wound infection.

Recommendations regarding cystic duct cholangiography are less obvious from this review. Routine cystic duct cholangiography at the time of cholecystectomy has been widely recommended;[8-10] such a recommendation is logically based on the fact that there are thereby fewer common bile duct explorations and more positive explorations; and, besides, the procedure has a lower morbidity than has exploration of the common bile duct. On the other hand, it has not been demonstrated conclusively that more stones are found as a result of the routine use of cystic duct cholangiography. In the large series of Kakos and colleagues[9] the use of cholangiography increased from 2.9% in 1951 to 93% in 1970, yet the incidence of common duct stones found remained between 11.5 and 16% and the recovery was highest early in the experience during the period 1956 to 1960, when cholangiography was not commonly performed.

In the present study, false-positive cholangiograms were frequent. Of greater concern is the finding that negative cholangiograms were proven misleading in 5 of 15 patients in whom exploration was performed despite the negative report. These patients were included among a total of 155 in whom cholangiograms were negative. The difference between the incidence of positive explorations when cholangiograms were used (63%) and when clinical indications were used (41%) is significant, but this is not as clearly different when one considers the findings in patients with common duct stones in whom the cholangiograms were negative. The explorations were done in these instances on clinical grounds.

Although operative cholangiography as currently performed is useful, false-positive and false-negative errors are common, the techniques are demanding, and use of the procedure should not alter routine indications for choledochotomy. The challenge at this institution is to improve the equipment and techniques for cystic duct as well as those of T-tube cholangiography in the operating theatre, to reach the standard attained in the department of radiology.

Experience concerning the problem of retained stones gained since the completion of this study supports the use of a stone basket as the best method for retrieval. Spontaneous disappearance of the stones is common, due either to false-positive cholangiography or passage of the calculi. Reoperation is recommended only in patients who do not tolerate clamping of the T-tube because of jaundice or infection and in whom removal by use of the stone basket has failed.

References

1. Stuart RD: Diagnosis and control of gonorrhoea by bacteriological cultures, with preliminary report on new method for transporting clinical material. *Glasgow Med J* 27: 131, 1946
2. Polk HC, Lopez-Mayor JF: Postoperative wound infection: prospective study of determinant factors and prevention. *Surgery* 66: 97, 1969

(Continued on page 468)

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REFERENCES

1. Leading Article: *British M J* :127 (Oct. 21) 1972. 2. Purssey, B. S.: *M J Australia 1*:989 (May 16) 1970. 3. Fielding, G; Rao, A; Davis, N. C. and Wernick, N: *M J Australia 2*:159 (July 24) 1965. 4. Gibson, R. M.: *British M J 1*:1326 (June 7) 1958. 5. Forbes, G. B.: *Lancet* :505 (Sept. 2) 1961.

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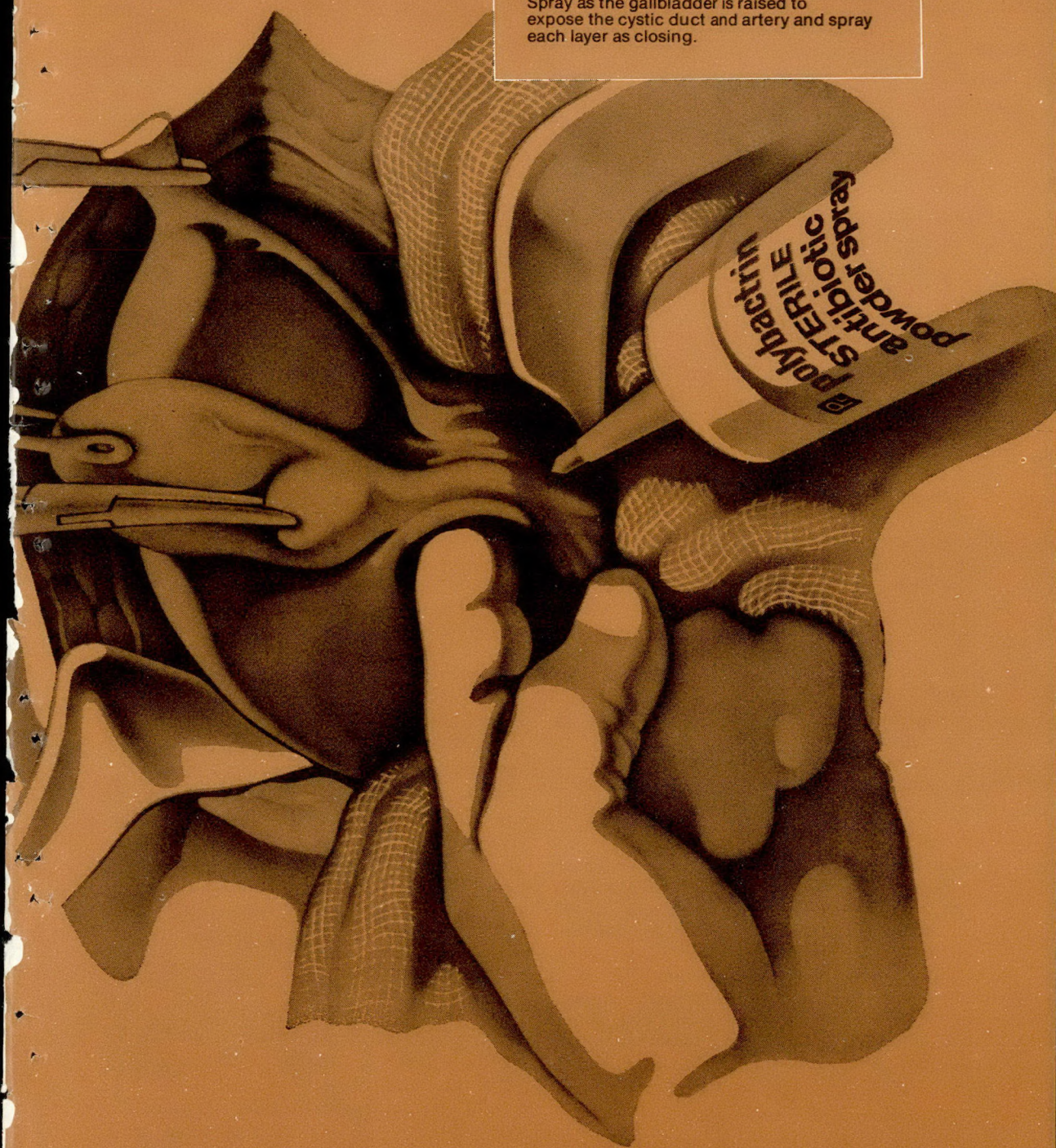

3. HEUER GJ: Factors leading to death in operations upon gallbladder and bile-ducts. *Ann Surg* 99: 881, 1934
4. ROBSON MC, BOGART JN, HEGGERS JP: Endogenous source for wound infections based on quantitative bacteriology of biliary tract. *Surgery* 68: 471, 1970
5. COLCOCK BP, PEREY B: Treatment of cholelithiasis. *Surg Gynecol Obstet* 117: 529, 1963
6. CHETLIN SH, ELLIOTT DW: Preoperative antibiotics in biliary surgery. *Arch Surg* 107: 319, 1973
7. DAVIDSON AI, CLARK C, SMITH G: Postoperative wound infection: computer analysis. *Br J Surg* 58: 333, 1971
8. SMITH R, SHERLOCK S: *Surgery of Gall Bladder,* London, Butterworths, 1964
9. KAKOS GS, TOMPKINS RK, TURNIPSEED W, et al: Operative cholangiography during routine cholecystectomy: review of 3,012 cases. *Arch Surg* 104: 484, 1972
10. NANSON EM: Operative cholangiography: plea for its general use. *Can J Surg* 18: 449, 1975

TNM CLASSIFICATION OF MALIGNANT TUMOURS OF THE BLADDER, PROSTATE, TESTIS AND KIDNEY

W. E. COLLINS, MD, FRCS[C]*

Summary: TNM classification is a short description of a cancer at a point in its natural history—the onset of definitive treatment—and should be considered in planning treatment, in assessing prognosis, in evaluating end results, in facilitating the exchange of information between treatment centres and thus in contributing to the continuing investigation of human cancer. For four cancers of urologic sites there are new TNM classifications. Although previous classifications of bladder cancer were satisfactory, the new classifications for kidney, prostate and testis are the first internationally accepted classifications for these three organs that are clinically practical. Widespread use of these classifications is recommended.

Résumé: La classification TNM est une brève description du cancer à un instant de son évolution naturelle—le début du traitement définitif. On devrait y recourir pour projeter le traitement, poser le pronostic, évaluer les résultats finals, faciliter l'échange de renseignements entre les centres thérapeutiques et, de la sorte, contribuer à l'étude continue du problème du cancer humain. En ce qui concerne quatre cancers urologiques, on y trouve de nouvelles classifications TNM. Bien que les classifications antérieures du cancer vésical aient été satisfaisants, les nouvelles classifications pour les reins, la prostate et les testicules sont les premières qui soient acceptées universellement pour ces trois organes et qui offrent un intérêt clinique pratique. Nous conseillons d'étendre largement l'usage de ces classifications.

THE TNM system, as elaborated by Denoix* and used by the committee on TNM classification of the International Union Against Cancer (UICC), is a short description of a cancer at a point in its natural history (at the onset of definitive treatment) based on clinical information in its primary application. From it, groupings may be devised to indicate stages, but it is not primarily a staging system. The basic principles established are applicable to all sites, regardless of treatment, and the classification may be supplemented later by information that becomes available from histopathologic examination or surgical exploration. Anderson* has shown that they are applicable for such deep-seated lesions as carcinoma of the colon and rectum.

The TNM classification and staging have five purposes; the classification and staging

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*ANDERSON WA: Stage classsifications and end results reporting for carcinoma of colon and rectum. *Cancer* 34 (suppl): 909, 1974

are worth while only if they serve one or more of these purposes. They should aid the clinician in the planning of treatment; they should give some indication of prognosis; they should assist in evaluation of treatment results; they should facilitate the exchange of information between treatment centres; and they should contribute to the continuing investigation of human cancer.

In the TNM classification the symbol T represents the degree of penetration of the primary tumour through or beyond the site of origin, N denotes the condition of the regional and juxtaregional lymph nodes, and M the absence or presence of distant metastases.

Microscopic confirmation of the degree of penetration of the primary tumour is expressed by the symbol P, and G refers to the pathologic grading of the tumour. In the classification of renal-cell carcinoma, invasion of veins is important and this information is expressed as V; similarly, in the bladder classification the invasion of lymphatics is expressed by the symbol L.

TNM Classification of Urologic Sites

New TNM classifications of tumours of four urologic sites (bladder, prostate, kidney and testis) have been developed by the UICC with the enthusiastic and effective help of many national groups, including the National Cancer Institute of Canada and the American Joint Committee for Cancer Staging and End Results Reporting. Revisions and changes in any system may be necessary as new data and knowledge are available, and a final and ideal system may not be achieved until we stop learning more about cancer.

Classification of tumours in these four urologic sites presents specific problems, but they have been classified according to a common plan. For this purpose, certain modifications to the hitherto accepted rules of the TNM system have been necessary as follows:

1. Minimal requirements for the meaningful categorization of a primary tumour, the lymph nodes and metastases are necessary; for example, arteriography and lymphography may be mandatory.

2. Lymph nodes beyond the regional nodes may now be treated; therefore, these juxtaregional nodes are also classified.

3. With tumours of the testis, radical orchiectomy performed for confirmation of the diagnosis provides the necessary information for assessment of the extent of the primary tumour.

The classifications of these tumours of urologic sites are not definitive. Though based on experience of large international groups of urologists, radiotherapists and pathologists, and supported by extensive data, they have yet to be fully tested in field trials. However, they represent the first workable classifications of tumours of the kidney, prostate and testis that have been acceptable to an international group.

Because these classifications do meet most, if not all, of the objectives for which they were developed, they are now ideal for clinical application. Some groups may wish to add designations of a surgical-evaluative classification and a postsurgical classification; there is no reason why they should not.

For two decades, hormonal therapy was used indiscriminately in the treatment of prostatic cancer. It was then impossible to assess the proper place for hormonal therapy in the management of prostatic cancer. Now, therapy is being used indiscriminately. Widespread use of TNM classification of prostatic cancer at this time will allow the place of radiation therapy to be evaluated.

At a recent international meeting on cancer of the larynx, presentations were not accepted unless the material had been classified by the TNM system. It is reasonable to assume that future end-stage reporting will not be acceptable unless the data required for TNM classification are collected prospectively. Therefore, widespread use of TNM classification of malignant tumours of these four urologic sites is recommended.

Sellers (personal communication, 1975) has developed check sheets for cancers of the bladder and prostate. These check sheets make classification exceedingly easy.*

Systems for classification of tumours follow.

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*Check sheets are available from the Ontario Cancer Treatment and Research Foundation, 7 Overlea Blvd., Toronto, Ont. M4H 1A8.

THE BLADDER

Rules for Classification

1. The classification applies only to epithelial tumours. Papilloma is excluded but such cases may be listed under the category G0.

2. There must be histologic or cytologic verification of the disease.

3. The following are the minimum requirements for assessment of the T, N and M categories:

- T categories: Clinical examination, urography, cystoscopy, bimanual examination under adequate anesthesia and biopsy or transurethral resection of the tumour (if indicated) prior to definitive treatment.
- N categories: Clinical examination, lymphography and urography.
- M categories: Clinical examination, chest radiography and biochemical testing. In the more advanced primary tumours or when clinical suspicion warrants, radiographic or isotope studies should be done.

If these requirements cannot be met the symbol TX, NX or MX will be used.

TMN Classification

T = Primary tumour

The suffix (*m*) may be added to the appropriate T category to indicate multiple tumours, thus: T2(*m*).

T1S Carcinoma in situ. Definite anaplasia of surface epithelium without the formation of papillary stuctures and without infiltration.

