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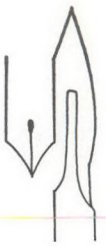

QUILL ON SCALPEL This section provides a medium through which Canadian surgeons can declare themselves, briefly and informally, on the day-to-day affairs of surgery.

TREATMENT OF CARCINOMA OF THE THYROID GLAND

IT is time that surgeons faced the facts concerning thyroid carcinoma. Total thyroidectomy is recommended in current textbooks and training programs as the treatment of choice for papillary or follicular cancers of the thyroid and some even recommend radical neck dissection if any local lymph-node spread is present. Advocates of total thyroidectomy seem undeterred by the lack of evidence that the extent of surgical resection influences the outcome. Careful assessment of the available evidence is required rather than opinions based on traditional concepts.

Black, YaDeau and Wollner[1] reviewed 418 cases of papillary carcinoma of the thyroid in patients followed-up over a 30-year period. The 10-year survival rates were 84 and 90% for patients with lesions greater and smaller than 1.5 cm in diameter, respectively, regardless of involvement of lymph nodes. The operations performed ranged from a subtotal lobectomy to a total thyroidectomy. Crile[2] followed 107 consecutive patients with papillary cancer of the thyroid for a median period of 11 years. There were 10 deaths, all within 5 years of the initial operation. The surgical procedure varied but most patients had a lobectomy. Medina and Elliott[3] reported 130 cases of thyroid cancer treated by operations ranging from subtotal lobectomy to total thyroidectomy with neck dissection, in approximately equal numbers, by 24 different surgeons. The survival could be related only to the age of the patient at diagnosis and the histologic type of the tumour. Complications were related to the magnitude of the operation, as would be expected. The 10-year survival in cases of papillary or follicular lesions was similar to that reported by others.[1, 2, 4] No reports in the literature suggest that radical local treatment for papillary or follicular lesions influences the prognosis, which is relatively good in any case. Although medullary carcinoma of the thyroid exhibits different behaviour with more rapid progression, evidence that the extent of resection alters the outcome is also lacking.[5]

The presence of multiple foci of cancer in the thyroid gland is often cited as an argument for radical local treatment. Nobody would dispute that multiple foci of papillary cancer often can be demonstrated histologically. The reported rate of multifocal malignant lesions ranges from 30%[6] to 87.5%[7] and perhaps this figure would be increased to 100% if the histologic search were intensive enough. One must, however, consider performance. It is rare for overt carcinoma to develop in a residual thyroid lobe.[6] What, then, is the natural history of these histologic foci of cancer stressed so greatly by some surgeons? What of the rate of histologically proven carcinoma in multinodular goitres that varies from 4 to 15% in different series?[8-11] It is estimated that thyroid nodules develop in approximately 5% of the adult population.[12, 13] According to Statistics Canada the annual death rate from cancer of the thyroid between 1950 and 1973 has remained fairly constant at around 6/1 million population.[14, 15] Even if one accepted the lowest figures for reported cases of nodular goitres and malignant lesions one would have to deduce that many people harbouring carcinoma in their thyroid glands live a normal life span without overt evidence of the disease.

There are only two possible explanations for these facts. First, in histologic appearance, a malignant tumour in many thyroid specimens may be a normal variant, which

is erroneously labelled "cancer" by the pathologist. Second, differentiated carcinoma of the thyroid may indeed be common, but if so, in most cases it must be confined by some unknown mechanism to a strictly localized microscopic disease. Whichever explanation proves to be true, one must conclude that radical operative procedures on the thyroid gland are irrelevant. Eventually immunologists may give us a better understanding of these facts but in the meantime the facts cannot be ignored.

It has also been argued that, for papillary and follicular tumours, once surgical treatment is complete, an ablative dose of iodine-131 (^{131}I) should be given to eliminate any residual thyroid tissue in the neck.[16] This is indeed aggressive therapy for such a disease. What potential benefit to the patient is evidenced by such treatment in exchange for its discomforts and hazards?

At the opposite end of this histologic spectrum, anaplastic thyroid tumours present a dismal prognosis. No form of therapy appears to influence the disastrous course except for short-term palliation. Why, then, do many surgeons recommend aggressive surgical and radiation therapy?

The message is clear. Papillary or follicular carcinoma of the thyroid should be locally excised. In most cases this means a subtotal or total lobectomy depending on the size of the tumour in relation to the size of the thyroid lobe: the remainder of the gland should be left alone if it is normal to palpation. Lymph nodes should be removed singly or in groups only when they contain tumour. The theoretical rationale for the use of thyroxine therapy is reasonable, though again it remains to be proved that thyroxine reduces the rate of clinical recurrence. Ablative ^{131}I therapy should be used only in patients with overt evidence of widespread disease. For anaplastic tumours therapy should be designed to offer meaningful palliation if and when possible.

The concept that the outcome for a patient with cancer is largely dependent on the extent of the surgeon's intervention is indeed attractive as a raison d'être for surgical intervention. The evidence, however, suggests otherwise and any surgeon performing radical procedures for carcinoma of the thyroid gland must ask himself what he is attempting to achieve in the light of the natural history of the disease.

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PELVIC EXENTERATION FOR CARCINOMA OF THE RECTUM

The overall rate of cure for carcinoma of the rectum is in excess of 50%. Pelvic recurrence is, however, a major technical problem. Several techniques have been tried to avoid suture-line recurrence after low anastomoses. These have included the "no touch" technique, use of iodized catgut, and rectal irrigation using water or chemical agents. In addition, preoperative radiation prior to abdominoperineal resection has been used, and pelvic exenteration has been effective in certain selected cases.

Cohen of the Massachusetts General Hospital recently reported (Abdominal Surgery *18: 25, 1976*) *his experience with a 49-year-old Negro woman admitted to hospital initially with vaginal bleeding. On palpation, a mass was present at the apex of the vaginal cuff, contiguous with a large rectal mass and the base of the bladder. At operation an ulcerating lesion measuring 4 x 6 cm was found 7 cm from the anal verge. A total pelvic exenteration with sigmoid colostomy and ureteroileal conduit was carried out. A flap of greater omentum was used to reconstruct the pelvic floor.*

Cohen points out that in patients who have rectal cancers with extensive lateral or posterior transmural invasion there is high risk of local recurrence. As many as 50% of pelvic recurrences involve structures anterior to the rectum, including the posterior vaginal wall, the cervix, uterus, bladder, prostate and seminal vesicles. When used for primary treatment of rectal cancers, cure rates with pelvic exenteration have been about one in three. However, pelvic exenteration is not an effective procedure to treat recurrences after abdominoperineal resection.

REVIEW ARTICLE

GASTROINTESTINAL HORMONES*

STEPHEN N. SULLIVAN, MD†

The availability of pure intestinal hormones and the development of radioimmunoassays for their measurement has expedited research into many aspects of gastrointestinal endocrinology. A complex balance evidently exists between the different intestinal hormones and also the rest of the endocrine system. Polyendocrinopathies have been described, and, so far, two diseases due to intestinal hormone excess (Zollinger-Ellison syndrome and the syndrome of watery diarrhea, hypokalemia and achlorhydria) elucidated. It seems likely that many more gastrointestinal endocrine diseases await discovery.

La disponibilité d'hormones intestinales pures et la mise au point de méthodes radio-immunologiques pour en faire le dosage ont stimulé la recherche dans plusieurs champs de l'endocrinologie gastro-intestinale. Un équilibre complexe existe évidemment entre les différentes hormones intestinales tout comme le reste du système endocrinien. Des polyendocrinopathies ont été décrites et jusqu'à maintenant, on a pu élucider deux maladies causées par une hypersécrétion d'hormone intestinale (le syndrome de Zollinger-Ellison et le syndrome de diarrhée liquide avec hypokaliémie et achlorhydrie). Il semble probable que plusieurs autres maladies endocriniennes gastro-intestinales seront découvertes.

IT is now evident that not only is the gastrointestinal (GI) tract a major endocrine organ[1] but also that there are complex relations between intestinal hormones and other endocrine organs. Two elaborate reviews on the subject have recently become available,[2, 3] and, in another publication, I published a brief summary.[4] The pertinent literature is made complex by interspecies variations and by the experimental use of nonphysiologic doses of impure hormones. In this paper I shall try to confine discussion to data obtained, where available, from the use of relatively pure hormone preparations in man.

APUD CELLS

The endocrine polypeptide cells of the gut belong to a family of cells to which, from their cytochemical and ultrastructural characteristics, the acronym Apud (amine precursor uptake and decarboxylation) refers. These cells, also found in the pituitary, thyroid and adrenal glands, and the pancreas and lungs[5] (Table I) are believed to be of neuroectodermal origin and to migrate from the neural crest.[6] The common origin of these cells may partially explain both the common amino-acid sequences in different hormones and some of the polyendocrinopathies — Wermer's syndrome (pituitary adenoma, islet cell tumour, parathyroid adenoma or hyperplasia) and Sipple's syndrome (medullary thyroid carcinoma, pheochromocytoma, parathyroid adenoma or hyperplasia).[7, 8] Tumours of this cell series have been termed apudomas.[9]

TABLE I.—HORMONES PRODUCED BY APUD CELLS

Cell type	*Hormone produced*
Gut polypeptide cells	Gastrin, secretin, CCK, "enteroglucagon", GIP, VIP, motilin
Pituitary melanotroph	MSH
Pituitary corticotroph	ACTH
Parafollicular C cell	Calcitonin
Pancreatic β cell	Insulin
Pancreatic α_2 cell	Glucagon
Pancreatic α_1 cell	Gastrin
Adrenal medulla	
Carotid body	
"Endocrine cells' of the lung	

The nomenclature for these cells is complicated and is in a state of flux; the trend seems to be to name the cells for the hormone they produce.

MODE OF ACTION OF GI HORMONES

The mechanism of release of GI hormones is not known but evidence points to cholinergic and adrenergic pathways. Anticholinergics inhibit the pancreatic secretory response to secretin releasers more than the response to exogenously administered secretin;[10] topical anesthetics applied to the intestinal mucosa reduce the response of the pancreas to intestinal stimulants,[11] and

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hexamethonium prevents the release of cholecystokinin (CCK).[12] Infusions of physiologic doses of adrenalin are known to release gastrin,[13] an effect that may be inhibited by β blockade. In the future, stimulators and inhibitors of GI-hormone release may be of therapeutic value in the management of diseases of GI-hormone deficiency and excess, which are sure to be described.

GI-hormone receptors have not been described but Grossman[14] has postulated that gastrin, CCK, secretin and glucagon act on one receptor with two interacting sites. Gastrin and CCK, which share a terminal pentapeptide, are thought to act at one site, and secretin and glucagon, which also have structural similarities, at the other. The result of a simultaneous action of hormones depends on whether it leads to competitive or noncompetitive augmentation or inhibition.

Gastrin and CCK are believed to act on the lower esophageal sphincter (LES) and small bowel by stimulation of postganglionic cholinergic neurons.[15] Their action on the gallbladder, however, may be through direct stimulation of the muscle.[16] One intestinal hormone, motilin, may act through direct release of acetylcholine from nerve endings.[17]

The histamine H_2-receptor antagonists metiamide and cimetidine are universal blockers of all gastric secretory stimuli, including vagal stimulation, gastrin, cholinergic agents, histamine and food,[18, 19] and it may be that histamine is the final step in the mode of action of all gastric stimulants.

Biochemically, the mode of action of intestinal hormones is still speculative. Cyclic adenosine monophosphate (AMP) is a factor in intestinal secretion[20] and prostaglandin activity,[21] and, while it is probably true that cyclic nucleotides mediate some of the action of intestinal polypeptide hormones, there is still not sufficient proof to implicate them.

Proven GI Hormones

Gastrin

Gastrin, the most extensively studied of the GI hormones, exists in several molecular forms (Table II[22-25]); however, the nomenclature for the different forms has not been standardized and each investigative group uses its own terms.

Three gastrin species have, by means of gel filtration, been reliably identified — gastrin-34, gastrin-17 and gastrin-13 — according to the number of amino-acid residues they contain.[22] The C-terminal amino-acid sequences of each molecule are identical and each may exist in a sulfated or nonsulfated form.

Gastrin-34 corresponds to the "big gastrin" of Yalow and Berson.[26] It is the major circulating form of gastrin in the fasting state and its secretion is stimulated by feeding; its half-life is reportedly 9 to 15 minutes.[27, 28] Gastrin-17, the heptadecapeptide form, is also released by feeding and has a serum half-life of 3 to 5 minutes. Gastrin-13 is a "minigastrin" with a short half-life of 1.8 minutes.[25, 29] Gastrin-34 and lesser amounts of gastrin-17 are the major circulating forms in pernicious anemia and the Zollinger-Ellison syndrome (ZES).

Three other forms of gastrin have been found in the circulation and in tissues. The biologically inactive N-terminal tridecapep-

TABLE II.—Species of Gastrin

Investigative group and nomenclature				*Properties*			
Walsh[22]	*Rehfeld*[23]	*Yalow*[24]	*Gregory*[25]	*Gram formula weight*	*Amino acids*	*Release by food*	$T_{\frac{1}{2}}$ *(min)*
—	mixture of large molecules	"Big, big gastrin"	—	20 000	?	No	90
—	Component I	—	—	Similar to proinsulin	?	?	?
Gastrin-34	Component II	"Big gastrin"	"Big gastrin"	~3900	34	Yes	9-15
Gastrin-17	Component III	Gastrin	"Little gastrin"	~2100	17	Yes	3-5
Gastrin-13	Component IV	—	"Minigastrin"	~1600	13	?	1.8

tide of gastrin-17 has been identified by selective radioimmunoassay in the serum of patients with gastrinoma.[30] A "big, big gastrin" found in the jejunum and serum of healthy individuals and in the serum and tumour tissue of patients with gastrinoma has been isolated by Yalow and others[24, 31] from the void volume of Sephadex gel filtration columns; serum concentrations are not affected by feeding and this form of gastrin circulates with a half-life of approximately 90 minutes. Rehfeld, Stadil and Vikelsoe[32] and Rehfeld[23] have found a gastrin designated Component I, that, since it elutes just before gastrin-34 on Sephadex G50-SF columns, is presumably larger than gastrin-34. These workers, however, have not been able to identify a homogeneous "big, big gastrin" and they suggest that it may be a heterogeneous mixture of gastrin species of differing sizes.[32]

Gastrin exists in large quantities in the gastric antral G cells and proximal duodenum and in lesser amounts in the gastric cardia, pancreatic islet D or α_1 cells, and in progressively diminishing amounts along the intestinal mucosa.[33] The relative amounts of the larger molecular species appear to increase further down the intestine.

The major stimuli for gastrin release are those associated with eating — vagal stimulation, antral distension and the contact of protein products with the gastric antrum. Besides these physiologic stimuli several pharmacologic stimuli are also known to release gastrin, including calcium (intravenous or oral),[34] epinephrine[13] and bile salts.[35] The release of gastrin by epinephrine has been suggested as the explanation for elevated gastrin levels in pheochromocytoma[36] and for the release of gastrin during insulin hypoglycemia after complete vagotomy.[37, 38] These effects may be prevented by either α or β blockade.[36, 39]

Inhibition of gastrin release follows acidification of the gastric antrum to a pH below 3. (Alkalinization of the antrum may enhance gastrin release by preventing feedback inhibition by acid, and the loss of antral acidification in pernicious anemia and atrophic gastritis leads to sustained gastrin release and high serum levels; elevated gastrin levels have also been reported in rheumatoid arthritis[40] but the reason for this elevation is not known.) Glucagon[41, 42] and secretin,[43, 44] which normally decrease gastrin release (and inhibit the action of gastrin), cause a paradoxical increase in patients with ZES. This has been suggested as a diagnostic test for this syndrome, as has calcium infusion.[45]

Recently, serum concentrations of calcitonin, the hypocalcemic hormone produced by the parafollicular C cells of the thyroid, have been shown to be elevated in ZES. Conversely, medullary carcinoma of the thyroid, a calcitonin-producing tumour, is associated with low serum-gastrin concentrations.[46] These data suggest that gastrin stimulates calcitonin release and that calcitonin, in turn, inhibits gastrin release. As well as inhibiting gastrin release in large doses, calcitonin also inhibits the acid secretory effects of gastrin in smaller doses.[47]

Anticholinergics, such as atropine, will block the vagal release of gastrin but will not prevent gastrin release during feeding. Anticholinergics will also impair the gastric secretory response to gastrin.

The major physiologic effects of gastrin appear to be related to gastric secretion of acid, pepsin and intrinsic factor. Gastrin may also be a major determinant of pressure in the normal LES,[48] though there is controversy on this point.[49, 50] Other secretory and motor effects have been observed on the pancreas, biliary tree and intestine (Table III[51-53]). Gastrin also has trophic effects on the stomach, duodenum and pancreas[54-56] and stimulates the secretion of secretin,[57] insulin[58] and calcitonin.[59] At present, these actions appear to have minor physiologic significance.

The sites of gastrin degradation have not

TABLE III.—ACTIONS OF GASTRIN

Secretory
Acid, pepsin and intrinsic-factor secretion
Pancreatic enzyme production
Increase in bile flow
Secretin stimulation, insulin and calcitonin release
Decrease in intestinal salt and water absorption[51]
Motor
Increase in LES pressure
Increase in gastric motility
Relaxation of ileocecal valve and sphincter of Oddi[52]
Weak intestinal motility stimulant[53]
Miscellaneous
Trophic effects on stomach, duodenum and pancreas

been fully defined, but evidence suggests that the small bowel,[60] gastric fundus[61] and kidney[62-64] are important in gastrin clearance. These organs[59, 60, 61, 63] appear to extract gastrin during stimulated gastrin release but not under basal conditions. Nephrectomy prolongs the half-life of gastrin,[62] and patients with acute[65] and chronic renal failure[66] have elevated basal gastrin levels. In our laboratory prolonged circulation of gastrin has been demonstrated in uremic patients following a test meal.[67] The loss of gastrin-degrading function in uremia may not be related to loss of glomerular filtration rate, but to the loss of normal functioning renal mass.[68] The liver appears not to be a major degrader of gastrin and, in contrast to the rapid inactivation of pentagastrin by the liver, exogenous and endogenous gastrin are not appreciably affected by passage through the portal circulation.[69, 70]

Cholecystokinin

Cholecystokinin is a 33-amino-acid polypeptide, released from the mucosa of the upper small bowel by the hydrolyzed products of fat and protein digestion, by high concentrations of acid,[71] and possibly by magnesium sulfate.[72] The five C-terminal amino-acid residues are similar to gastrins. This structural similarity to gastrin may account for some of the effects of CCK. In the presence of gastrin, CCK may act as a competitive antagonist of gastrin but in its absence acts as a partial agonist of some of the effects of gastrin.

The major effects of CCK (Table IV[73-75]) relate to stimulation of pancreatic enzyme secretion and contraction of the gallbladder. It also has motor effects on the sphincter of Oddi, small intestine,[72] colon[67] and pyloric sphincter.[77] Impure preparations may stimulate pancreatic glucagon and insulin secretion[78] but highly purified CCK has no effect.[2]

TABLE IV.—ACTIONS OF CHOLECYSTOKININ

Pancreatic enzyme secretion
Gallbladder contraction
Relaxation of sphincter of Oddi
Intestinal and colonic motility
Increase in pyloric sphincter pressure
Competitive inhibition of gastrin
Stimulation of gastric secretion in absence of gastrin
Release of alkaline phosphatase from small intestine[73]
Release of intestinal disaccharidases[74]
Small intestinal secretion[75]

Research into the effects of CCK has been hampered by the lack of a reliable radioimmunoassay for the hormone and of readily obtainable pure hormone. Commercially available CCK preparations may contain only 20% by weight of CCK. Radioimmunoassays for CCK have been reported[79, 80] but these have not yet been proved reliable. Thus, biologic assays have been used for CCK and, experimentally, the synthetic octapeptide of CCK or cerulein (a decapeptide structurally similar to CCK and obtained from the skin of the Australian tree frog *Hyla caerulea*) are frequently used.

Secretin

This topic was reviewed in 1972 by Hubel.[81]

Secretin is a 27-amino-acid polypeptide. Fourteen of the amino acids occupy the same position in secretin as in glucagon. Secretin is produced by the small granular S cells in the transitional zone between the crypts and the villi of the upper small bowel.[82]

The chief stimulus for release of secretin is duodenal acidification. The threshold for release is approximately pH 4.5 and the amount of secretin released is believed to be related to the rate of acid input and, hence, the length of bowel acidified. (However, the physiologic role of acid alone in stimulating secretin release has been questioned,[83] since the pH necessary for such release may not be present in the postcibal period.) Secretin may also be released by protein,[84] gastrin and bile salts.[85] The question of whether secretin is released by vagal stimulation or the products of fat digestion has not been resolved.

The main physiologic effect of secretin is stimulation of pancreatic volume and electrolyte secretion. Besides its effects on the pancreas, secretin has positive and negative secretory and motor effects elsewhere in the GI tract (Table V[73-76, 86-90]). It decreases the release of gastrin[91] and acts as a noncompetitive inhibitor of gastrin on the gastric parietal cells and the LES.[92]

Secretin may be a factor in the pathogenesis of peptic ulcer. The positive inotropic effects of secretin on the pyloric

sphincter[93] may be important in preventing duodenogastric reflux, which is thought to be of etiologic significance in gastric ulcer.[94] Impaired secretin release has been demonstrated in patients with duodenal ulcers[95] while exogenous secretin is a strong inhibitor of meal or pentagastrin-induced gastric secretions in such patients.[96]

Enteroglucagon

A substance with glucagon-like immunoreactivity has been identified in the intestinal mucosal L cell, gastric mucosal A cell and in plasma.[97, 98] There are species variations in mucosal location, and its exact location in man has not been identified. It appears, however, that the largest quantities are found in the ileum.[99] It can be distinguished from pancreatic glucagon by selective immunoassay and by its molecular weight (approximately 7000), which is twice that of a major pancreatic glucagon fraction.[100] Like gastrin, it may exist in small and large molecular forms.[101]

Unlike pancreatic glucagon, it is released into the circulation by glucose[98] and long-chain triglycerides.[102] After a partial gastrectomy[103] or vagotomy and pyloroplasty[104] (particularly in patients with a "dumping syndrome") and in patients with essential alimentary hypoglycemia (vide infra) large amounts of enteroglucagon may be liberated into the circulation following the ingestion of carbohydrates.

Enteroglucagon appears to be devoid of glycogenolytic activity and it has been hypothesized that it may competitively inhibit the hepatic actions of pancreatic glucagon.[105] Whether it stimulates insulin release has not been resolved, but available evidence suggests that it does not, since galactose, fructose, xylose, mannose and 3-0-methyl glucose all raise serum levels of enteroglucagon without affecting insulin levels.[106]

TABLE V.—ACTIONS OF SECRETIN

Secretory
Pancreatic volume and bicarbonate secretion
Increase in bile flow
Pepsin secretion
Brunner's-gland secretion
Increase in jejunal secretion and decrease in absorption[75, 86]
Decrease of gastric secretion
Release of insulin[87]
Decrease in stimulation of gastrin
Release of alkaline phosphatase from brush border[73]
Release of intestinal disaccharidases[74]
Elevation of serum calcium concentration[88]
Motor
Decrease in LES pressure
Decrease in gastric motility[89]
Decrease in small bowel[90] and colonic motility[76]
Increase in pyloric sphincter pressure

An enteroglucagon-producing renal tumour, causing severe small and large bowel stasis with marked hypertrophy of the small intestinal villi, has been reported. Following removal of the tumour all abnormalities remitted.[107, 108]

The physiologic role of enteroglucagon is unknown. It has been suggested that its release from the lower small intestine may "act to produce a slowing of further food transport and also to enhance long-term growth of the absorptive intestinal mucosa".[109]

Gastric Inhibitory Polypeptide

Gastric inhibitory polypeptide (GIP) is a 43-amino-acid polypeptide, with structural similarities to porcine secretin and glucagon, which has been isolated by Brown and Dryburgh[110] from an impure preparation of porcine CCK. It has been identified by radioimmunoassay in the serum of man[111] and is believed to be released from the D_1 cells of the upper small bowel mucosa[112] by food, particularly glucose and fat.[113]

In microgram doses it inhibits both antral and fundic motor activity and the gastric acid and pepsin secretory response to pentagastrin, histamine and insulin hypoglycemia.[114] GIP is believed to stimulate intestinal secretion,[115] and one case of pancreatic cholera has been attributed to a GIP-producing tumour.[116] No effect has been observed on the gallbladder or exocrine pancreas, but recently intravenous infusion of GIP has been demonstrated to potentiate the insulin secretory response to intravenous glucose.[117]

The physiologic implications of GIP will be discussed under the section on enterogastrone.

Vasoactive Intestinal Peptide

Vasoactive intestinal peptide (VIP) is a 28-amino-acid polypeptide with structural similarities to glucagon, secretin and GIP.[118] These structural similarities are related to its different actions, which in-

clude stimulation of pancreatic and intestinal secretion,[115] induction of hyperglycemia[119] and inhibition of gastric acid and pepsin secretion. It also has vasodilatory activity, from which it derives its name,[120] and inhibitory effects on tracheal, gastric and gallbladder smooth muscle.

VIP was originally isolated from the upper porcine small intestine but has now been demonstrated by radioimmunoassay to be distributed throughout the primate gut in quantities exceeding that of gastrin, secretin, or CCK.[121]

The physiologic function of VIP is presently unknown but, pathologically, it has been shown to be associated with the syndrome of watery diarrhea, hypokalemia and achlorhydria (WDHA) secondary to pancreatic or retroperitoneal neoplasms.[122, 123]

Motilin

Motilin is a 22-amino-acid polypeptide that has been isolated from the mucosa of the upper 1 m of the porcine small intestine.[124, 125] Its structure is distinct from that of the other gastrointestinal polypeptides.[126] Intravenous injection of nanogram doses in dogs leads to increased gastric antral and fundal motor activity and increased pepsin output with no increase in acid secretion.[124] In the dog the stimulus for its release is believed to be increased alkalinity of the duodenum.[127] However, in man, two recent reports suggested that motilin may be released by duodenal acidification[128] and in fact delay gastric emptying.[129] The mode of action of motilin may lie in release of acetylcholine from nerve endings.[17] The physiologic role of motilin is presently unknown but it may function as a regulator of constant gastric input into the duodenum.

Prostaglandins

Prostaglandins are oxygenated cyclic C20 fatty acids and, as such, are not polypeptide intestinal hormones. They are mentioned here only because under certain pathologic and pharmacologic circumstances they exert a hormonal effect on the GI tract.

