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THE PROBLEM OF STONES IN THE COMMON BILE DUCT WITH PARTICULAR REFERENCE TO RETAINED STONES*

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Operations on the biliary tract form an increasingly large proportion of general surgical operations. While some discussion continues over the advisability of removing a gallbladder containing "silent" stones, it seems to have been accepted that those patients harbouring symptomatic gallstones should undergo cholecystectomy provided they are in satisfactory condition. The technique of cholecystectomy has been standardized. Much discussion however continues over the advisability of adding exploration of the common bile duct to the operative procedure. It is axiomatic that unnecessary exploration of the duct is undesirable, but if exploration is not carried out in the presence of calculi the primary pathology will not be corrected. While failure to explore the common bile duct in the course of cholecystectomy may leave what may be termed an "unsuspected" stone in this area, failure to completely clear the duct of calculi at common duct exploration will leave a residual or "overlooked" stone or stones.

We have recently reviewed the operations carried out on the biliary tract at The Montreal General Hospital over the six-year period ending on January 1, 1962. While most of these operations consisted of cholecystectomies with or without common duct exploration, particular attention has been paid to operations involving recurrent exploration of the bile ducts in order to assess the problem of residual stones both from the diagnostic and therapeutic points of view.

Case Material

During the six-year period embraced by this study, 2090 cholecystectomies were performed at The Montreal General Hospital. Of these patients, 327, or 15.6%, underwent common bile duct exploration in addition to removal of the gallbladder. There were 12 deaths as a result of the combined procedure—3.7%. Common duct stones were discovered in 156 patients, 47.8% of the total explorations (Table I).

TABLE I.—Primary Biliary Operations, 1955 - 1961

Cholecystectomy	2090
Cholecystectomy	
Plus common bile duct exploration	327 (15.6%)
Stones recovered	156 (47.8%)
Retained stones in common bile duct following exploration	23 (7.1%)
Common bile duct stones following cholecystectomy	1

Subsequently 23 patients, 7.1% of those who had undergone exploration of the common bile duct, were shown to have retained stones. Eighteen of these fell into the group in which the initial exploration had been positive, that is, where stones had been removed at the primary operation. The incidence of retained stones among the 156 patients who had an initial choledocholithotomy was 11.5%. On the other hand, among the 171 patients in whom exploration of the common duct was unrewarding, five retained stones were found, an incidence of only 2.9% (Table II).

TABLE II.—Retained Stones Following Common Bile Duct Exploration—23 Cases

Following choledocholithotomy (18/156)	11.5%
Following negative exploration (5/171)	2.9%

Of the 2090 patients studied over the six-year period, only one who underwent simple cholecystectomy was subsequently

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found to have a stone in the common bile duct. However, during this period we encountered 19 patients with common bile duct stone who had previously undergone a cholecystectomy. Six of these patients had been operated upon at The Montreal General Hospital, but only one (mentioned immediately above) during the period of this study; in the remaining 13 patients the previous operations had been performed elsewhere. The explanation for this apparent discrepancy is evident in the study of these 19 patients which demonstrates that considerable time may elapse before the recognition of the unsuspected stone. One stone was discovered during the first postoperative year, eight during the five years following operation, and the remainder during varying periods up to 21 years after the initial operation. While it could be argued that some of these stones had formed in the bile ducts at some time following the initial operation, we believe that most or all of them arose primarily in the gallbladder.

TABLE III.—Retained Common Bile Duct Stones—52 Cases

Following cholecystectomy	19
Following common bile duct exploration	23
Following re-exploration of common bile duct	8
Misdiagnosis (carcinoma of pancreas)	1
Pancreatitis	1

A further group of 10 patients with retained stones makes up the total of 52 recorded in Table III. In seven of these, stones had been overlooked following re-exploration of the common bile duct for retained stones in the first two groups mentioned in Table III, and in one patient stones remained after two explorations of the common bile duct performed elsewhere. While these eight patients represent instances of twice-retained stones, they are included in the total because they are part of our total experience with residual common duct stones. In two other instances, stones were demonstrated at postmortem in patients dying with suspected carcinoma of the pancreas and pancreatitis; previous duct exploration had been negative.

A total, then, of 52 cases of retained stone were encountered during the period of the study, 19 following cholecystectomy alone, 23 following common bile duct exploration, and the 10 cases described above (Table III).

Treatment

Operation was carried out upon all of the 19 patients with retained stone following cholecystectomy alone. In addition to choledocholithotomy, a cystic duct remnant was found and removed in five of these patients, and in four the remnants contained stones (Table IV). In one patient, a cystic duct remnant which contained stones was removed and concurrent exploration of the bile duct revealed no calculi; however, two calculi were later demonstrated in the common bile duct at postmortem examination after the death of the patient from pulmonary embolus. Four of the remaining 18 patients had further retained stones and required reoperation.

TABLE IV.—Retained Stones after Cholecystectomy—19 Cases

Surgical removal (5 further retained stones)	19
Cystic duct remnant (4 with stones)	5

In those patients in whom stones were demonstrated in the common bile duct after cholecystectomy and bile duct exploration, surgical removal was carried out in only 11. Two of this group of 11 had further retained stones postoperatively. In five, the T-tube was removed without operation and four of the five patients have remained asymptomatic to date. Spontaneous passage of calculi was observed in two patients before the removal of the T-tube. Chloroform-ether irrigations were successfully carried out in four patients and the retained stone was an autopsy finding in one (Table V).

TABLE V.—Retained Stones After Common Bile Duct Exploration—23 Cases

Surgical removal (2 further retained stones)	11
T-tube removed without operation	5
Spontaneous passage with T-tube in place	2
Chloroform-ether irrigations	4
Autopsy finding	1

A total of 30 patients were re-explored for residual stones in this series, 19 after cholecystectomy and 11 after cholecystectomy and common duct exploration. Of these 30, seven had further retained stones: an incidence following reoperation of 23%.

In addition to these seven patients with twice-retained stones, one further patient with residual stones after two operations elsewhere makes a total of eight cases of twice-retained stones. In five of these, the common duct system was cleared after a third operation; in one, duct stones remain despite a third procedure; persistent stones were demonstrated after a fatal pulmonary embolus in another; and in the last patient the remaining stone was demonstrated at autopsy two years following the last operation (Table VI).

TABLE VI.—Twice-Retained Stones—8 Cases

Removal	5
Still present	1
Autopsy finding	2

Diagnosis of Common Duct Stone

1. *The Unsuspected Stone*

The unsuspected stone is one left in the duct system at the time of cholecystectomy in a patient in whom common duct exploration has not been carried out. While the indications for exploration of the common bile duct seem reasonably well established, the finer interpretations of these indications are very much more difficult. If the indications for exploration are not absolute but some question as to the advisability of duct exploration remains, operative cholangiography may be a very useful aid. Although routine cholangiography should probably not be recommended, it may be of considerable value in demonstrating unsuspected stones in certain situations.[5, 10] The techniques of cholangiography vary, but it is probably most easily accomplished by injection of a water-soluble contrast medium through a No. 6 ureteral catheter which has been passed through the cystic duct into the common bile duct. Saypol[12] utilizes this intraductal catheter to facilitate palpation of calculi within the duct lumen.

2. *The Overlooked Stone*

A stone is considered overlooked when it is left behind in the common duct despite duct exploration. Diagnosis may be made in several ways.

(a) *Operative choledochography.*—Most surgeons carry out a T-tube cholangiogram before removal of the T-tube after operation, but it seems obvious that the optimal time for diagnosis of the retained stone in the common bile duct is at the time of operation. This examination is carried out in the operating-room following placement of the T-tube. While lack of fluoroscopic control and the use of less specialized equipment may result in some diagnostic errors, obvious stones are readily visualized in this way.

(b) *Postoperative choledochography.* — As suggested above, this examination should be considered a routine examination for all patients in whom a T-tube has been placed at the time of operation. All 23 patients, in whom stones were diagnosed following common duct exploration at this hospital, had common duct stones demonstrated in this way. In order to avoid possible erroneous interpretation of these studies, stones should be clearly demonstrated on at least two examinations.

(c) *Clinical suspicion.*—It appears obvious that the diagnosis of retained stone must be entertained clinically in patients presenting to the physician or surgeon at an interval after a gallbladder operation before further confirmatory studies can be undertaken. A history of pain with a suggestive pattern, fever, intermittent jaundice or pale stools may prompt this diagnosis. Laboratory investigations may reveal an elevated bilirubin, although such elevations may be transient. Alkaline phosphatase may be raised even in the absence of bilirubin elevation. While one would hope that in the presence of a suspected stone more elaborate radiological studies could demonstrate its presence clearly, these studies frequently are of no assistance and a further operative procedure must be based on clinical and laboratory evidence alone.

(d) *Intravenous cholangiography.*—With the advent of this radiological procedure it was hoped that examination of the biliary tract after cholecystectomy would be very much facilitated. In practice the demonstration of residual stones in the common bile duct by means of the intravenous cholangiogram is infrequent. The usefulness of this examination is limited in the presence of an elevated bilirubin, and frequently opacification of the duct is not sufficient to outline calculi. The method may, however, be of value in confirming a clinical suspicion if gross dilatation of the common bile duct is demonstrated.[15] Intravenous cholangiography is of no value in the presence of jaundice.

(e) *Opacification of common duct stones.*—The so-called four-day Telepaque (iopanoic acid) test was introduced by Salzman and Warden[11] in 1958. The procedure is based on the ability of biliverdin to absorb the contrast medium over this period. In the presence of duct obstruction and infection, the bilirubin on the surface of the calculi tends to be converted to biliverdin and so opacification becomes possible. Salzman and Warden were able to demonstrate 10 of 13 common bile duct stones in this way and the method has the additional advantage that stones frequently may be outlined in ducts which cannot be adequately visualized by means of intravenous cholangiography. The test may be useful even in the presence of jaundice.

(f) *Transhepatic cholangiography.*—Cholangiography by needle puncture of the liver, first described by Carter and Saypol in 1952,[2] is a procedure which carries a relatively small morbidity. As physicians gain increasing experience with it, we believe that this technique will be used more frequently. In the presence of jaundice it often provides a more precise indication of the nature of the obstructing lesion and allows the surgeon to assess more deliberately the operative procedure which may be required for its correction.

Treatment of the Retained Stone

Retained stone in the common bile duct after cholecystectomy alone requires only one type of treatment—surgical removal. On the other hand, demonstration of stones in the bile duct following common bile duct exploration leaves one with a choice of therapeutic methods.

Before proceeding with a further operation for removal of the retained stone, several alternatives can be considered. If the calculus is located above the T-tube and adequate dilatation has been carried out at the time of operation, removal of the T-tube will be necessary to allow spontaneous passage. If, in the opinion of the surgeon, spontaneous passage is possible, the tube is removed and the patient is observed closely to avoid any serious complication that might result from duct obstruction. If a stone or stones are located distal to the T-tube, the tube should be left in position to determine whether spontaneous passage will occur. Biliary-flushing techniques have been used in the management of several patients in the present series and have been successful in four. Whether dissolution of calculi actually occurred or the flushing promoted spontaneous passage is debatable. Careful attention should be paid to the technique described for biliary flushing in order to avoid undue discomfort to the patient.[1, 13] Whether or not a complete biliary flushing routine is used, bile salts, magnesium citrate, cream and olive oil, and one of the nitrates should be administered to facilitate spontaneous passage. If these techniques are unsuccessful, operative removal of the stone or stones becomes essential.

Secondary operations on the biliary tree may be facilitated by using the techniques described by Cattell.[4] Demonstration of the duct and removal of calculi is not an extremely difficult operative technique. A failure to demonstrate patency of the ampulla will, of course, make trans-duodenal exploration necessary. In reviewing our cases of twice-retained stones, however, the 23% incidence of retained stones in 30 patients re-explored for removal of residual stones is alarming. Before completion of an operation for retained stones one

should use all possible means to ensure that the duct is cleared, including adequate operative T-tube choledochograms.

Discussion

1. *The Unsuspected Common Duct Stone*

While the indications for common bile duct exploration at the time of cholecystectomy are reasonably well established, the extreme variability in the incidence of common duct exploration suggests that many of these indications are relative. In 1931, Crump studied 1000 consecutive cases of calculous gallbladder disease at postmortem and demonstrated that 25% had stones in the common bile duct. A review of large series of surgically treated cases showed that the incidence of exploration varies from 10.5% of all cases (Glenn[6, 7]) to 45% (Cattell[3]). In Glenn's cases, exploration was positive in 69.1% and the overall incidence of common duct stone was 7.2%. Cattell, exploring a much higher percentage of his cases, found stones in only 36.7%, which however represented an overall incidence of 16.8%. In general it would seem that the more frequently the duct is explored, the more frequently stones are found. On the other hand, as more explorations are performed, the incidence of unrewarding exploration also rises. Our experience, exploration in 15.6% of primary biliary operations seems to approximate the average in the literature and 48% of these explorations resulted in successful choledocholithotomy.