TX The minimum requirements to assess fully the extent of the primary tumour cannot be met.

T0 No evidence of primary tumour.

T1 On bimanual examination a freely mobile mass may be felt: this should not be felt after complete transurethral resection of the lesion and/or, microscopically, the tumour does not extend beyond the lamina propria.

T2 On bimanual examination the indurated bladder wall is mobile. There is no residual induration after complete transurethral resection of the lesion and/or there is microscopic invasion of superficial muscle.

T3 On bimanual examination induration or a nodular mobile mass is palpable in the bladder wall that persists after transurethral resection of the exophytic portion of the lesion and/or there is microscopic invasion of deep muscle or extension through the bladder wall.

T3a Invasion of deep muscle.

T3b Extension through the bladder wall.

T4 Tumour fixed or invading neighbouring structures and/or there is microscopic evidence of such involvement.

T4a Tumour invading prostate, uterus or vagina.

T4b Tumour fixed to the pelvic wall and/or infiltrating the abdominal wall.

N = Regional and juxtaregional lymph nodes

The regional lymph nodes are the pelvic nodes below the bifurcation of the common iliac arteries. The juxtaregional lymph nodes are the inguinal nodes, the common iliac and para-aortic nodes.

NX The minimum requirements to assess the regional lymph nodes cannot be met.

N0 No evidence of involvement of regional lymph nodes.

The Bladder (continued)

N1 Involvement of a single homolateral regional lymph node.

N2 Involvement of contralateral or bilateral or multiple regional lymph nodes.

N3 There is a fixed mass on the pelvic wall with a free space between this and the tumour.

N4 Involvement of juxtaregional lymph nodes.

Subsequent information regarding the histologic assessment of the regional lymph nodes may be added to the clinical N category by means of negative and positive signs, thus: N– for nodes with no microscopic evidence of metastasis; or N+ for nodes with microscopic evidence of metastasis (e.g., N1–, N0+).

M = Distant metastases

MX The minimum requirements to assess the presence of distant metastases cannot be met.

M0 No evidence of distant metastases.

M1 Distant metastases present.

M1a Evidence of occult metastases based on biochemical and/or other tests.

M1b Single metastasis in a single-organ site.

M1c Multiple metastases in a single-organ site.

M1d Metastases in multiple-organ sites.

Note: The location of metastases should be specified. The lymph nodes beyond the regional and juxtaregional nodes and bone are regarded as single-organ sites.

P = Histopathologic categories

Assessment of the P categories is based on evidence derived from surgical operation and histopathology; that is, where tissue other than biopsy is available for examination. The suffix (*m*) may be added to the appropriate P category to indicate multiple tumours, thus P2(*m*).

P1S Preinvasive carcinoma (carcinoma in situ).

PX The extent of invasion cannot be assessed.

P0 No tumour found on examination of specimen.

P1 Tumour not extending beyond the lamina propria.

P2 Tumour with infiltration of superficial muscle (not more than halfway through muscle coat or infiltration of perivesical tissue).

P3 Tumour with infiltration of deep muscle (more than halfway through muscle coat) or infiltration of perivesical tissue.

P4 Tumour with infiltration of prostate or other extravesical structures.

G = Histopathologic grading

GX Grade cannot be assessed.

G0 No evidence of anaplasia (i.e., papilloma).

G1 Low-grade malignancy.

G2 Medium-grade malignancy.

G3 High-grade malignancy.

L = Invasion of lymphatics

LX Lymphatic invasion cannot be assessed.

L0 No lymphatic invasion.

L1 Superficial lymphatics invaded.

L2 Deep lymphatics invaded.

Note: The histopathologic categories and grading conform to the recommendations of WHO. (Ref. *Histological Typing of Urinary Bladder Tumours*, Geneva, WHO, 1973).

Stage grouping

No stage grouping is at present recommended.

THE PROSTATE

Rules for Classification

1. The classification applies only to carcinoma.

2. There must be histologic or cytologic verification of the disease, to permit division of cases by histologic type.

3. The following are the minimum requirements for assessment of the T, N and M categories.

- T categories: Clinical examination, urography, endoscopy and biopsy (if indicated) prior to definitive treatment.
- N categories: Clinical examination, lymphography and/or urography.
- M categories: Clinical examination, chest radiography, skeletal studies and determination of the acid phosphatase level on two or more occasions.

TNM Classification

T = Primary tumour

The suffix (*m*) may be added to the appropriate T category to indicate multiple tumours, thus: T2(*m*).

TX The minimum requirements to assess fully the extent of the primary tumour cannot be met.

T0 No tumour palpable. This category includes those cases of the incidental finding of a carcinoma in an operative or biopsy specimen. Such cases should be assigned an appropriate P, N or M category.

T1 Tumour intracapsular, surrounded by palpably normal gland.

T2 Tumour confined to the gland, smooth nodule deforming contour but lateral sulci and seminal vesicles not involved.

T3 Tumour extending beyond the capsule with or without involvement of the lateral sulci and/or seminal vesicles.

T4 Tumour fixed or invading neighbouring structures.

N = Regional and juxtaregional lymph nodes

The regional lymph nodes are the pelvic nodes below the bifurcation of the common iliac arteries. The juxtaregional lymph nodes are the inguinal nodes, the common iliac and para-aortic nodes.

NX The minimum requirements to assess the regional lymph nodes cannot be met.

N0 No evidence of involvement of regional lymph nodes.

N1 Involvement of a single regional lymph node.

N2 Involvement of multiple regional lymph nodes.

N3 There is a fixed mass on the pelvic wall with a free space between this and the tumour.

N4 Involvement of juxtaregional nodes.

Subsequent information regarding the histologic assessment of the regional lymph nodes may be added to the clinical N category by means of negative and positive signs, thus: N– for nodes with no microscopic evidence of metastasis; or N+ for nodes with microscopic evidence of metastasis (e.g., N1–, N0+).

M = Distant metastases

If lymphography indicates extension to the juxtaregional lymph nodes, a scalene node biopsy is recommended.

MX The minimum requirements to assess the presence of distant metastases cannot be met.

M0 No evidence of distant metastases.

M1 Distant metastases present.

M1a Evidence of occult metastases by biochemical and/or other test.

M1b Single metastasis in a single-organ site.

M1c Multiple metastases in a single-organ site.

M1d Metastases in multiple-organ sites.

Note: The location of metastases should be specified. The lymph nodes beyond the regional and juxtaregional nodes, and bone are regarded as single-organ sites.

P = Histopathologic categories

Assessment of the P categories is based on available material whether biopsy, transurethral resection, enucleation or total prostatectomy; the source is to be stated. The suffix (*m*) may be added to the appropriate P category to indicate multiple tumours, thus: P2(*m*).

PX The extent of invasion cannot be assessed.

P0 No tumour found on examination of specimen.

P1 Focal (single or multiple) carcinoma.

P2 Diffuse carcinoma with or without extension to the capsule.

P3 Carcinoma with penetration through the capsule and/or extension to the seminal vesicles.

P4 Extension into adjacent organs.

G = Histopathologic grading

GX Grade cannot be assessed.

G0 No evidence of anaplasia.

G1 Low-grade malignancy.

G2 Medium-grade malignancy.

G3 High-grade malignancy.

Stage grouping

No stage grouping is at present recommended.

THE TESTIS

Rules for Classification

1. Testis refers to the body of the testis and excludes the epididymis.

2. There must be histologic verification of the disease. Cases must be divided by histologic type. Malignant lymphoma is excluded.

3. The following are the minimum requirements for assessment of the T, N and M categories.

- T categories: Clinical examination and radical orchiectomy (which in this case is considered as a biopsy).
- N categories: Clinical examination, lymphography and urography.
- M categories: Clinical examination, chest radiography and biochemical tests.

TNM Classification

T = Primary tumour

In the absence of orchiectomy the symbol TX must be used.

TX The minimum requirements to assess fully the extent of the primary tumour cannot be met.
T0 No evidence of primary tumour.
T1 Tumour limited to the body of the testis.
T2 Tumour extending beyond the tunica albuginea.
T3 Tumour involving the rete testis or epididymis.
T4 Tumour invading the spermatic cord and/or scrotal wall.
T4a Invasion of spermatic crord.
T4b Invasion of scrotal wall.

N = Regional and juxtaregional lymph nodes

The regional lymph nodes are the paraaortic and paracaval nodes. After surgery on the scrotum the homolateral inguinal lymph nodes are included with the regional lymph nodes. The juxtaregional lymph nodes are the intrapelvic nodes, the mediastinal and supraclavicular nodes.

NX The minimum requirements to assess the regional lymph nodes cannot be met.
N0 No evidence of involvement of regional lymph nodes.
N1 Involvement of a single homolateral regional lymph node, which, if inguinal, is mobile.
N2 Involvement of contralateral or bilateral or multiple regional lymph nodes, which, if inguinal, are mobile.
N3 A palpable abdominal mass is present or there are fixed inguinal lymph nodes.
N4 Involvement of juxtaregional lymph nodes.

Subsequent information regarding the histologic assessment of the regional lymph nodes may be added to the clinical N category by means of negative or positive signs, thus: N– for nodes with no microscopic evidence of metastasis; or N+ for nodes with microscopic evidence of metastasis (e.g., N1–, N0+).

M = Distant metastases

As the primary tumour advances or if clinical suspicion warrants, skeletal or isotope studies should be done.

MX The minimum requirements to assess the presence of distant metastases cannot be met.
M0 No evidence of distant metastases.
M1 Distant metastases present.
M1a Evidence of occult metastases based on biochemical and/or other tests.
M1b Single metastasis in a single-organ site.
M1c Multiple metastases in a single-site.
M1d Metastases in multiple-organ sites.

Note: The location of metastases should be specified. The lymph nodes beyond the regional and juxtaregional notes — and bone are regarded each as single-organ sites.

P = Histopathologic categories

Assessment of the P categories is based on evidence derived from surgical operation and histopathologic examination after orchiectomy. The P categories correspond to the T categories.

P0 No evidence of primary tumour.
P1 Tumour limited to the body of the testis.
P2 Tumour extending beyond the tunica albuginea.
P3 Tumour involving the rete testis and/or epididymis.
P4 Tumour invading the spermatic cord and/or scrotal wall.
P4a Invasion of spermatic cord.
P4b Invasion of scrotal wall.

Stage grouping

No stage grouping is at present recommended.

THE KIDNEY

Rules for Classification

1. The classification applies only to renal-cell carcinoma. Adenoma is excluded but such cases may be listed under the category G0.

2. There must be histologic and cytologic verification of the disease. Any unconfirmed cases must be reported separately.

3. The following are the minimum requirements for assessment of the T, N and M categories:

- T categories: Clinical examination, urography and arteriography prior to definitive treatment.
- N categories: Clinical examination, lymphography and urography.
- M categories: Clinical examination, chest radiography and biochemical testing. In patients with more advanced primary tumour or when clinical suspicion warrants, radiographic or radioisotope studies should be done.

If these requirements cannot be met the symbol TX, NX or MX will be used.

TNM Classification

T = Primary tumour

In the absence of arteriography, the symbol TX must be used.

TX The minimum requirements to assess fully the extent of the primary tumour cannot be met.

T0 No evidence of primary tumour.

T1 Evidence of a small tumour without enlargement of the kidney. There is limited calyceal distortion or deformity and circumscribed vascular deformities, surrounded by renal parenchyma.

T2 Evidence of a large tumour with deformity and/or enlargement of the kidney or calyceal or pelvic involvement. The continuity of the cortex is preserved on arteriography.

T3 Evidence of spread into perinephric fat, peripelvic fat or hilar renal vessels.

T4 Evidence of invasion into neighbouring organs or abdominal wall.

N = Regional and juxtaregional lymph nodes

The regional lymph nodes are the paraaortic and paracaval nodes. The juxtaregional lymph nodes are the intrapelvic and the mediastinal nodes.

NX The minimum requirements to assess the regional lymph nodes cannot be met.

N0 No evidence of involvement of regional lymph nodes.

N1 Involvement of a single homolateral regional lymph node.

N2 Involvement of contralateral or bilateral or multiple regional lymph nodes.

N3 Fixed regional lymph nodes (assessable only at surgical exploration).

N4 Involvement of juxtaregional lymph nodes.

Subsequent information regarding the histologic assessment of the regional lymph nodes may be added to the clinical N category by means of negative and positive signs, thus: N– for nodes with no microscopic evidence of metastasis; or N+ for nodes with microscopic evidence of metastasis (e.g., N1–, N0+).

M = Distant metastases

MX The minimum requirements to assess the presence of distant metastases cannot be met.

M0 No evidence of distant metastases.

The Kidney (continued)

M1 Distant metastases present.

M1a Evidence of occult metastases based on biochemical or other tests, or both.

M1b Single metastasis in a single-organ site.

M1c Multiple metastases in a single-organ site.

M1d Metastases in multiple-organ sites.

Note: The location of metastases should be specified. The lymph nodes beyond the regional and juxtaregional nodes are regarded as single-organ sites, as is bone.

P = Histopathologic categories

Assessment of P categories is based on evidence derived from surgical operation and histopathologic examination—when tissue other than biopsy is available for examination.

PX Extent of invasion cannot be assessed.

P0 No primary renal-cell tumour found on examination of specimen.

P1 Tumour surrounded by renal parenchyma.

P2 Tumour extending to the capsule and/or invading the renal pelvis and/or calyces.

P3 Tumour extending beyond the capsule into the perinephric fat or the peripelvic fat or the renal pedicle.
P3a Extension to perinephric fat.
P3b Extension to peripelvic fat.
P3c Extension to renal pedicle.

P4 Tumour invading neighbouring organs or fixed to the abdominal wall, or both.

G = Histopathologic grading

GX Grade cannot be assessed.

G0 No evidence of anaplasia (i.e., adenoma).

G1 Low-grade malignancy.

G2 Medium-grade malignancy.