The effects of prostaglandins on the gut have been reviewed by Waller,[130] Bennett and Fleschler[131] and Wilson.[132] There is evidence both for the synthesis, release and degradation of prostaglandins in the gut and for action of ingested or injected prostaglandins on the gut. However, prostaglandins have not been demonstrated to act as GI hormones under normal physiologic conditions. Prostaglandins E_2 and $F_{2\alpha}$ are the major extractable forms found in the GI mucosa and pancreas of man. Their function is unknown, but it is suggested that they may act as local mediators of secretion and motility. The mode of action of prostaglandins is also unknown, but there is substantial evidence to suggest that they act through stimulation or inhibition of adenyl cyclase and hence, the "second messenger" cyclic AMP.[21]

The diarrhea that may be associated with thyroid medullary carcinoma, ganglioneuromas, pheochromocytomas, islet cell tumours and ileal carcinoids may result from prostaglandin production and release by these tumours.[133, 134]

Prostaglandins E_1, E_2 and A_1 have gastric antisecretory effects during basal and stimulated gastric acid secretion.[135-138] Prostaglandin analogues that are potent and orally active with few side effects may be of therapeutic benefit in gastric hypersecretory states[139] and it is possible that the ulcerogenic effects of acetylsalicylic acid and indomethacin may be related to their inhibitory action on prostaglandin synthesis.

Some of the other effects of exogenously administered prostaglandins in man are listed in Table VI.[140]

HYPOTHETICAL GI HORMONES

The existence of two hormones, "incretin" and "enterogastrone", has been postu-

TABLE VI.—EFFECTS OF PROSTAGLANDINS IN MAN

Prostaglandin $F_{2\alpha}$	*Prostaglandin E_1*
Increase in LES pressure[140]	Relaxation of LES
Contraction of circular and longitudinal smooth muscle	Contraction of longitudinal and relaxation of circular smooth muscle
Stimulation of intestinal secretions	Stimulation of intestinal secretion
	Inhibition of basal and stimulation of acid secretion

lated to explain the observed physiologic effects that follow eating, including augmented insulin secretion and feedback inhibition of gastric secretion and motility.

Incretin

This topic has been well reviewed.[2, 141-144] It is established that, for a given elevation in blood sugar concentration, oral administration of glucose leads to a higher and more sustained insulin response than intravenous administration.[145, 146] The same is true for amino acids.[147] It is presumed that the augmented insulin response is due to hormonally stimulated insulin release. Secretin,[87] impure CCK, gastrin,[58] glucagon, GIP,[117] VIP and duodenal extracts (insulin-releasing polypeptide)[148] are all capable of stimulating insulin secretion. It is not known which (if any) of the GI hormones is a true physiologic intestinal insulin secretogogue. Several hormones may act in concert to produce the observed effects. Release of these hormones may be inducible since carbohydrate restriction will blunt the insulin response to an oral glucose tolerance test.[149] The biguanide, phenformin, may inhibit insulin release after food by inhibition of intestinal hormone release[150] as well as by impaired glucose absorption.[151] The clinical ramifications of incretin will be discussed further under the section on alimentary hypoglycemia.

Enterogastrone

The introduction of fat, acid or hypertonic solutions into the duodenum is known to inhibit the gastric secretory response to gastrin, pentagastrin, histamine, insulin hypoglycemia and a meal. The term "enterogastrone" is applied to a hormone that, when released from the duodenal mucosa, would inhibit gastric secretion. Several possibilities exist (Table VII), including secretin,[96] CCK, GIP and glucagon. Other inhibitors of gastric secretion have also been described including sialogastrone (isolated from saliva[152]), bulbogastrone (isolated from the duodenal bulb[152]), gastrone B (found in human achlorhydric gastric juice and identified in the antral mucosa[153, 154]) and urogastrone (isolated from urine). The function of these substances is unkown.

Of all the possible enterogastrones, the GIP of Brown[110] is the most likely candidate. It alone (and perhaps VIP) inhibits the secretory response to all known gastric stimulants as well as inhibiting gastric motility. Under physiologic circumstances, however, enterogastrone may comprise several hormones acting in concert to produce the observed effect of inhibition of gastric secretion and motility.

Anatomical Loci of Activity

The multiple and varied effects of the intestinal hormones on the stomach and pancreas have been extensively investigated and described. It is only in recent years that more interest has been directed towards the LES, pyloric sphincter and large bowel. These aspects will be considered more fully.

Lower Esophageal Sphincter

Since the advent of continuous-perfusion esophageal manometry,[155] the physiologic and pharmacologic properties of the LES have been more accurately defined.[156] The chief function of the LES is to maintain a pressure barrier between the gastric cardia and the body of the esophagus. Positive inotropic influences are exerted on the sphincter by increased intragastric pressure, vagal stimulation, cholinergic drugs, alpha adrenergic drugs,[157] metoclopramide,[158] prostaglandin $F_{2\alpha}$[159] and gastrin.[160] Gastrin is the influence of major pharmacologic

TABLE VII.—Actions of Possible Enterogastrones

	Hormone			
Variable factor	*CCK*	*Secretin*	*Glucagon*	*GIP*
Releaser	Fat, acid	Acid	Hypoglycemia	Fat
Acid inhibition response to				
Gastrin	+	+	+	+
Histamine	−	−	−	+
Inhibition of gastric motility	+	+	+	+
Inhibition of pepsin	+	?	?	+

(and perhaps physiologic) importance and probably acts via stimulation of postganglionic cholinergic neurons. Negative inotropic effects are exerted by secretin,[92] glucagon,[161] CCK,[162] beta adrenergics,[157] anticholinergics,[156] prostaglandins E_1, E_2 and A_2,[163] smoking[164] and the ingestion of fatty food.[165]

Changes in intragastric pH also affect LES pressure, but whether these pressure changes are secondary to changes in serum gastrin levels or not is unclear. Higgs, Smyth and Castell[166] have observed pH-dependent sphincter-pressure changes without appreciable alteration in total serum gastrin as measured by radioimmunoassay. However, presently available immunoassays are not able to distinguish between the different gastrin species, so changes in the molar ratio of the different molecular species (and hence, biologic activity) may occur without affecting the total gastrin. This problem remains to be solved.

A number of patients with gastroesophageal reflux have a hypotensive LES that responds poorly to stimuli (the hypotensive, hyposensitive LES); the presence or absence of a hiatal hernia appears to be of little importance.[167] The disorder may be a combination of relative hypogastrinemia and end-organ resistance to gastrin. Postprandial (and possibly fasting) gastrin concentrations may be diminished while exogenous administration of gastrin causes little absolute increase in LES pressure.[168, 169] However, the exact physiologic mechanism of gastroesophageal reflux is unknown.

On the other hand, the disorder of achalasia is characterized by the presence of a hypertensive, hypersensitive LES,[170] which may fail to relax on swallowing. Inhibition of gastrin release via antral acidification will decrease the sphincter pressure.[171] Paradoxically, patients with pernicious anemia or ZES, diseases in which the serum gastrin values are grossly elevated, have sphincters of different competence. Poor sphincter function is found in pernicious anemia[172] while patients with ZES have excellent sphincter function.[173, 174]

Stomach

The actions of the polypeptide hormones on the gastric parietal cell and antral pump have been discussed. Gastrin stimulates both secretory and motor activity while secretin, CCK, glucagon and GIP inhibit both actions.

Pyloric Sphincter

The pylorus is a true sphincter and has a function in preventing duodenogastric reflux.[93] Pyloric pressure may be increased by intraduodenal instillation of acid, olive oil, amino acids, glucose and hypertonic solutions. Likewise, exogenous administration of secretin, and CCK increase pyloric sphincter pressure.[77] Gastrin inhibits the effects of these hormones.[175] Smoking will also decrease pyloric sphincter pressure.[176] Pyloric sphincter incompetence and reflux of duodenal contents may influence the development of gastric ulcers.

Pancreas

Several reviews of the hormonal control of pancreatic function have recently been published.[71, 78] The chief hormonal influences on the pancreas are as follows. Secretin increases the volume of pancreatic secretions and bicarbonate and insulin secretion while CCK stimulates pancreatic enzyme and glucagon release. Glucagon inhibits pancreatic exocrine function by influencing enzyme release and synthesis. Insulin, on the other hand, appears to have trophic effects on the pancreatic acinar cells. The *physiologic* role of the other GI hormones on pancreatic function is unknown.

Large Bowel

As already mentioned, at least two intestinal polypeptides affect the function of the colon. Intravenous infusion of CCK[177] or its endogenous release via oral administration of magnesium,[178] or duodenal infusion of fats and amino acids[179] will stimulate sigmoid colonic motility. Infusion of secretin will inhibit the motor response to CCK.[76] Neither of these hormones is believed to act on the rectum. Gastrin is not thought to have a motor effect on the large bowel.

The implications of the colonic effects of GI hormones will be considered in a discussion of the irritable bowel syndrome.

GI Hormones in Disease

An excess or deficiency of GI hormones will have varied manifestations. Only five disorders will be mentioned here: celiac disease, peptic ulcer disease, pancreatic cholera, alimentary hypoglycemia and the irritable bowel syndrome.

Hormone Deficiency

Theoretically, any disorder that damages the upper intestinal mucosa could lead to secondary deficiency of small bowel hormones. At first glance, celiac disease or gluten-induced enteropathy appears to be such a disorder. Hypofunction of the pancreas[180-182] and gallbladder[183, 184] following oral administration of hormone releasers has been described in celiac disease. These physiologic alterations would imply deficiency of secretin and CCK; however, Polak and colleagues[185] have described hypertrophy and hyperplasia of the intestinal secretin cells in celiac disease, suggesting possibly a poor release reaction. On the other hand, Low-Beer and associates[186] have demonstrated abnormally high fasting levels of CCK with a slow rise to normal levels following feeding in celiac disease. These results remain to be confirmed and explained.

Secretin deficiency has been proposed as an etiologic factor in peptic ulcer disease, and a deficiency of enterogastrone may account for the increased incidence of intestinal ulceration in celiac disease.[187]

As techniques improve, true primary and secondary deficiencies of GI hormones are likely to be described.

Peptic Ulcer Disease

Except for ZES, the role of intestinal hormones in peptic ulcer disease has not been fully defined. Gastrin may be a factor in the gastric hyperacidity observed in duodenal and distal gastric ulcers.[188] Recently, McGuigan and Trudeau[189] have demonstrated that patients with duodenal ulcer disease have an increased gastrin response to a standard protein meal, increased sensitivity to pentagastrin[190] and a higher and more prolonged gastrin response to insulin hypoglycemia.[191] Unlike ZES patients, they have neither fasting hypergastrinemia nor a paradoxical gastrin secretory response to glucagon and secretin. The possibility that the hypersecretion of duodenal ulcer disease results from deficient enterogastrone has also been considered[192] and it is of interest that Bloom and Ward[95] have demonstrated deficient secretin release in a small group of duodenal ulcer patients.

It has been postulated that gastric ulcers may be due to pyloric sphincter dysfunction and duodenogastric regurgitation of bile and intestinal juices.[77] Damage to the mucosa would allow back diffusion of hydrogen ions into the mucosa, thus explaining the hypoacidity frequently noted in these patients. The hypoacidity, in turn, would enhance gastrin release,[193] which could then block the normal pyloric response to CCK and secretin.[175]

Peptic ulcer disease also has a strong association with chronic renal failure,[194] cirrhosis and portosystemic shunting, and massive small bowel resection.[195, 196] The peptic ulcer disease of chronic renal failure may be due to hypergastrinemia[66] and gastric acid hypersecretion secondary to impaired renal degradation of gastrin.[61-64] There is, however, no direct correlation between hypergastrinemia and the presence or absence of peptic ulcer disease.[67] Similarly, the gastric hypersecretion that follows massive small bowel resection may be due to hypergastrinemia secondary to impaired extraction of endogenous gastrin by the small bowel,[60] or to enhanced secretion of gastrin secondary to a deficiency of small bowel gastrin secretory inhibitory substances.[197] Gastrin is not affected by passage through the portal circulation[70] and hypergastrinemia has not been documented in cirrhosis or following portosystemic shunting. The gastric hypersecretion that occurs in these situations may be secondary to increased sensitivity of the gastric parietal cell mass to normal levels of circulating gastrin.[198]

Surgical modifications of the upper gastrointestinal tract will affect gastrin levels. After vagotomy (truncal, selective or highly selective) basal and postcibal gastrin levels are elevated.[37] Pyloroplasty will partially attenuate the postcibal response.[199] Similar postcibal elevations have been observed in patients given atropine.[200] It has been stated that complete vagotomy will prevent the

gastrin secretory response to insulin hypoglycemia[201, 202] but the consensus of the available literature is that this statement is incorrect.[37] Gastrin release during insulin hypoglycemia persists following complete vagotomy.[37, 199] Continued gastrin secretion may be related to gastrin release via adrenergic influences.[13, 36]

After partial gastrectomy and gastrojejunal anastomosis (Billroth II) basal, and particularly postcibal, gastrin levels are diminished. On the other hand, partial gastrectomy and gastroduodenal anastomosis (Billroth I) affects the gastrin levels only slightly,[203] suggesting continued release of duodenal gastrin.

The relationship between recurrent ulceration and postoperative gastrin levels has not been elucidated but when additional data are available, ulcer surgery may become more rational.

Zollinger-Ellison Syndrome and Antral-G-Cell Hyperplasia

Isenberg, Walsh and Grossman[204] have recently published an excellent review of ZES. The disease is due to hypergastrinemia and the big and heptadecapeptide forms of gastrin account for the majority of the serum and tumour gastrin.[31, 205] As originally described, the syndrome included fulminant peptic ulcer disease, gastric hypersecretion and a non-β-cell tumour of the pancreas, but the clinical spectrum may include moderate to severe peptic ulcer disease, diarrhea, steatorrhea, vitamin B_{12} malabsorption and type I multiple endocrine adenomatosis.

With the discovery of hypergastrinemia with antral-G-cell hyperplasia (AGCH) as well as with pancreatic and duodenal gastrinomas the diagnostic work-up of ZES has been expanded. AGCH was originally described as ZES type I, with the classic form being called type II, but it is now clear that the two disorders are quite distinct and can be separated by biochemical and histologic criteria (Table VIII).[206, 207] A differential diagnosis based on clinical grounds, gastric acidity studies or fasting gastrin levels is fraught with difficulties, and the diagnosis is best established on the basis of elevated gastrin levels after infusions of calcium, secretin or glucagon in ZES and elevated gastrin levels after food in AGCH.[207]

Experience has shown that treatment for ZES should consist of *total* gastrectomy, the sole exception being an isolated duodenal gastrinoma (although metastases may be occult). Regression of metastatic tumour has been reported after total gastrectomy. If AGCH can be diagnosed accurately then antrectomy should be curative.[207, 208]

WDHA Syndrome

Watery diarrhea, hypokalemia and achlorhydria (WDHA syndrome, pancreatic cholera, Verner-Morrison syndrome) have been described with non-β islet cell tumours[209] and retroperitoneal tumours.[123] Achlorhydria is not invariable and the gastric acidity studies may be normal. The diarrhea may be cyclic or chronic. Other features of the syndrome may include hypercalcemia, dehydration, hypokalemic nephropathy, metabolic acidosis, flushing and glucose intolerance (possibly due to hypokalemia). The patients tend not to have a family history of endocrinopathy.

The hormone or hormones responsible have not been identified with certainty but must stimulate intestinal secretion while inhibiting gastric secretion. Suggested possibilities are secretin,[209] GIP,[116] VIP,[112] prostaglandins,[134] gastrin plus glucagon[210] and a "CCK-like" hormone.[211] At present, if the syndrome is a single entity (which it may not be), VIP is the most likely hormone responsible for the symptomatology.

Surgery is the treatment of choice, but 50% of the tumours are malignant and the majority will have metastasized by the time of surgery. Adrenocorticotropic hormone (ACTH) and steroid therapy have been beneficial in controlling the diarrhea of inoperable patients.[209]

TABLE VIII.—ANTRAL-G-CELL HYPERPLASIA *v.* ZOLLINGER-ELLISON SYNDROME

Features	*AGCH*	*ZES*
Fasting gastrin	High	Very high
Gastrin release by food	Yes	No
Gastrin release by secretin	No	Yes
Antral G cells	Hyperplasia	Normal
Pancreatic D cells	Normal	Hyperplasia or
Tumour	No	tumour

Alimentary Hypoglycemia

Postprandial hypoglycemia in the absence of pituitary, adrenal and liver disease or early diabetes is almost invariably of alimentary origin. Patients with rapid gastric emptying (either primary or secondary to gastric surgery) or enhanced glucose absorption frequently develop alimentary hypoglycemia. Postprandial hypoglycemia has also been described in patients with no obvious intestinal defects.[151] The pathogenesis involves several nonexclusive variables including blood sugar, insulin secretion and enteroglucagon levels.

Although early hyperglycemia is common, it is not essential for the development of hypoglycemia.[149] Likewise, hyperinsulinemia may also be absent.[212] Hyperenteroglucagonemia is a frequent finding.[105]

The pathophysiology probably involves varying combinations of hyperinsulinemia (secondary to hyperglycemia and incretin) and hyperenteroglucagonemia, which may inhibit the effects of pancreatic glucagon.[105]

Therapy involves the use of small, isocaloric, low carbohydrate meals to reduce hyperglycemia and to reduce induction of incretin[149] and enteroglucagon, anticholinergics to delay gastric emptying, and small doses of phenformin (50 mg) to reduce glucose absorption and incretin secretion.[150, 151]

Irritable Bowel Syndrome

Many of the patients seen by gastroenterologists are afflicted by the irritable bowel syndrome,[213] a complex disorder of abnormal esophageal, small intestinal[214] and colonic function.[215] The disorder is rightly called a syndrome and probably represents the interaction of psychic, environmental, dietary and GI influences. The role of GI hormones in the pathogenesis of the disorder is not fully defined but Harvey and Read[216] have recently demonstrated colonic motility disturbances and reproduction of symptoms during infusions of CCK in patients with the irritable bowel syndrome. Similar disturbances have been documented following presumed CCK release after oral magnesium sulfate administration.[178] These experimental results and the clinical observation that symptoms frequently follow the ingestion of food suggest, very strongly, that in some patients the irritable bowel syndrome may be secondary to disordered GI endocrinology. It is not yet known whether these patients are overproducing hormones or are just overly sensitive to normal hormone levels.

Study in the field of gastrointestinal endocrinology began over 70 years ago with the discovery of secretin by Bayliss and Starling. Interest in this field has grown rapidly in the last decade. In this review I have attempted to summarize the current state of knowledge in gastrointestinal endocrinology and to indicate the relevance of this knowledge to certain diseases of man. Much is still to be discovered.

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SELF-ASSESSMENT

SESAP II QUESTION

507. Which of the following statements concerning serum gastrin levels is/are correct?

(1) They can be measured by radioimmunoassay using gastrin labeled with iodine-125
(2) They usually increase markedly in patients who have had antrectomy and vagotomy
(3) They are useful in identifying patients with the Zollinger-Ellison syndrome
(4) They are useful in investigating the possibility of residual vagal function after vagotomy

For this question one or more of the answers given above is correct. Your answer should be:

A if only *1, 2 and 3* are correct,
B if only *1 and 3* are correct,
C if only *2 and 4* are correct,
D if only *4* is correct,
E if all are correct.

For the critique of Item 507 see page 372 of this issue.
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END-TO-SIDE ANASTOMOSES OF VEIN GRAFTS TO ARTERIES*

S. E. CARROLL, MD, FRCS[C], FACS

ALTHOUGH Linton[1] described the use of a small venous tributary in the acute angle of end-to-side anastomoses between a vein graft and artery, I have found a larger tributary of greater length more convenient. If short transverse limbs, proximally and distally, are added to the arteriotomy,[2] a rectangular anastomosis may be fashioned, helping to fix the intima (Fig. 1). This is particularly important in maintaining flow in both directions, for example, in the distal popliteal artery, below the origin of the anterior tibial branch. A larger venous tributary used in this way allows the surgeon to fashion the distal anastomosis with less risk of narrowing of the vein graft at the junction and gives extra length when this is crucial. Occasionally a tributary may be used at the distal end of the anastomosis, but in this situation the surgeon must be careful to remove valve tissue that may obstruct flow. With ingenuity a suitable tributary can almost always be found.

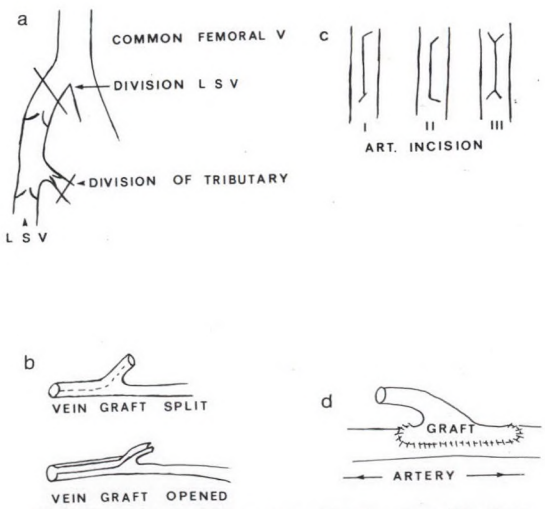

Fig. 1.—End-to-side anastomosis. (a) Method of removing long saphenous vein (LSV) with tributary. (b) Opening proximal vein into tributary. (c) Variations in arteriotomy. (d) Completed rectangular anastomosis.

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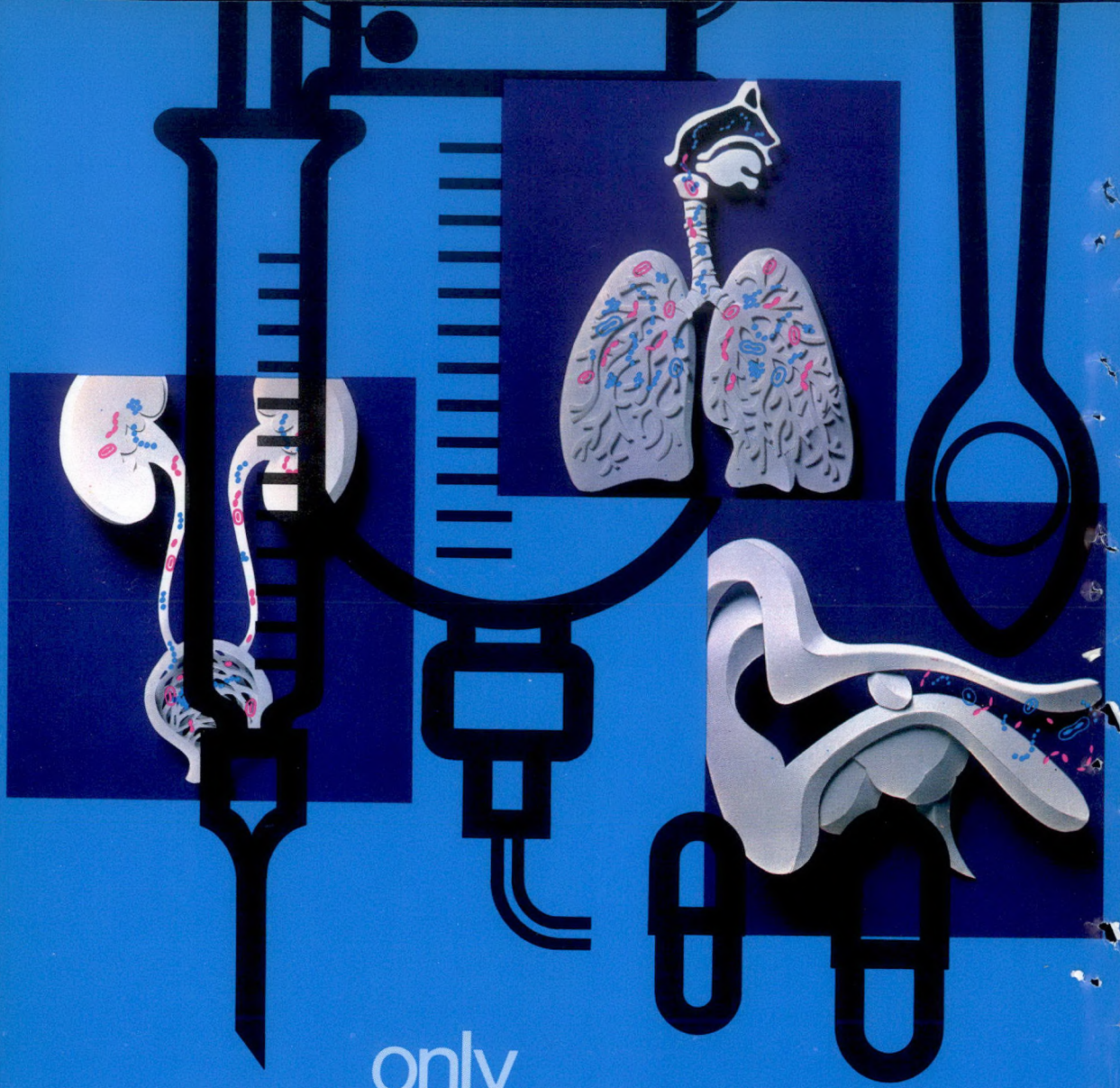

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J FOR SURGICAL JOURNALS

DAVID A. E. SHEPHARD

This journal is one of countless SURGICAL JOURNALS *published throughout the world. All have useful functions, and there are as many different types of surgical journals as there are functions and editors shaping them. As varied and as numerous as these journals are, however, their origin can be traced to one progenitor* — Philosophical Transactions — *just as the many antibody-secreting lymphocytes develop from one cell type. The history of surgical journals well illustrates this series' theme that surgeons' nonsurgical colleagues have always shaped important developments in surgery.*

The key developments in the history of surgical journals were these. In 1455, Gutenberg, in making available movable type, facilitated the spread of scientific knowledge. During the 16th and 17th centuries, many natural philosophers began to advocate the scientific method of enquiry and the direct observation of nature: Bacon advised his colleagues to "read not to contradict and confute, nor to believe and take for granted . . . but to weigh and consider"; and Descartes recommended "the methodic doubt of everything". Soon the importance of a single experiment or observation was recognized; books could no longer serve as means of rapid dissemination; correspondence among scientists then assumed the function of speedy communication; however, letters were laborious to write in any number and, out of fear that they might too readily be criticized, letters tended to be sent to colleagues who would be unlikely to reject their content, which hardly served the Baconian method. So the idea that letters be printed and published periodically arose, an idea that restored the principles behind scientific communication and also led to the development of the scientific periodical. The Transactions *were first published in 1665. It was the first truly scientific journal and became the model for those that followed.*

Scientific journals soon began to proliferate; they continue to do so. Their objective, however, has remained the same: today's readers, among whom are innumerable surgeons, share the thinking of the president of the Royal Society in 1661, Robert Moray, who realized the importance of "communication among us of whatever knowledge may further for posterity . . . most necessary of studies".