It is difficult to ascertain the true incidence of unsuspected stone following failure to explore the common bile duct. In this present study, only one patient out of 2090 undergoing cholecystectomy in this six-year period was subsequently operated upon for removal of a retained stone. Classically these stones frequently remain asymptomatic for many years and undoubtedly we will encounter further retained stones in this group as time goes on.

While it is difficult or impossible to overcome the problem that arises from the variable interpretations by individual surgeons of the established indications for common bile duct exploration, two additional procedures have recently become available which will assist the surgeon in his decision for or against exploration.

The first of these is operative cholangiography, and it would seem that with increased experience and perfection of techniques, the presence or absence of stones may be demonstrated with a high degree of accuracy. While it should probably be considered unwise to refrain from exploring the duct because the radiograph was negative, the use of this procedure in equivocal cases is certainly to be recommended. While some have suggested that cholangiography should be performed in all cases of cholecystectomy, the indiscriminate use of this procedure may be unwise, as postoperative pancreatitis on rare occasions may complicate its use.

A second more direct approach to the problem has been suggested by Saypol,[12] who utilizes a ureteral catheter in the common duct to facilitate palpation of intraductal calculi. We have used this technique with some success and believe that a wider use of this procedure, which may be combined with cholangiography, is to be recommended.

2. *The Overlooked Stone*

Residual stones after common bile duct explorations were demonstrated in 23 (7%) of 327 primary operations at The Montreal General Hospital. This figure is similar to those of Glenn and Johnston but is somewhat lower than others reported.[6, 8-10] In comparing quoted figures for stones retained in the duct, attention should be paid to whether or not the patients studied underwent choledocholithotomy. In our own group there was an 11.5% incidence of retained stones in those who had stones removed from the common bile duct at exploration, whereas those who had a negative duct exploration showed only a 2.9% incidence (Table II). While it might seem obvious that the absence of stones at exploration would make the possibility of overlooking a stone considerably less, it is important to realize the increased danger of inadequate duct clearance in a patient from whom calculi have been recovered. In patients who had retained stones re-

moved from the common bile duct at a second operation, an even higher incidence of further or "twice-retained" stones was demonstrated.

What can be done to avoid this very serious complication? While it seems accepted practice to carry out radiographic visualization of the common duct at some time after the operative procedure and before removal of the indwelling T-tube, a similar type of examination is less frequently performed at the time of operation. Assuming that this procedure is technically feasible, the information obtained may be very much more useful at the operating-table at a time when residual stones may be removed. While we believe that this examination should form a part of every operation of this nature, the markedly increased incidence of retained stones following choledocholithotomy makes such an examination imperative when stones have actually been removed from the common bile duct.

If, despite all precautions, residual stones are demonstrated in the duct at some time after the operative procedure, further therapy becomes necessary. While a further operation might seem essential, a review of our experience suggests that it may be worth while to delay for a short period of time in the hope that spontaneous passage of the stone may occur. The methods used to facilitate spontaneous passage have been described and the place of biliary-flushing techniques has been outlined.

If stones remain despite these maneuvers, re-exploration of the common bile duct is required. Following re-exploration, it is again emphasized that the biliary tree should be visualized at the operating-table by means of a T-tube choledochogram to ensure that the operation has indeed been successful. The 23% incidence of retained stone following removal of previously retained stones in our study convinces us that this additional procedure is essential.

Summary

A review of the experience at The Montreal General Hospital with common bile duct exploration over a period of six years is presented. An assessment of the incidence and management of retained stones has been made. The diagnosis and methods of treatment of retained stones have been outlined and the place of operative cholangiography has been discussed.

References

1. Best, R. R., Rasmussen, J. A and Wilson, C. E.: An evaluation of solutions for fragmentation and dissolution of gallstones and their effect on liver and ductal tissue, *Ann. Surg.*, **138:** 570, 1953.
2. Carter, R. F. and Saypol, G. M.: Transabdominal cholangiography, *J. A. M. A.*, **148:** 253, 1952.
3. Cattell, R. B.: The use of a long T-tube in surgery of the biliary tract, *Surg. Clin. N. Amer.*, **28:** 659, 1948.
4. Cattell, R. B.: A technic of exposure in secondary operations on the biliary tract, *Surg. Clin. N. Amer.*, **30:** 867, 1950.
5. Ferris, D. O.: Operative cholangiography: an aid in reducing the incidence of residual common duct stones, *Postgrad. Med.*, **26:** 301, 1959.
6. Glenn, F.: Common duct exploration for stones, *Surg. Gynec. Obstet.*, **95:** 431, 1952.
7. Glenn, F.: A 26 year experience in the surgical treatment of 5037 patients with nonmalignant biliary tract disease, *Surg. Gynec. Obstet.*, **109:** 591, 1959.
8. Havard, C.: Non-malignant bile duct obstruction, *Ann. Roy. Coll. Surg. Eng.*, **26:** 88, 1960.
9. Hicken, N. F., McAllister, A. J. and Call, D. W.: Residual choledochal stones: etiology and complications in one hundred ten cases, *A.M.A. Arch. Surg.*, 68: 643, 1954.
10. Johnston, E. V., Waugh, J. M. and Good, C. A.: Residual stones in the common bile duct: the question of operative cholangiograms, *Ann. Surg.*, **139:** 293, 1954.
11. Salzman, E. and Warden, M. R.: Telepaque opacification of radiolucent biliary calculi; the "rim sign", *Radiology*, **71:** 85. 1958.
12. Saypol, G. M.: Indications for choledochostomy in operations for cholelithiasis, *Ann. Surg.*, **153:** 567, 1961.
13. Torresyap, F. C.: Chloroform instillation of common bile duct; its problems with a report of an immediate untoward reaction, *A.M.A. Arch. Surg.*, **77:** 903. 1958.
14. Watkins, D. H. and Salzman, E.: Opacifying gallstones, *A.M.A. Arch. Surg.*, **80:** 986, 1960.
15. Wise, R. E.: Intravenous cholangiography, Charles C Thomas, Springfield, Ill., 1962.

Résumé

Le nombre des interventions sur la région biliaire forme une partie importante, et toujours croissante, de la chirurgie générale. Les techniques de cholécystectomie sont maintenant bien au point. Certaines discussions subsistent encore

quant à la modalité et à l'opportunité de l'exploration des voies biliaires; il est banal de dire que toute exploration non nécessaire doit être évitée; cependant, il est bien évident que lorsque celle-ci n'est pas faite, il y a un important risque d'oublier des calculs, et par là même, de ne pas traiter correctement l'affection en cause. Le présent article est une étude statistique des interventions de ce genre, faites à l'Hôpital Général de Montréal pendant une période de six ans finissant en janvier 1962. La plupart de ces interventions étaient des cholécystectomies avec ou sans exploration de l'arbre biliaire. Leur nombre a été de 2090, avec 12 décès (3.7%). Trois cent vingt-sept de ces malades subirent, outre la cholécystectomie, une exploration du canal cholédoque, et des calculs furent ainsi découverts dans 156 cas (soit 47.8% du nombre total d'explorations). Ultérieurement, il a été trouvé que 23 malades (soit 7.1% des explorations) étaient porteurs de calculs "insoupçonnés". L'auteur discute alors divers problèmes de diagnostic. Si les indications de l'exploration cholédoque ne sont pas nettes ou sont douteuses, il est indiqué de procéder à une cholangiographie per-opératoire; la technique varie selon les auteurs. Une des plus simples est d'injecter à l'aide d'un cathéter urétéral no. 6, passé dans le cholédoque à travers le cystique, un liquide radio-opaque aqueux. Lorsqu'un calcul demeure dans les voies biliaires après exploration, on parle de "calcul oublié" (overlooked). Le diagnostic peut être fait par divers moyens: la cholédocographie par tube en T lors de l'intervention; la cholangiographie intraveineuse; l'opacification du calcul par des substances du type de l'acide iopanoïque, basée sur la propriété qu'a la biliverdine d'absorber le contraste; et la cholangiographie trans-hépatique.

CHOLECYSTECTOMY WITH ROUTINE SPHINCTEROPLASTY*

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It is generally accepted that the results of cholecystectomy have been far from satisfactory. According to various reports in the surgical literature,[1-5] anywhere from 15% to 30% of patients undergoing cholecystectomy have persistent or recurrent symptoms postoperatively. Some investigators claim an even higher incidence of unsatisfactory results. Carter and Marraffino[3] in a series of 307 cholecystectomies observed recurrent symptoms in 63% of cases, an astonishingly high figure.

Post-Cholecystectomy Syndrome

The causes of the so-called post-cholecystectomy syndrome are multiple (Table I).[20-22] These different etiological factors may result in a persistence of preoperative symptoms or the development of a different type of symptom in the post-operative period.

Although some of these errors are avoidable, others may not be, with the limited investigative means at our disposal at the present time.

Erroneous preoperative diagnosis can to a certain extent be eliminated, but not entirely. Many of the disturbances outlined under this heading may coexist with gall-bladder pathology. I share with the majority of surgeons the view that a gall-bladder which is the site of symptomless pathology should nevertheless be removed even in the presence of symptoms attributable to another condition. Cholecystectomy of course will not cure these symptoms and

TABLE I.—Causes of the Post-Cholecystectomy Syndrome

1. *Erroneous preoperative diagnosis:*
   Faulty dentition, air swallowing, hiatal hernia, colonic dysfunction, overuse of laxatives, peptic ulcer, coronary artery disease, tension or anxiety states, cancer of any abdominal organ
2. *Incomplete surgery:*
   Cystic duct remnant[37]
   Overlooked ductal stones
   Overlooked malignancy
   Biliary fistula
3. *Injury during operation:*
   Bile peritonitis
   Bile duct stricture
4. *Residual disease in neighbouring or connected structure:*
   Cholangitis, hepatitis, pancreatitis
   Stenosis of sphincter of Oddi
   Abdominal adhesions
   Neuroma at the point of division of the cystic duct
5. *Physiological derangements:*
   Disturbances in bile flow after removal of a functioning gallbladder
   Biliary dyskinesia: hypotonic; hypertonic

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it is imperative that this should be explained to the patient preoperatively. However, in spite of a thorough preoperative investigation, there may be such an overlay of symptoms as to make it, on occasion, virtually impossible to sort them out adequately in the preoperative period. Although this group is generally included in the "bad results" of cholecystectomy, it is probably unfair to the surgeon to do so. The operation has accomplished its purpose, that is, removal of a pathological gallbladder (even if symptomless), and should not be considered unsuccessful when it failed to cure symptoms attributable to another condition.

The other causes noted in Table I are preventable through the exercise of careful and experienced surgery: cystic duct remnant, biliary fistulas, bile peritonitis and bile duct strictures are all avoidable pitfalls. Abdominal adhesions can, to a certain extent, be minimized.

Finally, a third group remains in which the results are not necessarily due to the incompetence of the surgeon but to the shortcomings of our present-day investigative and surgical management. Here, I am thinking of overlooked duct stones, overlooked malignancy in the region of the ampulla of Vater, pancreatitis, cholangitis, stenosis of the sphincter of Oddi, disturbances in bile flow after removal of a functioning gallbladder and biliary dyskinesia of the hypotonic or hypertonic variety.

The overlooked common duct stone is a continuous source of embarrassment to the surgeon and of grief to the patient. Twenty-five per cent of patients with calculous disease of the gallbladder will have stones in the common duct. This has been well demonstrated by various investigators, such as Crump[6] in a series of 1000 postmortem examinations, Mirizzi[7] by operative cholangiography and Maingot[8] in England; this is also confirmed in the present series. Reference to the experience of the most highly competent surgeons in this field reveals that in all patients undergoing cholecystectomy, stones are left behind in the common duct in from 5% to 10%.[9-11] This leads one to wonder about the incidence of this mishap in less experienced hands.

Early malignancies of the duodenal papilla, the ampulla of Vater, the terminal end of the common duct and the head of the pancreas are all readily missed.