G3 High-grade malignancy.

V = Invasion of veins

VX Extent of invasion cannot be assessed.

V0 Veins do not contain tumour.

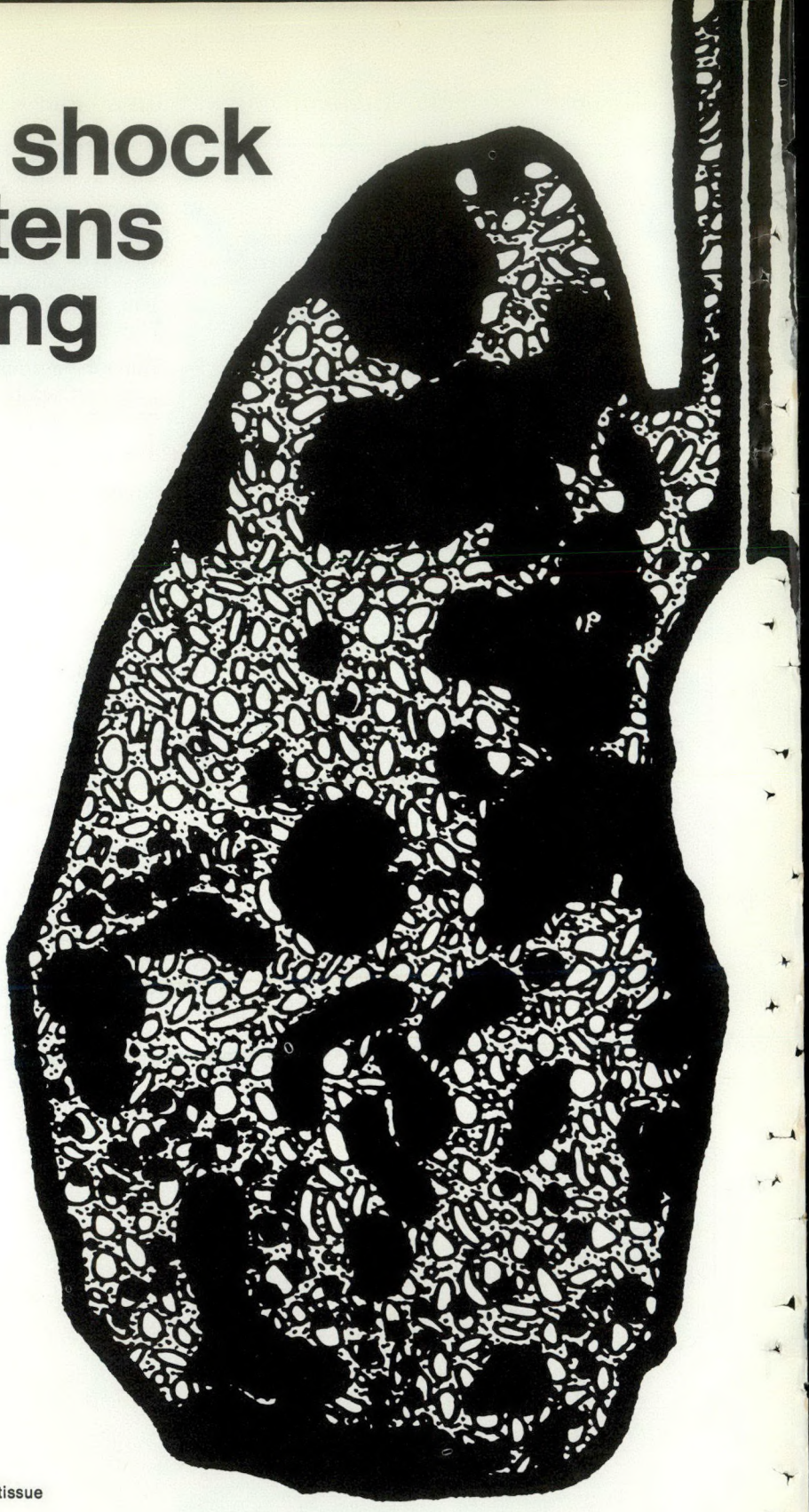
V1 Renal vein contains tumour.

V2 Vena cava contains tumour.

Stage grouping

No stage grouping is at present recommended.

when shock threatens the lung



Abstract visualization of lung tissue

Solu-Medrol

helps reduce pulmonary damage and increase survival rates

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

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

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

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

Prescribing information on following page

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

TESTING FOR COMPLETENESS OF VAGOTOMY

Of tests designed to assess the completeness of vagotomy, the Hollander insulin hypoglycemia test is the most widely used, though it is of no value during operation. A different approach is that of T. R. Weber, T. A. Miller and S. M. Lindauer (J Surg Res 18: 491, 1975) *who used a combination of 2-deoxy-D-glucose (2DG) and neutral red (NR) both during and after operation.*

A potent vagal stimulant, 2DG is thought to be associated with hypothalamic glucocytopenia, which in turn stimulates the dorsal motor nucleus of the vagus. Vagotomy abolishes this response. Neutral red is secreted selectively by the gastric parietal cells and, if NR is injected intravenously in the presence of vagal stimulation, the gastric juice turns pink, then purple. The appearance of NR in the gastric juice is prevented by vagotomy.

Weber and his colleagues used the combination of 2DG and NR diagnostically in 18 patients, all of whom also underwent Hollander's test. Tests were performed preoperatively, intraoperatively and postoperatively. Among six patients who had not undergone peptic ulcer surgery, the 2DG-NR test was positive preoperatively in all six as opposed to the Hollander test, which was positive in five; intraoperatively, there was no difference in these six patients between the two tests; and 3 montns postoperatively the 2NG-NR test was positive in none of four patients who underwent vagotomy whereas the Hollander test was positive in one of these four. A second group comprised 12 patients with a possible recurrence of ulcer after surgery. In these, the only difference was that in two patients preoperatively the 2DG-NR test was positive and the Hollander test was negative. These two patients were found to have intact vagus nerves and evidence of recurrent ulceration. Among the other 10 in this group, both the 2DG-NR and Hollander tests were negative in 7 (none of whom underwent a further operation) and were positive in 3, all of whom were found to have recurrent ulceration.

The 2DG-NR test is useful as a postoperative test in assessing the completeness of vagotomy, but its value as an intraoperative test needs further evaluation.

SOLITARY EPIDIDYMAL SCHISTOSOMIASIS*

L. H. HONORÉ, MB, ChB, FRCP[C]† and G. U. COLEMAN, MD, FRCS[C]‡

Summary: A 54-year-old Canadian presented with a 1-month history of painless swelling in the right testis. The diagnosis was thought to be a sperm granuloma, a leiomyoma, or an adenomatoid tumour of the epididymis; histologic examination, however, revealed evidence of schistosomiasis, probably due to *Schistosoma haematobium*. Solitary schistosomiasis of the epididymis has been reported previously in only two cases. Epididymal schistosomiasis has never been diagnosed preoperatively because it is so rare, but even if it were suspected preoperatively and confirmed by biopsy, chemotherapy alone would not prevent impairment of epididymal function due to scarring. Surgical excision of the lesion, therefore, is recommended.

Résumé: Nous avons observé, chez un Canadien de 54 ans, une tuméfaction indolore du testicule droit, datant d'un mois. Au point de vue diagnostique, on pensa d'abord à un granulome séminal, à un léiomyome ou à une tumeur adénomatoïde de l'épididyme, jusqu'à ce qu'un examen histologique eût révélé qu'il s'agissait d'une schistosomiase probablement attribuable à *Schistosoma haematobium*. Jusqu'alors on n'avait signalée que deux cas de schistosomiase épididymaire isolée. Cette infestation n'a jamais été diagnostiquée avant l'intervention en raison de sa rareté. Toutefois, même si elle était soupçonnée avant l'opération et confirmée par biopsie, la chimiothérapie seule ne pourrait empêcher l'altération de la fonction épididymaire par des cicatrices. Nous conseillons donc l'excision chirurgicale de la lésion.

SCHISTOSOMIASIS is endemic in Africa and is hyperendemic in the Nile valley, where the incidence of infestation of the population at large may attain 100%.[1] In these areas, schistosomiasis of the epididymis is not rare, but it is usually associated with overt rectal or vesical disease. As the sole presenting manifestation of schistosomiasis, however, epididymal schistosomiasis is extremely rare, even in these areas of high infestation, and only two cases of solitary epididymal schistosomiasis have been reported. The first case[1] was that of a 10-year-old Sudanese boy who had an orchiectomy for suspected orchioblastoma; pathologic examination revealed a normal testis with extensive granulomatous epididymitis due to *Schistosoma haematobium*. The second case[2] concerned a 23-year-old Sudanese who presented with a painless swelling in the tail of the epididymis; the lesion was shown to be that of schistosomiasis, though it was impossible to differentiate the infestation histologically between that of *S. haematobium* and that of *S. mansoni*. In addition, schistosomiasis of the spermatic cord without epididymal involvement has been reported.[3] The patient, a 50-year-old Ghanaian, presented with a bilateral, slowly enlarging, painless swelling in the scrotum and underwent a bilateral orchiectomy for presumptive seminoma; in this man severe schistosomiasis affected the cord, so that the veins were plugged and both testes became infarcted.

In these cases, the diagnosis of schistosomiasis typically was not even suspected before operation, and was made only after the surgical specimen had been studied pathologically. The patients have all been Africans and, to our knowledge, there is no record of solitary epididymal schistosomiasis presenting as a painless scrotal mass in a Caucasian. We report such a case in order to draw attention to this rare lesion, which we believe will become more common in Canada as a result of world travel and immigration.

CASE REPORT

A 54-year-old minister, who had spent 17 years in Africa with the Sudan Interior Mission, presented with a 1-month history of a painless swelling in the right testis. There were no other complaints and specifically none referable to the urinary or alimentary tracts, He had a history of recurrent urolithiasis and had passed a small stone about 3 months pre-

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viously. He looked fit. The only physical abnormality that was found was a slightly irregular, firm, nontender nodule (dimensions, 2 x 2 cm) in the globus major of the epididymis, separable from the testis. Intravenous pyelography showed only a small calculus in the left kidney. Results of urinalysis, urine smears and urine cultures were negative. Examinations of the blood revealed no abnormalities except for a mild eosinophilia (absolute count, 438 to 803 x $10^6/l$). The lesion was thought to be a sperm granuloma, a leiomyoma or an adenomatoid tumour of the epididymis; the globus major of the right epididymis was excised. The postoperative course was uneventful. Histologically, the diagnosis was schistosomiasis; as a result, urine and stool specimens were examined, though no parasites were found, and a course of niridazole (Ambilhar, CIBA; 750 mg *bid* for 7 days) was given.

Histopathologic Findings

Gross inspection showed diffuse fibrous thickening of the epididymis with tiny yellow spots, but no caseation necrosis was noted. The serosal membrane was smooth and devoid of tubercles. Microscopic examination revealed extensive granulomatous inflammation of the epididymal and paraepididymal connective tissues. The epididymal tubules and vasa efferentia were largely spared but a few tubules showed intramural inflammation and focal ulceration due to rupture of a nearby granuloma into their walls (Fig. 1). Three types of tuberculoid granuloma were present. The first type was solid, with a central Langhans type of giant cell, palisading epithelioid cells and peripheral infiltration with lymphocytes, plasma cells and eosinophils. The second type contained one or two ova lying free among the epithelioid cells or within the cytoplasm of a foreign-body giant cell (Fig. 2). The third type, made up of single or a few coalescent units, was characterized by central eosinophilic necrosis with entrap-

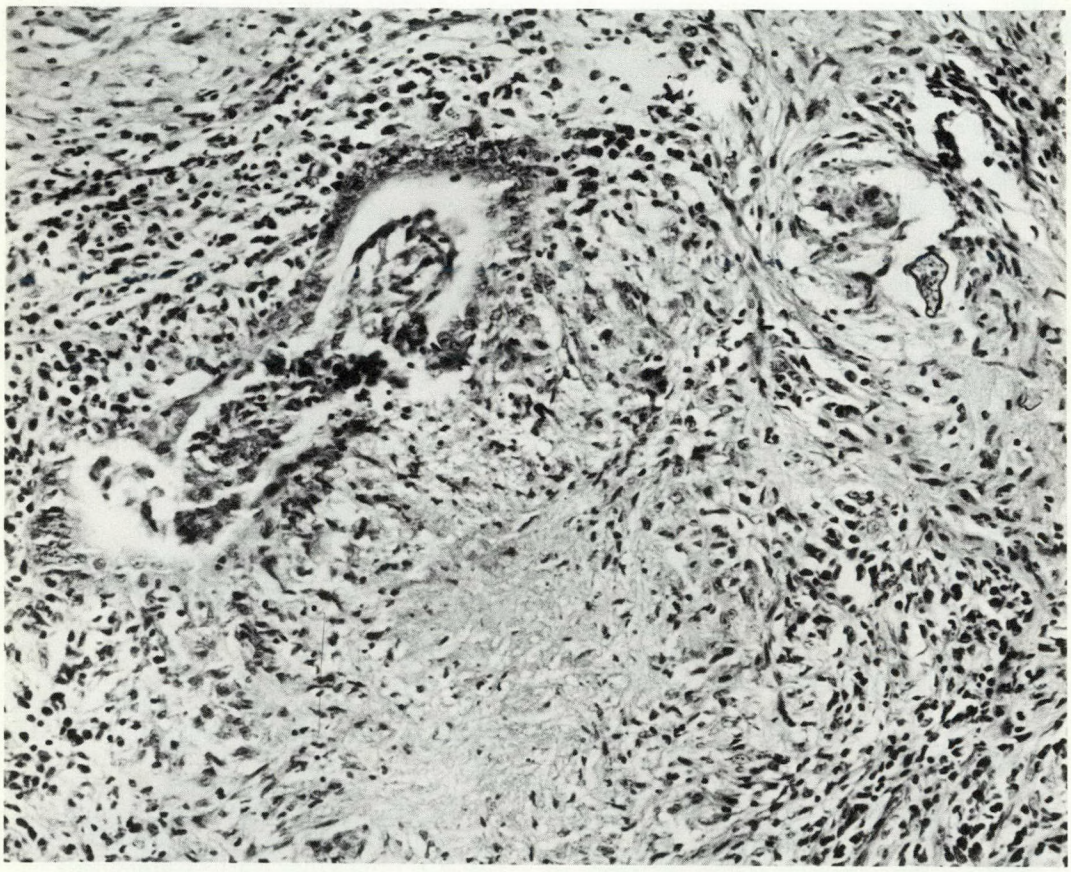

Fig. 1.—Inflammation in wall of epididymal tubule with focal ulceration (hematoxylin and eosin, x 210).