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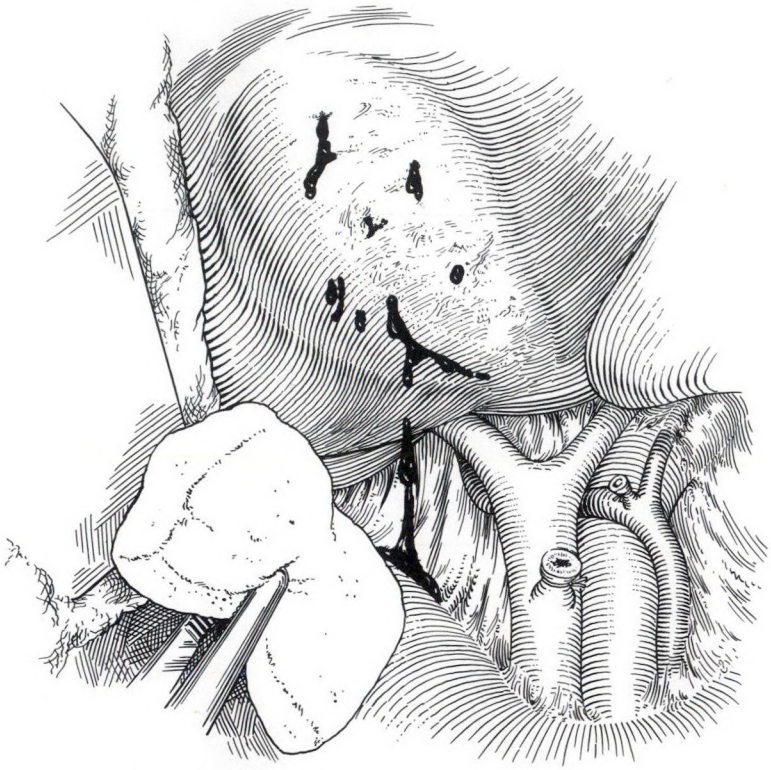

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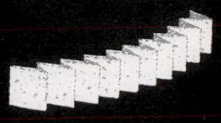

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packing cavities – obliterating dead space

Sterile Sponge, size 200
80 x 250 x 10 mm
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for general surgery

Sterile Sponge, size 100
80 x 125 x 10 mm
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for general surgery

Sterile Sponge, size 50
80 x 62.5 x 10 mm
box of four sponges, No. 7858

specially prepared for dry application and emergency hemostasis

Sterile Compressed Sponge,
size 100 – 12.5 x 8 cm
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for general and neurological surgery

Sterile Sponge, size 12 – 3 mm
20 x 60 x 3 mm
box of four sponges, No. 7852

for general and neurological surgery

Sterile Sponge, size 12 – 7 mm
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box of four sponges, No. 7853
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Precautions:

Gelfoam and Gelfilm are simple to use, and with conscientious observance of certain precautions satisfactory results may generally be expected where their use is indicated.

1. Gelfoam should be used discriminately in arterial bleeding because of the intra-arterial pressure. It is advisable to suture and reinforce where possible.
2. Although Gelfoam generally serves its purpose well in the presence of haemorrhagic blood dyscrasias, it should not be relied upon as the sole method of haemostasis in such conditions.
3. Gelfoam should not be used to stop menstrual bleeding. In postpartum and menorrhagic bleeding it serves only as a temporary vaginal tampon.
4. Gelfoam must be in snug contact with the bleeding surface in order to be effective.
5. Use Gelfoam as sparingly as possible in order to minimize the amount of implanted foreign material.
6. Do not overfill cavities with Gelfoam.
7. Do not use Gelfoam in grossly contaminated wounds which are so deep that drainage is interfered with. However, it may be used for temporary haemostasis in more superficial contaminated wounds, provided it is removed after it has served its haemostatic purpose.
8. Avoid prolonged exposure of Gelfoam to contaminated air.

Detailed information available on request.

EFFECTS OF AMBIENT AND STAGNANT HYPOXIA ON THE MECHANICAL AND ELECTRICAL ACTIVITY OF THE CANINE UPPER JEJUNUM*

A. MEISSNER, MD,† K. L. BOWES, MD and S. K. SARNA, PhD‡

The effects of ambient and stagnant hypoxia on the mechanical and electrical activity of the upper jejunum were studied in 32 anesthetized dogs. A 50 or 75% reduction in oxygen content of inhaled air produced ambient hypoxia; superior mesenteric artery (SMA) occlusion or thrombin-induced mesenteric thrombosis resulted in stagnant hypoxia. Induction of hypoxia was immediately followed by a transient increase in mechanical activity. A 50% reduction in oxygen content had no other effect. A 75% reduction in oxygen content resulted in a gradual decrease in electrical control activity (ECA) frequency and in the disappearance of electrical response activity (ERA), and in jejunal contractions; however, ECA persisted until cardiac arrest occurred after 30 to 45 minutes of hypoxia. Occlusion of the SMA resulted in a significant decrease in contractile activity but ECA was not affected. Thrombin-induced mesenteric thrombosis produced rapid and irreversible disappearance of both electrical and mechanical activities. Jejunal contractions and ERA are dependent upon an adequate oxygenated blood supply. ECA however, is highly resistant to reduction in oxygen content of perfused blood and continues until perfusion stops.

Les effets de l'hypoxie ambiante et stagnante sur les activités mécaniques et électriques du jéjunum supérieur ont été étudiés chez 32 chiens anesthésiés. Une diminution de 50 à 75% de la teneur en oxygène de l'air inhalé a produit l'hypoxie ambiante. L'occlusion de l'artère mésentérique supérieure (AMS) ou la thrombose mésentérique provoquée par la thrombine ont résulté en une hypoxie stagnante. L'induction de l'hypoxie a immédiatement été suivie d'une augmentation transitoire de l'activité mécanique. Une baisse de 50% de la teneur en oxygène n'a produit aucun autre effet. Une diminution de 75% du contenu en oxygène a entraîné une baisse graduelle de la fréquence de l'activité de contrôle électrique (ACE), et la disparition de l'activité de réponse électrique (ARE) et des contractions jéjunales. Toutefois, l'ACE s'est maintenue jusqu'à l'arrêt cardiaque qui est survenu après 30 à 45 minutes d'hypoxie. L'occlusion de l'AMS a entraîné une diminution significative de l'activité contractile mais l'ACE n'a pas été affectée. La thrombose mésentérique provoquée par la thrombine a produit la disparition rapide et irréversible, à la fois, des activités électriques et mécaniques. Les contractions du jéjunum et l'ARE sont trsè dépendantes d'une réserve sanguine adéquate en oxygène. L'ACE cependant, est très résistante à une diminution de la teneur en oxygène du sang de perfusion et persiste jusqu'à l'arrêt de la perfusion.

Two types of electrical activity can be recorded from the small bowel muscle of dogs and humans.[1] The first, electrical control activity (ECA) (slow waves, pacesetter potential), is omnipresent and has a maximum frequency of 18 cycles/min in the duodenum of the dog. It controls the appearance in time and space of a second type: electrical response activity (ERA) (fast activity, spike potential). ERA initiates mechanical activity; that is, whenever ERA occurs at a site, the muscle at that site contracts. ECA in the small bowel of the dog results from bidirectionally coupled relaxation oscillators.[2]

It has been suggested that ERA and ECA could determine the viability of bowel at laparotomy.[3, 4] Ligation of mesenteric vessels in the dog results in rapid disappearance of both types of small bowel electrical activity. However, bowel ischemia may occur clinically in low-flow or hypoxic states without occlusive vascular disease.[5] The relative importance of flow and hypoxia in the generation of electrical activity is not known.

In this study, in attempting to determine

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the relative importance of flow and oxygenation in the generation of electrical and mechanical activities of the small bowel, we compared the effects of ambient and stagnant hypoxia on small bowel electrical and mechanical activity in three groups of dogs.

Methods

Anesthesia

Adult, healthy dogs (weight, 15 to 20 kg) were fasted for 16 hours before each experiment. After induction of anesthesia with intravenous sodium pentobarbital (30 mg/kg body weight) the dogs were intubated with a plastic tube. To initiate controlled respiration, succinylcholine chloride (30 mg) was administered intravenously, and the endotracheal tube connected to a respirator. The dogs were ventilated 14 times/min with 80% nitrogen and 20% oxygen at a tidal volume of 15 ml/kg body weight. Partial pressure of oxygen (Po_2) in the inhaled gas mixture was equal to that of room air. Anesthesia was supplemented by sodium pentobarbital (10 mg/kg) and succinylcholine chloride (20 mg) as required.

Preparation of Jejunum and Monitoring of Jejunal Activity

At laparotomy a loop of upper jejunum was exposed and three bipolar silver wire electrodes[6] were implanted subserosally every 10 cm and oriented transversely to the bowel axis. The first pair of electrodes was placed 30 cm caudad to the ligament of Treitz. Contractile activity of the small bowel was recorded by extraluminal force strain gauges (R.B. Products, 153 Nautilus Dr., Madison, WI) aligned with the transverse axis of the small bowel and sutured to the serosal surface at 10-cm intervals. The first was attached 3 cm distal to the first bipolar electrode. Recordings were made on an eight-channel Beckman R411 dynagraph recorder. The myoelectric signals were filtered with upper and lower cut-off frequencies at 22 Hz and 1.6 Hz, respectively.

Production of Ambient and Stagnant Hypoxia

Group 1.—Ambient hypoxia was produced in this group by reducing the oxygen content of inhaled air by 50% (seven dogs) or 75% (seven dogs). Partial pressures of arterial and inhaled gas were determined before and every 30 minutes after oxygen reduction. The 50% reduction in oxygen lasted for 2 hours and the 75% reduction until cardiac arrest occurred. A continuous recording of small bowel electrical and mechanical activity was made for 1 hour before and 2 hours after establishing ambient hypoxia.

Group 2.—In this group of nine dogs stagnant hypoxia was produced by occluding the superior mesenteric artery (SMA) for 2 hours by tightening a hemostatic snare, in the form of a polyethylene tube (ID, 0.86 mm; OD, 1.27 mm), placed around the vessel. The distal branch of the SMA was isolated (50 cm caudad to the ligament of Treitz) and cannulated with an identical polyethylene tube, whose tip was positioned in the main trunk of the SMA. The femoral artery was then exposed and cannulated with a polyethylene tube (ID, 1.67 mm; OD, 2.41 mm). Each tube was connected to a transducer and hence to the recorder. Systematic and SMA blood pressures were recorded during the experiment. A decrease in blood pressure recorded in the distally placed polyethylene tube was interpreted as proof of SMA occlusion (stagnant hypoxia). Electrical and mechanical activities were recorded for 1 hour before, during the 2-hour period of artery occlusion, and for 1 hour after release of the snare.

Group 3.—In five dogs stagnant hypoxia was produced by direct injection of thrombin topical (150 NIH units/kg body weight; supplied by Parke-Davis & Co. Ltd., Montreal), which produced vein and SMA thrombosis. During the infusion (30 to 60 s) the SMA and vein were occluded. Electrical and mechanical activities were recorded for 1 hour before and 2 hours after thrombin injection. Full-thickness segments of the intestinal wall were examined histologically at the end of the experiments.

To complete the experimental preparation, the small bowel was replaced in the peritoneal cavity, the laparotomy wound was closed, and the connecting wires and tubes were brought out through the suture

line. Monitoring of the respiratory action throughout the study was by a transducer connected by a polyethylene tube to the respirator. A continuous electrocardiographic recording was made.

RESULTS

We recorded two types of electrical activity from the upper jejunum — electrical control activity (ECA) and electrical response activity (ERA) (Fig. 1).

In the 1-hour basal period, ECA in all dogs was phase-locked with an aboral direction of phase lag and a mean frequency of 17.3 ± 0.91 cycles/min (± SEM). Response activity was usually noted when contractions appeared, but, as the positions of electrodes and strain gauges were not identical, exact correlation did not always occur.

We recorded two patterns of contractile activity with the extraluminal force transducers,* the first consisting of groups of repetitive low-amplitude contractions appearing 4.8 ± 0.45 times per 5-minute recording period (total duration, 56.0 ± 6.22 s), and the second consisting of groups of high-amplitude repetitive contractions appearing 2.5 ± 0.31 times per 5-minute recording period (total duration, 140 ± 16.1 s).

Effects of Ambient Hypoxia (Group 1)

In all dogs, a 50% decrease in oxygen content of inhaled mixture (Po_2, 67.5 mm Hg) resulted in a decrease in arterial Po_2 from 61.6 to 35.9 mm Hg. A 75% reduction in oxygen content of inhaled air (Po_2, 37.4 mm Hg) resulted in a decrease in arterial Po_2 from 66.7 to 16.8 mm. Hg.

Immediately after 50 and 75% reduction of oxygen in inhaled air, there were high-amplitude repetitive contractions (mean duration, 4.8 ± 0.33 min). ERA was associated with the contractions but ECA did not change.

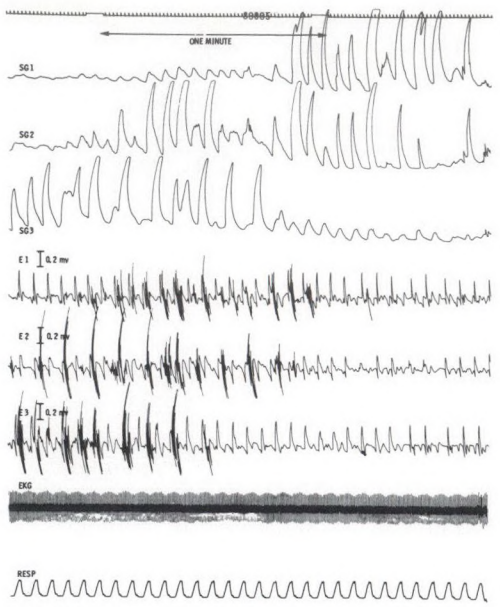

Fig. 1.—Types of electrical and mechanical activity of upper jejunum during control period. Mechanical activity (SG1-SG3) appeared intermittently either as groups of repetitive low-amplitude contractions (early part SG1) of repetitive high-amplitude (SG1-SG3) contractions. ECA (E1 - E3) appeared regularly 17.3 ± 0.91 times/min. ERA (early part E1-E3) was intermittently superimposed on ECA. Electrodes and strain gauges are at different positions (see text) so ERA and contractions do not exactly correspond.

Following the transient increase in mechanical activity and ERA, the patterns and frequencies of electrical and mechanical activities in dogs subjected to a 50% reduction in inhaled gas oxygen content rapidly returned to control levels. Systemic blood pressure did not change appreciably during hypoxia or after.

The 75% decrease in inhaled oxygen content resulted in a progressive decrease in ECA frequency from 17.1 ± 0.47 cycles/min to 11.9 ± 1.72 cycles/min 30 minutes after oxygen decrease ($P < 0.05$) (Fig. 2); ECA was, however, continuously present and phase-locked in an aboral direction, though at a lower frequency, until the heart stopped or fibrillated 42 ± 5.37 minutes after 75% oxygen decrease (Fig. 3). Systemic blood pressure was maintained until the heart slowed or its rhythm became irregular. After the initial transient increase in con-

*Quantitation of mechanical activity as recorded by external force transducers is difficult. Although ex-vivo quantitation of transducers is possible, the tension under which the gauge is sutured, the depth of sutures, slight deviations from the transverse axis, and the state of bowel when the transducer is applied all profoundly influence their sensitivity. These factors obviate the extrapolation of ex-vivo results to the in-vivo situation. For the purpose of this investigation we arbitrarily classified mechanical activity into low amplitude (< 1-cm deflection) and high amplitude (> 1-cm deflection).

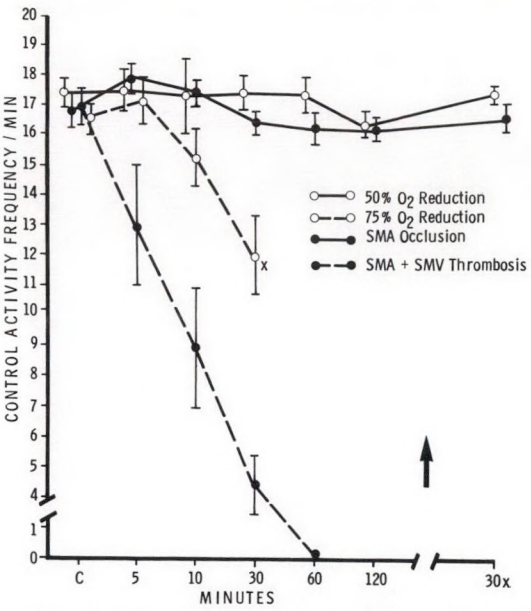

Fig. 2.—Mean ECA frequency before (C) and after either oxygen reduction or occlusion of the superior mesenteric artery (SMA). Vertical lines indicate ± SEM. Arrow indicates release of occlusion or reestablishment of normal oxygen level in inhaled air. X indicates recorded values 10 to 15 minutes before arrest of heart action.

tractile activity, low- and high-amplitude contractions and ERA disappeared. ERA and contractions were absent for the remainder of the experiment.

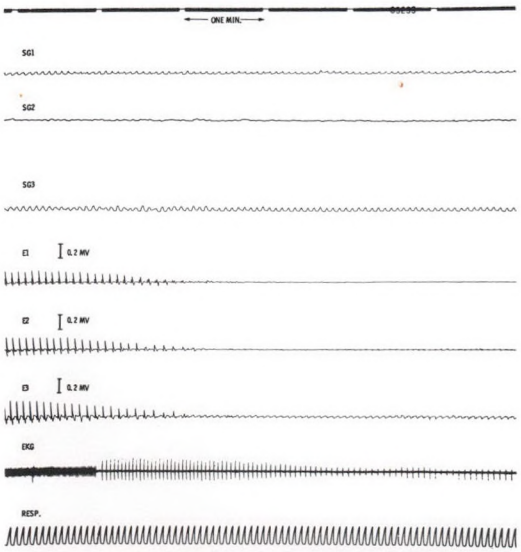

Fig. 3.—Electrical and mechanical activity of jejunum at time of circulatory arrest after 75% reduction in oxygen content of inhaled air. Note absence of contractile activity and persistence of ECA until moment of arrest.

Effects of SMA Occlusion (Group 2)

Traction on the plastic tube placed around the SMA produced a striking decrease in blood pressure within its branches. Throughout the occlusion period, however, the mean blood pressure in the SMA remained at 15 to 20 mm Hg. Immediately after occlusion there were high-amplitude repetitive contractions associated with ERA for 3.5 ± 0.75 minutes. ECA did not change. After this brief interval of increased contractile activity, there was a period of diminished activity that persisted to the end of the experiment (Fig. 4). Low-amplitude repetitive contractions were less common, appearing 2.5 ± 0.44 times per 5-minute period ($P < 0.05$). High-amplitude repetitive contractions diminished slightly but not significantly from a basal incidence of 2.7 ± 0.57 to 1.3 ± 0.44 times per 5-minute period. The total duration of the high-amplitude contractions, however, increased from 110.4 ± 21.3 to 210.1 ± 18.2 seconds ($P < 0.05$). Throughout the experiment ECA remained phase-locked in an aboral direction with a frequency of 16.8 ± 0.31 cycles/min.

After release of tape around the SMA and restored full blood flow, contractile activity returned to the pattern seen in the control period.

Effects of SMA and Vein Thrombosis (Group 3)

Direct administration of thrombin into the SMA produced intravascular coagulation in all small-diameter arteries and capillaries of the small bowel and in all tributaries of the superior mesenteric vein. The small bowel became cyanotic and hemorrhagic. There were diffuse subserosal and submucosal hemorrhages with extravasation of blood into the small bowel lumen.

A transient period (2.3 ± 0.24 min) of high-amplitude repetitive contractions immediately followed the thrombin injection. Then contractile activity and ERA disappeared and were not recorded again (Fig. 5). In four dogs ECA disappeared 6.5 ± 0.91 minutes after thrombin injection but in one it ceased 45 minutes after mesenteric thrombosis. ECA remained phase-locked and the direction of the phase lag was always aboral until it ceased.

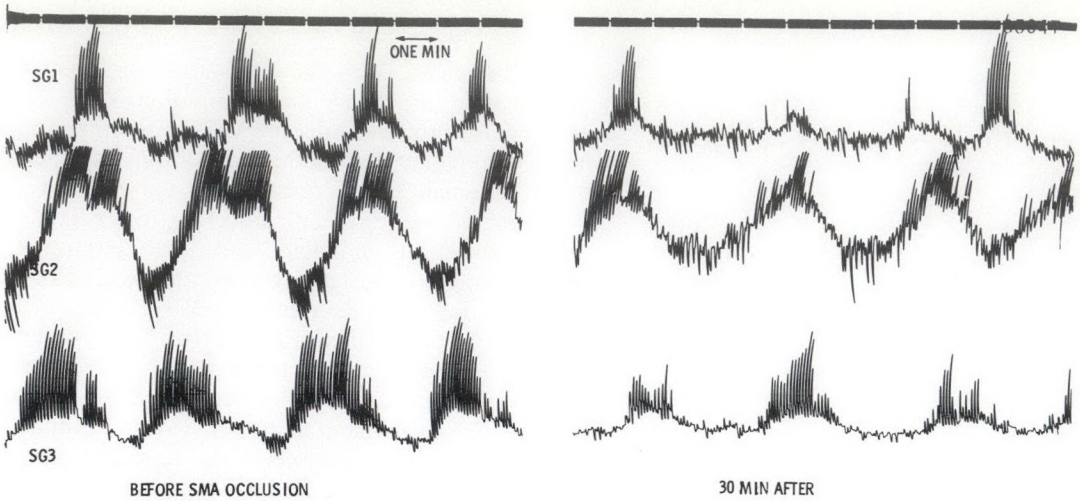

Fig. 4.—Mechanical activity of jejunum before and 30 minutes after occlusion of SMA.

Discussion

In this study ambient hypoxia produced by decreasing the oxygen content of inhaled air caused a transient increase in jejunal mechanical activity. When the oxygen reduction was minor (50%), normal contractile activity rapidly returned. When the oxygen reduction was greater (75%), all mechanical activity rapidly disappeared. Stagnant hypoxia, produced in these experiments by SMA occlusion, was also followed by an initial transient increase in mechanical activity. Thereafter, contractions persisted at a greatly reduced rate. SMA pressure following ligation persisted at 15 to 20 mm Hg indicating the presence of substantial collateral circulation through the pancreaticoduodenal arcade.

Throughout all of the procedures ECA

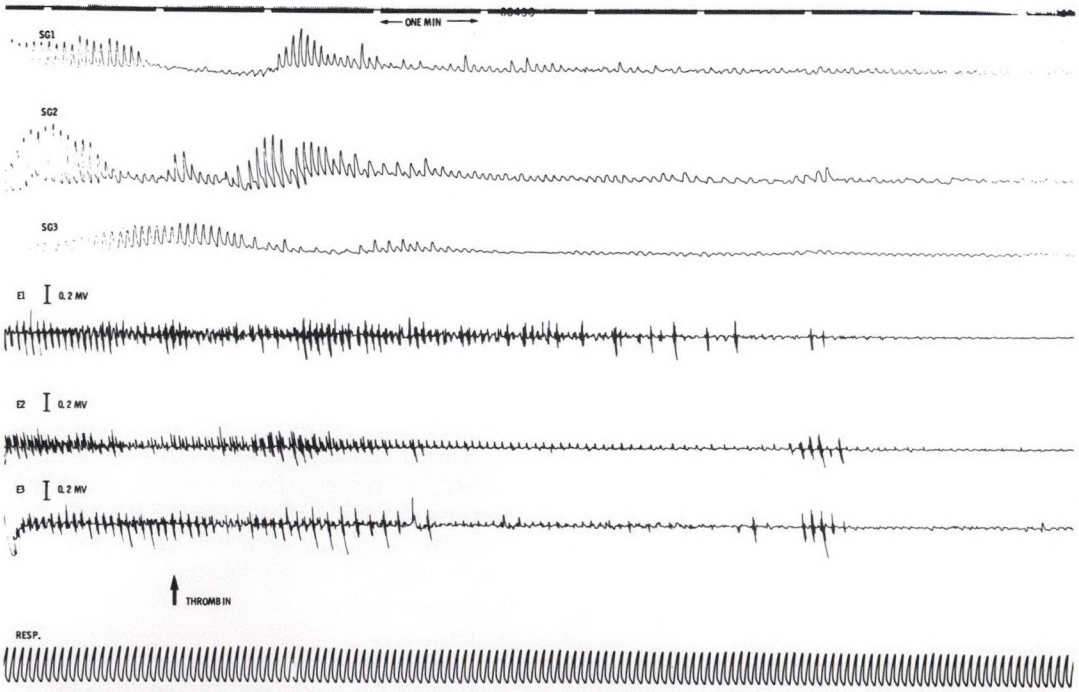

Fig. 5.—Jejunal electrical and mechanical activity before and after massive intravascular coagulation produced by injection of thrombin into SMA.

persisted and remained phase-locked in an aboral direction. Only after a 75% decrease in oxygen content of inhaled air did the frequency decrease. Even then ECA persisted until all flow ceased at the time of cardiac arrest. When the injection of thrombin into the SMA produced rapid cessation of flow ECA, ERA and all mechanical activity disappeared.

The persistence of ECA until the complete arrest of circulation indicates that it is comparatively resistant to hypoxia. ECA is primarily a myogenic function and does not require nervous or hormonal input for its generation. It is dependent upon the integrity of the cellular sodium pump.[7] Upon complete arrest of blood flow, rapid changes in cell membrane permeability, electrolyte concentration, and metabolite accumulation occurred. These changes probably resulted in the disappearance of ECA.

Mechanical activity, on the other hand, appears to be more sensitive to changes in arterial Po_2. It is difficult to attribute such rapid changes to neural degeneration; they are more likely due to changes in membrane permeability produced by hypoxia.

It has been suggested[4] that the recording of electrical activity at operation may be of value in determining the viability of bowel in low-flow states and after arterial or venous thrombosis and embolism. Recording at the time of operation, however, may be misleading. This study indicates that a normal jejunal ECA frequency can persist in spite of severe hypoxia. In addition, small bowel ischemia may progress following laparotomy. It has been suggested that all patients operated on for ischemic bowel disease have a second laparotomy 24 hours later to check for progression of the ischemia. The use of electrodes implanted into the small bowel with recording in the postoperative period in such patients may obviate the need for a second operation. Electrodes have been implanted into the stomach of patients undergoing laparotomy by Sarna, Bowes and Daniel[6] without side effects. The clinical application of small bowel electrical activity recording in ischemic bowel disease may take this form.