Much has been said and written about intravenous[12] and peroperative cholangiography.[9, 13-15] In spite of the enthusiasm of the protagonists of peroperative cholangiography for this method of demonstrating stones in the common duct and pathology at the terminal end of the duct, it is not unfair to state that this technique in the hands of the majority of surgeons has not, after a period of trial, received general acceptance because of its time-consuming tediousness and, still more important, the pitfalls and the difficulty in interpretation of the films.

Stenosis of the sphincter of Oddi,[16, 27-29] disturbances in bile flow after removal of a functioning gallbladder and biliary dyskinesia[38-40] are conditions that stimulate an ever-increasing interest among internists and surgeons concerned in the management of biliary tract disease. Fibrosis of the sphincter is now recognized as a definite entity. Goinard and Pelissier[16] in a study of 700 cholecystectomy cases reported its incidence (histologically controlled) at 8%. Cattell and his co-workers,[17, 27] and many others,[18, 29] recognize that fibrosis of the sphincter of Oddi is responsible for an appreciable number of the unsatisfactory results following cholecystectomy. The majority of fibrosed sphincters will be missed if one relies only on the commonly accepted indications for exploring the common duct.

Biliary dyskinesia occupies an important place in the post-cholecystectomy syndrome. It has been defined as "recurring episodes of pain following cholecystectomy in which no demonstrable organic cause can be found". It is assumed to be due to autonomic nerve imbalance. Hypotonic and hypertonic varieties have been described. It was demonstrated as far back as 1936 by McGowan, Butsch and Walters[19] that morphine-induced spasm of the sphincter of Oddi in a patient who had undergone cholecystectomy produced an increase in common duct pressure and pain identical to that experienced by the patient before the removal of the gallbladder. It has since

been recognized[20] that alkalis, physostigmine, pilocarpine, nicotine, acetylcholine and morphine will cause contractions and spasm of the sphincter of Oddi, whereas acids, scopolamine, atropine, adrenaline and notably amyl nitrite will cause relaxation of this sphincter.

There is at the present time no reliable way of determining which post-cholecystectomy patients are liable to suffer from biliary dyskinesia. Mallet-Guy[24] and Caroli and Gilles[25] have done extensive work on peroperative manometry in trying to assess the presence of hypertonicity or hypotonicity of the sphincter of Oddi. The interpretation of readings carried out on the premedicated and anesthetized patient is open to question. Besides, it cannot shed any light on a condition that may only prevail in the postoperative period, that is, after the gallbladder has been removed.

Routine Transduodenal Sphincteroplasty

In view of all the above-mentioned shortcomings of our present-day management of biliary tract disease, a new approach to the handling of these problems seemed to be warranted. It was reasoned that by adding routine transduodenal sphincteroplasty to cholecystectomy, many if not all of these shortcomings could be safely overcome. Apart from all other considerations, I have always thought that simple removal of the gallbladder with sparing of the sphincter of Oddi is physiologically unsound. These two structures are physiologically related, closure of the sphincter causing a reflux of bile into the gallbladder for purposes of storage. If one of these structures is sacrificed, the *raison d'être* of the other ceases to exist. Animals which have no gallbladder—the horse, the rat—have no sphincter of Oddi. Therefore, if one structure is eliminated the other should be, if physiological principles are to be respected.

It has been demonstrated in physiological experiments by Judd and Mann[26] that dilatation of the common duct occurred in dogs after cholecystectomy but did not if sphincterotomy was performed at the same time. Potter and Mann[23] then demonstrated that the pressure in the common duct increases markedly following cholecystectomy. Every surgeon knows that dilatation of the common bile duct is a frequent finding following cholecystectomy. This can only be the result of increased pressure which is not physiological and is probably the cause of pain.

Sphincterotomy and sphincteroplasty in itself is not a new concept and has been employed in the treatment of a variety of conditions. It is the recognized form of treatment for stenosis of the sphincter of Oddi.[16, 27, 29] The work of Doubilet and Mulholland[30-32] and Cattell and Warren[33] on sphincterotomy in the treatment of pancreatitis is well known. Mallet-Guy and Rose[24] have used the method extensively in the management of hypertrophy and hypertonicity of the sphincter. Colp[34] in 1946 presented eight cases in which sphincterotomy was used in the treatment of postoperative biliary dyskinesia.

Furthermore, the advantages of transduodenal exploration of the common duct have been recognized over the years. Wright[35] in England has made it a practice for 20 years to avoid opening the common duct, believing this procedure to be harmful and unnecessary. Mahorner[36] in 1949 reported 16 cases of supraduodenal and transduodenal exploration of the common bile duct. Even in this small group of patients, when the duodenum was opened he found many surprising conditions that would have been overlooked had it not been opened. This has also decidedly been my experience in the present series of cases. If sphincteroplasty is the recognized treatment for so many of the causes of the post-cholecystectomy syndrome, why not do it prophylactically in all cases of cholecystectomy, if it can be done effectively, within a reasonable period of time and without increasing the mortality and morbidity rates of the operation?

These objectives have been accomplished in 100 consecutive cholecystectomies by using the following technique.

Operative Technique

The gallbladder, cystic duct, common duct, pancreas and duodenum are inspected and palpated in the usual manner

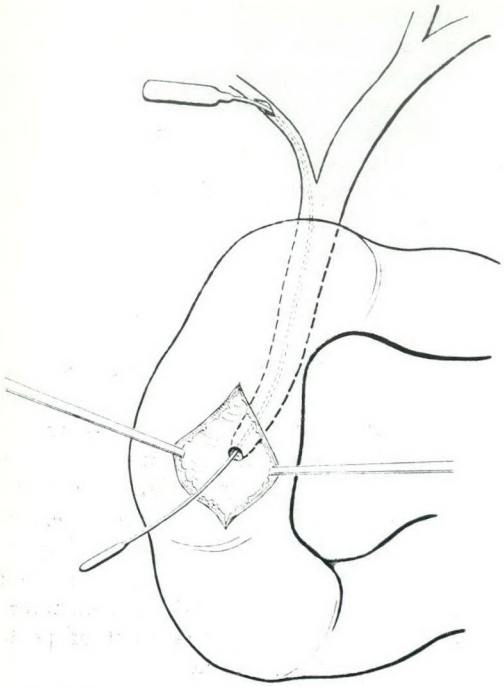

Fig. 1.—Bakes' dilator or probe passed into the duodenum via the cystic and common ducts makes it extremely simple to locate the duodenal papilla and sphincter of Oddi.

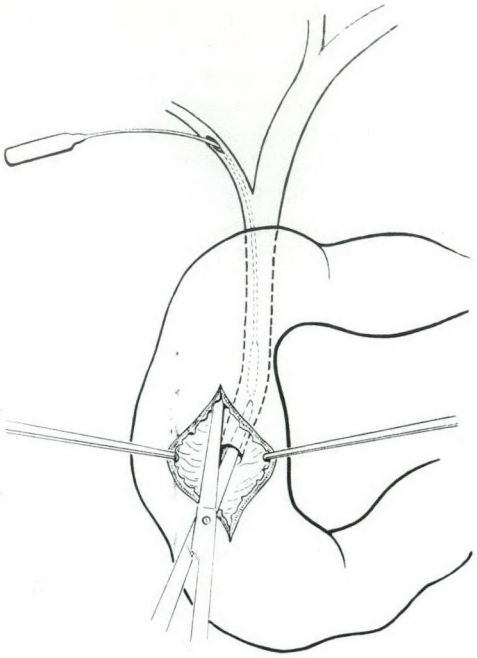

Fig. 2.—Duodenum open, section of the sphincter in upper outer quadrant is being carried out.

for detection of stones or other pathology. The cystic artery is dissected, ligatured and sectioned. The cystic duct is dissected and its junction with the common duct is exposed. The gallbladder is removed in the usual manner, except that the cystic duct is initially sectioned at its junction with the gallbladder. After peritonealization of the gallbladder bed, a small incision is made in the lateral wall of the cystic duct and a 3 mm. Bakes' dilator is inserted via the cystic duct into the common duct, through the sphincter of Oddi, into the duodenum (Fig. 1). Failure of the 3 mm. dilator to enter the duodenum is considered suggestive of stenosis at that point. Occasionally the cystic duct is too small to receive the 3 mm. dilator; a small probe is then used and passed into the duodenum.

A small incision (usually not more than 1″) is made in the anterior wall of the second portion of the duodenum. The duodenal contents are suctioned to prevent spillage. The tip of the Bakes' dilator is grasped and it then becomes an easy matter to locate the duodenal papilla and sphincter of Oddi. Any anomalies in the region are noted. The papilla is held up by the insertion of two silk sutures. The jaw of a pair of fine-pointed scissors or a special sphincterotome is inserted into the ampulla and the sphincter is incised in its upper outer quadrant (Fig. 2). If the scissors cannot be passed alongside the shaft of the dilator, the latter is pulled back into the common duct. If, because of stenosis, the dilator or probe cannot be passed into the duodenum, one cuts down on the tip of the dilator to enter the ampulla. The incision is deepened until the diameter of the opening reaches that of the common duct. This is felt to be of importance, as will be discussed in a moment. This deep section is facilitated by introducing silk sutures in the side wall of the incised duct and using them to exert traction in order to bring the duct into the wound as the incision becomes deeper. When the incision is completed, the duodenal mucosa is approximated to the wall of the incised duct with a series of interrupted 000 chromic catgut sutures (Fig. 3). This type of "longitudinal" incision and

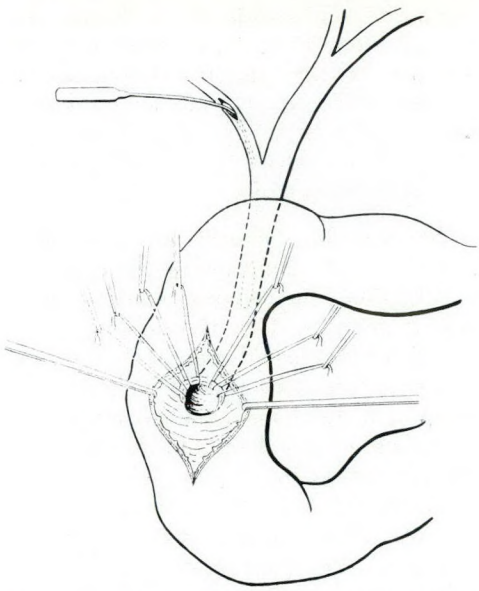

Fig. 3.—Sphincteroplasty has been accomplished. Note that the size of the opening is the same as the diameter of the common duct. The sectioned common duct wall is approximated to duodenal mucosa with a series of interrupted 000 chromic catgut sutures.

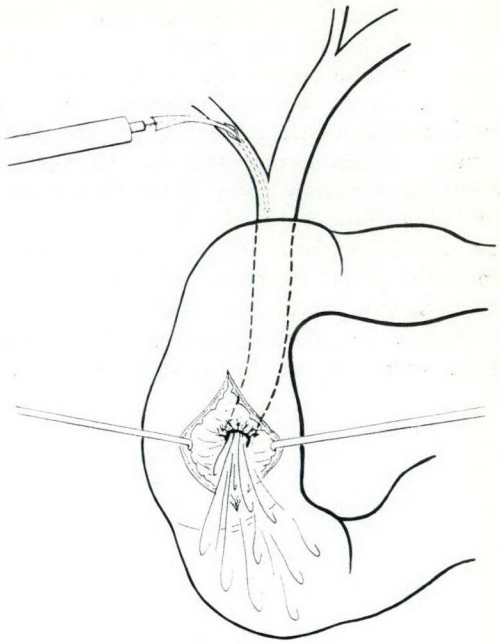

Fig. 4.—Common duct is being irrigated via catheter in the cystic duct.

transverse" closure produces a Mikulicz type of plasty which, in my opinion, is one of the factors maintaining patency of the aperture. As these chromic sutures are introduced, the silk traction sutures are removed. These interrupted chromic sutures are temporarily left long and their ends grasped by forceps.