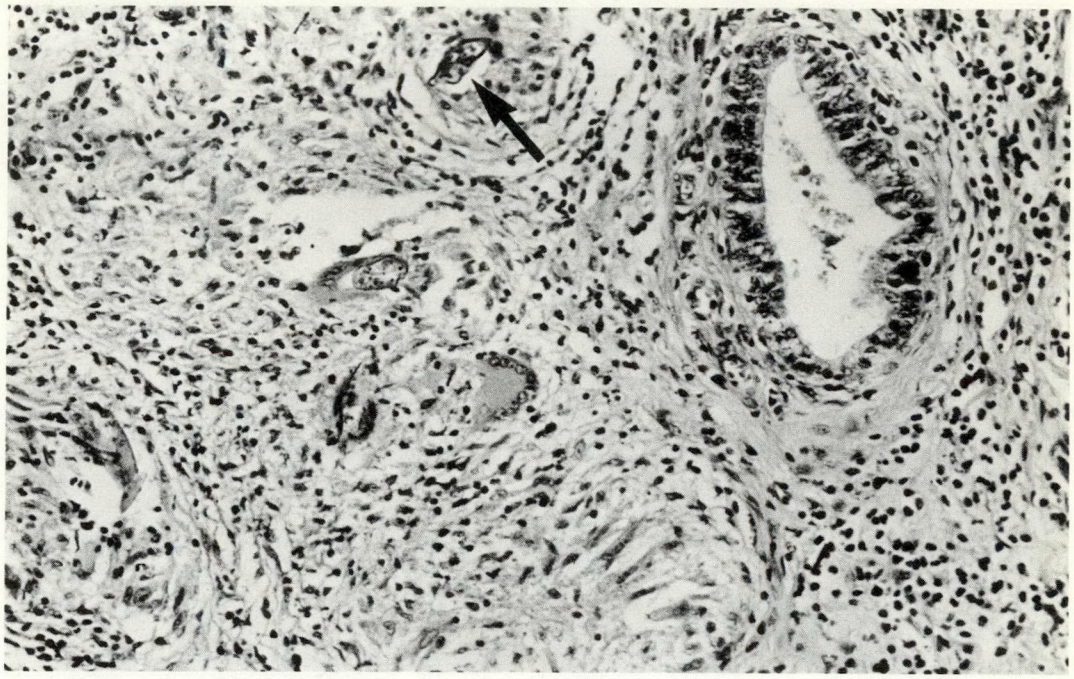

Fig. 2.—Interstitial tuberculoid granulomas with many schistosomal ova (arrow) (hematoxylin and eosin, x 210).

ment of degenerating ova (Fig. 3). These granulomas showed little fibrosis and no calcification; they were distributed widely throughout the epididymis, but tended to lie close to small blood vessels and lymphatic spaces. The small and medium-sized veins showed no intraluminal deposition of ova or intramural inflammation. Granulomas, particularly the small compact units, were abundant in the paraepididymal tissues, especially around blood vessels and underneath the tunica vaginalis. The serosa itself was not involved. Many schistosomal ova were seen, with varying degrees of degeneration. Some were well preserved with large numbers of conspicuous miracidia and a clear-cut refractile cell wall, while others showed a variable loss of detail and shrinkage. A few ova bore sharp terminal spines consistent with the appearance of *S. haematobium* (Fig. 4).

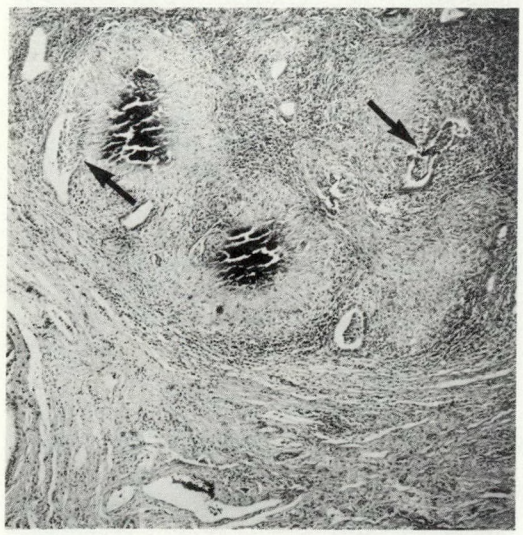

Fig. 3.—Granulomas with central eosinophilic necrosis. Note rupture into nearby tubule (arrows) (hematoxylin and eosin, reduced by 37% from x 52).

Discussion

Pathologically, the diagnosis in this case was clearly schistosomiasis of the epididymis, and the presence of terminal spines in many of the ova suggested that the organism was *S. haematobium*. The first reported case of epididymal schistosomiasis[1] was also that of infestation with *S. haematobium*, which appears to be the only form that can mature outside the portal system and cause disease, as in the conjunctiva[4] and the larynx.[5]

Schistosomal infestation is considered to evolve through three stages:[6] (a) skin penetration by the larvae with or without local symptoms and signs; (b) deposition of ova in veins, mostly in the portal and vesical venous systems with intestinal or urinary symptoms; and (c) progressive irreversible damage to organs as a result of venous occlusion. During the phase of parasitemia the ova can be seen in every organ, though rarely in the testis, epididymis and spermatic cord.[7] This relative sparing of these areas was noted by Alves, Woods and Gelfand,[8] who also noted that, in contrast, the seminal vesicles, prostate and terminal vas deferens are common sites of egg deposition. Whatever the cause of this differential distribution in the male genital tract, it probably underlies the rare involvement of the upper part of the tract. Why the epididymis should on occasion be selectively involved as in the present case is not clear, especially when there is no subjective or objective evidence of involvement of bowel or bladder. In fact, as in the two previous cases[1, 2] and in the present case, the absence of ova in urine and stool appears to be a distinct feature of solitary epididymal schistosomiasis. In sharp contrast, Honey and Gelfand[9] noted that hard painless swellings can be felt in the testes, epididymes and spermatic cords of patients excreting ova in the urine, though biopsy of these organs fails to show any deposition of ova.

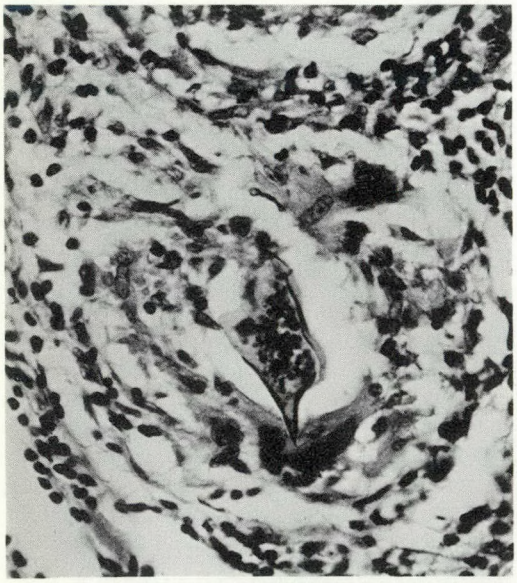

Fig. 4.—Ovum with miracidia and terminal spine (hematoxylin and eosin, reduced by 34% from x 890).

Our pathologic material does not allow us to draw any conclusion as to the peculiar vulnerability of the epididymis in this patient. The spread clearly was not ductal; most likely it was vascular. Though no large vein was seen containing intraluminal ova, the venular basis of the lesion is suggested by the predominantly interstitial inflammation and the abundance of granulomas in para-arterial locations in the epididymal interstitium and in the highly vascular tissues underlying the tunica vaginalis.

Though the diagnosis is easily made pathologically, the clinical diagnosis is regularly missed because of the general unawareness of this condition in western countries. The clinical forms of epididymal schistosomiasis have recently been summarized by Boulos and Karim,[2] as follows:

1. The granular or miliary form, in which hard tubercles are scattered along the spermatic cord, epididymis and their coverings.
2. The solitary form, commonly seen in the globus major and not uncommonly associated with nodules scattered along the cord—the "bilharzial rosary". (These nodules were absent in the present case.)
3. The massive form, with extensive infiltration of the spermatic cord in part or in all of its intrascrotal course, spreading down to the epididymis and testis, covering and matting them together. The spermatic fascia and cremasteric muscle may be affected and all structures are plastered together into one irregular solid mass.

Because of the rarity of this condition, no critical evaluation of therapy is available. In all the cases reported, treatment has been surgical excision, because the lesion was never recognized preoperatively. Theoretically, if the lesion was suspected before or at exploration, a diagnostic biopsy could precede any decision on whether to operate or to prescribe chemotherapeutic agents. Many objections can be raised against this basically rational approach. First, a sample biopsy, whether examined by means of a frozen section or by multiple routine sections, may fail to show the telltale ova, and the presence of tuberculoid granulomas may

lead to an erroneous pathological diagnosis of tuberculosis and subsequent inappropriate therapy. Second, in the absence of any previous experience with biopsy, one cannot exclude a serious potential complication—for example, spread of the infection into the nearby tissues with aggravation of local disease. Third, even if the correct diagnosis were made by biopsy, it is doubtful whether chemotherapy alone should be the treatment of choice. In all the cases so far reported, the epididymis has been severely affected, and chemotherapy, even if this was parasitocidal (which is by no means certain), could be expected to cause scarring and severe impairment of epididymal function. For these reasons we believe that, irrespective of whether or not the diagnosis is suspected preoperatively, the treatment of choice should be surgical excision with antiparasitic drug coverage.

REFERENCES

1. ELTAYEB AA: Schistosomiasis of epididymis. *Br J Surg* 56: 552, 1969
2. BOULOS PB, KARIM OA: Schistosomiasis of epididymis. *J R Coll Surg Edinb* 18: 158, 1973
3. JOSHI RA: Bilateral total infarction of testis due to schistosomiasis of spermatic cord. *Am J Trop Med Hyg* 11: 357, 1962
4. BADIR G: Schistosomiasis of conjunctiva. *Br J Ophthalmol* 30: 215, 1946
5. SHAHEEN H: Bilharziasis of larynx. *Arch Otolaryngol* 35: 286, 1942
6. SANJURJO LA: Parasitic diseases of genitourinary system, in *Urology*, v 1, third ed, edited by CAMPBELL MF, HARRISON JH, Philadelphia, Saunders, 1970, p 480
7. MAKAR N: *Urological Aspects of Bilharziasis in Egypt*, Cairo, Société Orientale de Publicité, 1955, p 50
8. ALVES W, WOODS RW, GELFAND M: Distribution of bilharzial ova in male genital tract. *Cent Afr J Med* 1: 166, 1955
9. HONEY RM, GELFAND M: *Urological Aspects of Bilharziasis in Rhodesia*, Edinbugh, Livingstone, 1960, p 20

HEMORRHOIDS, VARICOSE VEINS AND DEEP VEIN THROMBOSIS: EPIDEMIOLOGIC FEATURES AND SUGGESTED CAUSATIVE FACTORS*

DENIS P. BURKITT, MD, FRS, FRCS(Edin)

Summary: Three venous disorders—hemorrhoids, varicose veins and deep vein thrombosis—are common in Western societies, but are relatively rare in other societies. Impressions gained by the author from 20 years of surgical experience in Africa and answers to questionnaires sent to more than 100 hospitals in 20 African countries have led to formation of an etiopathogenetic hypothesis for these three disorders. Hemorrhoids and varicose veins may well be related to the occurrence of constipation, which, in turn, is related to a deficiency of fibre in Western diets. Deep venous thrombosis may be related to both valvular incompetence and an alteration in blood coagulability; the latter is related to alterations in the intestinal concentration of vitamin K. It is therefore possible that the occurrence of these three conditions might be prevented by adding cereal fibre to Western diets.

Résumé: On sait que trois troubles veineux, les hémorroïdes, les veines variqueuses et la thrombose des veines profondes, sont chose courante dans les sociétés du monde occidental, mais relativement rare dans d'autres populations. Après 20 années d'expérience chirurgicale en Afrique et avoir colligé les réponses aux questionnaires qu'il a envoyés à plus de 100 hôpitaux dans 20 pays Africains, l'auteur a formulé une hypothèse étiopathogénique susceptible d'expliquer ces trois pathologies. Les hémorroïdes et les varices peuvent fort bien avoir un rapport avec la constipation qui, à son tour, peut relever d'une insuffisance d'aliments fibreux dans les régimes de nos sociétés. La thrombose des veines profondes peut être causée à la fois par une incompétence valvulaire et une altération de la coagulabilité, cette dernière étant due à des altérations de la concentration intestinale de la vitamine K. Il devrait donc être possible de prévenir ces trois pathologies en ajoutant des aliments fibreux aux régimes alimentaires du monde occidental.

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*Presented at surgical grand rounds, Royal Victoria Hospital, Montréal, Qué., Feb. 6, 1975.

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HEMORRHOIDS are among the commonest of the diseases of Western man, varicose veins affect nearly one in five North American adults and deep vein thrombosis (DVT) is one of the commonest of all postoperative complications.

These three venous disorders are considered together because they have closely similar epidemiologic features. The same factor is postulated as a cause of the first two and a closely related factor as a cause of the third.