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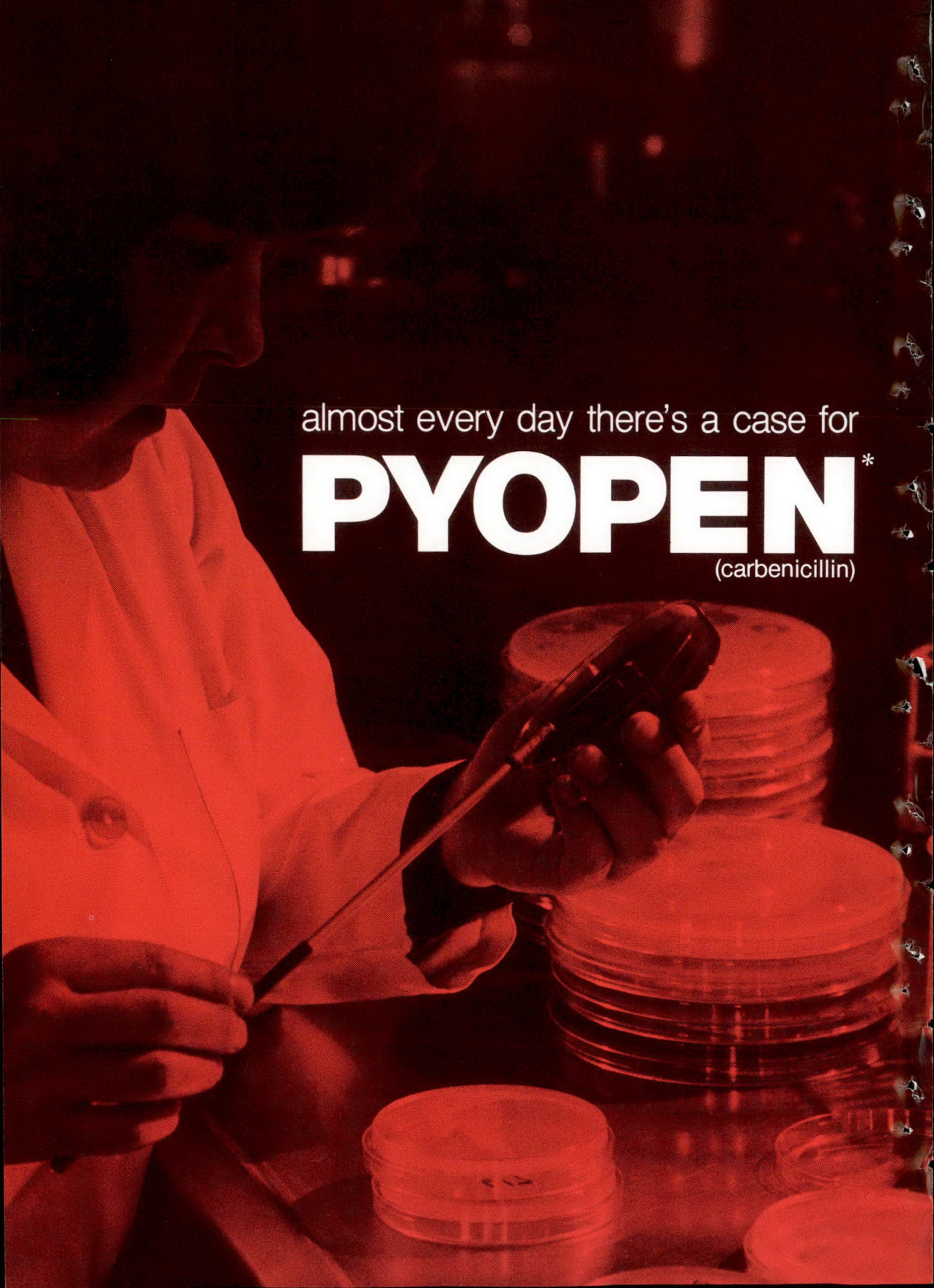
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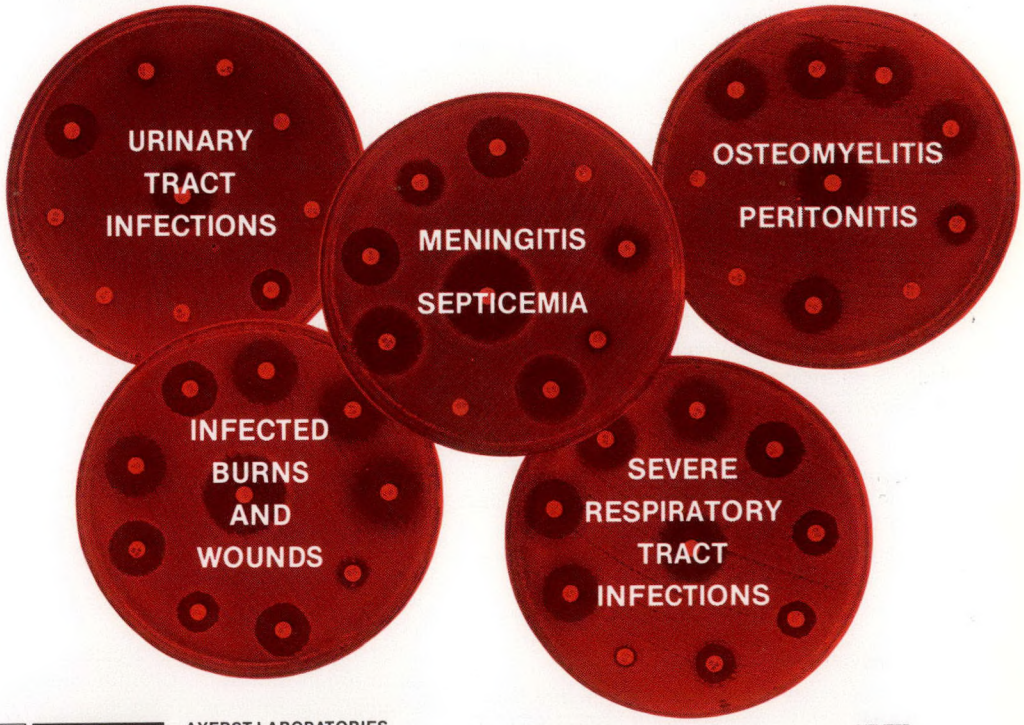

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MALADIE DE PAGET DU SEIN CHEZ L'HOMME

MAURICE FALARDEAU, MD, FRCS[C],* MLADEN RUSNOV, MD, FRCS[C]† et ROBERT LESAGE, MD, FRCP[C]‡

Un homme de 78 ans se présente pour une maladie de Paget du sein. Il s'agit d'une entité rare et nous croyons présenter le 22ème cas prouvé histologiquement bien qu'en 100 ans environ 40 articles et moins de 50 observations aient été publiés.

A la lumière de l'expérience récente, les auteurs ont opté pour une chirurgie plus limitée soit une mastectomie totale avec évidemment axillaire plutôt qu'une mastectomie radicale classique puisqu'il n'y avait ni masse sous-jacente cliniquement décelée ni adénopathie.

De plus, retenons que toute lésion eczématoïde du mamelon qui persiste plus de 2 semaines ou qui est unilatérale devient suspecte de malignité et devrait alors être biopsée. t

The case of a 78-year-old man with Paget's disease of the breast, described herein, appears to be only the 22nd histologically proven case of this rare condition; in over 100 years less than 50 cases have been reported. Since this patient had no underlying tumour or nodal involvement the operation consisted of total mastectomy with removal of axillary nodes only, rather than the classical radical mastectomy. All eczematoid lesions of the areola of the breast that persist for more than 2 weeks or are unilateral should be considered Paget's disease until proven otherwise by biopsy.

En 1874 Sir John Paget[1] a décrit pour la première fois la maladie de Paget du sein. La description de Paget s'ajoutait à l'observation de Velpeau de 1859 mais, selon Sekigughi,[2] c'est Erichsen qui, en 1879, proposat que cette entité porte le nom de maladie de Paget. Nous rapportons un cas de cette affection chez l'homme.

Affection peu fréquente, puisque le cancer de la glande mammaire est environ 100 fois plus rare chez le sexe masculin que chez le sexe féminin[3-6] et que la maladie de Paget constitue de 1 à 3% de tous les cas de néoplasie mammaire,[4, 7, 8] on s'attend à trouver un homme atteint de cette maladie sur 3 à 10 000 cas de cancer du sein. Au Centre d'Oncologie de l'Hôpital Notre-Dame, sur 5076 cas de néoplasie du sein qui ont été observés sur une période de 32 ans, on compte 7 femmes atteintes de maladie de Paget et seulement 2 hommes. Un de ces cas a été opéré initialement ailleurs et nous rapportons ici le second.

En 100 ans, environ 40 articles et une quarantaine d'observations ont été publiés dans la littérature mondiale sur ce sujet. Toutefois, selon Crichlow et Czernobilsky,[4] seulement 11 cas authentiques auraient été décrits jusqu'en 1969. Ces auteurs en ont rapporté deux autres, auxquels viennent s'ajouter les cinq cas de Coley et Kuehn[9] et d'autres publiés par Suzuki et Kubota,[10] Von Bartel et Wagner,[11] O'Grady et McDivitt,[7] Nance et collègues,[8] et Haagensen.[12] Enfin, celui que nous présentons ici, serait donc le 22ème.

Presentation Clinique

Un homme, âgé de 78 ans, est admis dans le service d'opthalmologie en mars 1974. Entre 1961 et 1969, il avait été hospitalisé à quatre reprises pour un infarctus du myocarde, une périarthrite de l'épaule droite, une cholécystite et une cataracte. En aucun moment, il ne fut mention de lésion au sein.

A l'examen physique, on découvre une lésion squameuse du sein droit. En rétrospective, le malade raconte que, depuis une dizaine d'années, il accuse localement un prurit modéré et que le mamelon saigne en certaines occasions.

Le dermatologiste consulté note une plaque érythémateuse, bien délimitée, squameuse, intéressant tout le mamelon droit, sans adhérence au plan profond, mesurant environ 3 cm de diamètre (Fig. 1); il n'y a pas de masse sous-jacente. Aucun ganglion axillaire n'est palpé. Le sein gauche est normal.

La mammographie ne décèle ni gynécomastie ni lésion tumorale et l'étude radiologique du squelette ne montre aucun signe de métastase osseuse. On procède alors à une biopsie qui démontre une maladie de Paget du sein. Le

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Les demandes de tirés-à-part doivent être adressées au: Dr. Maurice Falardeau, département de chirurgie, Hôpital Notre-Dame, 1560, rue Sherbrooke, est, Montréal, PQ H2L 4M1.

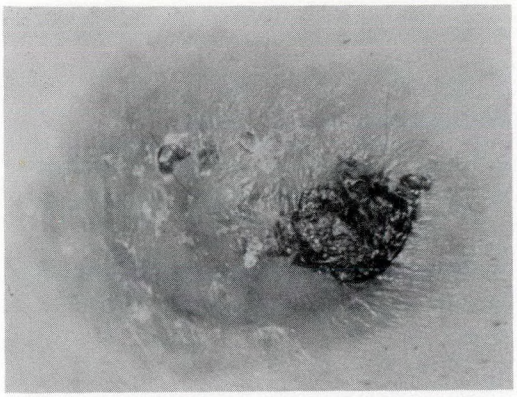

Fig. 1.—Aspect clinique d'une maladie de Paget.

malade subit ensuite une mastectomie simple (totale) avec évidemment ganglionnaire axillaire.

Le specimen anatomo-pathologique nous montre un fragment provenant du mamelon où l'épiderme est infiltré par de larges cellules à cytoplasme clair avec des noyaux irréguliers et parfois mitotiques (Figs. 2 et 3). Au niveau de la glande mammaire sous-jacente, on note des canaux remplis par une prolifération de cellules epithéliales néoplasiques. Il n'y a pas d'envahissement extracanaliculaire (Fig. 4). Il n'y a pas de métastase au niveau des ganglions axillaires.

L'évolution postopératoire est normale et 28 mois plus tard le malade est asymptomatique.

Discussion

Sur le plan clinique, le symptôme le plus fréquent de la maladie de Paget du sein est l'écoulement du mamelon avec excoriation et ensuite ulcération. Le malade se plaint la plupart du temps d'un prurit léger. On retrouve un eczéma du mamelon et de l'aréole avec ou sans masse sous-jacente et l'envahissement ganglionnaire est rare chez l'homme. Sur les 13 cas colligés par Crichlow et Czernobilsky,[4] 9 présentaient une masse et 5 seulement avaient une atteinte des ganglions.

Les changements cutanés précèdent-ils l'apparition de la néoplasie ou en sont-ils une manifestation secondaire? Treves[13] en 1954 rapporte un cas où la maladie est demeurée localisée à la peau pendant 14 ans sans qu'on n'ait pu déceler d'épithélioma de la glande ni de métastase ganglionnaire lors de la mastectomie. Des délais de 25 et 30 ans ont été rapportés respectivement par Sekigughi[2] et Fabry et Trautmann.[2]

De plus, selon Dockerty et Harrington[14] et Coley et Kuehn,[9] on peut retrouver une

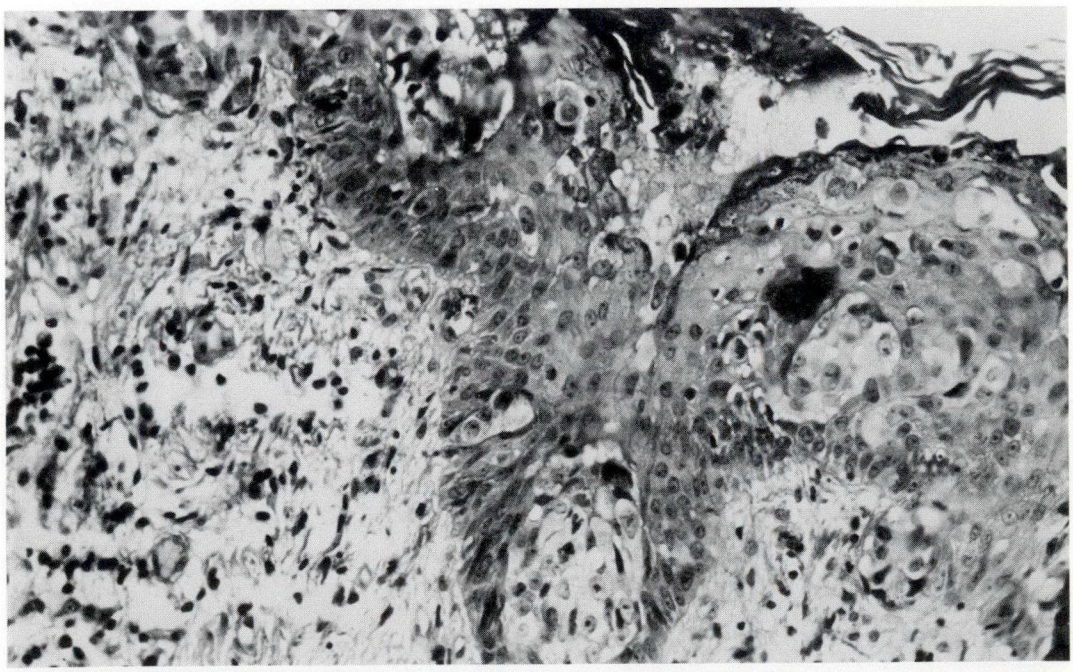

Fig. 2.—Envahissement de l'épiderme par des cellules de Paget (hematoxyline et eosine; le grossissement [x 160] a été réduit de 25%).

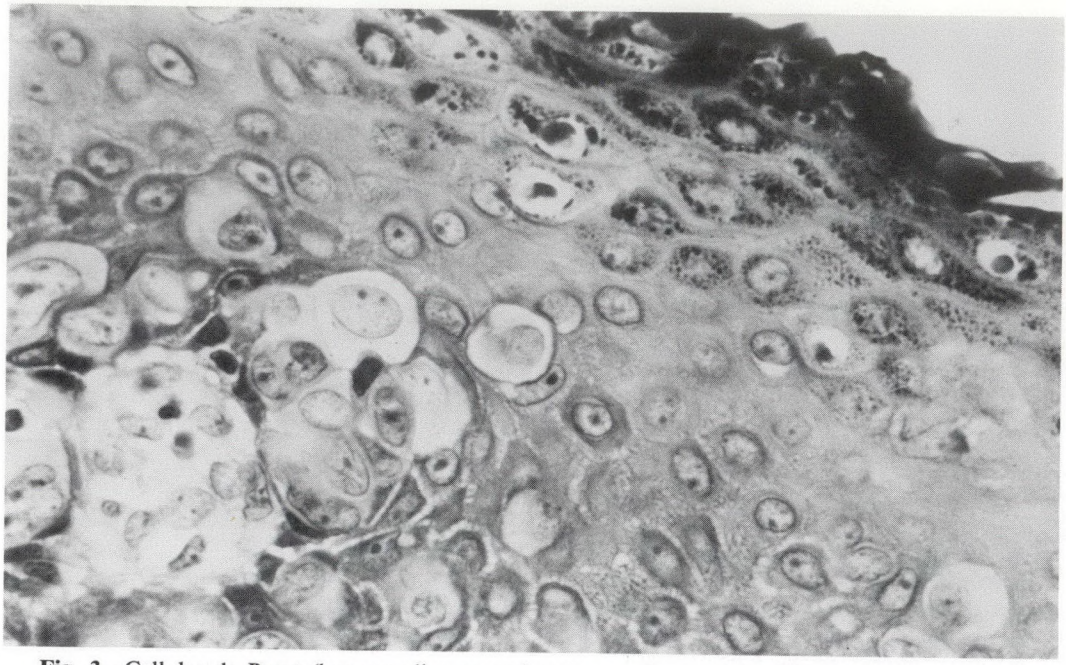

Fig. 3.—Cellules de Paget (hematoxyline et eosine; le grossissement [x 400] a été réduit de 25%).

maladie de Paget du mamelon à un stade pré-clinique, sans lésion eczémateuse macroscopique du mamelon mais avec des cellules de Paget typiques à l'histologie.

Enfin une maladie de Paget du sein doit toujours faire rechercher attentivement une néoplasie mammaire sous-jacente à la lésion du mamelon.

En pratique toute lésion eczématoïde ou excoriation du sein qui persiste plus de 2 semaines doit faire l'objet d'une biopsie. On doit considérer toute lésion unilatérale

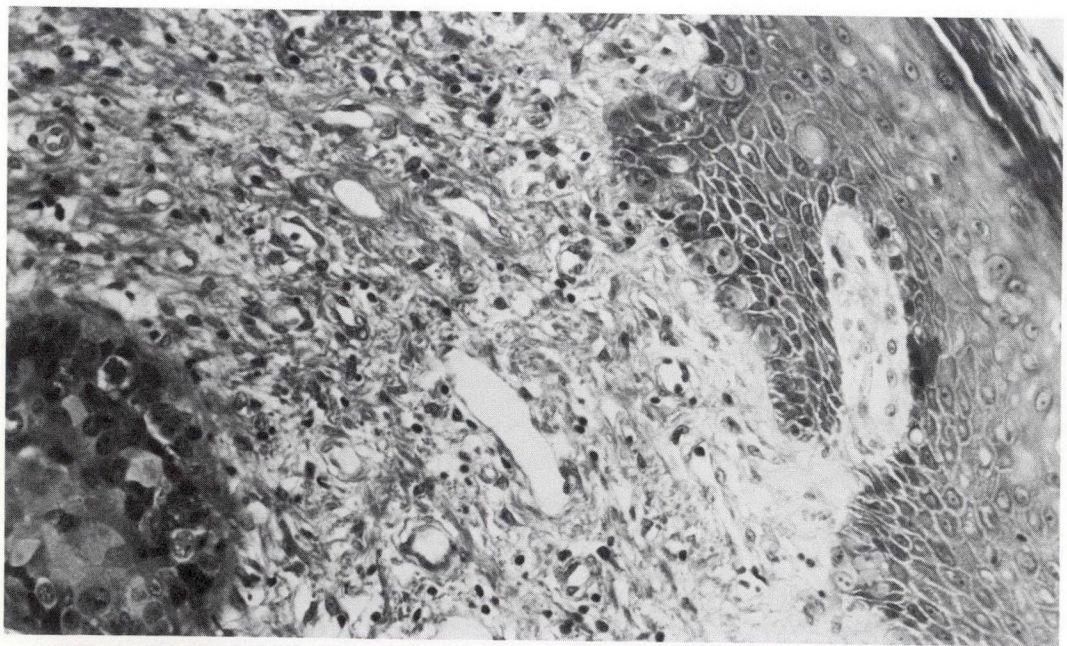

Fig. 4.—Prolifération néoplasique bien localisée à l'intérieur des canaux galactophores (hematoxyline et eosine; le grossissement [x 160] a été réduit de 25%).

comme une maladie de Paget jusqu'à preuve du contraire. La mammographie constitue un adjuvant précieux pour déceler la présence ou l'absence d'une masse sous-jacente.

Le diagnostic différentiel est à faire avec la maladie de Bowen, l'adénomatose bénigne du mamelon, l'eczéma simple, la folliculite, le mélanome amélanique, la croûte banale de l'hygiène défectueuse et la néoplasie ulcérée du sein envahissant le mamelon.

Sur le plan histopathologique, la maladie de Paget consiste en une infiltration de l'épiderme par de larges cellules à cytoplasme clair dites cellules de Paget mais décrites par Darier[15] en 1889 et le diagnostic définitif dépend de la présence de ces cellules de Paget.

Ceci nous amène à étudier la relation entre les changements épidermiques du mamelon et le cancer du sein sous-jacent. Il s'agit d'un envahissement de l'épiderme par des cellules néoplastiques d'origine canaliculaire.[4] Les cellules tumorales envahissent progressivement les canaux galactophoriques puis l'épiderme de surface.

Le traitement de cette maladie est des plus controversé. Jusqu'à récemment, seule la mastectomie radicale avec greffe[3, 10, 13, 16] cutanée était acceptée comme traitement valable. Des articles tout récents mettent en doute cette assertion.[12, 17]

La rareté de cette lésion chez l'homme interdit en fait d'adopter une attitude rigide.

Dans l'observation que nous rapportons ici, le patient n'a subi qu'une mastectomie totale avec évidemment axillaire. Selon les résultats histologiques, il semble bien qu'il n'y avait pas d'indication de faire davantage puisque les ganglions axillaires prélevés étaient indemnes d'envahissement.

D'une façon générale, le pronostic d'un cancer du sein chez l'homme serait moins bon.[18, 19] Le milieu hormonal mâle en serait-il responsable? Les hommes consulteraient-ils après un plus long délai? Enfin le sein de l'homme étant plus petit, l'envahissement des structures avoisinantes se ferait-il plus rapidement?

Holleb, Freeman et Farrow[17] croient que le pronostic a pu sembler moins bon parce que très peu de néoplasies du sein sont observées chez l'homme et que les références valables sont encore plus rares.

Nous croyons que la maladie de Paget avec masse palpable ne diffère que très peu des autres cancers du sein et doit être traitée comme tel. Cependant, si la présence d'une tumeur ne peut être décelée dans le sein ni cliniquement ni à l'aide de la mammographie et si l'extension de l'érosion du mamelon ne dépasse pas l'aréole, une mastectomie simple (totale) doit être considérée comme un traitement définitif, particulièrement chez les patients avec un risque opératoire élevée.

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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:

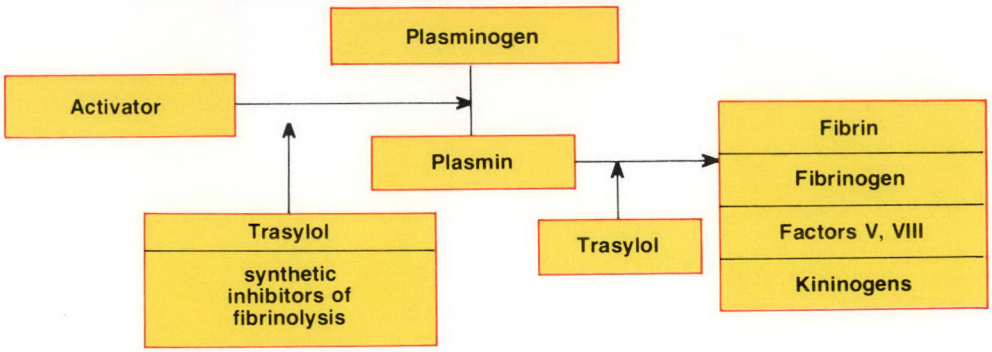
Placebo ..... 25.0% Mortality
Trasylol® ..... 7.5% Mortality

"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." *

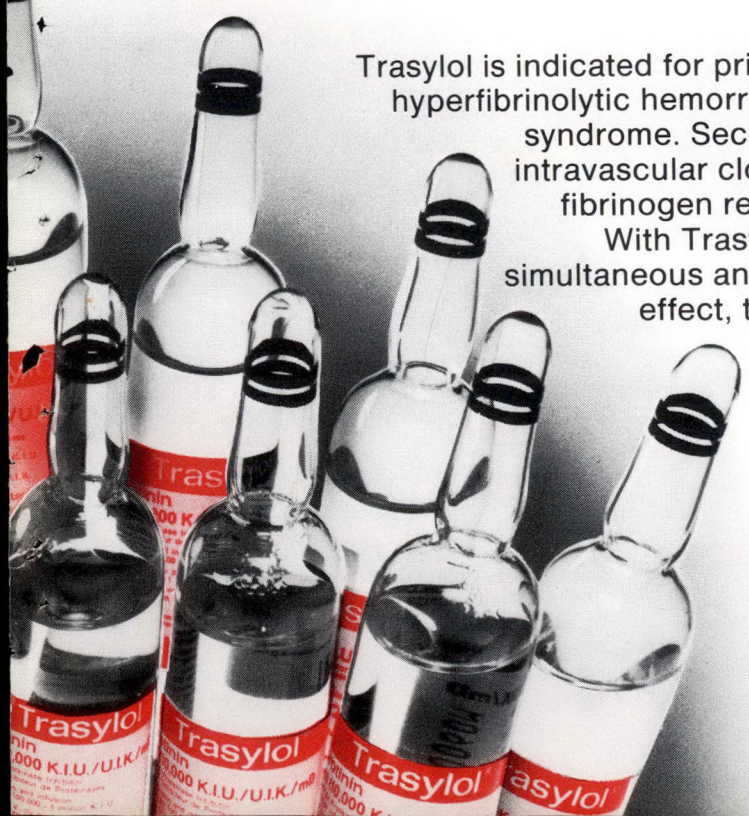
*Trapnell, J.E. et al, British J. Surg., March 1974.

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.

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ABSTRACTS OF PAPERS PRESENTED AT THE ANNUAL MEETING OF THE CANADIAN ORTHOPAEDIC RESEARCH SOCIETY, HELD IN OTTAWA, ONTARIO, MAY 25 AND 26, 1975

1. Augmentation of Bone Healing by Supplemental Direct-Current Electricity

D. A. MacKenzie and C. Knowles

Because the Harris fracture-healing model produces nonunion it is ideal for quantitating the ability of supplemental direct-current (DC) electricity to augment the rate and capacity of fracture healing.

In this preliminary study transverse single saw cuts were created at the junction of the proximal and middle thirds of the radius in a control group of mature dogs. Although these fractures were bilateral and unfixed, the radii were reasonably stable and the animals were able to walk on the 1st postoperative day. The reliability of the model was confirmed by creating bilateral saw cuts in six mature dogs. In all six dogs well-established, bilateral nonunion was demonstrated radiographically. Histologic examination confirmed the presence of cartilage in the gap.

The same procedure was performed in a second group of four dogs, but in addition they received 20 μA of *continuous* DC current on one side, a dummy lead being placed in the medullary canal on the other (control) side. In three dogs, bone union was demonstrated on non-screen radiographs and was confirmed by histologic examination.

In a third group of 10 dogs, a *pulsed* DC current unit was implanted. In the six dogs sacrificed, there were definite signs of advanced healing on the experimental side as judged by non-screen radiographs and histologic examination.

Department of surgery,
Montreal Children's Hospital,
Montreal, PQ.