The dilator is now removed from the cystic duct and it is replaced by a fine catheter which is tied into the cystic duct. A thorough irrigation of the common duct with physiological saline is carried out through this catheter (Fig. 4). At the same time the site of the plasty is held up by the assistant exerting traction on the chromic sutures, and the saline and calculi, if there are any, are seen to gush out through this opening. When the return is entirely clear, the catheter is removed from the common and cystic duct. A transduodenal instrumentation is now practised if deemed necessary. Desjardins forceps, probes and scoops are easily introduced into the common duct via the sphincteroplasty. It is astonishing how much easier instrumentation of the common duct can be by the transduodenal approach (Fig. 5). It is like fishing down directly into a well when

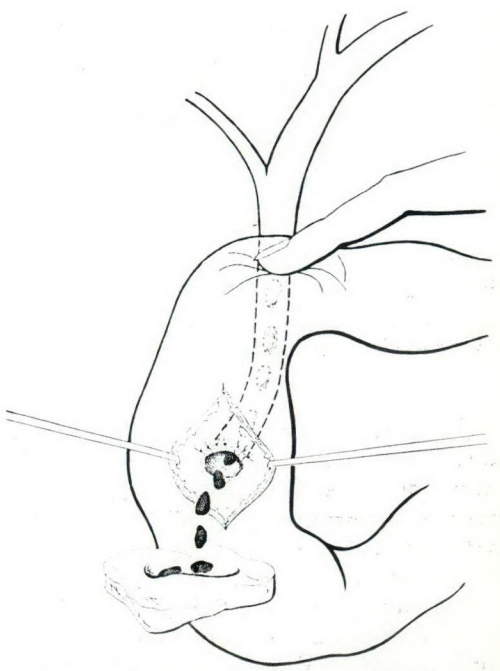

Fig. 5.—Calculi are being easily expressed from common duct into duodenum through the plasty opening.

compared with the awkward and difficult manipulations of the standard lateral-wall approach. The author is now experimenting with a direct vision choledochoscope to further improve the operative investigation. Finally, when exploration is complete, a small polyethylene tube, about 1″ in length and of a diameter that will fit loosely into the common duct, is fixed at the choledochoduodenal junction with a stitch of 000 chromic catgut so that its proximal extremity lies in the common duct and its distal extremity in the duodenum (Fig. 6).

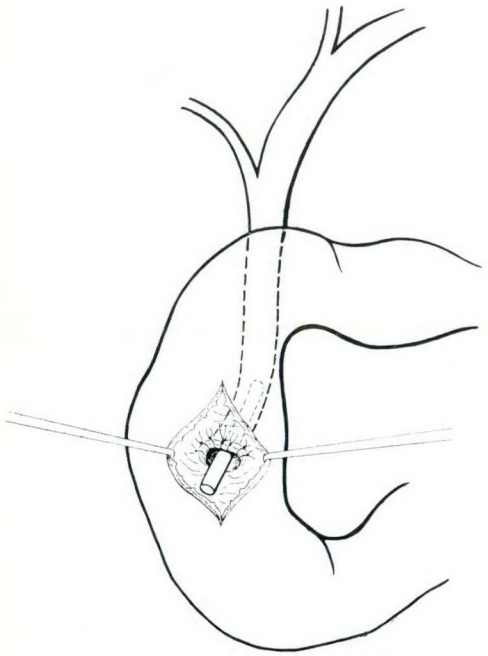

Fig. 6.—The position of the polyethylene tube bridging the plasty opening is illustrated. The tube is fixed in position with one 000 chromic catgut suture, which is absorbed in six to seven days, and the tube passes down the bowel.

The incision in the duodenal wall is now closed in two layers (an all-coats running suture of 00 chromic catgut and a serosal layer of interrupted 000 silk sutures). The cystic duct is sectioned almost flush with the common duct and the common duct peritonealized with interrupted 000 silk. Penrose drains are led out from the area of the foramen of Winslow and, after routine appendectomy, the abdominal wall is closed in layers. The transduodenal sphincteroplasty usually adds about 30 minutes to the operating time. The entire operation, including routine appendectomy, averages an hour and a quarter to an hour and a half.

Contraindications

The procedure should not be employed in severe acute cholecystitis. The presence of infection, the edema which may be present in the wall of the duodenum, or a very ill patient greatly increases the risk of the procedure. One would be particularly afraid of a duodenal fistula resulting from the closure of an edematous duodenal wall. The procedure has been performed without complication in two or three early cases of acute cholecystitis, where edema was limited to the gallbladder wall. Age in itself is not a contraindication. The oldest patient in this series was 72 and this additional procedure did not in any way affect her convalescence. Systemic diseases such as diabetes and heart disease should be taken into consideration and each case assessed on its own merits.

Operative Findings

To eliminate personal variations, all of the cases reported here were operated upon by the author. The results are presented in Table II. For purposes of this study any common duct with a diameter greater than 8 mm. was considered to be enlarged.

TABLE II.—Operative Findings in 100 Consecutive Cholecystectomies

Stones in the gallbladder	96
Dilatation of the common duct	18
Stones in the common duct	22
Unsuspected stones in the common duct	13
Stenosis of the sphincter of Oddi	10
Chronic pancreatitis	5
Benign stenosis of the common duct	1
Fibroma of the duodenal papilla	1

Of the 22 cases presenting with stones in the common bile duct more than one-half would ordinarily have been missed by accepted management of these cases. These stones which would have been missed were small and escaped detection by the usual method of palpation.

In 13 cases of unsuspected stones in the common duct, none of the accepted indi-

cations for exploration of the common duct were present. For the purposes of this study the following indications were accepted: (a) dilated common bile duct; (b) stones palpable in the common bile duct; (c) "tumour" palpable at terminal end of common bile duct; (d) history of or presence of jaundice; (e) gallbladder containing stones smaller than the calibre of the cystic duct; (f) when the clinical findings suggested cholelithiasis, yet at operation no stones could be palpated in the gallbladder or biliary ducts; (g) when aspiration of the common duct with a needle revealed other than normal golden-yellow bile. This means that 13 patients out of 100 operated upon for cholelithiasis would have left the operating-room with stones remaining in the common duct.

Stenosis of the sphincter of Oddi, 10 cases, was considered to be present when a 3 mm. Bakes' dilator could not be passed through the sphincter on the fully anesthetized and curarized patient, even when exerting a considerable amount of pressure. Five of these cases would ordinarily have been missed, as no indications were present for exploring the common bile duct.

Chronic pancreatitis, five cases, was assessed grossly when a hard generalized induration of the head of the pancreas was found. Local induration or borderline cases are not included in this group. This therefore is a conservative estimate.

From Table II it is evident that if transduodenal sphincteroplasty had not been carried out routinely the following lesions would have been missed: (a) 13 cases of common duct stones, (b) five cases of stenosis of the sphincter of Oddi, and (c) one fibroma of the duodenal papilla; and five patients with pancreatitis would have been deprived of useful therapy.

Therefore, of 100 patients, 24% would have received inadequate surgical management. This figure, of course, does not include the cases of biliary dyskinesia that might have occurred postoperatively if the sphincter of Oddi had not been sacrificed. There is, of course, no way of assessing this.

Mortality and Morbidity

It is important to determine whether this additional procedure has increased the mortality and morbidity rates of cholecystectomy. There was one death in the 100 cases. It occurred in the early part of the series in a 54-year-old woman with cardiac disease who died 48 hours after the operation in a state of apparent shock. At that time, the difficulties of the operation had not yet been completely ironed out. It is felt that this death could have been avoided had the operation been performed at a later date. Autopsy was inconclusive in determining the cause of death. There was no evidence of acute pancreatitis but a curious retroperitoneal edema was present which extended down to the region of the cecum. It was felt that there must have been some leakage at the site of sphincteroplasty. At that time suturing of the duodenal mucosa to common duct was not being done.

It must be mentioned that different methods of sphincteroplasty were tried during the time the first 25 patients were being operated upon, before adopting the now routine procedure described in this communication. At first, no tubes whatever were left in the common duct; for a time duodenal mucosa was not sutured to the common duct wall; an attempt was made to leave a T-tube in the common duct with a long branch extending into the duodenum, and tubes were inserted in the common and pancreatic ducts and exteriorized through the duodenal wall. However, nearly all of these procedures produced stormy and alarming convalescences, with considerable elevations of temperature and pulse increases for periods of five to six days. At least four or five cases presented the clinical picture of acute pancreatitis. This experience stresses the importance of proper operative technique, for as soon as the present method was adopted, 75 consecutive cases were performed without any incident whatever. There was no complication of any kind and all these patients were discharged from hospital seven or eight days after operation. It is therefore justifiable to conclude that this additional maneuver adds nothing to the mortality and morbidity rates of cholecystectomy.

Follow-up Study

It has been possible to follow-up 85 of the 100 patients for a period ranging from three years to four months (the patients most recently operated upon and included in this series). There has been one post-operative death *(vide supra)*. Another patient died two years after operation from primary carcinoma of the liver of which there was no evidence at the time of operation. Seven patients (8% of the follow-up group) have a variety of symptoms which seem to be triggered by the ingestion of fatty foods. They are relatively well and satisfied as long as they adhere to the dietary restriction of certain fats. Eight patients (9%) have what they describe as occasional attacks of pain similar to their preoperative pain, lasting from three to four minutes. These attacks occur from once a week to once a year. They are occasionally associated with meals but seem to be more particularly related to bouts of nervous tension. It is interesting to note that the majority in this group are high-strung and tense individuals. Sixty-eight patients (80%) are completely well and have no symptoms of any kind and the majority can eat practically anything. *None of these 85 patients has required any further operation on the biliary tract and none has suffered from jaundice at any time.*

Discussion

The morbidity and mortality rates of sphincteroplasty due to acute pancreatitis, as reported in the literature,[41, 42] is somewhat staggering. Deucher[41] reports a mortality rate of 12%. It is felt that the operative technique (as described above) is of major importance in the prevention of this catastrophe; not a single case of acute pancreatitis occurred during the use of this technique in the 100 consecutive cases reported here.

Manipulation of these delicate structures must be as gentle as possible. Considerable trauma with consequent edema and obstruction to the opening of the pancreatic duct can be caused by clumsy and tedious search for the duodenal papilla. Finding of the duodenal papilla may be difficult because it is a small structure lost in duodenal folds. This difficulty has been overcome by the introduction of the dilator through the cystic duct into the duodenum. This is a sure, non-traumatic, rapid guide to the ampulla. No mention has been made of mobilization of the second part of the duodenum. This at times may be necessary, particularly in obese patients where exposure is difficult. It will facilitate what could otherwise be a very laborious procedure in a particularly obese patient. However, it is felt that this maneuver should not be contemplated unless absolutely necessary. It traumatizes the head of the pancreas and exposes the retroperitoneal tissues to duodenal and biliary spillage. Also, no mention is made of attempts to localize the opening of the pancreatic duct. This was carried out in the early cases and it was realized that the necessary probing and sponging caused a considerable amount of congestion and edema of the delicate mucosa. Convalescence was always more difficult in patients in whom the pancreatic duct had been probed and cannulated. It was abandoned as an unnecessary maneuver.

It is important that section of the sphincter should be carried out in the upper outer quadrant. This eliminates the possibility of traumatizing the pancreatic duct. Also, the section should be carried as deeply as necessary in order to obtain a sphincteroplasty opening equal to the diameter of the common duct. This is necessary if any stones which might escape exploration are subsequently to pass into the duodenum. It is astonishing how deep this incision has to be made occasionally, as much as ¾″ in some patients. There is, in a good percentage of cases, a marked narrowing of the common duct just proximal to the ampulla of Vater which must be sectioned if the anticipated results are to be achieved. No definite length of incision can be established; each case has to be assessed individually.

There is considerable difference of opinion in the surgical literature as to whether the duodenal mucosa should be sutured to the common duct wall. I feel strongly that this should be done in all cases for the following reasons:

1. It provides a better guarantee that healing will occur without stenosis. This type of suturing more or less applies the Mikulicz principle of plasty, that is, longitudinal incision with transverse closure. A fundamental principle in surgery of any muscular sphincter is that a single transverse section does not produce incontinence.

2. It prevents pancreatic fluid digestion of the area exposed by sphincterotomy. In sectioning the sphincter there is some separation of the mucous membrane of the wall of the duodenum from the cut edge of the duct. Pancreatic fluid digestion of this area may occur.

3. It prevents extraduodenal leakage and peritonitis if section has inadvertently gone too far in the duodenal wall.

It is important that no instrumentation be carried out through the plasty opening before transcystic irrigation is accomplished. Otherwise stones distal to the cystic duct might be forced back into the hepatic ducts. By irrigating first, all stones or sludge distal to the cystic duct will be flushed out into the duodenum.