The understanding of these problems has been hampered by the assumption of Western medical authors, too often held, that diseases common in their experience must also be common elsewhere. This erroneous approach has regrettably preserved hypotheses that are untenable in the light of epidemiologic evidence.

My convictions are based on 20 years of surgical experience in Africa, where I worked mainly in a large teaching hospital but had surgical responsibilities that entailed regular visits to nearly every hospital in Uganda. Subsequent research interests led me to visit over 100 hospitals in some 20 different African countries, and to make several prolonged tours visiting hospitals in the Indian subcontinent. Impressions thus gained have been reinforced by replies to questionnaires sent monthly to more than 160 hospitals in Africa and Asia asking for the number of patients seen with any of these three diseases. The information derived from these questionnaires forms the basis of this communication.

GEOGRAPHIC DISTRIBUTION

The prominence of these three diseases in the Western world contrasts with their relative rarity within rural communities in developing countries. This rarity has been largely hidden from Western medicine because physicians tend to report what is common in their experience rather than what is rare.

The prevalence of these three venous disorders is highest in affluent countries in the Western world, lowest among peoples living traditionally in developing countries and intermediate in countries with standards between these extremes.

All these conditions have a similar prevalence in black and white Americans.

Hemorrhoids

In this communication hemorrhoids will be considered as dilatations of the veins in the superior hemorrhoidal plexus; the present definition does not include such conditions as perianal hematomas and mucosal prolapse, which are often included loosely in a broader term.

A diagnosis of hemorrhoids has only been accepted if there was some prolapse or bleeding lest almost any perianal condition be included.

Monthly returns from 77, mainly rural, hospitals in Africa indicate that, for each hospital, less than three patients with bleeding or prolapsed hemorrhoids are diagnosed annually.

Hemorrhoids appear to be considerably more prevalent in India than in Africa.

Varicose Veins

Africans rarely suffer from varicose veins. Physicians specifically searching for the condition usually estimate the rate to be less than 1%, sometimes much less than this. Many with over 20 years' experience have reported that they see barely one patient annually,[1-3] though a few have reported much higher prevalences.[4]

Replies to questionnaires received from more than 140 hospitals in Africa reveal that more than 50% of them estimated an annual incidence of less than five cases. In only 10 hospitals were more than 20 cases reported, and in 21 not even 1 case a year was noted.

Varicose ulceration is almost unknown in Africa. I saw no case in 20 years in a 600-bed teaching hospital. Only 4 of 60 doctors in different hospitals in Africa who replied to a questionnaire had ever seen a case.

Deep Vein Thrombosis

The frequency of DVT appears to be similar to that of varicose veins. Monthly reports from 47 African hospitals show that fewer than one case is diagnosed clinically per hospital per year. This rarity has been confirmed by autopsy findings[5] and also by the paucity of clinical or radiologic evidence of its dreaded sequel, pulmonary embolism.

The diagnosis of DVT has inevitably rested on clinical grounds. Admittedly it has been suggested that in 50% of cases diagnosed clinically no thrombosis exists, but on the other hand the diagnosis is not made clinically in 50% of patients with thrombosis. This possible error in overdiagnosis or underdiagnosis suggests that prevalence estimates made on clinical findings by those alert for the condition may not be too inaccurate.

In communities in which DVT is rare, pulmonary embolism is exceedingly rare, and this complication is unlikely to be consistently missed.

The Effect on Prevalence of Westernization

The prevalence of each of the three diseases increased in non-western countries after contact with Western culture. Though still rare among traditionally living communities, their incidence is increasing among the more highly educated and in urban communities. Hemorrhoids almost invariably become more common preceding the development of varicose veins. I. A. M. Prior (personal communication, 1975) has demonstrated the steady increase in the prevalence of the latter, from that in Polynesian peasants, who are little affected, through the prevalence in Polynesians living in urban communities to that of New Zealand Maoris, in whom the prevalence of varicose veins exceeds even that of their white compatriots. The changing prevalence related not to genetic factors but to manner of life. Similar observations have been made in Africa and India.

The incidence of DVT appears to increase at about the same time as that of varicose veins increases.

Related Diseases and Physiologic Phenomena

Not only do patterns of geographic distribution throw light on the etiology of disease but so also do observed relations between diseases. The three venous disorders considered are related epidemiologically to such bowel diseases as diverticulosis, appendicitis and cancer, and to such apparently unrelated conditions as hiatus hernia, gallstones, and ischemic heart disease. Diverticular disease never occurs in a community until several decades after varicose veins have become relatively common. Moreover, patients with demonstrable colon diverticula are more than twice as likely as expected to have varicose veins also.[6] These observations suggest a shared causative factor.

A high prevalence of each of these three diseases is generally associated with prolonged intestinal transit times and the passage of small firm stools, whereas the reverse is true for communities with low prevalences. Moreover, the amount of fibre eaten is related directly to stool bulk and softness, and indirectly related to intestinal transit time.[7]

Conventional Concepts of Causation in the Light of Epidemiologic Evidence

Hemorrhoids

Incrimination of anatomic features such as the absence of valves in the portal venous system and the manner of emergence of venules through the wall of the anal canal must be discounted. There is no evidence of anatomic differences between areas of high and low prevalance.

The same applies to the blaming of any other factors not related to geographic distribution.

Varicose Veins

The widely held hypothesis that man's erect posture is a fundamental cause of varicose veins is quite untenable in the light of its geographic distribution. Gravity, however, may contribute after valve failure.

Nor can heredity be considered a primary cause in view of the epidemiologic features. No longer can constrictive clothing be blamed, and certainly not pregnancy—a normal physiologic process that is most common in communities among whom varicose veins are rare. Reports from India and parts of Africa suggest that the occurrence of varicose veins is higher in men than in women.

Deep Vein Thrombosis

It is generally assumed that DVT is the result primarily of the circumstances of hospitalization, and in particular of surgery and of obstetric delivery. This attitude takes no

account of the fact that similar surgical operations and obstetric deliveries using the same techniques and anesthetic methods are associated to a much smaller degree with DVT in developing countries than they are in the Western world.

The contrast between the prevalence of DVT in developing countries and in the affluent West is well illustrated by the frequency of 1.7 per 10 000 deliveries in Thailand compared with 134.7 per 10 000 deliveries in the United States.[8]

An Alternative Hypothesis

Cleave[9, 10] was the first to relate all these venous disorders to constipation, although he postulated mechanisms different from those suggested herein.

These venous disorders, together with the associated diseases already listed, have all been related to the fibre-depleted diets characteristic of modern Western civilization.[10-13] Fibre-depleted diets are the fundamental cause of constipation.[7, 14] Constipation results in both the increased pressures within the bowel that are believed to cause diverticular disease[15, 16] and appendicitis[17] and the increased intra-abdominal pressures that occur with straining during evacuation of firm feces. These increased pressures tend to force the gastroesophageal junction upwards into the thoracic cavity, and with, it has been postulated, the development of hiatus hernia.[18] These pressures are also believed to be an important cause of both hemorrhoids and varicose veins.

A different but related cause will be postulated with respect to DVT.

Hemorrhoids

The superior hemorrhoidal plexus drains into the superior hemorrhoidal veins. All forms of abdominal straining force blood retrogradely down these veins, thus increasing the pressures within the veins of the superior hemorrhoidal plexus. In all abdominal straining, with the single exception of that required for evacuating hard stools, these raised intravascular pressures are compensated for by extravascular pressures supplied by reflex contraction of the anal sphincters (Fig. 1). It is only during defecation that raised intravascular pressures

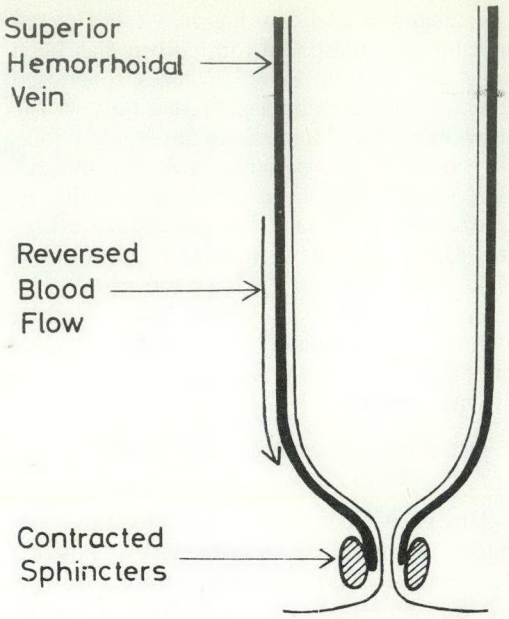

Fig. 1.—External pressure from contraction of anal sphincters counteracting increased pressure within the superior hemorrhoidal venous plexus. (Reproduced by permission from Burkitt DP: Dietary fibre and pressure diseases. *J R Coll Phys Lond* 9: 138, 1975.)

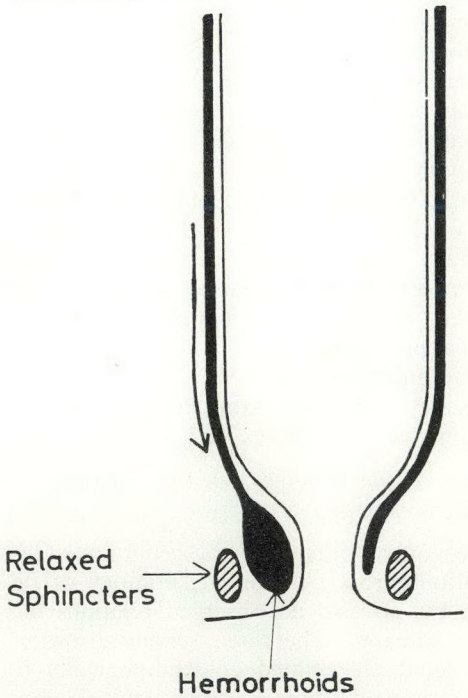

Fig. 2.—Relaxation of anal sphincters, during defecation, leaving raised intravenous pressures unopposed with resultant dilatation of veins. (Reproduced by permission from Burkitt DP: Dietary fibre and pressure diseases. *J R Coll Phys Lond* 9: 138, 1975.)

are unopposed by pressures from without. During defecation the anal sphincters relax (Fig. 2). Oft-repeated, increased and unopposed intravenous pressures are believed to be the underlying cause of hemorrhoids. Tenesmus, even with an empty rectum, has the same effect.[19]

Varicose Veins

Increased intra-abdominal pressures are readily transmitted through incompetent saphenous valves, as is demonstrated by the standard cough-impulse test for valve competence. It must therefore be assumed that such pressures, which can well exceed 200 mm Hg, must be sustained by these valves so long as they remain competent (Fig. 3). It is reasonable to suppose that oft-repeated pressures exerted in all directions in a liquid medium might lead to dilatation of the veins and that the increased circumference would become too great for the valve cusps to occlude. And more than 25 years ago it was shown that varicose veins were unaccompanied by any pathologic changes in the valves, and that instead they were associated with stretching of the circumference so that there was a gap between the attachments of the valve cusps (Fig. 4).[20]

An additional causative factor is possibly the adoption of raised toilets. In the traditional squatting position, leg veins are, by means of pressures between the abdomen and thighs, protected from the effects of increased intra-abdominal pressure. A raised toilet seat exposes the valves to these pressures by minimizing flexion of the thighs.

These factors may not account for the development of all varicose veins but they are believed to be important in the majority.

Deep Vein Thrombosis

At least two factors are believed to be important in the pathogenesis of DVT. It seems reasonable to assume that, if the superficial and perforating veins undergo changes, including dilatation in the presence of valvular incompetence, the deep veins may also be affected.[21] If so, retarded venous circulation during enforced recumbency could predispose to thrombosis.

A more important factor is likely to be a change in blood coagulability. The prevalance of DVT is maximal in communities whose residents have retarded intestinal transit and small stool volume, and minimal when the reverse obtains.

In clinical estimation, the prevalence of DVT and resultant pulmonary embolism can apparently be appreciably reduced if the fibre intake of surgical patients before and after operation is increased (C. Latto, personal communication, 1975; N. J. Blacklock, personal communication, 1975). The following possible mechanism is postulated and is being investigated.

Stools of persons living in western countries, where the incidence of DVT is maximal, contain a relative preponderance of anaerobic rather than aerobic organisms, in comparison with stools from developing

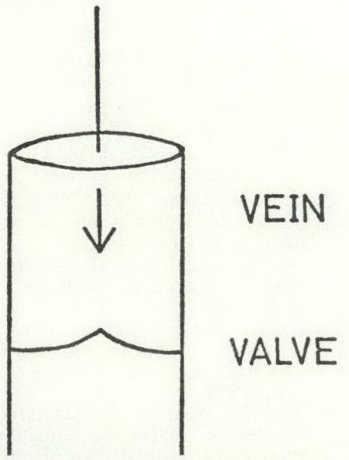

Fig. 3.—Competent venous valves sustaining transmitted abdominal pressure (> 200 mm Hg).

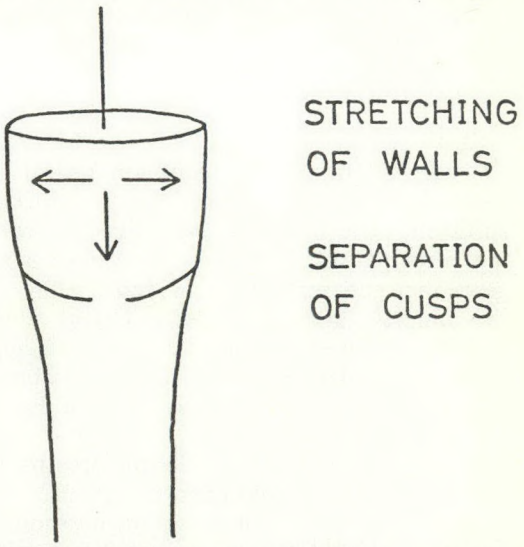

Fig. 4.—Dilated veins with incompetent valves transmitting raised intra-abdominal pressures.

countries where DVT is minimal. Anaerobic organisms have been implicated in the production of vitamin K, and in fact hemorrhagic states resulting from excessive doses of antibiotics have been treated by the administration of vitamin K. Vitamin K, in turn, is essential for the synthesis of activated factor X, which is required in the conversion of prothrombin to thrombin. Therefore the abnormal intestinal behaviour associated with Western civilization may indeed alter clotting factors.