2. Aurosomes in Rabbit Articular Cartilage

A. F. Oryschak and F. N. Ghadially

Although gold salts are used in the treatment of rheumatoid arthritis, little is known about the morphology and distribution of gold in articular tissues. The aim of this study was to find out whether gold injected into the joint enters articular cartilage.

Sodium aurothiomalate (Myochrysine) injected into the knee joints of rabbits produced lysosomes (aurosomes) of a characteristic morphology in the chondrocytes of articular cartilage. Such lysosomes are morphologically distinct from others and from those present in joints injected with sodium thiomalate. With the aid of electron-probe x-ray analysis, gold and phosphorus were demonstrated in the aurosomes.

Numerous coated vacuoles also developed in the chondrocytes in joints injected with sodium aurothiomalate. It is thought that these vacuoles are involved in the transport of a gold-protein complex and that the aurosomes evolved from the coalescence of such vacuoles with primary lysosomes.

Department of pathology,
University Hospital,
Saskatoon, SK.

3. Biofeedback Applied to Patients with Above-Knee Amputations

G. R. Fernie, J. P. Kostuik, C. McLaurin and B. Zimnicki

In training a patient with an above-knee amputation it is important to teach him to ensure that the knee joint of the prosthetic limb is fully extended before he places any weight upon it. If not he will be unstable and may fall. A simple device helps train amputees in this aspect of walking. The device consists of a buzzer that sounds when the knee is flexed and is silent when the knee is fully extended. It has been used effectively for over a year at the amputee centre of the Toronto Hospital. Biofeedback techniques are being applied to correct other common errors made by amputees. In addition to aiding the physiotherapist in the training sessions, these devices also permit patients to use their time in hospital better by enabling them to exercise in the absence of the physiotherapist but still with a degree of automatic supervision.

The experienced amputee might benefit by the provision of continuous proportional feedback of the angle of flexion of the knee

joint, so a second device has been designed to fulfil this need. This system uses tactile stimulation of the skin of the stump.

Amputee Research Centre,
Toronto Hospital,
Weston, ON.

4. Blood Supply of the Cortex in Growing and Adult Bone

A. Trias

The role of the arterial and venous systems in the bone cortex was examined in the femora of dogs and rabbits. Study of the anatomy revealed two distinct vascular networks. The first, seen only in young growing bone, is a functional network of vessels of capillary calibre, which form rectangular meshes, longitudinally oriented, and which do not divide by dichotomy but anastomose with each other with no change in calibre. This system is continuous with the deep layer of the periosteum and that of the endosteum and permeates the whole cortex. As the haversian systems are formed, a second, new, system appears — the supply system. It consists of arteries and veins radiating from the bone marrow, penetrating the cortex in a straight line and then branching in arborescent fashion. The vessels anastomose freely with the mesenchymal system.

In the younger cortical bone, when the functional system prevails, the flow appears to be centripital. In adult bone the arterial cortical flow via the supply system is centrifugal, but the blood returns centripitally to the marrow before leaving the bone mainly through metaphyseal veins. The changes in cortical circulation from growing to adult bone reflect its changing histologic structure.

Department of orthopedics,
Centre Hospitalier Universitaire,
Université de Sherbrooke,
Sherbrooke, PQ.

5. Collagen Architecture of Normal and Osteoarthritic Human Articular Cartilage

R. U. Repo, K. Newland and L. Johnston

The architecture and the morphologic disintegration of collagen in osteoarthritic articular cartilage was investigated by scanning electron microscopy in 14 tibial plateaus (7 were normal by the criteria of Collins).

The collagen was exposed by partial removal of proteoglycans with 4 M guanidinium hydrochloride and was dehydrated by sublimation with camphene to minimize artefactual distortion of the tissue.

The study of normal articular cartilage showed that the tangential zone of collagen is arranged generally along the split lines of Hultkrantz, but below this the split lines do not correspond to any recognizable collagen orientation.

Osteoarthritic specimens demonstrated deep microfissures and were direct extensions of fibrillation defects seen macroscopically. Selected specimens of early osteoarthritic tibial plateaus demonstrated microscopic fissuring of the collagen framework in planes perpendicular to the split lines of Hultkrantz, suggesting that these fissures may represent fatigue failure of collagen occurring near the free edge of the meniscus and the weight-bearing portion of the plateau.

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University of Western Ontario,
London, ON.

6. Collagen Polymorphism in Ossifying Bony Rudiments of the Human Fetus

D. J. Gates and W. M. Rigal

Different types of collagen exist in bone and cartilage. The synthesis of bone (type I) and cartilage (type II) collagens in cultured bony rudiments of the human fetus was investigated as a preliminary study of collagen polymorphism in pathologic bone formation in man. Normal long-bone rudiments from 6- to 16-week-old fetuses were cultured under lathyritic conditions, in vitro, for 12 hours in the presence of ^{14}C-lysine and ^{3}H-proline. The various developmental regions were dissected from the explants after freezing in liquid nitrogen, then subjected to a sequential extraction procedure designed to facilitate solubilization and removal of the newly synthesized (lathyritic) and pre-existing, unlabelled collagens. Extracts containing labelled and unlabelled collagens were combined after dialysis, and collagen subunits were separated on carboxymethyl-cellulose cation exchange columns

using a linear sodium chloride gradient. Peaks of radioactivity were identified by collagen subunit type, and relative concentrations of bone ($[\alpha_1(I)]_2\alpha_2$) and cartilage ($[\alpha_1(II)]_3$fl) collagens were calculated for each region of the explants. Changes in the molar ratio of $\alpha_1:\alpha_2$ in calcified and noncalcified regions indicate that the appearance of type I collagen is a prerequisite to calcification in the ossifying bony rudiments of the human fetus.

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Edmonton, AB.

7. Comparison of Joint-Force Loading Patterns for Varus, Valgus and Flexion Deformities at the Knee

I. J. Harrington

A bioengineering analysis of force transmission at the knee was carried out by the dynamic three-dimensional technique of Morrison, and the results were compared with those calculated from a static frontal plane analysis. Varus, valgus and flexion deformities were assessed.

Major differences occur for joint-force magnitude and location of the centre of joint pressure at the knee using the two different methods of analysis. The discrepancies are most apparent for flexion deformities.

In valgus limbs, the centre of joint pressure may be located in the medial joint compartment for an appreciable portion of the stance phase of the gait cycle, and at periods when joint-force loading is maximal.

These results suggest that the centre of joint-force pressure cannot be predicted accurately by static analytical methods. The rationale of performing high tibial osteotomies based on static frontal plane calculations is questionable.

Since an osteotomy to provide ideal joint loading throughout the stance phase of the gait cycle cannot be designed, the most practical method of osteotomy might be simple, anatomical restoration of knee alignment.

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Toronto East General & Orthopaedic Hospital,
Toronto, ON.

8. Effects of Electrical Stimulation on Bone Growth In Vitro and on Fracture Healing

W. G. de Haas and J. Watson†*

A noninvasive technique of electrical stimulation of bone growth and fracture healing was studied in vitro and in a patient with a fracture. The growth of embryo chick tibias was found to accelerate in pulsed magnetic and pulsed electric fields, and healing in osteotomized radii in rabbits was likewise accelerated, though inconsistently, when radii were subjected to a pulsed magnetic field. In the case of the patient, a 50-year-old man with a post-traumatic pseudarthrosis of the tibia, treatment in a pulsed magnetic field for 6 weeks resulted in bone union 6 months later.

The principle use of a pulsating magnetic field to induce an electric field at fracture sites promises to have clinical application.

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†Department of electrical engineering,
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Swansea, Wales.

9. Immunogenicity of Osteosarcoma in the Rat, Induced by Murine Sarcoma Virus-Moloney

E. P. Urovitz, F. Langer, A. E. Gross, A. A. Czitrom and S. K. Stylianos

The immunogenicity of a viral induced rat osteosarcoma was studied by the lymphocyte microcytotoxicity test. Intratibial injection of murine sarcoma virus-Moloney (MSV-M) resulted in the development of palpable tumours at the injection site, which histopathologically appeared as osteosarcomas. In 73% of animals these tumours progressed and metastasized to lungs. Lymphocytes from these "progressor" animals demonstrated an ability to kill osteosarcoma cells in vitro (as quantitated in the microcytotoxicity test) while serum from these animals abrogated or blocked the cell-mediated cytotoxicity. In the remaining animals the tumours either failed to develop or regressed spontaneously. Lymphocytes from these "regressor" animals also demonstrated cytolytic activity against osteo-

sarcoma cells in vitro, but serum failed to block the lymphocyte-mediated cytolysis. Both regressor and progressor groups demonstrated humoral cytotoxic antibodies to tumour antigen on the basis of the ability of their serum to kill tumour cells in vitro.

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10. Interface Between Bone and Polymethylmethacrylate Under Load-bearing

J. Miller, D. Burke* and J. W. Stachiewicz†*

The increased awareness by physicians of loosening or breaking of the components of total joint arthroplasty has emphasized the need for experimental studies on the interface between the implants and host bone. A suitable model was designed for laboratory animals to serve as a vehicle for examining this interface. The model consisted of the replacement of a 1.9-cm segment of the midshaft of the dog's femur with a metallic intramedullary device. The device was cemented into place with polymethylmethacrylate. After varying periods of full weight-bearing, the bone and implant were recovered and histologic thin sections obtained by a technique that preserved the surgical polymer.

There were two impressive findings. First, blood left on the endosteal surface of the bone at the time of the operative procedure weakened the bone-cement interface and may have contributed to failure. Gaps of 500 to 1000 μ, filled with blood, were seen, in contrast to very thin gaps where the bone was prepared by scrupulous cleaning before insertion of the polymer. Second, cracks appeared in the surgical polymer, in a radial fashion, running from the metallic implant to the bone-cement interface. These were often multiple, occasionally huge, and probably were the product of "hoop stress" — that is, tensile forces developing in the cement as a result of shrinkage of the methacrylate around an unyielding metallic core. Calculations indicated that this hoop stress can be large enough to exceed the tensile strength of the polymer.

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†Department of mechanical engineering,
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Montreal, PQ.

11. Method of Hemagglutination for the Study of Collagen-Glycosaminoglycan Interactions

L. B. Conochie, J. E. Scott, W. P. Faulk and A. Bailey

It has been postulated that the function of various connective tissues in the body is related to differences in their molecular composition and internal architecture. The interaction of collagen and glycosaminoglycans in articular cartilage may be important in determining its structure. Changes in this interaction may have a bearing on the susceptibility of articular cartilage to undergo changes related to age and wear-and-tear.

A simple method of hemagglutination, originally designed to detect and measure antibody can also monitor collagen-glycosaminoglycan and collagen-proteoglycan interaction in vitro under physiologic conditions of pH and ionic strength.

Tanned sheep erythrocytes coated with soluble collagen are agglutinated in the presence of certain connective-tissue polysaccharides. The "strength" of the collagen-glycosaminoglycan interaction is assessed by serial dilution of the glycosaminoglycan solution until the end point of agglutination is achieved.

In this system, chondroitin 4-sulfate and dermatan sulfate interacted strongly with collagen. Chondroitin 6-sulfate and heparan sulfate interacted less strongly, and hyaluronate and keratan sulfate were extremely weak interactors with collagen. This interaction requires that the triple helical native collagen molecule be intact, since mild heat denaturation of the collagen abolishes the interaction. In control experiments, with uncoated or albumin-coated erythrocytes, there was no agglutination in the presence of the connective tissue glycosaminoglycans.

This method of hemagglutination is rapid, simple, economical and requires only small quantities of purified material.

Department of surgery,
Montreal General Hospital,
Montreal, PQ.

12. Microcrystalline Collagen: An Effective Hemostatic Agent to Reduce Bone Bleeding

E. L. Thrasher, W. H. Harris and R. H. Cobden

An effective hemostatic agent that will reduce bleeding from bony surfaces, yet not inhibit osteogenesis is essential in orthopedic surgery. Bone bleeding from osteotomy of the greater trochanter, iliac-bone-graft donor sites, intertrochanteric osteotomies or fractures, and many other skeletal injuries is an important factor in operative and postoperative blood loss. Bone wax, oxidized cellulose and thrombin gelatin foam are commonly used despite the lack of quantitative data confirming their value. Bone wax reduces bone bleeding but interferes with osteogenesis.

Microcrystalline collagen, a new agent extracted from bovine hide corium and prepared as microcrystals (length, $< 1\ \mu$), maintains the tertiary structure of the collagen and thus binds platelets. Its efficacy as a hemostatic agent applied to cancellous bone was studied in a series of osteotomies of the greater trochanter in 53 dogs. Microcrystalline collagen reduced blood loss by 73% compared with control values and was appreciably better than other test agents. It reduced blood loss without interfering with union of the greater trochanter after repositioning.

In a series of patients undergoing total hip replacement a similar study was carried out. Various agents were applied to the cancellous bleeding surface of the trochanteric osteotomy. Microcrystalline collagen reduced bleeding from the test site by 77% and did so without interfering with union of the greater trochanter.

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13. Natural History of the Patient with an Infected Total Hip Replacement

G. A. Hunter

Review of the natural history of 127 patients with deep infection after total hip replacement revealed that 19 died after the insertion or excision of the prosthesis. No patient died who had a successful implant in the appropriate position under a dry wound.

Of the patients still living only 17 retained their hip implant in position without further wound complications. The remaining patients had their hip implants excised; most had dry wounds.

Poor management, despite early recognition of the infection resulted in a high rate of excision of the hip prosthesis.

The results of this survey indicate that a second total hip prosthesis should not be inserted following deep infection of the first implant.

Important considerations are the difficulties of distinguishing between a positive wound culture and clinical infection of the wound in arthroplasty of the hip, the bacteriologic aspects of deep infections with reference to the use of prophylactic antibiotics, and the dangers of metastatic infection in the postoperative period.

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14. Pattern of Cortical Bone Loss in Experimental Disuse Osteoporosis

H. K. Uhthoff, C. Palmer and Z. F. Jaworski

The effect of disuse on the humerus, radius, ulna and third metacarpal was studied in eight adult dogs over a period of 2 to 24 weeks. The dogs were immobilized in a shoulder spica; no surgical trauma was introduced.

Radiologic and histologic measurements suggest that bone is not lost gradually, but in a phasic pattern. Early negative bone balance was followed by positive balance at 12 weeks, which in turn was followed by a second, more-pronounced, negative balance. Measurement of the contribution of the periosteal, endosteal and haversian envelopes to bone loss demonstrated an impressive periosteal bone loss. At 24 weeks all cortices had regained a normal density. Any study on the prevention or treatment of disuse osteoporosis should consider the phasic behaviour of bone loss and the contribution of the three envelopes

to it, as well as the individual behaviour of each bone.

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Ottawa, ON.

15. Permanent Deformation of Bone: An Experimental Model in the Dog

C. F. Moseley, V. H. Frankel, A. H. Burstein and K. G. Heiple

Study of two cases of traumatic bending of long bones without evidence of fracture has demonstrated, at follow-up, new bone formation particularly on the concave aspect; in one case an onion-skin appearance was noted.

An animal model was developed to study, in vivo, the nature of, and the response of bone to, plastic deformation.

An instrument applying a four-point bending load to the canine fibula during a sterile procedure was designed so that the load-deformation curve could be monitored during application of the load. One fibula was subjected to loading into the plastic region. This was demonstrated by the shape of the load-deformation curve and by the visual, palpable, and radiologic evidence of residual deformation. With that load-deformation curve as a reference the other fibula was loaded within the elastic region only as a control.

Histologic examination and examination by ultraviolet light for tetracycline fluorescence have failed to demonstrate either the morphologic basis of plastic deformation or a relation between the remodelling pattern and the loading configuration.

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16. Prospective Biopsy Study of Collagenous Tissues in Arthritic Patients for Evidence of Immune Complex Deposition

E. Bennett, S. Richer and D. Cooke

Immunoglobulins (IgG, IgA, IgM) and complement components (B_{1C} were previously identified in the surface layers of articular collagenous tissue biopsies of many patients with rheumatoid arthritis (RA), in a location and form suggesting immune complex formation. The work was extended as a prospective study in which randomly selected arthritic patients, all of whom were candidates for reconstructive surgery, were included. In addition to cartilage and synovial tissue biopsies, the disease state and severity were assessed, and immunologic parameters in serum and synovial fluid were measured. Data on 208 patients studied for evidence of immune complex deposition in cartilage have been correlated with their diagnostic groups. In patients with classical RA, more than 92% had positive findings. Of those with noninflammatory arthritis, findings were positive in 52% of patients with primary degenerative arthritis and 20% of patients with secondary degenerative arthritis. Findings in nonarthritic joint biopsies were positive in 5%. The relatively high incidence of positive findings in the primary degenerative group suggests a potential relation between some of these cases and RA, and the potential for immune mechanisms to be involved in pathogenesis. The proportion of positive findings in patients with classical RA is highly significant when compared with the proportion in any other group studied ($P < 0.001$). These data support the notion that cartilage-localized immune complexes in RA play an integral role in chronicity, perhaps as a source of persisting antigen.

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Kingston, ON.

17. Resurfacing the Articular Cartilage of Adult Rabbits by Multiple Perforations Through Subchondral Bone

N. Mitchell and N. Shepard

Articular cartilage was removed from both distal femora of adult rabbits. One knee served as a control; the other was studied after multiple perforations had been made through the subchondral bone. Animals were sacrificed at intervals up to 1 year and cartilage regeneration was studied by light and electron microscopy. Initially a cartilaginous material, staining heavily with safranin 0, filled the holes, and under light and electron microscopy this material resembled hyaline cartilage. By 12 months

resurfacing of the cartilage had occurred, though the material lost its hyaline appearance after 8 months and resembled dense collagenous tissue. Since this tissue withstood wear for 1 year it is speculated that it may have some use in temporary resurfacing of partial cartilage defects.

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18. The Reversibility of Tissue Differentiation Around Screws

H. K. Uhthoff and J. P. Germain

Previous studies have demonstrated the influence of mechanical factors on *cell* differentiation — movement around screws inserted into compact bones led to bone resorption and absence of movement led to bone formation. The present study of 12 adult dogs showed that the morphology and function of *tissues* were also subject to mechanical factors. A 4-week-old callus, formed under conditions of mechanical neutrality, was resorbed when subjected to gross movement. On the other hand bone resorption resulting from movement around the screw ceased and bone formation started when the movement was suppressed. The results, obtained over an 8-week interval, were based on radiologic, histologic and fluorescence microscopic examinations. It is concluded that not only the differentiation of undifferentiated cells but also the state of differentiated tissues are influenced by local mechanical factors.

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19. Scanning Electron Microscopy of Superficial Defects in Articular Cartilage

F. N. Ghadially and A. F. Oryschak

Superficial defects approximately 2 mm in diameter were produced by removing a thin shaving of cartilage from the medial femoral condyle of the rabbit. On the surface of these defects many chondrocytes and their lacunae, laid bare by this procedure, were seen. In specimens collected over the 4- to 14-day period after operation, the lacunae became progressivly shallower and their margins rounded and obscured. At 3 to 4 weeks a few, small, thread-like and ribbon-like structures were seen arising from the margins and surface of the defects. With the passage of time these became quite prominent, and at 6 months numerous wave-like, band-like, rope-like and thread-like formations were seen coursing over the floor of the defects.

Collectively these formations may be referred to as "flow formations" for they appear to derive from streaming or flowing of cartilage substance, engendered by the pressure of load-bearing and shearing forces in the joint. The importance and ultimate fate of these new structures, revealed by scanning electron microscopy, remain to be determined.

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20. Stress Analysis of the Subtrochanteric Region of the Femur

G. V. B. Cochran, J. Fielding and R. E. Zickel

The subtrochanteric fracture is a clinical problem in biomechanics; the relative frequency of nonunion or failure of fixation, or both, is related to high mechanical stress. Experiments were designed to determine subtrochanteric stresses in relation to loading, muscle forces and devices for fracture fixation.

The subtrochanteric segment of six intact human femora was instrumented in vitro, with electrical resistance strain gauges. Static loads were applied in three configurations: directly to the femoral head, simulating two-leg stance; indirectly by apparatus, simulating single-leg stance with active abductors; and indirectly, simulating single-leg stance with active abductors *and* tensor fascia lata. Strain measurements during loading were obtained and data converted to stress.

For two-leg stance, experimental results supported the theoretical stress calculations of Koch and of Rybicki and colleagues. For single-leg stance, results indicated that abductors alone greatly increase subtrochanteric strain, up to 600% over two-leg stance.

Counteracting forces, represented by the tensor fascia lata, exert a protective effect, limiting stress to acceptable levels. After osteotomies, performed to simulate fractures, stresses in the fragments varied with type of internal fixation, muscle action and loading configuration. The addition of plate fixation to *intact* specimens, representing healed fractures, produced substantial "stress protection"; bone stress was reduced 30 to 50% near the plate, and medial-lateral distribution was altered markedly. In contrast, a "Zickel" nail intramedullary device, provided secure fixation while maintaining more physiologic stresses in bone with lower stress in the metal.

Alteration in stress patterns caused by internal fixation may be important in fracture healing in view of the recognized relation of mechanical stress to the deposition and remodelling of bone. Regarding strength of internal fixation, the "device-bone unit", rather than the strength of the device alone, is an essential concept.

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New York, NY.

21. Traumatic Dislocation of the Hip: A Microangiographic, Histologic and Radiologic Study

Clive P. Dincan and Sun-Shik Shim

Experimental study of traumatic posterior dislocation of the hip in 210 rabbits (60 mature, 150 immature) revealed that the dislocation caused circulatory embarrassment to the femoral head in both adult and immature rabbits. The major causative factor was damage to the extraosseous epiphyseometaphyseal vessels of blood supply and drainage. Disturbance of the circulation in immature animals worsened with continued dislocation reaching a maximum within 24 hours. Recovery did not start until 7 days after dislocation.

The perfusion deficit was most severe in immature animals and was maximal in the anteromedial portion of the femoral head, which was either devoid of perfusion or considerably underperfused within 10 minutes of dislocation. Recovery of perfusion within the femoral head of immature animals coincided with the development of an extraosseous network of epiphyseal blood supply and drainage on the posteroinferior femoral neck.

Reduction of the dislocated hip in growing animals damaged the blood supply to the femoral head, but early reduction enhanced complete recovery of blood supply. Reduction 12 hours or longer after the dislocation did not benefit the rate and extent of return of perfusion in the femoral head.

In adult animals, the intraosseous epiphyseometaphyseal anastomoses across the obliterated growth plate minimized the effects of damage to the extraosseous epiphyseal nutrient system.

Aseptic necrosis of the femoral head, demonstrated histologically, occurred in most animals regardless of skeletal maturity or reduction of the hip dislocation. It was more common and extensive in immature animals.

Abnormal radiologic features within the femoral head were seen infrequently between 5 and 10 weeks after dislocation, despite the high incidence of aseptic necrosis, but correlated well with the histologic findings.

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DEXON VERSUS CONVENTIONAL SUTURES IN HERNIA REPAIR*

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An unselected study of 87 inguinal herniorrhaphies was carried out over a 2-year period using polyglycolic acid (Dexon) sutures in 46 procedures and conventional sutures in the remaining 41. Tissue reaction was the same with both types of suture; however, the incidence of recurrence was lower with the use of conventional sutures. This study has not confirmed the superiority of Dexon sutures reported in other studies.

Une étude portant sur 87 cas non sélectionnés d'herniorrhaphies inguinales a été réalisée sur une période de 2 ans, alors que des sutures d'acide polyglycolique (Dexon) ont été utilisées dans 46 interventions et des sutures conventionnelles dans les 41 autres opérations. La réaction tissulaire a été identique avec les deux types de sutures; toutefois, la fréquence des récidives a été plus faible avec l'emploi des sutures conventionnelles. Cette étude n'a pu confirmer la supériorité des sutures Dexon signalée dans d'autres études.

POLYGLYCOLIC acid (Dexon) suture is a relatively new absorbable nonprotein material. Reports are unanimous in asserting that polyglycolic acid is absorbable, has superior tensile strength to conventional suture material and causes minimal tissue reaction.[1-8] Postlethwait[1, 2] reported that one third of the initial strength of polyglycolic acid is lost in 7 days and about 80% by 2 weeks. Lichtenstein[9] stated that any suture material that loses most of its strength within 2 weeks should never be used to close supportive structures (aponeurotic tissues of the abdominal wall). Rabbits regain less than 30% of the original tensile strength at the wound site within 2 weeks, and after 2 months the wound is only about 41% as strong as normal tissue.[9] Postlethwait[2] concluded that longer retention of strength by the polyglycolic acid suture would be desirable.

We compared Dexon with conventional suture material used for repair of 87 inguinal hernias in 76 patients.

METHODS

Numbered envelopes prepared in advance were opened by the supervising nurse in the operating room. Numbers were chosen from a random table and the surgeons used the suture material designated. Sutures designated as conventional were Dacron, cotton or silk. Cotton alone was used for all layers in a few cases. Conventional sutures were used in 41 repairs. Dexon suture was used for all layers in 46. In several patients undergoing bilateral repair, polyglycolic acid sutures were used on one side and conventional sutures were used on the other.

RESULTS AND DISCUSSION

Surgeons who were unaware of the suture material used evaluated the wound sites at the follow-up examinations. Factors adversely affecting wound healing, such as obesity, systemic disease and age were not taken into consideration in patient selection. Patients were followed up and examined after a period ranging from 9 to 37 months postoperatively. Criteria used in these examinations were: (a) recurrence, (b) early and late complications, and (c) hypertrophy of scar tissue.

In all, 80 operative repairs in 69 patients were evaluated (follow-up rate, 91%). Of these, 41 were repairs with Dexon and 39 with conventional sutures. Six recurrences were observed in the Dexon group (14.6%) and three in the conventional group (7.7%), indicating no superiority of Dexon suture in the repair of inguinal hernias. In fact, there is a low probability that the use of nonabsorbable material is more suitable in preventing recurrence ($\chi^2 = 0.4$, 1 df).

The postoperative complication rate in our study was similar in the two groups (Table I). With respect to scar tissue formation, two operative scars in each group were more prominent than the rest.

Gallitano and Kondi[5] reported that the

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TABLE I.—POSTOPERATIVE COMPLICATION RATE

Complications	*Dexon suture*	*Conventional sutures*
Slight induration and tenderness	1	1
Slight edema and ecchymosis	4	1
Hematoma (no drainage required)	0	2
Small subcutaneous abscess (drained)	0	1
Total	5	5

rate of incisional hernias with Dexon (used in fascial layers) was markedly diminished in closures of abdominal incisions. In our cases we found a 7% difference in the rate of recurrence in inguinal hernia repairs.

CONCLUSIONS

In spite of the impressive results from other reports indicating less tissue reaction from polyglycolic acid suture than from other suture materials, our study showed no substantial difference. We are not convinced of the advantages of polyglycolic acid suture for closure of supportive structures and therefore we routinely use Ethiflex suture (synthetic Teflon-Dacron) for closure of the fascial layers in the repair of inguinal hernias.

We acknowledge the help of professor Charles Rand, Department of epidemiology, faculty of medicine, University of Western Ontario.