Finally, I feel that probably the most important part of the procedure lies in leaving the small polyethylene tube to bridge the sphincteroplasty for the few days that are necessary to allow for the disappearance of the inevitable edema which arises at the site of the plasty. In the first few cases this tube was omitted and the convalescence in every case was quite stormy. Postoperative edema at the site of the plasty will inevitably obstruct the flow of bile and distend the bile passages; it may cause the cystic stump to "blow" and may cause regurgitation of bile into the pancreatic duct. This simple little tube allows the bile to flow freely into the duodenum. The tube is passed down into the bowel in seven or eight days, when the dangerous period of edema is over. It is easy to assess its position and follow its progress radiologically down the bowel by fixing one or two small Cushing silver clips to its distal extremity. It also eliminates the necessity of leaving T-tubes or other catheters in the common duct, a procedure extremely traumatic to a very delicate structure.

The entire procedure of transduodenal exploration of the common duct in fact eliminates much of the trauma to the common duct. There are no incisions in the wall of the common duct. No irritating and traumatic tubes are left behind to give rise to infection, cholangitis and hepatitis.

There has been some argument about duodenal closure. All incisions have been closed longitudinally without ill effects. It is felt that a transverse closure is not necessary and even at times a little more difficult to execute because of the "dog-ear" effect at the extremities of the incision.

Sphincteroplasty does permit duodenal reflux or regurgitation of duodenal contents into the biliary tract. The fear has been frequently expressed in the literature that this may set up cholangitis and fatal infection. This concept is entirely false. It is not reflux that causes cholangitis but bile stasis such as is encountered in stenosis of the biliary tract, notably at the site of choledochointestinal anastomoses. Experience with several hundred cases of sphincteroplasty reported in the literature,[16] and the present series, confirms this opinion.

The above-described procedure has been carried out during 100 consecutive cholecystectomies. In the course of this experience it has been amply demonstrated that the procedure has the following merits:

1. It eliminates the danger of missing early neoplasms of the duodenal papilla, the ampulla of Vater, the terminal portion of the common duct and the head of the pancreas. By opening the duodenum, visual and digital inspection of these structures is made possible.

2. It eliminates the problem of the residual stone. Stones and biliary sludge distal to the cystic duct are flushed out by irrigation. Instrumentation and choledochoscopy will reveal whatever stones have escaped irrigation. Finally, in the unlikely event that any stone has escaped all of these maneuvers, it can be assumed that it will pass spontaneously into the duodenum because the sphincteroplasty opening has the same diameter as that of the common duct.

3. It eliminates the danger of overlooking cases of stenosis of the sphincter of Oddi.

4. It is a recognized form of treatment for certain types of pancreatitis. Many cases of cholecystitis are associated with greater or lesser degrees of pancreatitis. Doubilet and Mulholland[30, 31] and others have demonstrated the value of sphincteroplasty in the management of these conditions. It is therefore a useful supplement to the management of those cases of cholecystitis which are associated with a certain degree of pancreatitis of biliary origin.

5. It is the best, easiest and least traumatic way of exploring the common bile duct. Reference has already been made to the technical advantages of this avenue of approach to the common duct.

6. It eliminates the problem of leaving tubes in the common bile duct. At best these are a source of trauma to a delicate structure, a source of infection, cholangitis and hepatitis. One shudders at the trauma that is caused to the common duct when a T-tube is removed, with its consequent laceration and scarring of the common duct wall. It is indeed a marvel of nature that such a crude insult to the common duct does not result in greater morbidity.

7. It eliminates the danger of missing a ligatured common duct. Simple introduction of a dilator down the common duct is an immediate guarantee of its patency.

8. It settles the problem of biliary dyskinesia. If the plasty is properly carried out, incontinence of the sphincter is assured and postoperative pain owing to spasm of this structure is thereby eliminated.

9. It eliminates the necessity of peroperative manometry and cholangiography. Manometry ceases to be necessary if the sphincter is going to be sacrificed in any case. Cholangiography is unnecessary since direct visualization replaces radiographic visualization.

Summary

The causes of the post-cholecystectomy syndrome have been reviewed. Routine sphincteroplasty with cholecystectomy for the treatment of cholelithiasis is advocated to minimize the occurrence of this syndrome. The operative technique is described and discussed.

Operative findings in 100 consecutive cases are reported in detail. The advantages of this technique are outlined.

The follow-up study of 85 of these 100 cases is presented.

It is felt that this approach to surgery of the gallbladder has considerably improved the postoperative results, as evidenced in the cases presented.

References

1. Eliason, E. L. and North, J. P.: Morbidity following cholecystectomy, *Ann. Surg.*, **109:** 580, 1939.
2. Bettman, R. B. and Lichtenstein, A.: End-results following cholecystectomy, *Amer. J. Med. Sci.*, **194:** 788, 1937.
3. Carter, R. F. and Marraffino, B.: Symposium on chronic diseases; causes and relief of symptoms following cholecystectomy, *New York J. Med.*, **40:** 1648, 1940.
4. Meyers, S. G., Sandweiss, D. J. and Saltzstein, H. C.: End results after gall bladder operations with an analysis of the causes of residual symptoms, *Amer. J. Dig. Dis.*, **5:** 667, 1938.
5. Nygaard, K. K.: On post-cholecystectomy colics; with report of a case, *Acta Chir. Scand.*, **81:** 309, 1938.
6. Crump, C.: Incidence of gall stones and gallbladder disease, *Surg. Gynec. Obstet.*, **53:** 447, 1931.
7. Mirizzi, P. L.: Operative cholangiography; its contribution to physiopathology of common bile-duct, *Lancet*, **2:** 366, 1938.
8. Maingot, R.: Abdominal operations, 2nd ed., Appleton-Century-Crofts Company, Inc., New York, 1948.
9. Ferris, D. O.: Operative cholangiography; an aid in reducing the incidence of residual common duct stones, *Postgrad. Med.*, **26:** 301, 1959.
10. Smith, S. W. *et al.*: Problems of retained and recurrent common bile duct stones, *J. A. M. A.*, **164:** 231, 1957.
11. Hicken, N. F., McAllister, A. J. and Call, D. W.: Residual choledochal stones; etiology and complications in one hundred ten cases, *A.M.A. Arch. Surg.*, **68:** 643, 1954.
12. Sandweiss, D. J. and Fulton, H.: Intravenous cholangiography; results in one hundred cholecystectomized patients with upper abdominal symptoms, *J. A. M. A.*, **159:** 998, 1955.
13. Ferris, D. O. and Weber, H. M.: Evaluation of routine operative cholangiography, *A.M.A. Arch. Surg.*, **73:** 197, 1956.
14. Mirizzi, P. L.: Operative cholangiography, *Surg. Gynec. Obstet.*, **65:** 702, 1937.
15. Johnston, E. V., Waugh, J. M. and Good, C. A.: Residual stones in the common bile duct: the question of operative cholangiograms, *Ann. Surg.*, **139:** 293, 1954.
16. Goinard, P. and Pelissier, G.: Total sphincteroplasty without drainage of the common bile duct in the treatment of biliary tract disease, *Surg. Gynec. Obstet.*, **111:** 339, 1960.

17. CATTELL, R. B. AND COLCOCK, B. P.: Fibrosis of the sphincter of Oddi, *Ann. Surg.*, **137:** 797, 1953.

18. TROMMALD, J. P. AND SEABROOK, D. B.: Benign fibrosis of the sphincter of Oddi: report of eight cases, *Western J. Surg.*, **58:** 89, 1950.

19. MCGOWAN, J. M., BUTSCH, W. L. AND WALTERS, W.: Pressure in the common bile duct of man; its relation to pain following cholecystectomy, *J. A. M. A.*, **106:** 2227, 1936.

20. BOCKUS, H. L.: So-called postcholecystectomy syndrome, *In:* Postgraduate gastroenterology; as presented in a course given under the sponsorship of the American College of Physicians in Philadelphia, December 1948, edited by H. L. Bockus, W. B. Saunders Company, Philadelphia, 1950, p. 561.

21. BERK, J. E.: Post-cholecystectomy syndrome, *Amer. J. Dig. Dis.*, **6:** 1002, 1961.

22. SHINGLETON, W. W. AND PEETE, W. P.: The postcholecystectomy syndrome, *Amer. Surg.*, **28:** 29, 1962.

23. POTTER, J. C. AND MANN, F. C.: Pressure changes in the biliary tract, *Amer. J. Med. Sci.*, **171:** 202, 1926.

24. MALLET-GUY, P. AND ROSE, J. D.: Per-operative manometry and radiology in biliary tract disorders, *Brit. J. Surg.*, **44:** 55, 1956.

25. CAROLI, J. AND GILLES, E.: La radiomanométrie biliaire; étude technique, *Sem. Hôp. Paris*, **21:** 1278, 1945.

26. JUDD, E. S. AND MANN, F. C.: The effect of removal of the gall-bladder: an experimental study, *Surg. Gynec. Obstet.*, **24:** 437, 1917.

27. CATTELL, R. B., COLCOCK, B. P. AND POLLACK, J. L.: Stenosis of the sphincter of Oddi, *New Eng. J. Med.*, **256:** 429, 1957.

28. BLOCK, M. A. *et al.*: Stenosis of the sphincter of Oddi, as a cause of jaundice, *A.M.A. Arch. Surg.*, **76:** 888, 1958.

29. COLCOCK, B. P.: Stenosis of the sphincter of Oddi, *Surg. Clin. N. Amer.*, **38:** 631, 1958.

30. DOUBILET, H. AND MULHOLLAND, J. H.: Surgical treatment of recurrent acute pancreatitis by endocholedochal sphincterotomy, *Surg. Gynec. Obstet.*, **86:** 295, 1948.

31. DOUBILET, H. AND MULHOLLAND, J. H.: Recurrent acute pancreatitis: observations on etiology and surgical treatment, *Ann. Surg.*, **125:** 609, 1948.

32. DOUBILET, H. AND MULHOLLAND, J. H.: Eight year study of pancreatitis and sphincterotomy, *J. A. M. A.*, **160:** 521, 1956.

33. CATTELL, R. B. AND WARREN, K. W.: The choice of therapeutic measures in the management of chronic relapsing pancreatitis and pancreatolithiasis, *Gastroenterology*, **20:** 1, 1952.

34. COLP, R.: Treatment of postoperative biliary dyskinesia; report of 8 cases of endocholedochal sphincterotomy, *Gastroenterology*, **7:** 414, 1946.

35. WRIGHT, A. D.: Surgery of the biliary tract, *Ann. Roy. Coll. Surg. Eng.*, **27:** 373, 1960.

36. MAHORNER, H.: Combined supraduodenal and transduodenal exploration of common bile duct, *Ann. Surg.*, **129:** 766, 1949.

37. MORTON, C. B., 2ND: Post-cholecystectomy symptoms from cystic duct remnants, *Ann. Surg.*, **139:** 679, 1954.

38. STRODE, J. E.: Biliary dyskinesia from surgical viewpoint, *Ann. Surg.*, **117:** 198, 1943.

39. DREILING, D. A.: The postcholecystectomy syndrome; the functional aspect of biliary colic persistent after cholecystectomy, *Amer. J. Dig. Dis.*, **7:** 603, 1962.

40. BACHRACH, W. E., SMITH, J. L. AND HALSTED, J. A.: Spasm of the choledochal sphincter accompanying sudden stress, *Gastroenterology*, **22:** 604, 1952.

41. DEUCHER, F.: Pancréatite mortelle après drainage transpapillaire du canal cholédoque, *Gastroenterologia (Basel)*, **88:** 311, 1957.

42. WALTERS, W., TAMA, L. AND MAGISANO, J.: Acute hemorrhagic pancreatitis associated with choledochal sphincterotomy, *Surg. Clin. N. Amer.*, **41:** 979, 1961.

RÉSUMÉ

Différents rapports dans les journaux médicaux de diverses origines s'accordent à constater l'existence d'un syndrome "post-cholécystectomie". Les causes en sont multiples: diagnostic pré-opératoire erronné, chirurgie insuffisante laissant persister un certain degré de pathologie, erreurs techniques pendant l'intervention, affection concomittante (pancréatite, cholangite, sténose du sphincter etc.), troubles fonctionnels. La dyskinésie biliaire est de plus un important facteur étiologique; elle semble être due à un trouble de l'innervation autonome de la région, et se traduit par des épisodes douloureux à répétition. L'auteur pense que l'apparition de ce syndrome pourrait être évitée par un traitement plastique du sphincter d'Oddi. L'ablation de la vésicule biliaire avec conservation du sphincter semble illogique: les deux organes existent simultanément en fonction l'un de l'autre, et les animaux qui n'ont pas de vésicule n'ont pas non plus de sphincter. La technique est la suivante: la vésicule et l'arbre biliaire sont soigneusement inspectés, puis l'artère cystique est ligaturée et sectionnée. Le canal cystique est disséqué et sa jonction avec le cholédoque bien visualisée. La vésicule est enlevée de façon usuelle, mais après section préalable du canal cystique; le lit vésiculaire est péritonéalisé, et une petite incision est pratiquée dans la paroi latérale du cystique: ceci permet d'introduire un dilatateur à travers le sphincter jusque dans le duodénum. Ce dernier est ouvert sur une petite longueur, ce qui permet d'accéder à l'ampoule de Vater et d'inciser celle-ci, par sa face interne, jusqu'à ce que l'on obtienne une ouverture de même calibre que celui du cholédoque. Cette intervention a donné d'excellents résultats. L'auteur a pu suivre post-opératoirement un groupe de 85 malades ainsi traités pendant des périodes variant entre quatre mois et trois ans: aucun d'entre eux n'a nécessité de réintervention sur ses voies biliaires, ni présenté de jaunisse.