Moreover, removal of all fibre from the diet can radically alter patterns of intestinal bacteria within a few days.[22]

It is not known whether the demonstrated difference between the types of fecal bacteria in Western and developing countries is due to increased fat or diminished fibre intake, or to some other dietary changes. It has, however, been suggested (I. McDonald, personal communication, 1975) that prolonged transit favours the development of anaerobes, and that hardness of feces, which ensures that the centre of a mass does not become exposed to the surface, has a similar effect.

Cleave[9, 10] postulated that hemorrhoids resulted from the direct pressure of hard fecal masses on the hemorrhoidal veins, with consequent obstruction of venous return, and that varicose veins and DVT were related to obstruction of venous return from the lower limbs caused by pressures on the common iliac veins by a loaded cecum or pelvic colon.

Possibility of Prevention

If these various hypotheses can be confirmed, all these three common disorders could be partially eliminated by restoring sufficient fibre to our diet and thus preventing constipation. Available knowledge suggests that the restoration of cereal fibre is the simplest and least costly. Cereal fibre can be restored to the diet by replacing white by wholemeal bread, or adding about 30 g (1 oz) of millers' bran to our food daily, or by doing both.

This is highly effective in the treatment not only of constipation and diverticular disease but also of first-degree hemorrhoids; and clinical evidence has shown that it may also reduce the prevalence of DVT.

References

1. Milton-Thompson DG: Varicose veins in tropical Africa. *Lancet* 1: 1174, 1974
2. Williams EH: Varicose veins in tropical Africa. *Ibid*, p 1291
3. Worsfold JT: Varicose veins in tropical Africa. *Lancet* 2: 1322, 1974
4. Daynes G, Beighton P: Prevalence of varicose veins in Africans. *Br Med J* 3: 354, 1973
5. Thomas WA, Davies JN, O'Neal RM, et al: Incidence of myocardial infarction correlated with venous and pulmonary thrombosis and embolism. Geographic study based on autopsies in Uganda, East Africa and St. Louis, U.S.A. *Am J Cardiol* 5: 41, 1960
6. Latto C, Wilkinson RW, Gilmore OJ: Diverticular disease and varicose veins. *Lancet* 1: 1089, 1973
7. Burkitt DP, Walker AR, Painter NS: Dietary fiber and disease. *JAMA* 229: 1068, 1974
8. Chumnijarakij T: Incidence of postpartum deep vein thrombosis in tropics. *Br Med J* 1: 245, 1974
9. Cleave TL: Neglect of natural principles in current medical practice. *J R Nav Med Serv* 42: 55, 1956
10. Idem: *The Saccharine Disease,* Bristol, Wright, 1974
11. Cleave TL, Campbell GD, Painter NS: *Diabetes, Coronary Thrombosis and Saccharine Disease,* Bristol, Wright, 1969
12. Burkitt DP: Some diseases characteristic of modern western civilization. Possible common causative factor. *Clin Radiol* 24: 271, 1973
13. Burkitt DP, Trowell HC, editors: *Refined Carbohydrate Foods and Disease,* New York, Academic Press. In press
14. Jones AF, Godding EW, editors: *Management of Constipation,* Oxford, Blackwell, 1972
15. Painter NS: Aetiology of diverticulosis of colon with special reference to action of certain drugs on behaviour of colon. *Ann R Coll Surg Engl* 34: 98, 1964
16. Painter NS, Burkitt DP: Diverticular disease of colon: deficiency disease of western civilization. *Br Med J* 2: 450, 1971
17. Burkitt DP: Aetiology of appendicitis. *Br J Surg* 58: 695, 1971
18. Burkitt DP, James PA: Low-residue diets and hiatus hernia. *Lancet* 2: 128, 1973
19. Graham-Stewart CW: What causes hemorrhoids? New theory of etiology. *Dis Colon Rectum* 6: 333, 1963
20. Adams JC: Etiological factors in varicose veins of lower extremities. *Surg Gynecol Obstet* 69: 717, 1939
21. Burkitt DP: Varicose veins, deep vein thrombosis, and haemorrhoids: epidemiology and suggested aetiology. *Br Med J* 2: 556, 1972
22. Winitz M, Adams RF, Seedman DA, et al: Studies in metabolic nutrition employing chemically defined diets. II. Effects on gut microflora populations. *Am J Clin Nutr* 23: 546, 1970

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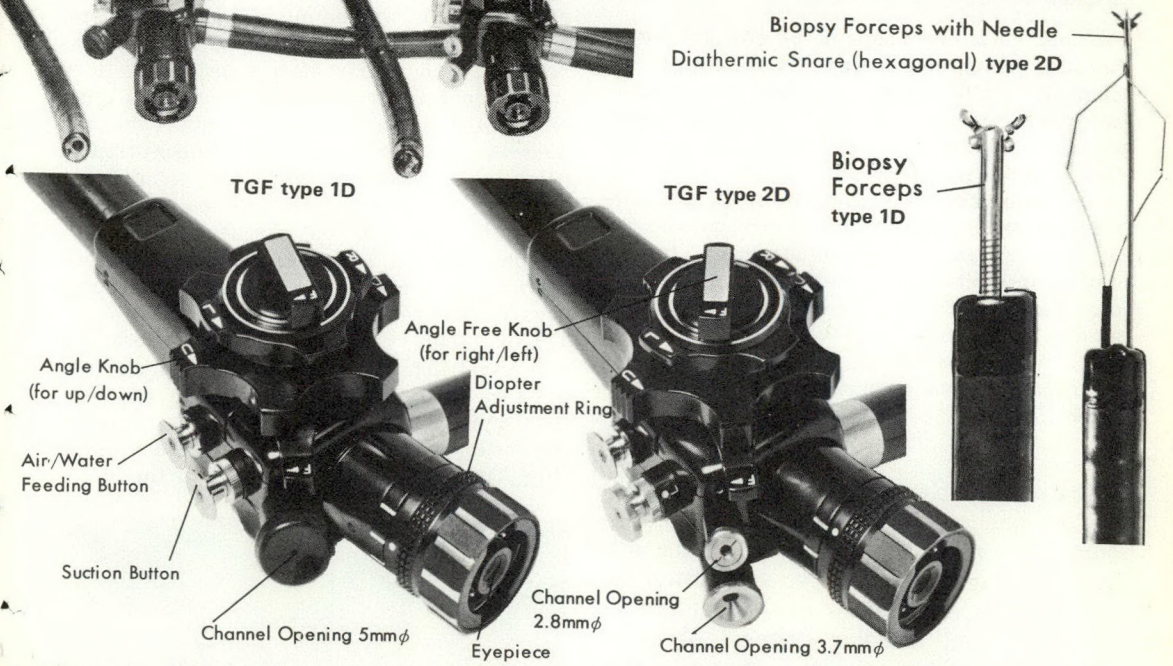

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UNUSUAL CASE OF MASSIVE GASTROINTESTINAL BLEEDING — PSEUDOANEURYSM OF THE HEAD OF THE PANCREAS

J. K. PRASAD, MB, BS, FRCS,* K. S. CHATTERJEE, MB, BS, FRCS (Edin)* and D. W. B. JOHNSTON, MD, FRCS[C], FACS†

Summary: Massive and repeated gastrointestinal bleeding with hemobilia arising from pseudoaneurysm of the pancreas occurred in a 58-year-man. The usual surgical methods of treatment were not practical because of peripancreatitis and difficulties in exposure. Catheterization of the gastroduodenal artery facilitated making the diagnosis of the pseudoaneurysm, but the accompanying necrosis of the duodenum and the proximal jejunum contraindicated the usual methods of embolization; instead, hemorrhage from the feeding vessel was stopped by transarterial electrocoagulation.

Résumé: Chez un homme de 58 ans, est survenue une hémorragie massive et récidivante accompagnée d'hémobilie, provenant d'un pseudoanévrysme du pancréas. Les techniques opératoires habituelles n'étaient pas pratiques, par suite d'une péripancréatite et de difficultés d'accès du champ. Le sondage de l'artère gastro-intestinale avait facilité le diagnostic de pseudo-anévrysme. Malheureusement, la nécrose concomitante du duodénum et du jéjunum proximale constituait une contre-indication aux modes habituels d'embolisation. Nous avons donc, à la place, enrayé l'hémorragie par électrocoagulation transartérielle du vaisseau nourricier.

BECAUSE gastrointestinal bleeding secondary to pancreatitis is relatively rare, pancreatitis is not often considered in the differential diagnosis of massive gastrointestinal bleeding. In an analysis of 1500 cases of gastrointestinal bleeding Palmer[1] observed only one case that originated from the pancreas. Wolstenholme[2] reported three cases of major gastrointestinal hemorrhage associated with pancreatic pseudocyst treated successfully in intracystic suture-ligation of the feeding vessel together with cystogastrostomy; one case was treated with pancreaticoduodenectomy. Spanos, Kloppedal and Murray[3] reported two cases of aneurysm of the gastroduodenal artery treated successfully by operation, one by ligation and one by excision.

We report a case of massive gastrointestinal bleeding from a pseudoaneurysm of the head of the pancreas, with successful treatment by selective, closed electrocoagulation of the feeding artery.

CASE REPORT

A 58-year-old man with a 12-year history of pancreatitis was admitted to hospital with complaints of upper abdominal pain, weakness and fatigue. He gave a history of tarry stools for 2 months. He was pale and emaciated, the epigastrium was tender and the liver was enlarged (liver edge, 2 finger-breadths below the costal margin). The hemoglobin concentration was 3 g/dl and the hematocrit was 11%; occult blood was detected in stool samples. Barium and endoscopic examinations of both the upper and lower gastrointestinal tract were negative.

Laparotomy 6 weeks after admission did not reveal the source of bleeding, but a hard mass was felt in the head of the pancreas. Further endoscopic examinations were negative. An arteriogram 1 month after laparotomy (Fig. 1) indicated that the source of the bleed-

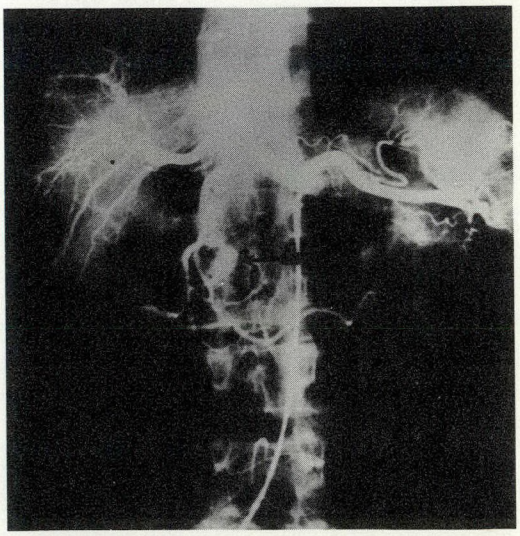

Fig. 1.—Arteriogram showing collection of contrast medium in pseudoaneurysm of pancreas (arrow).

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ing was either a duodenal ulcer or a pseudoaneurysm of the head of the pancreas.

A massive gastrointestinal hemorrhage 3 months after admission necessitated a second laparotomy. An extensive gastroduodenotomy revealed no evidence of duodenal or gastric ulceration, but blood mixed with bile was observed to be coming from the duodenal papilla. A Whipple's operation was started but the operation had to be abandoned because the portal vein was surrounded by acutely inflamed tissue and extensive fibrosis.

The postoperative course was complicated by peritonitis. A third laparotomy was performed. Gangrene and sloughing of the anterior duodenal wall were observed; these were not associated with the duodenotomy incision, which had healed well. The duodenum was necrotic and gangrenous; two Foley catheters were inserted into the second part of the duodenum with suction drainage. Necrosis of the proximal jejunum also required resection. Hyperalimentation was instituted. Recovery from the operation was satisfactory, but profuse bleeding recurred; he required a total of 64 units of blood.

Arteriography, repeated with the intention of occluding the pseudoaneurysm with Gelfoam emboli, showed that the pseudoaneurysm had doubled in size since the first arteriogram (Fig. 2). A direct branch of the gastroduodenal artery was identified as feeding the pseudoaneurysm, but this arterial branch could not be entered selectively because of the acute angle it made with the gastroduodenal artery. It was realized that Gelfoam embolization of the gastroduodenal artery might cause duodenal ischemia, and this, in view of the previous gangrene of the duodenum, was considered too hazardous. Instead, a guide wire (diameter, 0.95 mm) with a J-shaped tip was advanced through the catheter in the gastroduodenal artery, and the tip of the catheter was positioned in the artery leading to the pseudoaneurysm.* A clinical electrocoagulation unit (Valley-Lab SSE2-K, Boulder, CO 60301, USA†) (setting, 7) was used for 2.5 seconds. The guide wire was withdrawn. Injection of contrast medium demonstrated complete occlusion of the artery leading to the aneurysm (Fig. 3).

Since this procedure there has been no bleeding into the gastrointestinal tract. Length of follow-up is presently 40 weeks.

Discussion

A pseudoaneurysm of the pancreas is probably formed by digestive erosion of an artery close to the pancreas (e.g., splenic, gastroduodenal, or pancreaticoduodenal) by the enzyme activity of the contents of a

*Dr. R. E. Gold, department of radiology, University Hospital, London, Ont. performed this procedure.

†Canadian distributor: Sterisystems Ltd., 47 Baywood Rd., Rexdale, Ont. M9V 3Y9.