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USE OF THERMOGRAPHY FOR THE EARLY DIAGNOSIS OF DEEP VEIN THROMBOSIS FOLLOWING HIP OPERATIONS*

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Up to 50% of patients suffer from deep vein thrombosis (DVT) after major hip surgery. Frequently DVT cannot be diagnosed clinically. To the present, venography alone has been used in these patients, but it is time consuming, necessitates an intravenous dye injection and is not without complications. Now, however, the technique of thermography is available as an additional diagnostic aid.

The results of thermography were assessed in 24 patients who had recently undergone major hip operations and compared with those obtained by venography. Thermography did identify DVT in the lower leg veins of patients with no clinical symptoms, but higher obstructions were only diagnosed by venography. Thermography gave one false-positive result later disproven by venography.

Thermography has the advantage of being noninvasive and economical; it will become more useful when smaller portable systems are developed.

Jusqu'à 50% des patients qui subissent une chirurgie majeure de la hanche, ont a souffrir de thrombose veineuse profonde (TVP). Fréquemment, la TVP ne peut être diagnostiquée cliniquement. Jusqu'à présent, seule la phlébographie a été utilisée chez ces patients, mais elle est fastidieuse, requière l'injection intraveineuse d'un colorant et n'est pas sans complication. Toutefois, on peut maintenant avoir recours à la thermographie comme technique de diagnostic additionnelle.

Les résultats thermographiques ont été évalués chez 24 patients qui avaient subi depuis peu une intervention chirurgicale majeure de la hanche, et ils ont été comparés à ceux obtenus par phlébographie. La thermographie a pu identifier les TVP dans les veines inférieures de la jambe chez des patients exempts de symptômes cliniques, mais les obstructions supérieures n'ont pu être diagnostiquées que par phlébographie. La thermographie a donné un faux résultat positif qui a pu, plus tard, être rejeté par phlébographie.

La thermographie a l'avantage d'être une technique non-envahissante et économique; elle deviendra plus utile lorsque des systèmes portatifs, moins encombrants auront été mis au point.

THE proportion of patients in whom deep venous thrombosis (DVT) developed after hip surgery has been reported to be as high as 50%.[1, 2] Clinical signs may be misleading or totally absent in many patients. Lambie and colleagues,[3] who reported on 111 surgical patients considered to be at high risk, found that this complication developed in almost half the patients and of them, the diagnosis was unsuspected clinically in two thirds despite careful scrutiny; of those in whom the diagnosis was made clinically, the diagnosis was falsely positive in a quarter. Orthopedic surgeons are unsure of the value of prophylactic anticoagulants in patients with proven DVT[4-8] and there is no proof that such treatment actually decreases the incidence of fatal pulmonary embolism; neither is there general agreement on the anticoagulant drug of choice nor the ideal method of administration.[9-13]

Because clinical diagnosis is fraught with error, there is need for a simple, noninvasive, rapid, readily repeatable, diagnostic test to identify DVT in the lower limb for all susceptible patients with or without demonstrable clinical signs. Cooke and Pilcher[14] considered the chemical activity in the limb accompanying, and consequent upon, a thrombotic episode. They suspected that increased heat, though subclinical, could be present from an early stage and subsequently reported the successful use of thermography to detect subclinical increases of limb heat in patients with DVT. This work and that of Pilcher[2] stimulated our study.

METHODS AND PATIENTS

Principles of Thermography

Under standard conditions, the thermal contours or patterns that exist on exposed human skin are determined by applying the

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principle that heat is conducted to the skin secondary to variations in blood flow.

The infrared radiation emitted by the skin can be collected optically, transformed into electrical impulses, amplified and presented in display form. This is the essence of the AGA thermovision system 680 (Agatronics Ltd., Toronto, Ont.) that we have used. It has been described in detail by Clark.[15] The immense advantage of a technique as noninvasive as routine photography is obvious.

Technique of Screening

Each patient is taken by stretcher to a room where the constant ambient temperature is maintained between 20 and 22°C. The patient is exposed (except for a T-binder) below the umbilicus for 20 minutes before examination. The legs at the ankles are supported on a bolster under the Achilles tendon, which separates the ankles by 15 cm and keeps the calves clear of the stretcher by 5 cm. Twenty minutes is ample time for the surface temperature of the leg to equilibrate with the ambient temperature.

The time taken to examine one patient averages 20 minutes (after 20 minutes of cooling). As recommended by Cooke and Pilcher,[14] the thighs and calves are examined separately. The thermographic patterns are recorded in shades of grey (white = warm; black = cool) and coloured isotherms on Polaroid film. All thermographic examinations have been performed and interpreted by one of us (LJM).

In addition to thermography, venography was performed in patients whose first thermogram after hip surgery was performed between the 2nd and 4th postoperative day and then every 3 or 4 days throughout the postoperative period. In such patients one satisfactory venogram is obtained after the first thermogram, usually between the 3rd and 5th postoperative day. Each patient is then observed until fully ambulatory or until the time of discharge from the orthopedic unit. The presence or absence of clinical signs of DVT were recorded in all patients by one of us (AK).

Patients

In the 12-month period ending July 1974 we were able to complete this protocol for 24 patients. The details concerning sex, age and surgical procedure are summarized in

TABLE I.—SUMMARY OF RESULTS OF THERMOGRAPHY AND VENOGRPAHY IN 24 PATIENTS*

Patient	*Age, sex*	*Diagnosis*	*Procedure*	*Clinical signs of DVT*	*Thermogram*	*Venogram*
1	57 M	F L hip	IF	−	−	−
2	66 M	OA L hip	TH	−	−	−
3	67 F	OA R hip	TH	−	−	−
4	69 M	OA R hip	TH	−	−	−
5	85 F	F R hip	IF	−	−	−
6	60 M	Moore's P	Revised to TH	−	−	−
7	61 F	OA R hip	TH	−	−	−
8	70 F	Failed TH	Revision of TH	−	−	−
9	70 F	OA R hip	TH	−	+	+
10	78 F	F L hip	IF	?	+	+
11	77 F	F R hip	IF	+	+	+
12	49 F	F L hip	IF	−	+	+
13	71 M	Nonunion, F R hip	TO & BG	+	+	+
14	72 F	Nonunion, F R hip	Moore's A	+	+	+
15	69 F	AN L hip	TH	?	+	+
16	67 F	F L hip	IF	+	+	+
17	77 F	F L hip	Thompson P	−	+	+
18	56 M	F L hip	IF	+	+	+
19	75 F	OA L hip	TH	−	−	+
20	68 F	F L hip	IF	?	−	+
21	76 F	F R hip	IF	−	−	+
22	65 F	OA R hip	TH	−	−	+
23	62 M	F R hip	IF	−	+	−
24	53 M	OA R hip	VO	?	+	−

F = fracture, L = left, R = right, OA = osteoarthritis, P = prosthesis, TH = total hip replacement, IF = internal fixation, AN = aseptic necrosis, TO = trochanteric osteotomy, BG = bone graft, A = arthroplasty, VO = varus osteotomy.

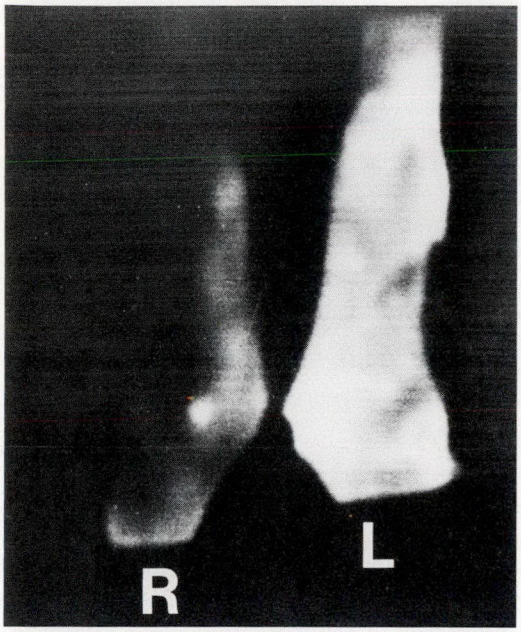

Fig. 1.—Positive thermogram — marked increase in heat in whole limb (white = warm).

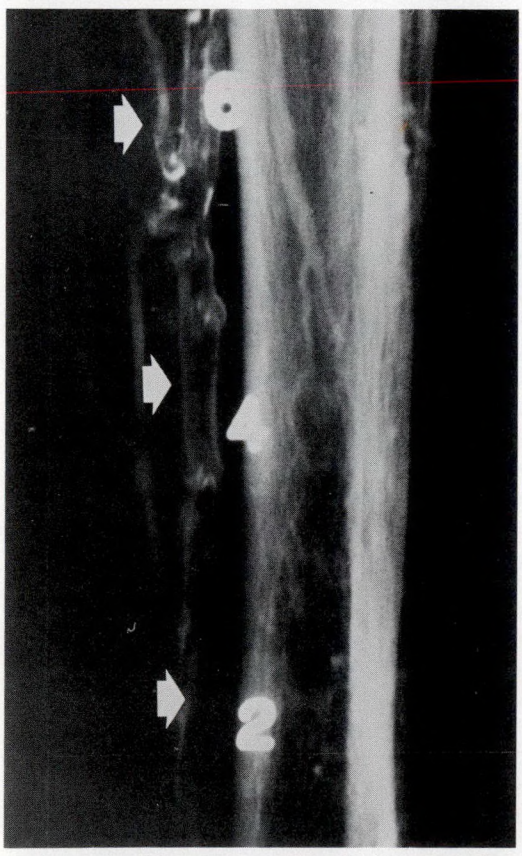

Fig. 2.—Positive venogram indicating extensive clot in soleal vein.

Table I; this table also indicates the clinical, thermographic and venographic findings in all the patients.

Results

Eight patients (1 to 8) showed no evidence of DVT on clinical, thermographic or venographic examination.

Ten patients (9 to 18) showed evidence of DVT on thermographic (Fig. 1) and venographic (Fig. 2) examination. Five of these (nos. 11, 13, 14, 16 and 18) had clinical evidence of DVT at the time of the first thermographic examination. In two (10 and 15) the clinical evidence was equivocal. Three patients (9, 12 and 17) had no clinical suggestion of DVT throughout the postoperative period. In patient no. 16, a 67-year-old woman with an intertrochanteric fracture of the left hip, internal fixation with Richards screw and plate was done 24 hours after injury. The patient developed clinical signs of DVT in the left leg on the 3rd postoperative day. Thermogram on the 3rd postoperative day was positive (Fig. 1). Venogram on the 4th postoperative day was also positive (Fig. 2).

Two patients showed evidence of DVT on venography, but serial thermograms were normal. In one (no. 20) the clinical evidence was equivocal. One patient (no. 19) had no clinical suggestion of DVT.

In two patients (21 and 22) localized high femoral thrombosis in the abnormal leg was demonstrated by venography. We could not prove by means of thermography, the presence of high femoral thrombosis on the operative side. The increased heat in the upper thigh due to the operation obscured the thermogram immediately and this heat increase persisted throughout the period of observation. There was no clinical suggestion of DVT in either patient. In patient no. 21, a 76-year-old woman with an intertrochanteric fracture of the right hip, internal fixation with Richards screw and plate was carried out within 24 hours of the accident. There were no clinical signs of DVT throughout the postoperative period. Thermography was normal on the 5th, 8th and 12th postoperative days (Fig. 3). Venogram on the 6th postoperative day was positive (Fig. 4).

Two patients had normal venograms, but

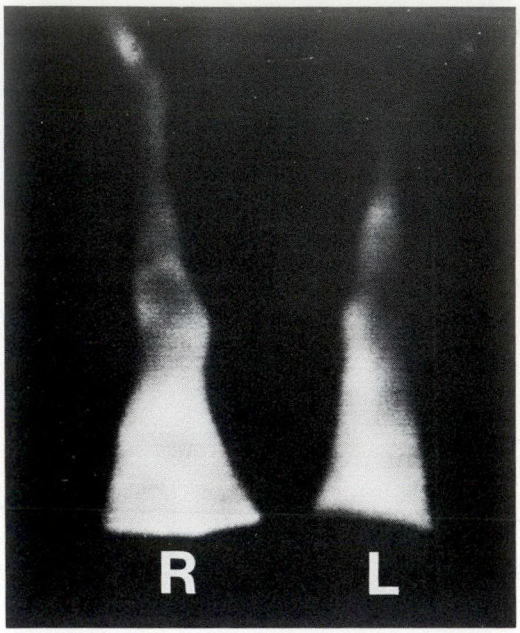

Fig. 3.—Thermogram demonstrates increased heat in upper thigh around operative site — a constant thermographic finding in postoperative hip surgery.

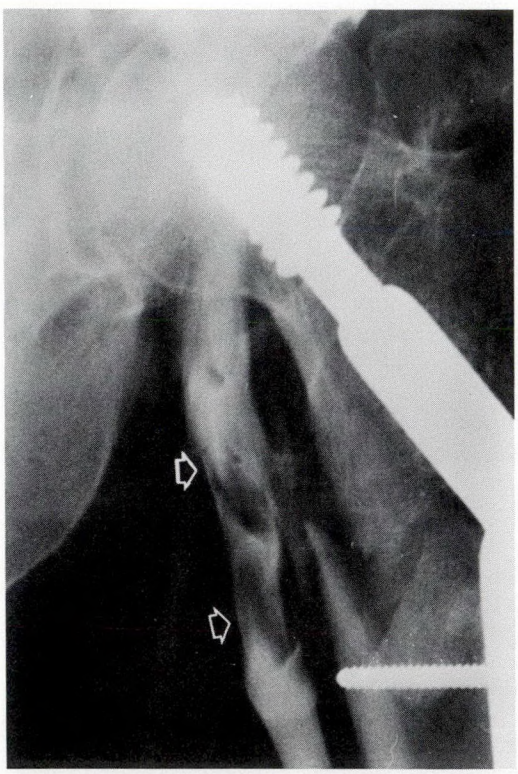

Fig. 4.—Positive venogram indicating presence of clot high in femoral vein. There was no clot in distal venous system.

definitely positive thermograms. One (no. 24) had extensive ecchymosis and swelling of the lower leg following a femoral osteotomy; clinically it was obvious that the thermogram would be of no diagnostic value. In the other patient (no. 23) there was no clinical suggestion of DVT. However, we were unable to find a cause for this false-positive thermogram.

Among 10 patients with normal venograms there was one false-positive thermogram and among 5 patients with venographic evidence of DVT in the calf there were two false-negative thermograms.

Discussion

In the early diagnosis of DVT of the lower limb, venography is the only method of examination that has an accuracy approaching 100%. It is time consuming, necessitates an intravenous injection of dye and is not without complications. Because it is noninvasive and because the cost of each test is reduced by two thirds, thermography has obvious advantages over venography.

We did not find thermography as accurate as did Cooke and Pilcher.[14] However, as a screening tool for the examination of patients with no clinical suggestion of DVT, it is useful in the identification of thrombosis of the soleal and popliteal veins. Because of the heat generated by the postoperative reaction after hip operations, thermography is of no value in identifying patients with localized high femoral thrombosis on the side that has been operated on. Although none of our patients had venographic evidence of iliofemoral thrombosis on either side, the presence of postoperative reaction following hip operations would make such a diagnosis difficult, thermographically, but would not be a problem in patients on medical services who had not had a recent surgical procedure involving the hip or leg. The definitive diagnosis of DVT in patients with positive thermograms, as well as those with suggestive clinical findings, still must depend on venography.

Although the thermovision system is mobile, it is unwieldy. In a hospital where patients are accommodated two to a room, the logistics of wheeling the apparatus from one room to another are practically impos-

sible. The suitability of a battery-operated, completely portable, small unit for this purpose (AGA thermovision 750) is being investigated.

Conclusion

Following hip operations, thermography of the lower limb is a useful screening technique in diagnosing deep venous thrombosis of the soleal and popliteal veins. It is economical and noninvasive. The thermovision system used for this study is mobile, but unwieldy. It is hoped that a completely portable, small unit will soon become available.

We are indebted to the department of visual education, St. Michael's Hospital, Toronto, for their unstinting and cheerful aid in the preparation of the prints, and to Miss K. Arthurs for her patience and help in the preparation of the manuscript.

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PROPHYLACTIC ANTIBIOTIC THERAPY AND HEART VALVE REPLACEMENT*

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Patients undergoing cardiac bypass for heart valve replacement maintained adequate blood concentrations of cloxacillin throughout the duration of bypass, provided their initial blood concentration was in the therapeutic range. Blood levels related to the time between the last preoperative dose of antibiotic and operation. Maximal values were achieved if an intraoperative bolus of drug was given.

Des patients qui ont subi une dérivation cardiaque pour le remplacement d'une valvule cardiaque ont maintenu des concentrations adéquates de cloxacilline pendant tout le temps ou ils ont été sous dérivation, en autant que les concentrations initiales étaient à l'intérieur des taux thérapeutiques. Les taux sanguins étaient reliés à l'intervale de temps écoulé entre la dernière dose d'antibiotique administrée avant l'opération et l'intervention elle-même. Les valeurs maximales ont été obtenues lorsqu'une dose massive de médicament a été donnée pendant l'intervention.

BECAUSE of the associated mortality,[1] infection of valve prostheses remains of major concern to the cardiovascular surgeon. Currently, patients undergoing heart valve replacement receive prophylactic antibiotic therapy in the intraoperative and early postoperative period. Although the benefits of such a practice are questionable, the current low rate of early postoperative valvulitis[2] makes it unlikely that a definitive study of risks *v.* benefits would, or could, be undertaken.

Current concern, we believe, should be directed to the appropriateness of antibiotic used, judged by the data available on organisms causing prosthetic valvulitis and their corresponding antimicrobial sensitivity. Further, the optimal timing and duration of such therapy as well as the optimal drug dosage warrant consideration. The latter is of importance since data .are conflicting. One study indicated that despite the agent used, cardiac bypass was associated with a precipitous drop in blood antibiotic concentrations to subinhibitory values.[3] A second study suggested that provided prepump values were satisfactory such a phenomenon did not occur.[4] Our study attempts to clarify this controversy.

MATERIALS AND METHODS

Twelve adult patients (seven women, five men) undergoing single valve replacement (nine aortic, three mitral) in late 1974 and early 1975 were studied. The average age was 58 years (range, 16 to 76 yr). In all cases the preoperative serum creatinine concentration was less than 1.5 mg/dl and there was no evidence of hepatic dysfunction as judged by normal values for serum bilirubin, alkaline phosphatase, lactic dehydrogenase and serum glutamic oxaloacetic transaminase concentrations.

Ten patients received ampicillin plus cloxacillin, while two, with a history of an allergy to penicillin, received lincomycin. The dose of each antibiotic in all cases was 0.5 g every 6 hours. The medication was given orally 1 day before operation and by intramuscular injection on the day of operation. In the later part of the study, additional antibiotic was given in standard dosage intraoperatively by intravenous bolus injection.

The time of the last dose of antibiotic prior to the initiation of cardiac bypass, to the nearest half-hour, was recorded, as were the times at which intraoperative blood samples were obtained. These were taken on three occasions: just before initiation of bypass; 30 minutes later, while on bypass; and immediately on completion of bypass. All blood samples were taken from the femoral artery line, allowed to clot and then spun down. The resultant serum samples were stored at $-70°C$ until assayed.

The volume of blood used in priming the pump oxygenator, as well as of any blood given intraoperatively, was recorded, as were those of other solutions given during the operative period.

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Serum cloxacillin levels were determined and the minimum inhibitory concentration (MIC) and minimum bacteriocidal concentration (MBC) estimated. The MIC and MBC were ascertained with the aid of a nonpenicillinase-producing strain of *Staphylococcus aureus* (ATCC 25923). The patient's serum was serially diluted with antibiotic medium no. 3 (Difco Laboratories, Detroit, MI). An 18-hour culture of *S. aureus,* grown in beef-heart infusion broth (Difco Laboratories), was diluted 1:100 and 1 drop of this, containing approximately 2.5 x 10^5 colony-forming units (CFU), added to each dilution. Following overnight incubation at 37°C the specimens were inspected for turbidity, the MIC of greatest dilution showing none. All dilutions were subcultured on blood agar at 37°C overnight, the MBC being the greatest dilution demonstrating no growth on subculture.

To determine serum cloxacillin concentrations a penicillin-resistant *S. aureus* (hospital strain) was used. It was prepared in a fashion similar to the above but diluted to approximately 6.0 x 10^6 CFU. Of this, 1.5 ml was added to 150 ml of antibiotic medium no. 11 (Difco Laboratories) in agar, the mixture poured into a glass-bottom tray (250 mm^2) and allowed to cool. Cloxacillin standards of known concentration (20.0, 10.0, 5.0, 2.5, 1.25 μg/ml) were prepared in pooled human serum. The known standards and unknown patient samples were allowed to saturate 6-mm filter paper discs and these discs were then firmly pressed onto the test plate. The standards were tested in quadruplicate and the unknowns in duplicate. In all cases the discs were randomly applied. After overnight incubation the zone of bacterial inhibition around each disc was measured with Vernier calipers to the nearest 0.5 mm and the average obtained for each sample essayed. The standards were then plotted on semilogarithmic paper and the unknowns extrapolated from the resultant graph.

Initially, patients received 250 to 500 ml of blood in the form of a pump prime with the occasional patient receiving an additional unit of whole blood intraoperatively. In the latter part of the study, patients often received no blood. An additional 2 to 3 *l* of electrolyte solution and dextrose were given intraoperatively. The average duration of cardiac bypass was 114 minutes (range, 78 to 161 min).

Results

There was one death in the early postoperative period, unrelated to infection. Among the 11 survivors there was no evidence of infective endocarditis at 3-month postoperative follow-up.

The MIC and MBC were determined to a maximum of 1:32. Eight of 10 patients on ampicillin-cloxacillin prophylaxis had adequate concentrations throughout. The remaining two, with lower concentrations, had received their last preoperative dose of antibiotics 9 hours before cardiac bypass. Similarly, low concentrations were achieved in the two patients with lincomycin prophylaxis although one of these had received additional drug intraoperatively.

Thus patients who received ampicillin-cloxacillin prophylaxis within 4 hours of operation had adequate antistaphylococcal activity in their serum throughout cardiac bypass. Lincomycin prophylaxis gave less satisfactory levels; however, the sample number was small.

The cloxacillin values were more than adequate to inhibit the growth of *S. aureus,* cloxacillin-sensitive *Staphylococcus albus, Streptococcus pyogenes* and *Diplococcus pneumonia*[5, 6] throughout the period of cardiac bypass provided the initial value was within the therapeutic range. If serum cloxacillin concentrations were satisfactory at the outset of cardiac bypass they remained so throughout the period of the bypass. Blood values are directly related to the time interval after the administration of the last dose of antibiotic. These data are presented in Fig. 1.

Discussion

The value of prophylactic antibiotics in surgery is in dispute. Some people believe that antibiotics, used in this way, expose the patient to the toxic and allergic risks inherent in the administration of all antimicrobials, that they do not lower the rate of infection, that the normal flora is eradicated, resistant bacteria proliferate and that

these new opportunistic pathogens themselves cause infection that is even more difficult to treat. None the less in surgical procedures associated with a high rate of postoperative infection, the administration of an antibiotic chosen for its effectiveness against pathogens of importance in that particular procedure has been associated with a substantial reduction in the rate of infection.[6,7]

For procedures associated with a low infection rate similar information is lacking. Goodman and coworkers[8] attempted to do a prospective study on the protective role of antibiotics in cardiac surgery. Two cases of potentially preventable *D. pneumoniae* endocarditis occurred in a placebo group and resulted in termination of the study before any statistically valid conclusion could be reached. Nevertheless this study makes it difficult to justify a further similar examination of this question in patients currently undergoing heart valve replacement.

Current concern should be to define the most appropriate drug, the ideal dosage, and the best timing and duration of therapy. The choice of ampicillin and cloxacillin at our centre reflects the importance of gram-positive cocci, particularly *S. aureus, S. epidermidis* and streptococci in causing prosthetic valvulitis.[9] Lincomycin has a spectrum of activity similar to that of cloxacillin and is used in patients with a history of penicillin allergy.

Our results indicate that the combination of ampicillin and cloxacillin achieves satisfactory concentrations of activity against penicillin-sensitive staphylococci even when the last dose of drug is given some hours before operation. However, in view of the prevalence of penicillinase-resistant *S. aureus* in hospitalized patients, blood concentrations of cloxacillin alone are of obvious importance. It is apparent that to achieve maximal blood concentrations of an antibiotic it should be administered as close to the time of operation as possible. Indeed the two patients with no detectable cloxacillin in their blood stream had received no antibiotic for 9 hours before operation. These results are in keeping with a recent study by Kluge and coworkers[4] but differ from an earlier study by Benner.[3] Benner found that, irrespective of prepump anti-

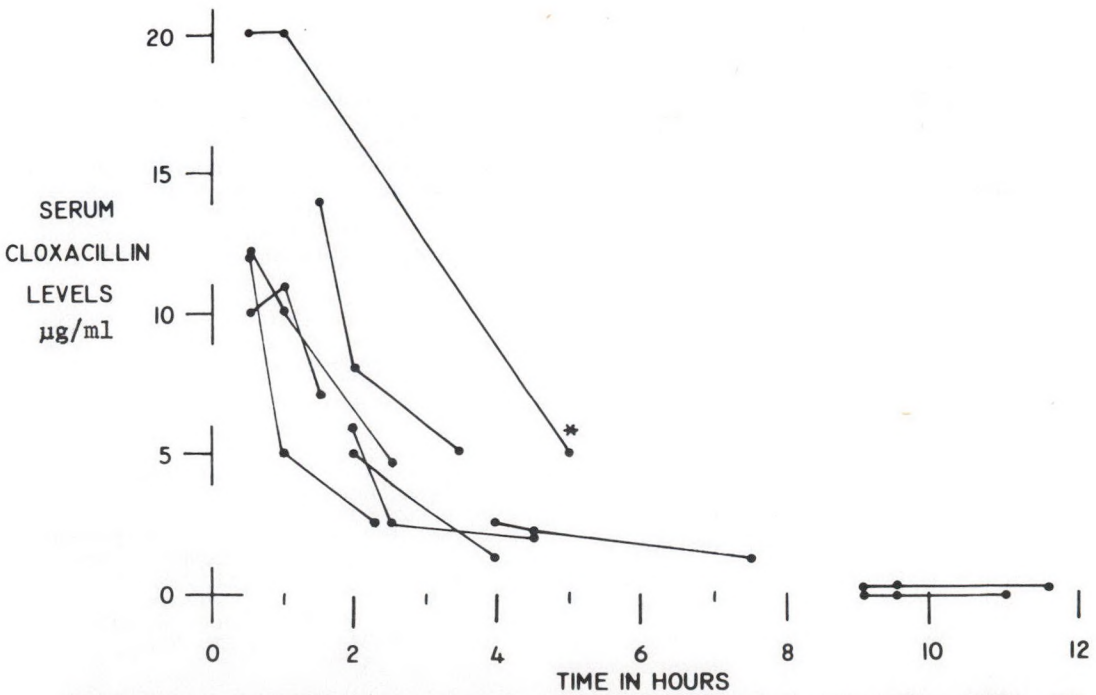

Fig. 1.—Serum cloxacillin concentrations are plotted for each patient at three time periods. "0" represents time at which patient received last dose of drug (0.5 g) before operation. Patients with highest concentrations received drug shortly before operation. * = sample taken in recovery room.

biotic blood concentrations, a precipitous decline occurred with the initiation of cardiac bypass so that concentrations quickly became inadequate. Benner did not investigate the cause of the phenomenon; however, refinements in cardiac bypass technique as well as marked reduction in the amount of blood used during operation may explain this difference.