MALIGNANT POLYPS OF THE COLON*

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THE present study was undertaken to determine the adequacy of local removal in the treatment of malignant polyps of the colon. Among 802 cases of carcinoma of the left half of the colon registered at the Saskatoon Cancer Clinic between 1950 and 1959, there were 64 patients with malignant polyps treated by various methods. This review is based on a study of these 64 cases. No cases of familial or multiple polyposis are included. Also excluded were polyps found in association with a carcinoma of the colon that had been resected. For the purposes of this paper, a malignant polyp is considered to be any case of carcinoma in polyp (either sessile or pedunculated) where that carcinoma shows early, usually Grade I, changes in the epithelium, with no invasion through the muscularis mucosae.[3]

There were three types of polyps. The first group was composed of 23 sessile smooth-surfaced polyps; nearly all of these were under 2 cm. in maximum diameter. The second group was composed of 20 sessile papillary-surfaced polyps, or villous papillomas; all of these were over 2 cm. in diameter, the largest measuring 6 x 8 cm. The third group consisted of 21 pedunculated polyps, some of which were smooth-surfaced and some papillary-surfaced, the papillary-surfaced lesions being larger, generally over 2 cm. in diameter.

In reviewing the location, 72 polyps had to be considered, as some of the 64 patients had more than one polyp. The majority of polyps were quite low, and well within the reach of the sigmoidoscope. There were 53 polyps below the level of the peritoneal reflection (0 to 14 cm. from the anal opening); 14 were located from 14 to 25 cm. above the anal opening; only five were above the 25 cm. level, that is, completely above the reach of a sigmoidoscope.

A consideration of the age and sex of these patients (Tables I and II) reveals that most of these tumours develop after middle age, and are slightly more common in the male than in the female.

TABLE I.—AGE DISTRIBUTION IN YEARS

40-49	*50-59*	*60-69*	*70-79*	*80-89*
8	14	22	17	3

TABLE II.—SEX DISTRIBUTION

Males	37
Females	27

Table III shows that the most significant symptoms these patients have is rectal bleeding. An uncommon but interesting symptom is the excessive mucus, present in five; each of these patients had a fairly large villous papilloma. However, none of these had the severe electrolyte disturbance described by some authors in villous papillomas with mucous diarrhea.[2]

TABLE III.—SYMPTOMS

Prolapse	7	Excessive mucus	5
Bleeding	38	Pain	12
Constipation	7	Pressure	5
Diarrhea	11	Routine sigmoidoscopy	14

Various methods were used in treating these malignant polyps (Table IV); 43 were treated by local removal and 25 were treated by radical removal. Local removal refers to either local excision of

TABLE IV.—METHOD OF TREATMENT

Transrectal local removal	28
Laparotomy with local removal	19
Abdominoperineal resection	21
Anterior resection	4

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the entire polyp in one piece, snare fulguration, or piecemeal removal. The pedunculated polyps are more readily removed in one piece through the sigmoidoscope than are the sessile polyps, and in the latter, piecemeal removal frequently is required.

TABLE V.—Results of Treatment

	Pedunculated	*Sessile (smooth)*	*Sessile (papillary)*	*Total*
Local removal....	13	15	6	34
Abdomino-perineal.....	5 (1 death)	5	11	21
Anterior resection.	0	4 (2 deaths)	0	4
Deaths from recurrences....	0	0	1	1
Recurrence and well.....	0	0	1	1

Excludes three patients who died of other diseases.

TABLE VI.—Follow-Up Study of Treated Cases

Alive and well	*Pedunculated*	*Sessile*	*Villous*	*Total*
2 to 5 years...	7	14	5	26
5 to 12 years..	10	8	13	31
Deaths	1 death after radical surgery	2 deaths after radical surgery	1 death at 18 months of recurrence	

Excludes 3 patients who died of other diseases.

Of the 31 patients alive and well five years or longer, 15 were treated by local removal.

Tables V and VI give the results of treatment and follow-up study from two to 12 years and allow some very interesting conclusions to be drawn.

There were no deaths from recurrence in the groups with pedunculated malignant polyps, or with smooth-surfaced sessile malignant polyps.

There was one death due to recurrent disease from a sessile papillary malignant polyp (villous papilloma). In this case, on the basis of a biopsy, the lesion was identified as a papillary malignant polyp, although the attending surgeon thought it looked like an obvious carcinoma, and described it as such on the proctoscopy report. However, the patient was 79 years of age and quite debilitated and only local treatment was carried out. The tumour recurred as invasive carcinoma after two attempts at local excision, and eventually caused death from metastases after 18 months.

There was one recurrence of a large sessile papillary malignant polyp (villous papilloma) in an 89-year-old debilitated woman in whom only repeated local curettages were performed, as it was believed that she would not tolerate the radical surgery necessary for full removal. However, she remains as well as her age and general condition permit four years after her first treatment.

Most significantly, three deaths occurred after radical surgery, and in each of these the pathological report after radical excision showed a very low grade of malignancy that undoubtedly would have been adequately managed by local excision.

Case 1.—A 60-year-old patient died 10 days after anterior resection for a small sessile 1 cm. polyp of Grade I malignancy at a level 7 cm. above the anus.

Case 2.—An 89-year-old patient died four days after an anterior resection for a 1 cm. malignant polyp at 13 cm. above the anus. No residual tumour was present in the resected colon; it had apparently been fully removed with the biopsy.

Case 3.—A 66-year-old patient died three weeks after an abdominoperineal resection for a 2 cm. pedunculated Grade I malignant polyp 9 cm. above the anus.

Three other deaths occurred at various intervals after treatment; these were all deaths from other forms of disease.

Table VI shows that 31 patients (approximately half of the series) have been followed up for five years or longer without recurrence; 15 of these were treated by local removal only.

No recurrences followed removal of 16 pedunculated malignant polyps, 12 of which were treated by local excision. Of the four patients treated by radical surgery, one died after operation.

There were no recurrences in 22 sessile smooth-surfaced polyps, 15 of which were treated by local surgery. Among the seven patients treated by radical surgery, there were two deaths.

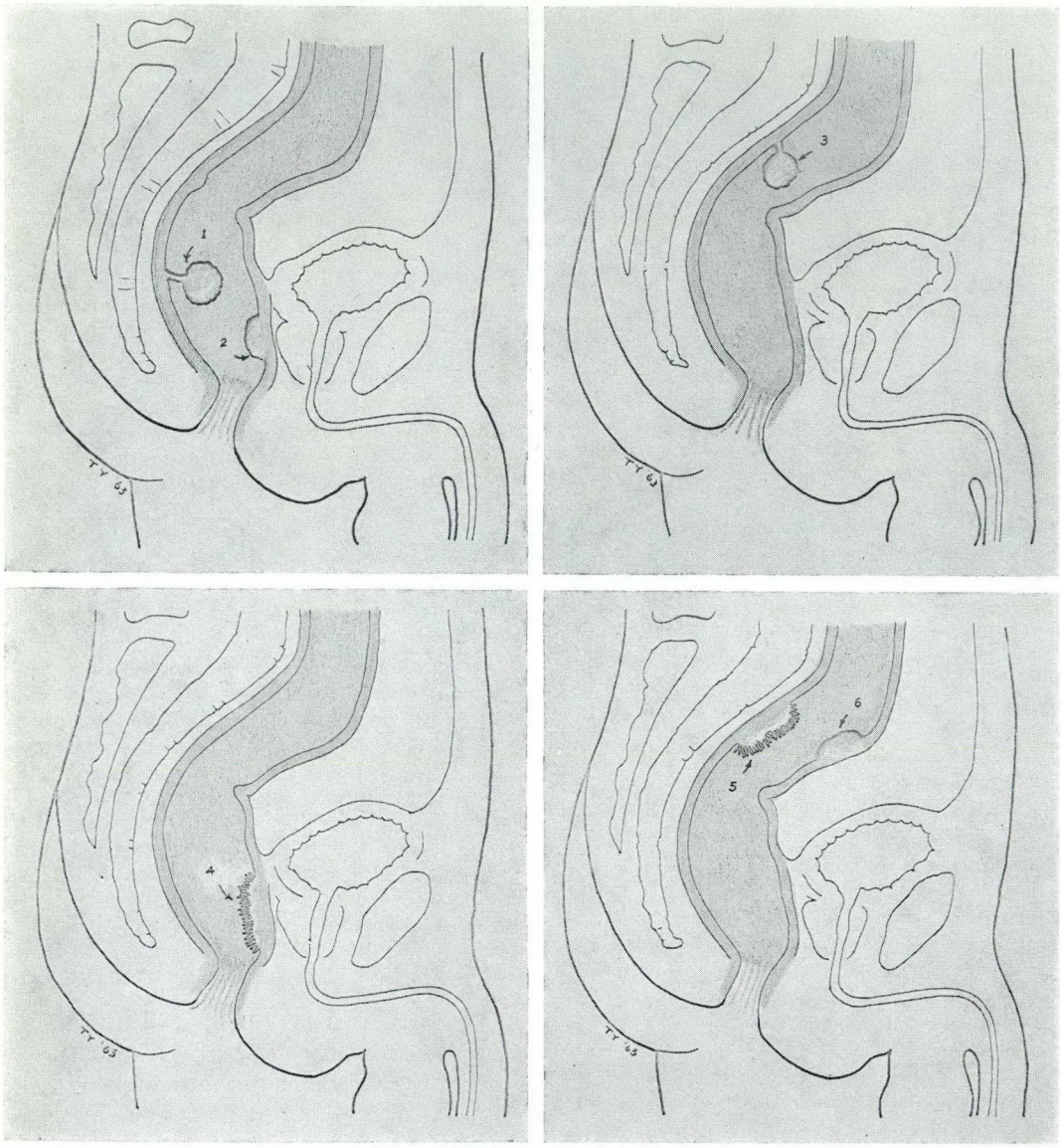

Fig. 1.—(1) Low pedunculated and (2) smooth sessile polyps are readily removed from below. Local removal is adequate for non-invasive malignant polyps. (3) High pedunculated polyps must be removed by colotomy. Even with Grade I malignancy and no invasion of muscularis mucosae, local excision is adequate. (4) Low villous papillomas can be removed by wide local transrectal excision or by low anterior resection, or other sphincter-preserving operation. Abdominoperineal resection should be avoided if possible. (5) High villous papillomas should be removed by wide segmental resection of colon. (6) High smooth-surfaced sessile polyps above the reach of biopsy by sigmoidoscope should be similarly excised.

Discussion

It is quite apparent in this series that there were more deaths (three) due to radical surgery for low-grade malignant polyps than to recurrence of disease after inadequate local surgery. Only one death can be attributed to failure of local surgery, and in this case the treatment was chosen largely because of the patient's poor general condition.

Malignant papillary sessile polyps (villous papillomas) appear to have a greater malignant tendency, because they are larger and recur more often. It is possible

that papillary change in the epithelium is evidence of a more advanced or older stage of polyp growth. This is in agreement with Helwig's observations.[4]

This study was an attempt to determine the adequacy of local removal of malignant polyps. It appears that malignant polyps (Grade I lesions which have not penetrated the muscularis mucosae) can be safely treated by local removal if they are pedunculated, or even if they are sessile with a smooth surface, whereas papillary sessile polyps (villous papillomas) are, both because of their larger size and their more malignant tendency, less safely treated by local surgery. In spite of this conclusion we hesitate to advocate routine treatment which is too conservative—as we do not believe that our follow-up study is long enough to allow valid conclusions. However, some conservatism in the management of these lesions seems indicated in view of our experience that three patients have died from probably unnecessary radical surgery for low-grade malignancies, whereas only one died from recurrence after local treatment.