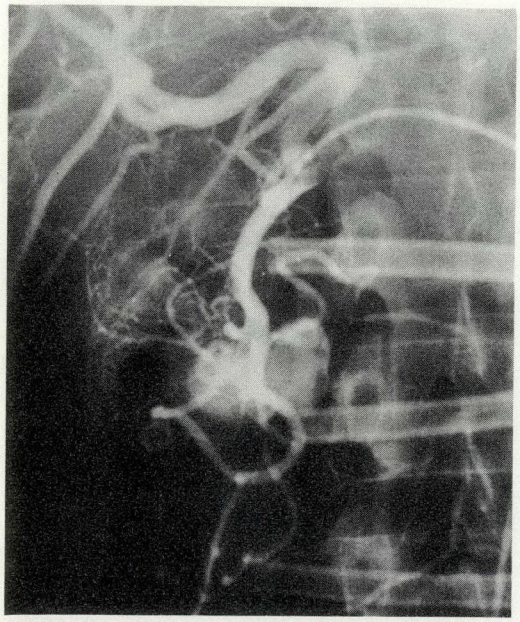


Fig. 2.—Second arteriogram. Note increased size of pseudoaneurysm, before electrocoagulation.

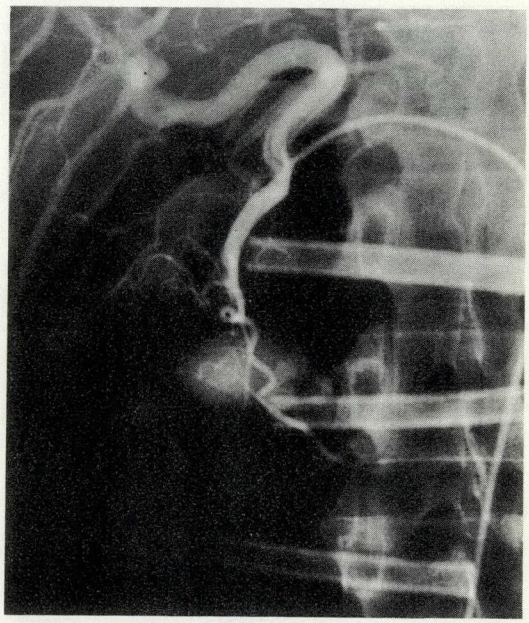


Fig. 3.—Third arteriogram. Note decreased size of pseudoaneurysm, after electrocoagulation.

The Effect of Trasylol® in Acute Pancreatitis

*** Results**

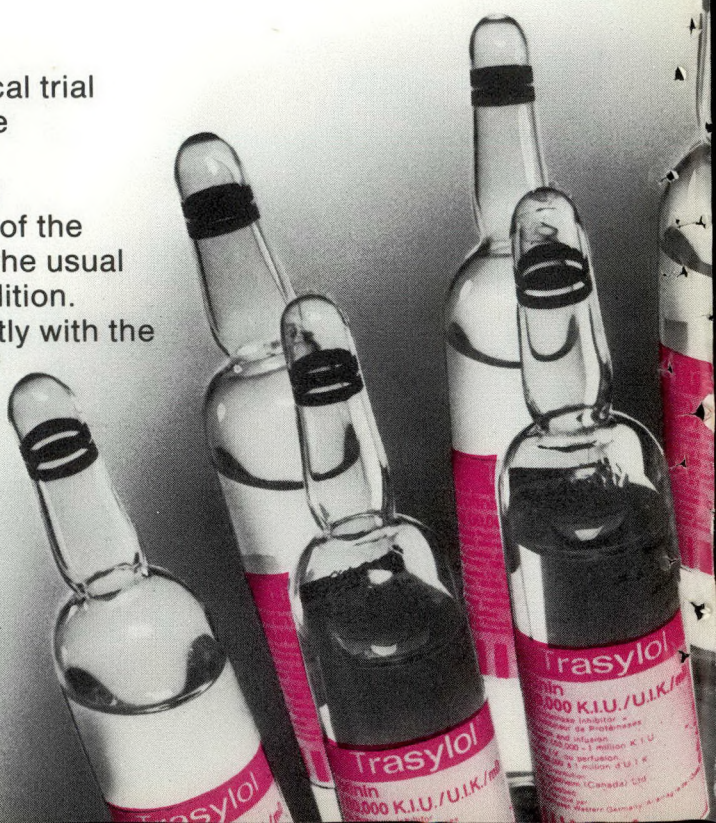
Course of illness	Group A (Trasylol)		Group B (Placebo)	
	No.	%	No.	%
Mild	30	56.6	22	42.3
Moderate	13	24.5	9	17.3
Severe	6	11.3	8	15.4
Died	4	7.5	13	25.0
Total	53	99.9	52	100.0

Trasylol® was shown to reduce mortality in acute pancreatitis to a significant extent:

Placebo ..... 25.0% Mortality
Trasylol® ..... 7.5% Mortality

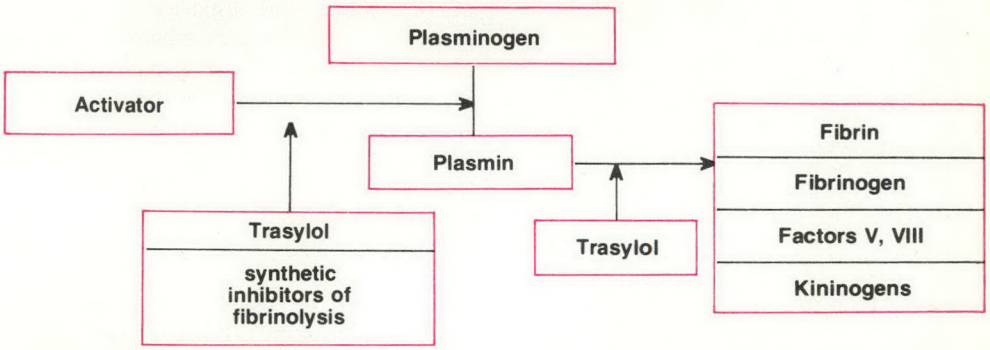
"Because the number of deaths were reduced, the spectrum of the disease as a whole was altered." *

Trapnell's recent double-blind clinical trial involving 105 patients confirmed the effectiveness of Trasylol in acute pancreatitis. In addition to reducing mortality and altering the spectrum of the disease, Trasylol largely abolished the usual effect of increasing age in this condition. Trasylol should be given concurrently with the usual measures for the treatment of pancreatitis, such as pain relief, fasting, gastric suction, etc. "It (Trasylol) can therefore now be regarded as a drug which is both effective and beneficial in the treatment of acute pancreatitis." *



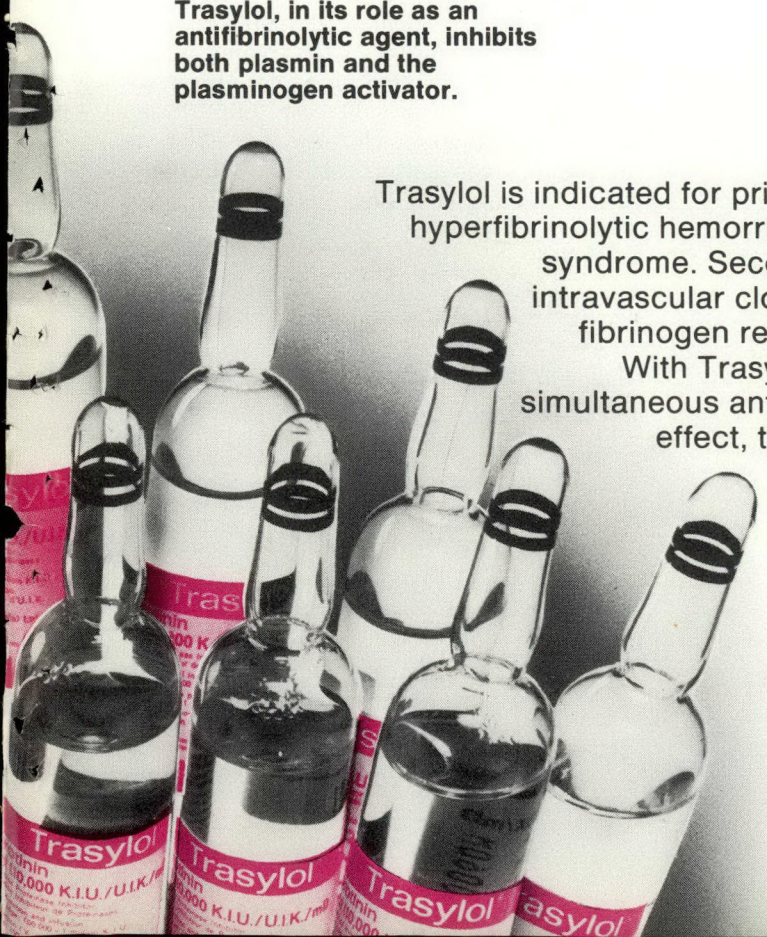
*Trapnell, J.E. et al, British J. Surg., March 1974.

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.

FBA Pharmaceuticals Ltd.
Distributed by:
Boehringer Ingelheim (Canada) Ltd.

pseudocyst. The wall of the pseudoaneurysm is subjected to arterial pressure and may either perforate into an adjacent segment of the gastrointestinal tract or, as in this case, into the pancreatic ductal system, leading to a severe hemorrhage.

Bleeding into the upper gastrointestinal tract can also result from gastric mucosal erosion during acute pancreatitis, but in such cases conservative treatment with blood transfusion is usually successful, and endoscopy confirms the pathologic basis of the lesion.

The introduction of selective angiography of the celiac and superior mesenteric arteries has been a major advance in the diagnosis and treatment of pseudoaneurysm of the pancreas. Not only is the diagnosis confirmed but also the feeding vessel is identified. Once the diagnosis has been made, treatment has generally been either a pancreaticoduodenectomy for a lesion in the head of the pancreas, or intracystic ligation of the feeding vessel, combined with cystogastrostomy or cystoduodenostomy. However, Greenstein, DeMaio and Nabseth[4] successfully treated a case by wiring the cystic cavity to induce thrombosis, and transcatheter occlusion of the feeding vessel with Gelfoam or clotted blood has also been successful. In the present case transarterial electrocoagulation of the artery leading to the pseudoaneurysm provided the selectivity of the vascular occlusion that was required.

We thank Dr. R. E. Gold of the department of radiology, University Hospital, London, Ont., for performing the diagnostic arteriography and the therapeutic electrocoagulation.

References

1. Palmer ED: *Upper Gastrointestinal Hemorrhage,* Springfield, IL, Thomas, 1970
2. Wolstenholme JT: Major gastrointestinal hemorrhage associated with pancreatic pseudocyst. *Am J Surg* 127: 377, 1974
3. Spanos PK, Kloppedal EA, Murray CA: Aneurysms of gastroduodenal and pancreaticoduodenal arteries. *Ibid,* p 345
4. Greenstein A, DeMaio EF, Nabseth DC: Acute hemorrhage associated with pancreatic pseudocysts. *Surgery* 69: 56, 1971

General Reference

Inglis FG, McKee NH: Unusual cause of upper gastrointestinal bleeding: rupture of splenic artery aneurysm into stomach with survival. *Can J Surg* 15: 276, 1972

BOOK REVIEWS

THE CERVICAL SPINE. Robert Wayne Bailey. 263 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1974. $21.75.

This book contains a remarkable amount of valuable information. It begins with coherent accounts of basic embryology and anatomy, and excellent reviews of neuroanatomy and neurologic diagnoses. The chapter on congenital anomalies by Poznanski particularly is detailed and informative.

The anterior approach to the spine, which Bailey helped to pioneer, is graphically illustrated in detail.

An interesting suggestion is made that at least some flexion deformities due to ankylosing spondylitis can be treated by skull traction followed by fusion, rather than by osteotomy as has been popularized by Urist and Simmons.

In the chapter on neurologic aspects of spinal injuries by Kahn one could question the advisability of laminectomy. In most instances, it seems that anterior decompression and stabilization is a more logical approach.

In summary, there is little extraneous material in this book which, as the author points out, is the first of its kind devoted entirely to the cervical spine, and as such is a most valuable source of information.

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FLUID, ELECTROLYTE AND NUTRIENT THERAPY IN SURGERY. Edward E. Mason. 352 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1974. $13.50.

This book covers a wider area than the title suggests. The opening chapters outline clearly the subjects of water balance, extracellular solute, carbon dioxide, and nonrespiratory defence of neutrality, with problems encountered in surgery. The author uses simple tests and clinical observations for abnormalities of volume, concentration and chemical composition. The chapter on water balance in particular is comprehensive yet succinct.

The ensuing chapters reflect the interests and works of the author. A valuable chapter, packed with important facts concisely but comprehensively, covers basic nutrition, and then intravenous hyperalimentation. Next follows a clear review of the various bypass operations used to treat extreme obesity. Among these, the gastric bypass, developed and used by the author is, in his opinion, the procedure of choice; and with respect to the intestinal bypass, Mason emphasizes too strongly fluid and electrolyte problems, which are actually not a general occurrence, with the procedure of Scott. Ileal bypass for hyperlipidemia is discussed, with an excellent presentation on the control of hyperlipidemia.

The chapters on circulation and shock and on acute renal failure are brief, fairly comprehensive, and up-to-date. A superb section on calcium and phosphorus metabolism comes next; it is packed with facts relevant to the surgeon. The book ends with a chapter on fluid resuscitation in the burned patient, by one of the author's colleagues, C. E. Hartford; it is an excellent summary of fluid replacement, covering all electrolyte changes including those resulting from topical treatment.

The bibliographies are pertinent and up-to-date. The book serves as a useful, concise and stimulating review of current electrolyte therapy and physiology in surgery.

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INSTRUCTIONAL COURSE LECTURES. Volume XXIII 1974. The American Academy of Orthopaedic Surgeons. 274 pp. Illust. The C. V. Mosby Company, St. Louis, 1974. $25.75.