It is apparent that larger doses of cloxacillin could safely be used in this group of patients. However, it is not clear that this would offer any significant advantage. A larger dose of ampicillin might extend its spectrum of activity to sensitive *Escherichia coli,* and nonpenicillinase-producing *Proteus* spp. Although they are frequent colonizers and cause urinary and respiratory tract infections among patients postoperatively, these organisms are less important in the etiology of valvulitis.[1] Lincomycin, although based on a small patient sample, does not appear to provide adequate blood concentrations in the dosage used.

Most prophylactic regimens for open-heart surgery are initiated in the 24 hours before operation and continued for a variable length of time postoperatively. Restricting prophylaxis to the immediate preoperative period attempts to avoid the rapid change in endogenous microflora that such therapy causes. This period might be shortened further because the penicillins are rapidly cleared from the blood stream and interstitial concentrations lag behind those of the serum by 1 to 2 hours.[10]

Experimental data from Burke's study[11] indicate that prophylaxis is most effective around the time of contamination. If the operative period is when major contamination occurs, as Kluge and colleagues[12] suggest, then this is a crucial time for intensive prophylaxis. We therefore believe that the addition of antibiotics intraoperatively is a useful adjunct to heart valve replacement surgery. How long such prophylaxis should continue after operation in unclear. Prolonged antimicrobial therapy is associated with side effects including overgrowth by resistant microorganisms, diarrhea, drug rashes, drug fever and superinfection. We therefore discontinue such treatment once the patient's chest tubes and indwelling catheters are removed, usually about the 4th postoperative day. With this approach our incidence of postoperative valvulitis over the past year has been less than 1%.

Our data indicate that, with current techniques, provided cloxacillin blood concentrations are adequate at the onset of cardiac bypass, they remain so throughout the operative period. There appear to be no major advantages to increasing the dose of cloxacillin above 0.5 g although this could safely be done. Based on the findings in a small number of patients, a 0.5-g dose of lincomycin provides suboptimal therapy for the eradication of *S. aureus.*

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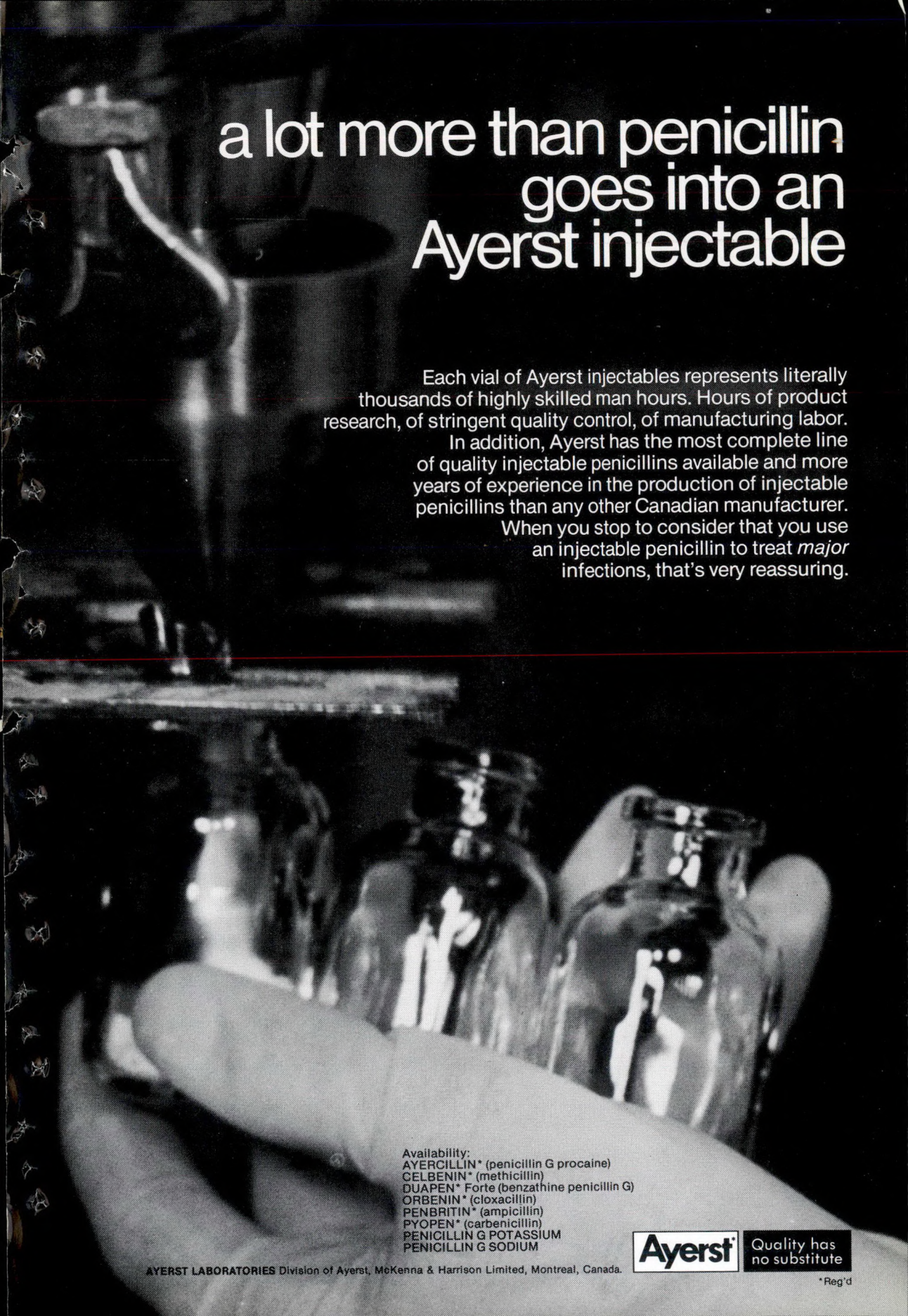

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DIFFUSE CAVERNOUS HEMANGIOMA OF THE SPLEEN

G. C. EJECKAM, MB, BS*

Diffuse hemangioma of the spleen occurred in a 59-year-old man. The presenting features were a dull ache and heaviness in the left upper quadrant for 3 weeks, severe left-sided pain and fever immediately before hospitalization, and a tender mass in the left upper quadrant. The condition was diagnosed at laparotomy; splenectomy was performed. In this case intrahemangiomatous hemorrhage had occurred, but not rupture of the spleen, which is a potentially lethal complication. Other complications of diffuse splenic hemangioma are thrombosis, infarction, infection with abscess formation, and partial calcification of the vascular spaces. The condition is rare; only 56 cases have been reported.

Un hémangiome diffus de la rate est apparu chez un homme de 59 ans. Les symptomes comprenaient une douleur diffuse et une lourdeur présentes depuis 3 semaines dans le quadrant supérieur gauche, une douleur sévère du côté gauche et de la fièvre juste avant l'hospitalisation, et une masse sensible dans le quadrant supérieur gauche. Le diagnostic a été posé à la laparotomie: une splénectomie a été effectuée. Dans le présent cas, une hémorragie hémangiomateuse est survenue sans qu'il y ait toutefois rupture de la rate, cette complication pouvant être mortelle. Les autres complications de l'hémangiome diffus de la rate sont la thrombose, l'infarctus, l'infection avec formation d'abcès, et une calcification partielle des espaces vasculaires. Cette affection est rare: seulement 56 cas ont été signalés jusqu'à maintenant.

DIFFUSE hemangioma of spleen is a rare condition; by 1961 only 56 cases had been reported in the world literature.[1] Diagnosis remains a problem and occasionally exploratory laporotomy is required. This case report illustrates some of the features of the condition.

CASE REPORT

A 59-year-old man was admitted to hospital with a 3-week history of dull ache and heaviness in the left upper quadrant. Two days before admission he experienced a sharp severe pain on the same side and became febrile. There were no urinary symptoms or change of bowel habit and his appetite remained unchanged. Physical examination revealed a tender mass in the left upper quadrant; neither jaundice nor generalized lymphadenopathy were noted. The provisional diagnosis was between malignant lymphoma and carcinoma of colon. Results of barium enema examination were normal. Exploratory laparotomy was performed.

The spleen was found to be enlarged and was removed. It weighed 530 g and measured 15 x 9 x 5 cm. The capsule showed patchy fibrous thickening. Splenic tissue had been almost completely replaced by multiloculated hemorrhagic cysts (Fig. 1).

Microscopy revealed the features of diffuse cavernous hemangioma (Fig. 2). The vascular channels were lined by swollen or flat endothelial cells, and the parenchyma manifested hemorrhage, with organization, and calcium deposition with giant-cell reaction (Fig. 3). Iron and calcium stains were strongly positive.

DISCUSSION

Virchow[2] recognized four types of splenic hemangiomas: hemangioma simplex, cavernous hemangioma, hemangioma telangiectoides and angioblastoma. The hemangioma in the present case had elements of hemangioma simplex and cavernous hemangioma. Cavernous hemangiomas are uncommon in

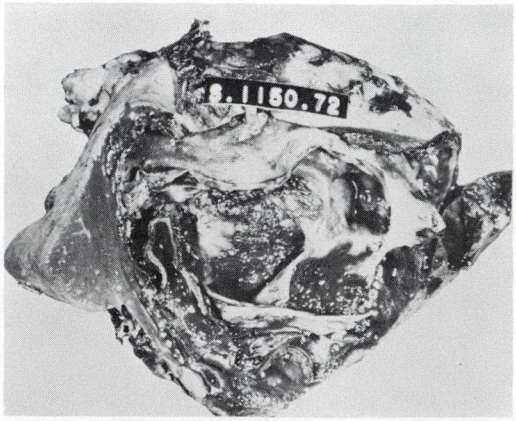

Fig. 1.—Section through spleen showing multiloculated hemorrhagic cystic spaces, with blood clots within spaces. Note area of intact splenic parenchyma on left.

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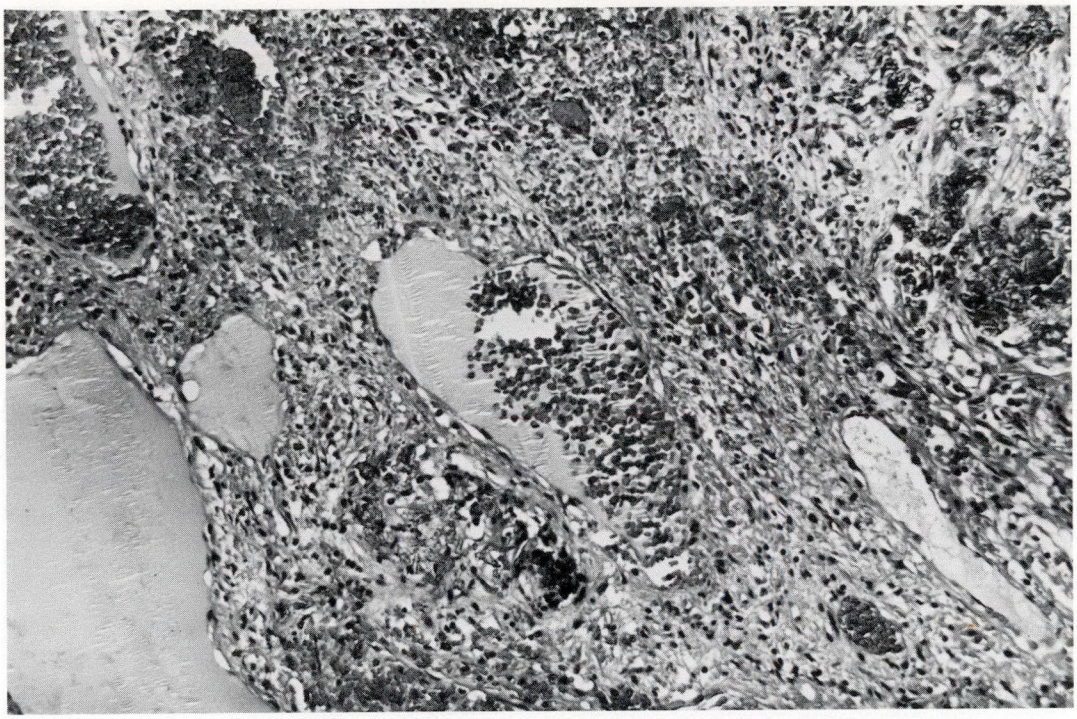

Fig. 2.—Features of cavernous hemangioma, with some capillary vascular formation. Fibrous elements are increased in intervascular areas (hematoxylin and eosin, reduced by 15% from x 150).

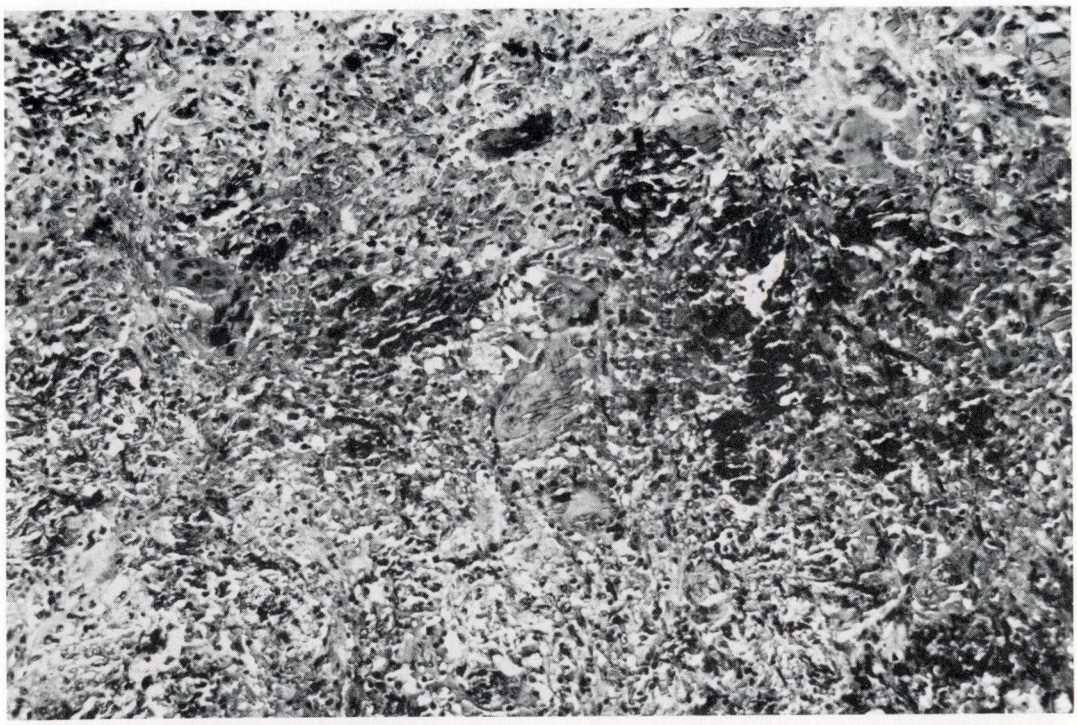

Fig. 3.—Diffuse hemorrhage and organization. Note Gandy-Gamna bodies in parenchyma (hematoxylin and eosin, reduced by 15% from x 60).

the spleen: they may be asymptomatic throughout life and only incidentally discovered at autopsy.[3-5] Occasionally splenic enlargement is found during routine physical examination or symptoms related to splenomegaly are noted.[6, 7] An enlarging left upper abdominal mass, persistent or intermittent pain, vomiting, dyspnea and palpitations, all, either individually or in combination, may indicate a splenic hemangioma. In the patient whose case is reported herein, the sharp pain was probably caused by hemorrhage into the angiomatous spaces with sudden tension of the splenic capsule.

Rupture of the spleen is a complication of intrahemangiomatous hemorrhage. This is fatal if unrecognized. The other chief complications are thrombus formation, infarction, infection with abscess formation and partial calcification of vascular spaces. The combination of focal fibrous scars containing deposits of hemosiderin and calcium — Gandy-Gamna bodies — are indicative of recurrent hemorrhages, organization of blood in some of the hemangiomatous spaces.

In the present case there was evidence of a mild normocytic, normochromic anemia but there were no target cells, schistocytes, neutrophilia or thrombocytosis, indicating autosplenectomy. Also absent were severe anemia and consumption coagulopathy, which have been described as presenting clinical features.[8-10]

Splenic hemangiomas are benign tumours. Reports of malignant transformation of splenic hemangiomas[11-14] must be assessed critically, as adequate documentation is still lacking.

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CONSERVATIVE MANAGEMENT OF EXTRAUTERINE PREGNANCY*

MICHAEL B. QUANE, MAO, FRCOG

An abdominal pregnancy in a 28-year-old nulliparous woman with a fertility problem was treated conservatively. The clinical antenatal course was unremarkable. A healthy 2000-g infant was delivered at term by laparotomy. The placenta was removed at the same time. Three years later the patient had a ruptured tubal pregnancy which was treated by salpingectomy. The literature on extrauterine pregnancy is reviewed briefly.

Une grossesse abdominale survenant chez une nullipare de 28 ans qui présentait un problème de fertilité, a reçu un traitement conservateur. L'évolution clinique prénatale a été sans histoire. Un enfant de 2000 g en bonne santé a été accouché par laparotomie. Le placenta a également été retiré. Trois années plus tard, la patiente a présenté une grossesse tubaire avec rupture qui a été traitée par salpingectomie. La littérature sur la grossesse extra-utérine est revue brièvement.

THE literature on the subject of extrauterine pregnancy is pessimistic; maternal morbidity is significant and fetal death rate is high. Bright and Maser[1] could find only 12 authentic case reports of abdominal pregnancy with maternal and infant survival to 1961. It is therefore understandable that few attempts have been made to treat cases diagnosed in the first trimester conservatively. Is conservative management of such cases ever justifiable?

CASE REPORT

The Clinical Course

A 28-year-old nulliparous woman, with an unremarkable past history, presented with a fertility problem; she had been trying to become pregnant for 2 years, without success. The physical findings, including a pelvic examination under anesthesia, were unremarkable.

Carbon dioxide insufflation was carried out; the gas passed with no demonstrable peristalsis. An endometrical biopsy was done; the curettings showed features consistent with tubercular endometritis, but tubercle bacilli were not identified. The patient was treated with antituberculous drugs for 14 months, after which endometrial biopsy and culture were repeated and reported as normal.

The patient presented 5 months later with a history of secondary amenorrhea for 6½ weeks, intermittent nausea, slight urinary frequency and breast tenderness; she suspected she was pregnant. Results of a complete general examination were normal.

The patient returned for follow-up 1 month later with a 10-week history of amenorrhea, slight backache, left lower quadrant discomfort and slight bleeding for 12 hours.

Pelvic examination under anesthesia revealed a soft and slightly enlarged uterus and a tangerine-sized solid mass of limited mobility in the region of the left appendage. The result of the urine pregnancy test was positive and extrauterine pregnancy was suspected.

The patient and her husband wished the pregnancy to continue despite the risks, which were fully explained to them. Probable genital tract turberculosis and a 4-year history of infertility encouraged me to agree with this decision; the chance for a normal pregnancy was considered remote.

The patient remained in hospital for 9 weeks. In that time she remained well except for a 2-week period of intermittent abdominal discomfort associated with swelling of the pregnancy mass to twice its usual size. The swelling was resonant and soft; it subsided following the passage of flatus and there was no associated constipation, vomiting or pain.

At 19 weeks the patient was discharged and followed on a weekly basis. The mass continued to grow, but the patient complained only of occasional abdominal discomfort. The margins of the mass seemed to be irregular. Initially it filled the left lower quadrant; subsequently it crossed the midline at the umbilicus, and became more symmetrical. Fetal movements were first felt by the patient at 14 weeks, and the fetal heart was first heard at 29 weeks. The head engaged in the pelvic brim at 34 weeks.

The Delivery

The patient was admitted to hospital for elective laparotomy at term. Immediately before laparotomy a blood transfusion was begun and the patient was examined vaginally.

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The uterus could not be outlined; the cervix was not dilated and the fetal head, which was in the pelvic cavity, had no direct relation to the cervix, which lay to the front and slightly to the left of the head.

The abdomen was opened through a vertical, subumbilical, midline incision. The fetus lay longitudinally in the peritoneal cavity; an incomplete sac had formed around it; the pouch of Douglas was inferior; the posterior leaf of the left broad ligament and the placenta were anterior. The placenta had developed normally on the posterior leaf of the left broad ligament. The broad ligament itself had been drawn high up into the peritoneal cavity, and in this way formed much of the anterior and left anterolateral wall of the sac. Superiorly, the wall of the sac was formed by the transverse colon and mesentery. The posterior parietal peritoneum formed the posterior wall of the sac. The sac was formed on the right side anterolaterally in part by adhesions between the omentum and the small intestine. The uterus lay above and slightly to the left of the symphysis pubis. The right appendage was free; the left appendage formed a part of the mass including the broad ligament and placenta.

The Baby

The infant was removed with ease by dividing the loose adhesions between the small intestine and the omentum on the right side. The baby (a normally developed 2000-g female) breathed spontaneously and remained well.

The Placenta

A decision was made to remove the placenta. This was done by approaching it from the attachment between the transverse colon and its mesentery, and the amniotic membranes. The membranes were peeled off easily with care taken to avoid damage to the middle colic artery. Brisk bleeding was encountered in separating the placenta from its main maternal blood supply in the left broad ligament. At this stage, the rate of blood transfusion was increased by the application of positive pressure. Hemostasis was secured by removing the posterior portion of the left broad ligament and the left fallopian tube and ovary. The abdomen was closed without drainage. The patient's general condition remained good throughout. The estimated blood loss was 2*l;* 5 units of blood had been transfused. The mother's convalescence was uneventful; the mother and baby were discharged on the 18th day.

Subsequent Course

Three years later, while on vacation, the patient complained of vomiting, intermittent abdominal pain relieved by frequent bowel action, breast tenderness and amenorrhea for 5 weeks following a regular 26-day cycle. Nonspecific gastrointestinal upset was diagnosed and the patient was treated conservatively. Her symptoms did not subside completely and continued for 8 days, but she was well enough to continue her vacation.

The abdominal pain recurred 4 days later and was associated with slight vaginal bleeding and a recurring feeling of faintness. On admission to hospital, a pelvic examination was done and a right-sided appendage mass, about the size of a hen's egg, was palpated. A blood transfusion was started and the abdomen was opened; approximately 1.5 *l* of free blood was found in the peritoneal cavity. A rupturing pregnancy was noted at the fimbriated end of the right tube; a right salpingectomy was performed. At the time of surgery, the previous operation site was inspected and found to be healthy and clear of adhesions. The convalescence was uneventful, and the patient was discharged from hospital 10 days later in good health.

Postscript

In the 7 years that have elapsed since the birth of this baby, the child has remained perfectly well. At the time of writing, the child was considered to be physically normal and of above-average intelligence. The pelvic findings in the mother reverted to normal. The endometrium has been biopsied and cultured twice in this time with negative results. The mother's general health has remained excellent.

Discussion

Frequency of Extrauterine Pregnancy

It is difficult to obtain meaningful comparative data on the frequency of abdominal pregnancy because the statistics are reported by a variety of authors in different ways. Beecham and Beecham[2] reported the frequency of abdominal pregnancy as 1 in 2081 births, while Eastman and Hellman[3] reported 1 in 15 000 deliveries and Grech[4] recorded a hospital rate of 1 in 1814 admissions.

Discrepancies occur for three reasons. First, abdominal pregnancy seems to be most

often recorded in countries where medical services are underdeveloped and where records are sometimes inadequate. Second, in relation to advanced abdominal pregnancy, cases are recorded under two headings: abdominal pregnancy and extrauterine gestation. These terms have been applied loosely; for example, Naidu and Reddy[5] recorded eight cases of advanced extrauterine gestation, in which two of the pregnancies had remained confined to one horn of a bicornual uterus. Third, the term "advanced" has been used by authors in different ways: Clark and Bourke[6] took it to mean that the gestation period was over 12 weeks; Mitra,[7] over 5½ months; and King[8] used the term for gestations longer than 28 weeks.

Terminating Pregnancy

Current thinking tells us that the intra-abdominal pregnancy should be terminated as soon as it is diagnosed, because of the low fetal salvage rate and the high maternal mortality and morbidity in late pregnancy. Ziel[9] reported a maternal mortality rate of from 14 to 32% and a fetal mortality approaching 100%. The chance of a baby developing normally appeared to be about 10%.

Removal of the Placenta

It is widely believed that total removal of the placenta lessens morbidity, even though there is an associated high rate of maternal mortality, secondary to hemorrhage.

Most surgeons believe that all loose membranes of the sac should be removed, and the cord, if left in situ, not ligated, because of the possible subsequent development of chorioamniotic cysts. If the placenta is left in situ, absorption may occur as early as 4 months and as late as 6 years after delivery.

Primary Peritoneal Implantation

Most cases of abdominal pregnancy are secondary to peritoneal implantation of the ovum. Though it is extremely doubtful if primary peritoneal implantation ever occurs, Miller[10] recorded a 23-day pregnancy implanted in the peritoneum below the right uterosacral ligament; he was convinced that this was a case of primary implantation.

Extra- and Intrauterine Pregnancy

Combined abdominal and intrauterine pregnancy has been documented by Sehdev and Sehdev;[11] a liveborn male infant (weight, 1456 g) with no apparent congenital abnormalities was delivered by cesarian section and at the same time an 896-g male stillborn with undescended testicles and a right club foot was removed surgically from the abdomen.

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11. SEHDEV HS, SEHDEV J: Combined abdominal and intrauterine pregnancies in African primigravida. *Can Med Assoc J* 95: 1322, 1966

BOOK REVIEWS

D'ABREAU'S PRACTICE OF CARDIOTHORACIC SURGERY. 4th ed. J. Leigh Collis, D. B. Clarke and R. Abbey Smith. 710 pp. Illust. Edward Arnold (Publishers) Ltd., London; The Macmillan Company of Canada Limited, Toronto, 1976. $93.00.

This edition of professor d'Abreau's textbook is again a useful description based on experience in a single practice.

The section on pulmonary surgery is excellent; the descriptions are practical and oriented to patient management. The section on valvular procedures, based on the author's experience, is informative and practical; on the other hand, the chapters on congenital heart disease, coronary artery disease and pacemakers, which reflect an admitted limited experience, are inadequate. The book ends with good sections on thoracic injuries, the esophagus and the diaphragm.

Although the sections on cardiac surgery have limitations, those on thoracic surgery are welcome. The single-author approach avoids some of the errors, contradictions, omissions or duplications of multiauthor textbooks.

M. BRAIS

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ADVANCES IN CANCER SURGERY. Edited by John S. Najarian and John P. Delaney. 608 pp. Illust. Stratton Intercontinental Medical Book Corporation, New York; Longman Canada Limited, Toronto, 1976. $28.50.