It is suggested that the following routine might be used in the management of malignant polyp of the colon, particularly in patients over 60 years of age or in those of a younger age group who are debilitated. For treatment purposes these polyps should be divided into two groups:

1. Those that can be well visualized by the sigmoidoscope.

2. Those that are above the level that allows good visualization by the sigmoidoscope.

Management of Polyps that can be Visualized through the Sigmoidoscope

(a) *Pedunculated polyps.*—Many of the pedunculated polyps in this series visualized through the sigmoidoscope were removed in pieces, but, if possible, they should be removed intact by cutting the base with biopsy forceps. The electric snare removes these polyps very nicely but it may interfere with microscopical examination of the base. After the polyp has been removed intact or in pieces, microscopical examination will determine if it is a low-grade lesion with no invasion through the muscularis mucosae; if this is the case, no further treatment is necessary. Continued observation and follow-up examination, however, are indicated. Should evidence of invasive malignant change be seen, radical surgery is indicated.

(b) *Sessile smooth polyps.*—These can be handled in the same manner as the pedunculated type, except that the higher ones may be difficult to remove satisfactorily via the sigmoidoscope. In these instances, laparotomy and colotomy may be necessary to remove the polyp.

(c) *Sessile papillary polyps (villous papillomas).*—With or without malignant change on biopsy, this is a more dangerous tumour because it is sometimes quite large (up to 6 x 9 cm. in the present series), and it has a distinct tendency to malignant degeneration, local recurrence and even distant metastases.

If on multiple biopsy the lesion is benign or of low-grade malignancy, is located quite low in the rectum and is not too large, it can be adequately treated by complete excision by the transrectal route with or without cutting the sphincter. Again careful follow-up examination is indicated.

The larger villous papillomas which completely encircle the bowel or those lesions which are too high for transrectal removal require resection from above, and in view of their low grade of malignancy are ideal for sphincter-preserving operations. In the very debilitated patient, piecemeal removal from below may be indicated.

In the patient with villous papilloma suffering major electrolyte imbalance due to profuse mucous diarrhea, emergency resection may be indicated as a life-saving procedure; we have had no experience with this type of case.[2]

Management of Polyps that cannot be Visualized through the Sigmoidoscope

Polyps above the 25 cm. level are considerably less common than below this level. Generally they are diagnosed by barium enema or double-contrast enema. Occasionally they are discovered at routine abdominal exploration. In any patient with polyps above the reach of the sigmoidoscope, the surgeon at laparotomy is faced

with the problem of having to deal with a polyp without the benefit of preliminary biopsy.

Management of Pedunculated Polyps above 25 cm.

Generally speaking, pedunculated polyps are benign or of low-grade malignancy and radical surgery is seldom indicated. Laparotomy is indicated and palpation of the polyp will determine or confirm its pedunculated nature.[1] Palpation of the whole colon should be carried out to exclude other polyps or tumours; some surgeons may prefer to examine the colon with the sigmoidoscope. After completion of the examination an incision is made over the polyp.[1, 5] If it has a smooth-surfaced benign appearance, local removal with a wide rim of mucosa at the base is indicated. Very rarely will pathological examination show anything but benign tumour or low-grade non-invasive malignant changes. Should invasive malignant changes be seen, however, more radical surgery will be indicated.

If, on the other hand, at colotomy the polyp has a fungating or obviously malignant appearance, the colon should be closed without biopsy of the lesion to prevent spillage, and radical excision performed. Such a situation rarely arises because frankly malignant tumours are usually readily recognizable on radiological examination or on palpation of the unopened colon.

Management of Sessile Polyps above 25 cm.

In view of the fact that both by barium enema and by palpation of the colon the sessile polyp is difficult to distinguish from a true carcinoma, the only safe management in the presence of these polyps is to perform radical excision. If there is reasonable suspicion that the lesion is of low-grade malignancy, limited wedge-resection may be performed. Frozen section on the resected specimen may indicate that more radical resection should be carried out.

In those tumours that have been biopsied by the sigmoidoscope but are too high for removal from below, extent of resection can be planned according to the reports of the biopsy.

Resection and anastomosis are indicated for all high-level villous papillomas.

SUMMARY

A total of 64 patients with 72 malignant polyps treated by various methods are reviewed. Of this number, the polyps were pedunculated, or smooth-surfaced and sessile, in 44 patients, while the remaining 20 had villous papillomas. Follow-up study of from two to 12 years showed no recurrence in any of 44 patients with pedunculated polyps or smooth-surfaced sessile polyps, whereas three deaths occurred following apparently unnecessary radical surgery for low-grade malignant polyps in this group. Of the 20 villous papillomas treated and followed up, there was one death from recurrence with metastases.

It is recommended that pedunculated and smooth-surfaced sessile polyps, if of non-invasive malignant change, be treated by local excision, whereas villous papillomas, being larger and probably representing a more advanced stage of tumour growth, must be treated by wide local excision in the lower lesions (where adequate biopsy shows non-invasive malignant changes or a benign lesion) and by wide segmental or anterior resection in the higher lesions that cannot be biopsied from below.

REFERENCES

1. BACON, H. E. AND PEALE, A. R.: Appraisal of adenomatous polyps of the colon; their histopathology and surgical management, *Ann. Surg.*, **144:** 9, 1956.
2. CAREY, R. J. AND BURBANK, C. B.: Mucus secreting villous adenoma of the colon presenting as circulatory collapse, *New Eng. J. Med.*, **267:** 609, 1962.
3. FISHER, E. R. AND TURNBULL, R. B., JR.: Malignant polyps of rectum and sigmoid; therapy based upon pathologic considerations, *Surg. Gynec. Obstet.*, **94:** 619, 1952.
4. HELWIG, E. B.: Evolution of adenomas of large intestine and their relation to carcinoma, *Surg. Gynec. Obstet.*, **84:** 36, 1947.
5. MCLANAHAN, S. AND MARTIN, R. E.: Colotomy, coloscopy, and colectomy in the management of polyps of the large intestine, *Ann. Surg.*, **145:** 689, 1957.

RÉSUMÉ

Cet article étudie l'opportunité de la résection locale dans le traitement des polypes malins du

côlon. Dans les archives de la Clinique du Cancer de Saskatoon, on trouve entre 1930 et 1939, 802 cas de cancers de la moitié gauche du côlon. Parmi ceux-ci, il y a 64 cas de polypes malins qui furent traités par diverses méthodes, et qui servent de base à la présente étude. Les polypes malins sont définis par les auteurs comme tout cas de carcinome à forme polypeuse (sessile ou pédonculé) présentant des modifications précoces de l'épithélium, sans envahissement de la muscularis mucosæ. Il y a lieu de distinguer trois types de polypes: (1) un premier groupe englobe 23 cas de polypes sessiles à surface lisse, dont le diamètre n'excède pas 2 cm.; (2) viennent ensuite 20 cas de polypes sessiles, mais à surface villeuse; (3) le troisième groupe comprend 21 cas de polypes pédiculés, à surface lisse ou villeuse. Quant à leur localisation, elle était très basse, et ils étaient facilement atteignables avec le sigmoïdoscope. Il apparaît que ces tumeurs se développent après l'âge moyen, et sont légèrement plus fréquentes chez l'homme que chez la femme. Parmi les symptômes, on trouve, par ordre de fréquence: le saignement, la douleur, la diarrhée, le prolapsus et enfin l'excrétion de mucus. Divers traitements furent employés: résection locale (excision du polype en une seule pièce, fulguration) dans 43 cas, et ablation radicale dans 25. Les conclusions de cette statistique se résument comme suit: l'étude de ces cas, ré-examinés entre deux et 12 ans après l'intervention, n'a pas permis de trouver de récidive lorsqu'il s'agissait de polypes pédonculés ou de polypes sessiles à surface lisse; il y eut par contre une mort par récidive dans le groupe des polypes papillomateux. Il semble donc que les polypes pédonculés et les polypes à surface lisse soient guérissables par une simple excision locale, tandis que les autres formes, qui représentent peut-être une évolution de la tumeur, sont justiciables d'une chirurgie plus complète (résection antérieure ou segmentaire).

DIAGNOSIS AND MANAGEMENT OF STOMAL ULCER*

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THE study reported in this communication concerns 41 patients with proved stomal ulcer encountered at the University of Alberta Hospital, Edmonton, over the 15-year period, 1945 to 1960. The diagnosis of 40 of these stomal ulcers was confirmed at operation and one post mortem. Duodenal ulcer was the original lesion in all but one patient. Only two of the patients were female.

The original history and the surgical treatment of the primary peptic ulcer were reviewed to determine whether there was any correlation between these factors and subsequent stomal ulceration. In this series, no age group appeared to be particularly vulnerable to recurrent peptic ulceration. The belief that stomal ulcer follows operation more frequently in patients whose original ulcer symptoms began at an early age is not supported by our findings.

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TABLE I.—THE SYMPTOM-FREE INTERVAL FOLLOWING THE PRIMARY PEPTIC ULCER OPERATION IN 39* PATIENTS

Time interval	*No. of patients*
0 - 6 months	13
7 - 12 months	10
13 months—5 years	12
Over 5 years	4

*It was not possible to obtain the record in two of the 41 patients.

SYMPTOM-FREE INTERVAL

The time interval between the primary peptic ulcer operation and the occurrence of stomal ulcer symptoms ranged from a few days following operation to 24 years (Table I). Thirteen of the patients reported symptoms within the first six months. Eight had symptoms within the first postoperative month.

The average symptom-free interval following gastric resection was 10 months, and after gastroenterostomy 36.5 months (Table II). Similar intervals were reported by Priestley and Gibson[11] and Everson and Allen.[3]

TABLE II.—The Average Symptom-Free Interval Following Primary Gastric Resection and Gastroenterostomy

Procedure	*Interval in months*
Gastric resection	10.0
Gastroenterostomy	36.5

Clinical Findings

In this series, the symptoms of stomal ulcers (as obtained from chart records) were almost identical to those of duodenal ulcers (Table III). Pain occurred in 36 out

TABLE III.—Clinical Findings in 41 Patients with Stomal Ulcer

Clinical findings	*No. of patients*
Pain	36
Hemorrhage (massive in 7)	17
Weight loss	8
Obstruction	8
Diarrhea	3
Perforation	3

of the 41 patients. Seventeen patients bled sufficiently to have anemia, hematemesis or melena. Massive hemorrhage was present in seven. Weight loss occurred in eight, and the findings of partial or complete obstruction were present in an additional eight patients. Diarrhea occurred in three. Perforation was present in three patients and was the presenting feature at the time of admission.

The findings included four patients with gastrojejunocolic fistula. On reviewing the symptoms in this group, it was evident that weight loss, diarrhea and fecal vomiting were the striking features (Table IV).

TABLE IV.—Symptoms of Gastrojejunocolic Fistula in Four Patients

Symptoms	*No. of patients*
Pain	3
Weight loss	3
Diarrhea	3
Fecal vomiting	2

Radiological Findings

In 39 of 41 patients, radiological examination was performed before the surgical confirmation of the stomal ulcer (Table V).

TABLE V.—The Results of Radiological Examination of 39 Patients with Proved Stomal Ulcer

Radiological findings	*No. of patients*
Positive for ulcer	28
Suggestive for ulcer	6
Negative	5
Positive diagnosis	72%

The findings were diagnostic in 28 patients (72%). The examination was suggestive of ulcer in an additional six patients. Everson and Allen[4] reported similar findings and indicated that a positive radiological diagnosis of 75% was an optimum figure. The stomal ulcers following subtotal gastrectomy are more readily visualized radiologically than those after gastroenterostomy.

Surgical Treatment of Stomal Ulcer

The surgical treatment of the stomal ulcer is dependent upon the type of primary surgical procedure and the specific presenting complication of the individual patient. In this series (Table VI), stomal

TABLE VI.—The Type of Primary Surgical Procedure which Preceded the Development of Stomal Ulcer in 41 Patients

Primary operation	*No. of patients*
Gastroenterostomy	18
Vagotomy and gastroenterostomy	2
Gastric resection	21
—less than 70%	(8)
—70% or greater	(13)

ulcer followed gastroenterostomy in 18 patients; vagotomy and gastroenterostomy in two patients, and gastric resection in 21 patients. Twenty of the primary resections were Billroth II in type, and one was Billroth I. Thirteen of the resections were 70% or greater in extent, while eight were less than 70%.

The analysis of the surgical treatment in this series is based upon the original procedure for the primary peptic ulcer.