The "Instructional Course Lectures" are well known to orthopedic residents and surgeons. This volume contains, as the editors have pointed out in their preface, a great deal of variety from the point of view of subject material and much that is of contemporary importance with regard to total joint replacement of the hip and knee.

Now that total replacements of the hip and knee are standard operative procedures for many orthopedic surgeons, it is becoming obvious that complications, some of which have been unpredictable, must be recognized and managed. There is much overlap in the large number of articles presented by surgeons from the United States who have been performing joint replacements since the concept was introduced in that country. However, this is not necessarily a fault at a time when the scope and concept of joint arthroplasty are expanding at an extremely rapid rate.

The series of articles on the role of the orthopedist in the management of juvenile rheumatoid arthritis attempts to be comprehensive and is reasonably successful in achieving this goal. An article by Fuller and Duthie on the timed appearance of some congenital malformations in orthopedic abnormalities is unique. White and his collegues have attempted

to make the biomechanics of the spine understandable for those without a biomechanical or engineering background. Much of the literature on biomechanics of the locomotor system is simply unintelligible to most orthopedic surgeons and residents, and this article deserves commendation for its approach.

This volume is highly recommended for its timing and for its content.

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INTRAVENOUS ANAESTHESIA. John W. Dundee and Gordon M. Wyant. 341 pp. Illust. Churchill Livingstone Edinburgh; Longman Canada Limited, Toronto, 1974. $34.25.

Since Dundee's book "Thiopentone and Other Thiobarbiturates" was published in 1956, an immense amount of literature concerning intravenous anesthetic agents, both barbiturate and nonbarbiturate, has accumulated. Both Wyant, joint author of this new book, and Dundee have made substantial contributions to the investigation of many of these agents; and as experienced anesthetists and investigators they have collaborated in a timely and comprehensive review of the present state of intravenous anesthesia.

The barbiturates, eugenols, steroids, tranquillizers, drugs used in neuroleptic techniques and those used to produce dissociative anesthesia are considered in turn. The chemistry and pharmokinetics of each group are discussed, followed by presentation and analysis of the laboratory and clinical evidence, and a thorough review of the clinical applications.

Thiopentone and methohexitone have been thoroughly investigated and extensively used for many years, yet the experimental evidence concerning them is often conflicting. The authors are to be congratulated for giving each item of evidence its due weight, indicating areas—particularly in relation to the newer agents—where knowledge is incomplete and further investigation is required. By drawing on their combined clinical wisdom and investigational experience, the authors have succeeded in summarizing a wealth of detail. The use of historical data reminds us that newer techniques have their origins in the past, and that the place of some of the newer agents in anesthetic practice has yet to be finally evaluated.

This book offers a useful perspective to those already in clinical anesthetic practice and is a useful reference source for those engaged in research. It should also be required reading for all residents in anesthesia.

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KAZANJIAN & CONVERSE'S SURGICAL TREATMENT OF FACIAL INJURIES. Vols. 1 and 2. 3rd ed. John Marquis Converse. 1482 pp. Illust. The Williams & Wilkins Company, Baltimore; Burns & MacEachern Limited, Toronto, 1974. $74.25.

The third edition of this book has been published in two volumes—a practical improvement since each volume is now handy to read —and the whole text of this work has been revised and updated.

The first volume is divided into chapters on the comparative phylogeny of the face, wound healing, and a résumé of plastic surgical techniques as adapted to maxillofacial surgery.

There follow sections on the treatment of facial fractures, on the mandible, the maxilla, the nose, the zygoma and the orbit. Indications for the simple closed, or operative open reduction of fractures, and more elaborate treatments are detailed.

The coverage of external fixation devices (Roger Anderson, acrylic resin splint) is now more complete, though outmoded plaster head splints are still advocated. Chapters concerning facial fractures in children, naso-orbital and fronto-ethmoidal fractures are more detailed and contain practical case histories.

In the field of craniofacial surgery for congenital malformations the author has been greatly influenced by advances made by fellow workers.

It was a pleasure for me to see that in the traumatic Lefort I osteotomy, immediate bone grafting at the pterigomaxillary junction is proposed for the comminuted, middle third fractures. Also, techniques of craniofacial surgery are applied to traumatic lowering of one orbital frame or hypertelorism.

The second volume is dedicated to reconstructive surgery. The chapter on rhinoplasty is improved by the accompaniment of coloured drawings. Also included are the extramucous rhinoplasty and correction of septal perforations. Concerning mandibular and maxillary deformities, contemporary methods of vertical osteotomies with bone grafting, sagittal split of the mandible, Lefort I, II and III osteotomies with their relative indications, have all been added with due credit to their initiators. More delicate and complex segmental and infrabasilar osteotomies are well explained and demonstrated. Soft-tissue reconstructions are

also covered, with special attention to the burned face.

This work is a basic textbook that should be in the library of every resident interested in or dealing with plastic surgery and facial fractures. Every plastic and maxillofacial surgeon would be well advised to own this new edition.

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PROGRESS IN CARDIOLOGY. 3. Edited by Paul N. Yu and John F. Goodwin. 349 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1974. $18.95.

"Progress in Cardiology" is a relatively new addition to the growing number of publications in cardiology that attempt to review existing knowledge in this field. This book, an annual publication, maintains the excellent standard set in previous years. The range of topics covered is broad enough that major sections should have wide appeal for the student, researcher, or practitioner of cardiology. Although it appears to be more suitable for the cardiologist, the book includes subjects that should be of immediate interest to the practising cardiovascular surgeon. The areas covered by this monograph include: reviews of the epidemiologic considerations in coronary artery disease; the anatomy and physiology of cardiac impulse formation and conduction; the physiology of ventricular arrhythmias; the use of exercise stress testing; the early clinical course following acute myocardial infarction; the renin angiotensin system in hypertension; the Eisenmenger syndrome; the effects of adrenergic blockade on the heart; cardiac valve replacement; prevention of thrombosis; echocardiography; and measurement of pulmonary water.

Each subject is timely and detailed. Most bibliographies are well referenced and provide a good source for further study. The editors appear to have given each of the contributors considerable latitude in preparing their reviews. As a result, most of the subjects dealt with are complete and up-to-date.

This monograph is an excellent source of current information. The price is quite reasonable considering its size.

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SURGICAL DISEASE IN PREGNANCY. Hugh R. K. Barber and Edward A. Graber. 763 pp. Illust. W. B. Saunders Company, Philadelphia; W. B. Saunders Company Canada Limited, Toronto, 1974. $32.45.

This comprehensive, complete review of the subject deals with every aspect of pregnancy, especially within the realm of surgery encountered by obstetricians and gynecologists. It also includes discussions on every other subspecialty of surgery, as each relates to pregnancy, including general topics on body fluids, radiation and chemotherapy. The editorial comments included with each chapter add to the excellent format of the book. The contributing authors are well known in their fields. I highly recommend this text as a reference book, especially for those preparing for final examinations.

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VASCULARIZATION AND TISSUE DIFFERENTIATION. F. A. Kiss. 167 pp. Illust. Akadémiai Kiadó, Budapest, 1975. $9.50. Paperbound.

This paperback reviews the current status of tissue revascularization into newly growing tissues. Although its title will not attract the attention of physicians unfamiliar with this particular field, the relevant research attains great import in view of our great and continual dependence on angiogenesis and tissue neosynthesis in surgical practice, in which wound healing, fistula closure and osseous union, for example, are so important.

What accounts for the successful repair and regrowth of tissues following injury? Available evidence, the author informs us, leans heavily toward the view that the initial step is the appearance of mesenchymal cells, which differentiate into capillary and red blood cells. These primitive cells then differentiate into the appropriate tissue being repaired. This introduction to the subject is followed by a series of sophisticated short papers that summarize much of the important experimental data from the field. The experiments described, many of which are the author's own work, are artfully detailed with regard to technique and method; they are also arranged in a logical, orderly sequence and each develops a cogent point, neatly and succinctly summarized, before being applied in the development of the hypothesis for the subsequent experiment. All of these

data are adroitly illustrated with simple and easily decipherable light and electron photomicrographs.

The book's main theme centres around the effects of adrenal extract, which appears to have potent angiogenic and osteogenic properties and which also is capable of stimulating vascularization in scar keloid, cornea, cartilage and even the myocardium. Hence, the number of potentially interested readers of this monograph would have to be expanded to include orthopedic and plastic surgeons who are interested in ways of bringing new blood supply to nonhealing bones or soft tissue.

Overall I rate the book as good, with limited usefulness for the clinician who reads this journal; but for anyone particularly interested in wound healing I rate it as excellent. Unfortunately the binding of my copy was of extremely poor quality and split with the first reading.

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THE YEAR BOOK OF PLASTIC AND RECONSTRUCTIVE SURGERY 1975. Editor: Frederick J. McCoy, Associate editors: Reed O. Dingman, John C. Gaisford, B. W. Haynes, Jr. and others. 351 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1975. $25.00.

This book contains chapters on: the head; the skin, subcutaneous tissue and hair; the neck and thorax, the abdomen and genitalia; the extremities; burns; surgical management, including shock, and wound healing; neoplasms; transplantation; and general topics. The selection of the content reflects the fact that the overall choice of articles submitted to the medical editors for their consideration in this book was not originally done by specialists in the field There is a great emphasis on articles chosen from the two journals, *Plastic and Reconstructive Surgery* and the *British Journal of Plastic Surgery*—an emphasis that is probably unnecessary, as specialists in this field read these journals already. There is also too much emphasis on case reports, but not enough on general review articles. The abstracts are too detailed to be skimmed through quickly and yet not detailed enough to obviate reading the original article if there is an interest in that subject. The indexing is sometimes difficult to follow.

Although this book does not cover well the entire world literature, it will be useful to the surgeon who cannot readily consult a large medical library, because it does contain abstracts from journals that are not readily accessible.

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NOTICES

LENS IMPLANTATION SEMINAR

A seminar on intraocular lens implantation will be held on Nov. 15, 1975, at the Queen Elizabeth Hotel, Montréal. Speakers include Miles Galin, Henry Hirschman, Norman Jaffe, Marvin Kwitko and Donald Praeger. The seminar covers the basic principles and indications of the intraocular lens. The lens models presently used (Binkhorst, Copeland, Worst, Fiederov) will be described and the means used in implantation at the time of intracapsular, extracapsular, and phacoemulsification cataract extraction will be demonstrated. The technique of implanting an intraocular lens in an aphakic eye will be covered. Preoperative, operative and postoperative care will be emphasized. The long-term results of the faculty members will be detailed. Formal lectures will be combined with individual instruction. For further information, write to: Dr. M. L. Kwitko, 5591 Côte des Neiges Rd., Suite 1, Montréal, Qué. H3T 1Y8.

SURGICAL RESEARCH

The 11th Congress of the European Society for Surgical Research (formerly the European Society for Experimental Surgery) will be held in Dublin, Ireland, on Apr. 27-30, 1976. Further information concerning this meeting may be obtained from: The Irish Medical Association, Conference Centre, 10, Fitzwilliam Place, Dublin 2, Ireland.

INDEX TO ADVERTISERS

Books Received

Acute Aortic Dissections. Constantine E. Anagnostopoulos. 255 pp. Illust. University Park Press, Baltimore, 1975. $24.50.

Clinical Embryology for Medical Students. 2nd ed. Richard S. Snell. 481 pp. Illust. Little, Brown and Company (Inc.), Boston, 1975. $12.50, paperbound; $17.50, clothbound.

Colpopoiesis from the Colon. M. Kun. 173 pp. Illust. Akadémiai Kiadó, Budapest, 1975. $11.00.

Common Duct Stones. Frank Glenn. 135 pp. Illust. Charles C Thomas, Publisher, Springfield, IL, 1975. $11.50.

A Concise Surgery of the Acute Abdomen. John A. Shepherd. 208 pp. Churchill Livingstone, Edinburgh; Longman Canada Limited, Toronto, 1975. $19.75. Paperbound.

Current Management of Trauma in Surgery and General Practice. Edited by Teruo Matsumoto. 382 pp. Illust. Charles C Thomas, Publisher, Springfield, IL, 1975. $23.50.

Digestive Surgery. Proceedings of the 2nd World Congress of "Collegium Internationale Chirurgiae Digestivae" Strasbourg, June 9-10-11, 1972. Edited by L. F. Hollender and G. D'Onofrio. 969 pp. Illust. Piccin Medical Books, Padua, 1974. $60.00.

Hoffmann's Double Frame External Anchorage. Methods, Applications and Results in 160 Observations. Henry Connes. Translated by W. A. Birnbaum. 117 pp. Illust. Editions GEAD, Paris, 1973. F 90,00. $2.20 (approx.). Paperbound.

Physiological Basis of Anaesthesiology. Theory and Practice. Proceedings of the First International Seminar (Milan—May 17-20, 1973). Fondazione Giovanni Lorenzine. Edited by W. W. Mushin, J. W. Severinghaus, M. Tiengo and S. Gorini. 367 pp. Illust. Piccin Medical Books, Padua, 1975. $16.00.

Problems of Recurrent Hernia. Robert C. Kimberly. 63 pp. Illust. Charles C Thomas, Publisher, Springfield, IL, 1975. $6.50. Paperbound.

Salivary Glands and the Facial Nerve. John Conley. 391 pp. Illust. Grune & Stratton, New York, George Thieme Publishers, Stuttgart; Longman Canada Limited, Toronto, 1975. $98.00.

Stress Fractures. Michael Devas. 240 pp. Illust. Churchill Livingstone, Edinburgh; Longman Canada Limited, Toronto, 1975. $54.00.

Surgery of the Liver, Pancreas and Biliary Tract. Edited by John S. Najarian and John P. Delaney. 658 pp. Illust. Stratton Intercontinental Medical Book Corporation, New York; Longman Canada Limited, Toronto, 1975. $28.00.