This volume was developed from a continuing education course sponsored by the department of surgery, University of Minnesota. It contains several groups of papers of varying quality. The first group deals with principles of cancer therapy including environmental carcinogens, virology, cancer chemotherapy and immunotherapy, radiotherapy and factors influencing metastases. Subsequent sections are organized on a systemic or regional basis. These include discussions on various aspects of the lymphomas, head and neck tumours, cutaneous malignancies, intrathoracic tumours, sarcomas and breast cancer. The final section covers a variety of topics including groin and axillary dissection, pediatric malignancies, intrascapulothoracic and hemipelvectomy amputations, testicular and ovarian masses. Most sections also contain a panel discussion, though on three occasions the discussion concerns papers that are located in later sections of the book. Gastrointestinal, biliary, pancreatic and hepatic malignancies are not discussed because they were considered at an earlier course; surgical technique is not emphasized, though some authors provide a few personal tips.

The book will not be attractive to the personal libraries of most Canadian surgeons, as most of the subjects are more throroughly covered in standard texts and, of course, abdominal malignancies are omitted entirely. Moreover, the publication of oral presentations requires rigorous editing to achieve the desirable degree of brevity.

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ADVANCES IN NEPHROLOGY. Volume 5. From the Necker Hospital. Edited by Jean Hamburger, Jean Crosnier and Morton H. Maxwell. 364 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1975. $29.50.

This excellent review of advances in nephrology is published annually from the Necker Hospital in Paris, France, under the auspices of professor Hamburger. The nephrology group of Necker Hospital has a wealth of both clinical and laboratory experience in all areas of nephrology; they are especially knowledgeable in the field of renal transplantation.

This year's volume concentrates on glomerular disease and renal transplantation. All of the chapters are concisely and clearly written; they will be easily understood by clinicians working in these fields. The chapter on recent advances in the understanding of rejection by professor Hamburger is outstanding, and is highly recommended to anyone seeking a current view of this phenomenon.

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CHEMOTHERAPY OF UROGENITAL TUMORS. Gerald P. Murphy and Arnold Mittelman. 268 pp. Illust. Charles C Thomas, Publisher, Springfield, IL, 1975. $24.50.

This book is a monograph in the Bannerstone division of American lectures in living chemistry. This series was conceived to ad-

(Continued on page 366)

when shock threatens the lung

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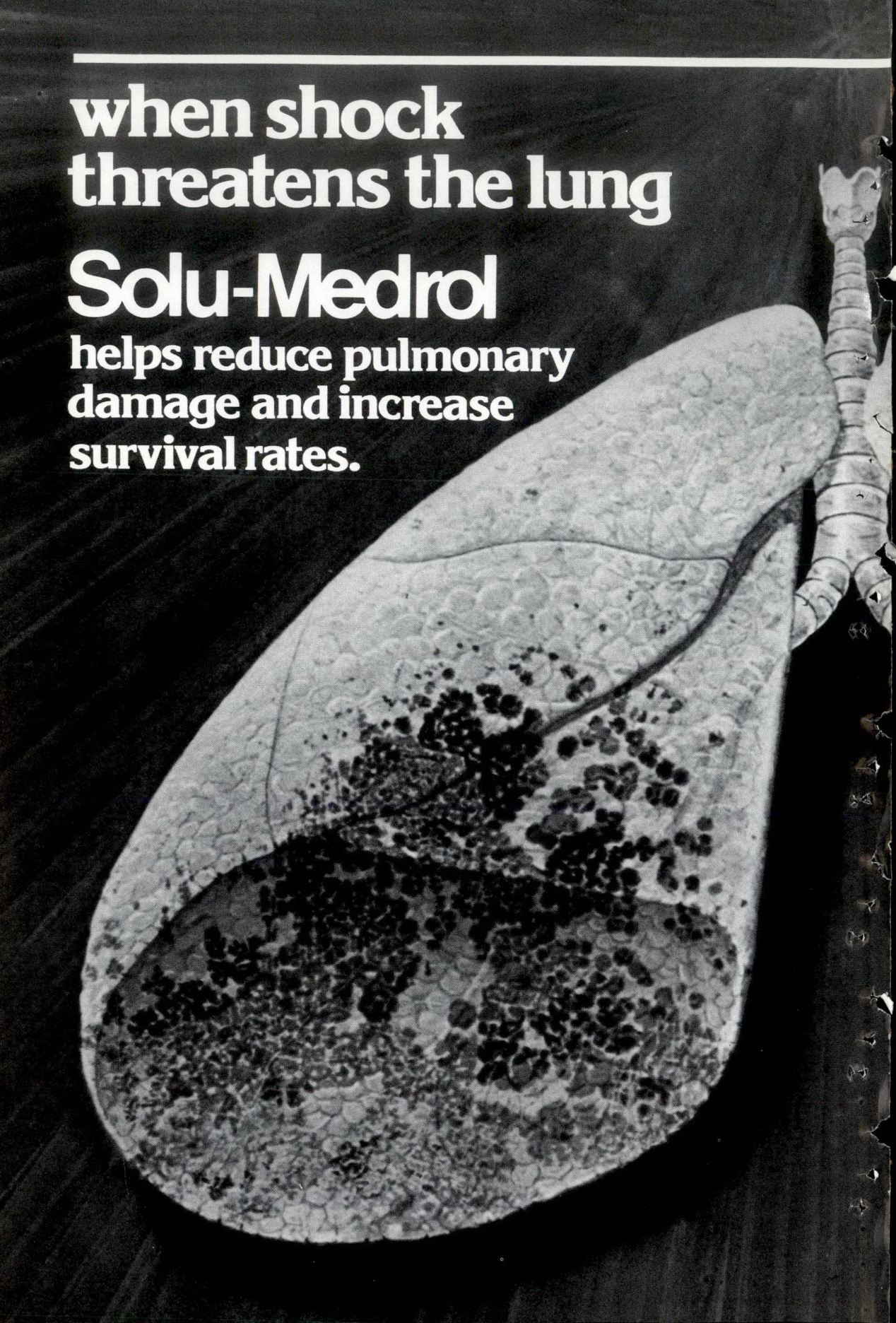
helps reduce pulmonary damage and increase survival rates.



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

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

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

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

Prescribing information on page 366

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.

(Continued from page 363)

vance the newer knowledge of chemical medicine in the cause of clinical practice, and this book certainly fulfils that requirement. It joins a rapidly growing number of books on cancer chemotherapy and oncology, all of which attempt to keep practising physicians up-to-date in the rapidly changing field.

As noted in the foreword by Dr. Willet Whitmore, "among the useful purposes served by this volume are the collation and organization of the scattered and scant information concerning the chemotherapy of urologic neoplasms and the indication of the already implemented or proposed means of expanding knowledge in this area". The authors have enlisted the aid of Dr. Stephen Carter of the National Cancer Institute, who has contributed three chapters. Specific tumours covered in the book include those of the kidney, prostate, testicle and bladder, and squamous cell carcinoma, neuroblastoma, Wilms' tumour and adrenal tumours. There is also a chapter on genitourinary sarcomas and other infrequent neoplasms. The last chapter, on animal models used for experimental chemotherapy of genitourinary tract tumours, is a synopsis of laboratory research being done in this area and adds to the value of the presentation.

This small volume is clearly written, easy to read and well illustrated. An excellent review of previous studies, it also fully documents present efforts and makes recommendations regarding future areas of research.

I strongly recommend this book to anyone who is interested in the chemotherapy of these tumours, particularly urologists, general surgeons and medical oncologists.

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Ottawa Clinic,
Ottawa, ON.

HAND SURGERY. 2nd ed. J. Edward Flynn. 712 pp. Illust. The Williams & Wilkins Company, Baltimore; Burns & MacEachern Limited, Toronto, 1975. $53.50.

The first edition of Flynn's textbook on hand surgery received wide acceptance. With the addition of 21 new contributors to the second edition, the value of the textbook should be enhanced. Each chapter is a well-written, self-contained item by an authority on the subject. For this reason it is not necessary to describe highlights within the book. The format makes for easy subject identification. To keep costs

low, the print is small and the text is closely packed, but once the reader becomes accustomed to this arrangement, it is quite acceptable.

This book will be a welcome addition to the library of the hand surgeon and should be placed in all medical libraries as a valuable reference source.

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INSTRUCTIONAL COURSE LECTURES. Volume XXIV, 1975. American Academy of Orthopaedic Surgeons. 328 pp. Illust. The C. V. Mosby Company, St. Louis, 1975. $26.80.

The American Academy of Orthopaedic Surgeons offers each year to the medical community 120 instructional course lectures over a 5-day period. A large number of formal papers and audiovisual programs are included. This text covers a few of the lectures. There is no particular theme and the material is selected at random. However, over the years they have formed a collective review of current orthopedic topics. The material is of interest to all orthopedic surgeons but is aimed primarily at residents and young orthopedists.

This year 30 acknowledged experts discussed a wide range of topics; among these were some of special interest such as biomaterials, resistant congenital club foot, peripheral nerve suture techniques, traumatic instability of the wrist and surgical approaches to intrinsic finger muscle dysfunction.

An annual series of lectures followed up by a documentation of the better ones in this way is a useful educational technique; other specialties would do well to emulate this method of postgraduate education.

L. H. Bartlett

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METHOD OF UROLOGY. Arthur W. Wyker, Jr. and Jay Y. Gillenwater. 365 pp. Illust. The Williams & Wilkins Company, Baltimore; Burns & MacEachern Limited, Toronto, 1975. $17.60.

The authors have tried to provide a volume that "fills the gap between the definitive reference books and the simplified manuals". "Method of Urology" is an outgrowth of the teaching program at the University of Virginia.

This book has many worthwhile features: it supplies a useful review of recent urologic thought, includes a concise, relevant and current bibliography at the end of each chapter and is written clearly. However, it has some drawbacks. First, unrelated topics, classifications and points of interest are lumped together into brief alternately numbered and lettered paragraphs; this frequently confuses the issues involved. Second, the authors have tried to include many points of view but have frequently failed to draw together and interpret the data. Finally, too often the authors have mixed anectodal information and scientific fact.

Should further editions aim at correcting some of the problems, the authors will have made a significant contribution to the urologic literature. In its present form the book is useful; it does accomplish the authors' stated objectives.

B. M. Mount

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POLYPOID LESIONS OF THE GASTROINTESTINAL TRACT. 2nd ed. Claude E. Welch and Stephen E. Hedberg. Vol. II in Major Problems in Clinical Surgery. 220 pp. Illust. W. B. Saunders Company, Philadelphia; W. B. Saunders Company Canada Limited, Toronto, 1975. $13.90.

This small monograph is another definitive work in the series entitled "Major Problems in Clinical Surgery", the second edition of the Welch treatise of several years ago. A major addition to the second volume of this text results from the development of colonoscopy. Contained within this work is a description of colonoscopy, detailed as though the author were desirous of teaching everyone this procedure. Its uses and its abuses are well reviewed and the current state of the art is well presented.

Definitions of the various types of polypoid lesions, once again presented, still defy clarity and precision, probably because the lesions are not so distinct that they can be easily defined. Polypoid lesions are divided into adenomatous, villoglandular, villous, polypoid and malignant. An interlocking discussion shifts back and forth between the various cate-

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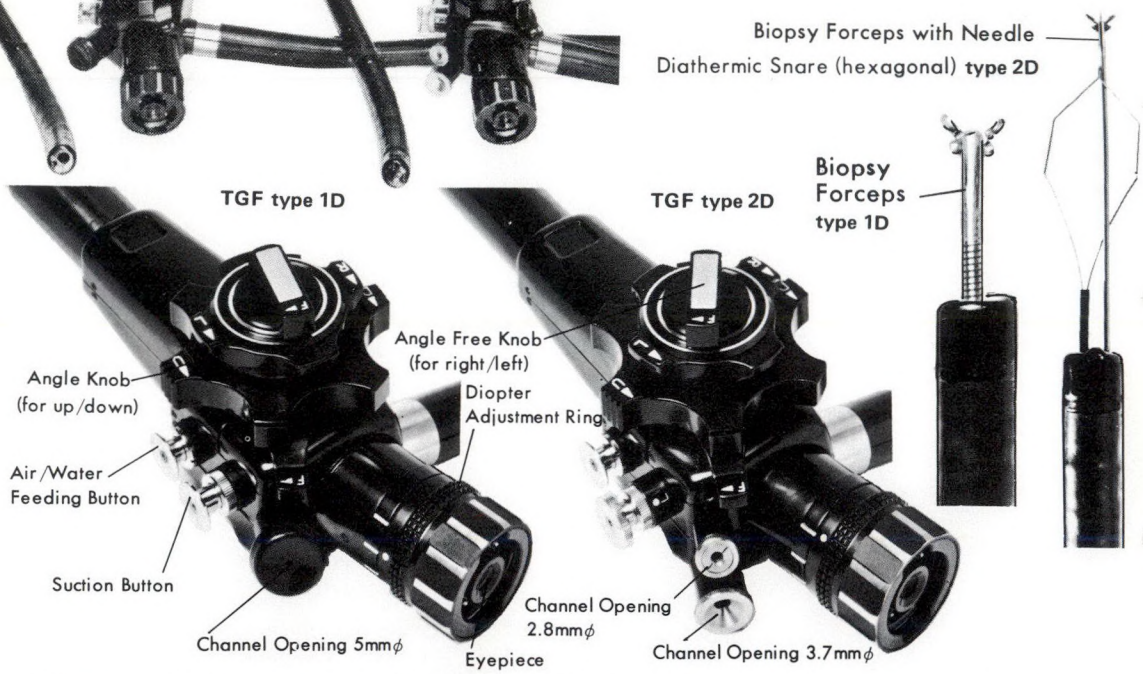

These new instruments were developed from the well known Olympus model GIF-D2 forward view gastrointestinal fiberscope with the accent on operating channels. The TGF-1D having 1 channel of **5mm** allows the use of retrieving tools for foreign bodies, big particle biopsies and various other accessories.

The TGF-2D with 2 channels is excellent for polypectomy. When coupled with a power supply for Diathermy and the Diathermic Snare, theTGF will make the safest and most effective system available in the current market for endoscopic removal of polyps in the stomach.

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gories, perhaps related to the changing criteria of pathologists and uncertainties regarding the malignant potential of the various pathologic findings. There is a fairly long discourse on the problems of cancer originating in polyps, with a good discussion of the literature, and a reasonably comprehensive statement of the author's own position on this complicated topic.

The book departs from the issue of polypoid lesions, per se, by providing recommendations for the management of colonic polyps. These are given by a thoughtful, careful expert in the field, and are buttressed by an extensive discussion of operative techniques; once again this is probably too detailed for those not conversant with the field, and insufficiently detailed for the expert surgeon.

The discussion concerning the remainder of the gastrointestinal tract (esophagus through small bowel) and the polypoid lesions occurring within this segment of the intestinal tract is less well done and less thorough than the discourse on the colon.

The book contains a good bibliography and is a handy reference work; probably it belongs in the library of every surgeon who operates on the colon.

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

Stress fracture is too often not considered in the differential diagnosis of diffuse aching pain. Dr. Devas has in this short monograph collected and categorized this type of injury for us.

In the introduction the author describes the pathogenesis of this type of injury so common to the young and healthy. Signs and symptoms are well described with adequate detail; the value of these is reinforced by well-reproduced radiographs. It is unfortunate that the excellent figures are often widely separated from the related text. There is at times a trend to redundancy because example cases are described and the detail is repeated in the accompanying radiograph. The author's thoughts on certain types of avascular necrosis being initiated by compression-type stress fractures are interesting and worthy of further investigation.

This book brings to light, in a simple and organized way, a collective reminder of a much forgotten injury. It serves to remind the reader that the diagnosis of a stress fracture must be suspected and made clinically.

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SURGICAL DISORDERS OF THE PERIPHERAL NERVES. 2nd ed. Sir Herbert Seddon. 336 pp. Illust. Churchill Livingstone, Edinburgh; Longman Canada Limited, Toronto, 1975. $43.25.

Except for a few changes, this second edition of Seddon's monograph appears to be identical to the first. In some respects this lack of change has led to omissions in the book's content. Thus, the recent advances in clinical neurophysiology, microsurgical techniques and perineural nerve repairs are alluded to in the preface, but are not described in the text. Likewise, despite recent developments in the field, the chapter on electrical phenomena is unchanged; intraoperative functional assessment at the fascicular level is not referred to. The work of Narakas on the surgical management of brachial plexus injuries and of Millesi on nerve grafts are detailed, but new microsuture and microsurgical techniques for nerve repair are barely mentioned; the section on operative treatment is therefore somewhat out of date.

In spite of its limitations, this book is highly recommended to all concerned with the repair of peripheral nerves; it is the most comprehensive review on the subject of peripheral nerve surgery to date and is an essential companion volume to Sunderland's book "Nerves and Nerve Injuries".

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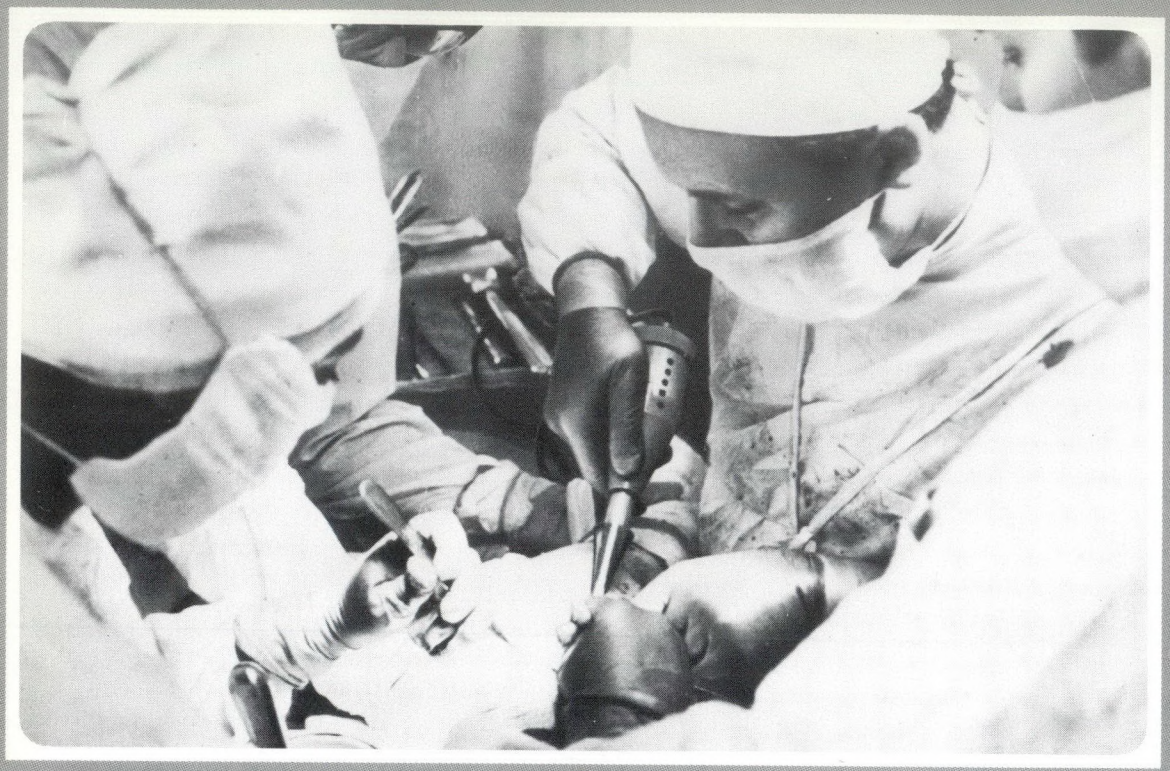
TRANSPLANTATION TODAY. 3. Edited by Michael Schlesinger, Rupert E. Billingham and Felix T. Rapaport. 992 pp. Illust. Grune & Stratton, Inc., New York; Longman Canada Limited, Toronto, 1975. $43.50.

There are few areas in medicine where the applied science changes as rapidly as it does in the field of transplantation. Several textbooks have been written on transplantation by physicians and surgeons over the last 10 years and most of them now are of historical interest only. It is of importance, therefore, that the new information currently published in over a dozen immunologic and clinical journals be



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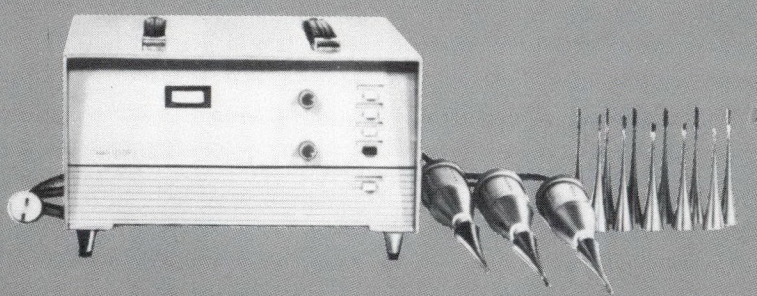

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brought together at regular intervals so that physicians and medical scientists interested in the applied aspects of transplantation can remain abreast of the field.

The Transplantation Society (an international society embracing both basic scientists and clinicians) meets every 2 years. Dr. Rapaport, who is editor of *Transplantation Proceedings*, the official journal of the Transplantation Society, has taken on the task of publishing the proceedings of the international meeting as an updated "textbook" of transplantation in the year following the meeting of the society. This represents the third such issue. Because the contents of this meeting contain both invited papers and free communications, the content is frequently highly technical and of a basic science nature. Nevertheless, of the 992 pages in this volume, one-third of the content is of direct interest to those doing clinical transplantation.

The rapid changes occurring in the field of histocompatibility make the introductory symposium on histocompatibility immunogenetics and the section on the role of transplantation antigens in human transplantation and susceptibility to disease important for the reader who wishes to update his knowledge in this field.

A special section deals with tolerance or enhancement as a solution to the clinical problems of transplantation. We learn that the in-vitro mechanisms elucidated from sophisticated studies may not be of great clinical importance and that the real roles for the delicate immunoregulatory mechanisms are not yet understood.

The correlation of in-vitro immune responses with clinical rejection is dealt with in detail. It points up the weakness of looking at any single part of a complex (immune) response, in attempting to explain highly variable clinical courses. In spite of these negative findings, the reader is impressed with the abundant scientific information and the potential of applied assays in dissecting with greater accuracy the immune response in the transplant recipient.

The section on clinical transplantation is a follow-up report of 124 long-term transplants of 8 to 12 years' duration. Although generally, patient survival was considerably less in the period preceding 1966, the overall patient survival was 56% in the related nonidentical transplants and 41% in the cadaveric transplants. The primary causes of death in the long-term survivors were sepsis, late rejection and liver failure. Interesting new areas of endeavour include the transplantation of pancreatic islet cells with a resulting subsequent correction of the renal lesion in diabetes.

The use of single allele shared skin allografts for the treatment of burns is reported; this is an area of great clinical promise. The most significant advance at a clinically applied level is in the field of bone-marrow transplantation. Several centres (primarily the Seattle group) have demonstrated that bone-marrow transplantation is the current treatment of severe aplastic anemia.

It is essential, in my opinion, for any clinical scientist interested in transplantation to have available to him either in his own library or through his local medical library a copy of "Transplantation Today", volume 3. The information contained in this text is dated but is still the most current available.

C. R. STILLER

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London, ON.

VASCULAR SURGERY. Edited by William H. Edwards. 257 pp. Illust. University Park Press, Baltimore, 1976. $24.50.

This book on vascular surgery covers a broad range of topics. It is easy to read and provides lessons from clinical experience by leading vascular surgeons on techniques, diagnosis and treatment.

The chapter on cerebrovascular insufficiency is clear and concise; readers will find it extremely helpful as a guide for the management of these diseases.

The book contains illustrative case histories of cerebrovascular occlusive disease; of special interest are the case presentations of vertebrobasilar insufficiency and the subclavian steal syndrome. Also useful are the many important clinical points concerning aortoiliac and peripheral vascular diseases, the comprehensive coverage of the management of renovascular hypertension and the specific technical details of surgery for resection of common aneurysms.

The vascular injuries are well described; this section includes both aortic and arterial injuries and associated thromboembolism.

General surgeons who are practising vascular surgery will find this book extremely helpful; vascular surgeons will enjoy comparing their own clinical experiences with those described in this book.

M. A. NAQVI

336 Kings Road,
Sydney, NS.

INDEX TO ADVERTISERS

Books Received

Anesthesia for the Uninterested. Edited by Alexander A. Birch and John D. Tolmie. 187 pp. Illust. University Park Press, Baltimore, 1976. $7.50, paperbound.

Anorectal Malformations and Associated Diseases. Progress in Pediatric Surgery. Volume 9. Executive Editors: P. P. Rickham, W. Ch. Hecker and J. Prévot. 154 pp. Illust. University Park Press, Baltimore, 1976. $19.50.

Congenital Malformations of the Heart. Daniel A. Goor and C. Walton Lillehei. 430 pp. Illust. Grune & Stratton, Inc., New York; Longman Canada Limited, Toronto, 1975. $37.50.

Lethal Diseases of the Ascending Aorta. Edited by Constantine E. Anagnostopoulos. 150 pp. Illust. University Park Press, Baltimore, 1976. $14.50.

Myocardial Revascularization. A Surgical Atlas. Quentin R. Stiles, Bernard L. Tucker, George G. Lindesmith and Bert W. Meyer. 165 pp. Illust. Little, Brown and Company (Inc.), Boston, 1976. Price not stated.

Plastic and Reconstructive Surgery of the Breast. Edited by Robert M. Goldwyn. 565 pp. Illust. Little, Brown and Company (Inc.), Boston, 1976. $48.50.

Postoperative Congenital Heart Disease. Edited by Ammon Rosenthal, Edmund H. Sonnenblick and Michael Lesch. 166 pp. Illust. Grune & Stratton, Inc., New York; Longman Canada Limited, Toronto, 1975. $16.75.

Practical Cryosurgery. Edited by H. B. Holden. 168 pp. Illust. Pitman Medical Publishing Co. Ltd. Distributed by Year Book Medical Publishers, Inc., Chicago, 1975. Price not stated.

CRITIQUE OF ITEM 507 (SESAP II)

Radioimmunoassay using gastrin labeled with iodine-125 is the method currently employed to measure serum gastrin levels. The measurements in the report by McGuigan and Trudeau indicated that gastrin concentrations are significantly reduced after antral resection (P less than 0.001). High levels of gastrin are useful in identifying patients with the Zollinger-Ellison syndrome; levels above 500 picograms are diagnostic of this syndrome (normal levels are those below 150 pg).

Vagotomy has been shown to depress the responsiveness of acid-secreting parietal cells to both histamine and gastrin, but gastrin levels are of no value in investigating the possibility of residual vagal function after vagotomy; residual vagal function is determined by the Hollander insulin test.

B

Reference

507/1. McGuigan JE, Trudeau WL: Serum gastrin levels before and after vagotomy and pyloroplasty or vagotomy and antrectomy. N Engl J Med 286: 184-188, 1972