(a) *Stomal Ulcer Developing after Gastroenterostomy*

The treatment (Table VII) of the 18 patients in this group was resection in 12;

TABLE VII.—The Type of Operation in 18 Patients with Stomal Ulcer Following Gastroenterostomy

Type of operation	*No. of patients*
Resection	12
Revision of gastroenterostomy	2
Vagotomy	2
Other	2

revision of gastroenterostomy in two and vagotomy alone in two. Of the remaining two patients, one had an antral exclusion for a large inflammatory mass in the prepyloric region and the other had a closure of a perforation.

(b) *Stomal Ulcer Developing after Vagotomy with Gastroenterostomy*

The two patients in this group were treated (Table VIII) by a 70% subtotal gastrectomy.

TABLE VIII.—The Type of Operation in Two Patients with Stomal Ulcer Following Vagotomy and Gastroenterostomy

Type of operation	*No. of patients*
Resection	2

(c) *Stomal Ulcer Developing after Resection*

TABLE IX.—The Type of Surgical Treatment in 21 Patients with Stomal Ulcer Following Gastric Resection

Type of operation	*No. of patients*
Vagotomy alone	8
Re-resection alone	3
Vagotomy and re-resection	5
Others	5

The treatment (Table IX) of the 21 patients in this group was vagotomy alone in eight; re-resection alone in three; and a combination of both procedures in five. The remaining five patients required special additional procedures which were tailored to correct the presenting perforation or fistula.

Complications of Stomal Ulcer Operation

Of the 40 patients who underwent operation for stomal ulcer, 13 developed complications (Table X). Ten of the complications were of a major nature, and, of these, eight were due directly to the surgical procedure and two were the result of associated disease. Of the complications due directly to the surgical procedure, stomal obstruction occurred in two; anastomotic leakage in two; massive hemorrhage in two, and an intra-abdominal abscess, which was followed by a small bowel obstruction. in one patient. One patient died of peritonitis following perforation of the stomal ulcer before he could be prepared for operation.

TABLE X.—The 10 Major Complications Following Stomal Ulcer Operation

Complications	*Number*
Specific	
Stomal obstruction	2
Anastomotic leak	2
Hemorrhage (massive)	2
Small bowel obstruction	1
Perforation with peritonitis	1
Non-specific	
Pulmonary embolism	1
Arteriosclerotic heart disease and heart block	1

Of the complications not directly attributable to the surgical procedure, one was a non-fatal pulmonary embolus and one consisted of arteriosclerotic heart disease with death occurring from heart failure on the fifth postoperative day. Of the four patients with gastrojejunocolic fistula, all had extensive definitive surgery and only one developed a complication (non-fatal pulmonary embolus).

Recurrences

Four of the 40 patients (10%) developed recurrence of stomal ulceration. The symptoms of recurrence became evident from one to 27 months (average 14 months) after their first stomal ulcer operation. The condition of two of the patients who did have extensive surgery was subsequently brought under control by medical treatment, and the follow-up of one and one and a half years has indicated satisfactory progress. A Hollander test was performed on one patient in this series and free hydrochloric acid was present, indicating an incomplete transthoracic vagotomy. The remaining two patients had further surgical

treatment, consisting of gastric resection (80% and 85%) and vagotomy with good results.

Mortality Following Stomal Ulcer Operation

In this series there were three deaths, a mortality rate of 7.3% (Table XI). The one patient who died as a direct result of surgery developed an anastomotic leak and a subphrenic abscess.

TABLE XI.—The Cause of Death in Three Patients with Stomal Ulcer

Cause of death	
1. Anastomotic leak	
2. Cardiac failure (five days after operation)	
3. Perforation with peritonitis (no operation)	
Overall mortality	7.3%

One patient with arteriosclerotic heart disease with bundle-branch block died on the fifth postoperative day from heart failure. The postmortem findings revealed no intra-abdominal complications.

One patient died of peritonitis following the perforation of a stomal ulcer. An operation was not performed as the patient was moribund on admission and could not be resuscitated before death occurred.

Follow-Up Study

Three patients died in the immediate postoperative period. One patient died of unrelated causes 14 months after operation and one patient is senile. Questionnaires were mailed to the remaining 36 patients and 24 replies were received (Table XII).

TABLE XII.—The Results of the Follow-up Study of 24 Patients Operated upon for Stomal Ulcer

Follow-up	*No. of patients*
Pain-free	18
Strength gain	19
Improved	22
Weight gain	11

The duration of follow-up of the 24 patients who replied ranged from four months to 12 years, with the average follow-up period of four years and 10 months. Eighteen patients were free of pain, and a gain in strength was reported by 19. Twenty-two patients (92%) felt improved. Eleven patients (45%) reported a gain in weight, which averaged 15 lbs. Harvey[7] had similar results on a follow-up study of patients after 75% gastrectomy for duodenal ulcer.

Eight patients (one-third) had symptoms of dumping (Table XIII). The symptoms of dumping were mild in four and moderately severe in four patients. A review of the literature reveals that the incidence of dumping ranges from 25% to 50% among patients who undergo primary peptic ulcer operations, as reported by Armstrong and Penick,[1] MacQueen,[9] Everson *et al.*,[5] and Weir and Bennett.[14]

TABLE XIII.—The Severity of the Dumping Syndrome Present in Eight Patients

Dumping syndrome	*No. of patients*
Mild	4
Moderate	4
Severe	0

A survey of the types of meals eaten revealed that 21 ate regular diets, while the other three ate small dry meals and avoided certain foods (fats). Only one of eight patients with the dumping syndrome followed a satisfactory dietary regimen. It is possible that the degree of postprandial distress in the remaining seven patients could be improved by appropriate dietary methods.

Discussion

All but one of the stomal ulcers occurred following primary surgical treatment of duodenal ulcers. Stomal ulceration is very rare following partial gastrectomy for gastric ulcer.[12]

Incidence

The incidence of stomal ulceration after the surgical treatment of duodenal ulcer cannot be determined accurately in this series as over one-third of the patients underwent primary surgical treatment at other centres. It is generally agreed that the rate of stomal ulceration (Table XIV)

TABLE XIV.—THE INCIDENCE OF STOMAL ULCERATION FOLLOWING VARIOUS SURGICAL PROCEDURES FOR DUODENAL ULCER

Type of operation	*Recurrence %*
Billroth II, 75%	3
Vagotomy and hemigastrectomy	2—3
Vagotomy and drainage procedure	10
Gastroenterostomy	30—40

after a 75% Billroth II gastrectomy is 3%.[12] The recurrence rate is much higher following a Billroth I procedure of the same magnitude.[6, 13] After vagotomy and hemigastrectomy, the ulcer recurrence rate is in the vicinity of 2% to 3%.[7] The stomal ulcer incidence following vagotomy and a drainage procedure is approximately 10%.[2] Recurrent ulceration following gastroenterostomy is from 30% to 40% if the patients are followed up for sufficiently long periods of time (20 years).[12]

Treatment

Approximately one-half of the stomal ulcers in this series followed a gastric resection for duodenal ulcer. The majority of the gastrectomies were 70% or more. This study emphasizes that an extensive resection does not necessarily preclude stomal ulceration. Sixteen out of 21 patients who developed stomal ulcers after gastrectomy had a subsequent vagotomy (Fig. 1). Of the two patients who developed recurrent ulceration after gastrectomy and vagotomy for an original stomal ulcer, the vagotomy in one patient is known to be incomplete, as indicated by a positive Hollander test.

This study supports the view that vagotomy is the procedure of choice in the treatment of stomal ulcers which follow adequate gastric resection. Patients with the added complications of obstruction, perforation, gastrojejunocolic fistula and massive hemorrhage require excision of the ulcer in addition to vagotomy. Transthoracic vagotomy is indicated where great technical difficulty is anticipated in the transabdominal approach, and was employed in two patients. A re-resection is generally necessary if the original operation has been inadequate (less than 50%).

Twenty of the 41 patients with stomal ulcer had a gastroenterostomy and two of these had an associated vagotomy. The majority of the patients had a subsequent gastric resection of 70% or more with good results (Fig. 2). A review of the patients who had procedures other than gastric resection revealed that the majority required further and more extensive surgery to correct the stomal ulceration and its complications. This statement also applies to the older patients in this series. Therefore, gastric resection with vagotomy is the procedure of choice for stomal ulcer following gastroenterostomy.

Intensive medical treatment for two or three weeks preoperatively is important in reducing the technical difficulties and the postoperative morbidity. However, the conservative management of stomal ulcers after inadequate surgery fails in the majority of patients.

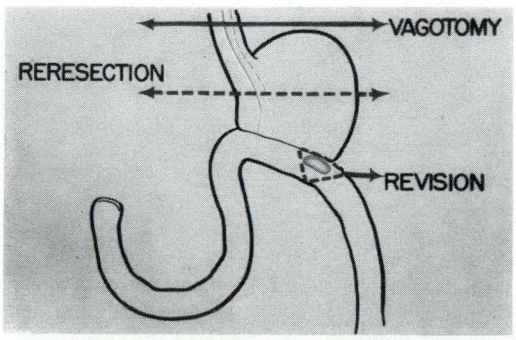

Fig. 1.—The treatment of stomal ulcer after gastric resection. Vagotomy is the procedure of choice. Re-resection and revision are performed only when required.

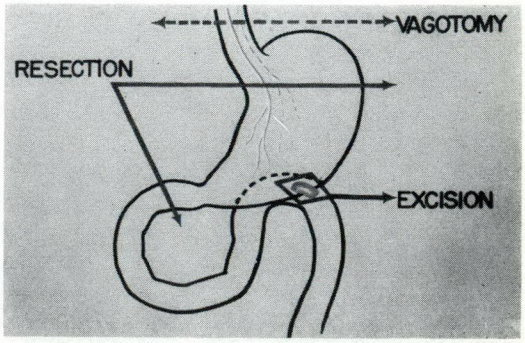

Fig. 2.—The treatment of stomal ulcer after gastroenterostomy. The procedures of choice are resection and excision of the ulcer. Vagotomy may be utilized as an additional procedure.

An operative procedure for stomal ulcer requires a thorough exploration of the abdomen to ascertain the cause (Table XV), which includes an incomplete vagotomy, inadequate gastric resection, retained pyloric antrum, ulcerogenic tumours of pancreatic islet cell origin within the pancreas or in aberrant locations, long afferent loop with stasis, or a faulty anastomosis.

TABLE XV.—The Various Causes of Stomal Ulceration

Etiology of stomal ulcer
1. Incomplete vagotomy
2. Inadequate resection
3. Retained pyloric antrum
4. Ulcerogenic tumours
5. Long afferent loop
6. Faulty anastomosis

Stomal Ulcer Recurrence

The recurrence rate of surgically treated stomal ulceration is high, 10% in this series. Therefore, an aggressive surgical approach is necessary to control the severity of the ulcer diathesis in the recurrent cases. The four patients who had such a recurrence were treated by combined gastrectomy and vagotomy to control stomal ulceration.

We have previously reported one case of intractable peptic ulceration which resulted in the death of a 32-year-old patient who possessed several islet cell tumours within the pancreas.[8] This case is not included in this study. These ulcerogenic tumours may occur within the wall of the duodenum.[10] Occasionally, clinically enlarged lymph nodes with metastatic involvement may be the only abnormal findings suggestive of islet cell tumour.

Summary

Stomal ulceration occurs predominantly in male patients after operations performed for duodenal ulcer. Vagotomy is the procedure of choice for stomal ulcer occurring after subtotal gastrectomy, provided that the presence of a residual antrum and pancreatic tumours has been excluded. Gastric resection with vagotomy is the procedure of choice for stomal ulcer occurring after gastroenterostomy. Whenever possible, gastrojejunocolic fistula is treated in one stage by vagotomy and definitive management of the fistula. The recurrence of surgically treated stomal ulcers is high. Therefore, the treatment should be aggressive and radical.

References

1. Armstrong, R. A. and Penick, R. M.: Surgical treatment of benign peptic ulcer; analysis of 462 cases, *Ann. Surg.*, **152:** 109, 1960.
2. Dragstedt, L. R., II: Vagotomy and gastroenterostomy or pyloroplasty; present technique, *Surg. Clin. N. Amer.*, **41:** 23, 1961
3. Everson, T. C. and Allen, M. J.: Gastrojejunal ulceration, *A.M.A. Arch. Surg.*, **69:** 140, 1954.
4. Everson, T. C. and Allen, M. J.: Recurrent or persistent peptic ulceration following secondary operations for peptic ulcer; analysis of 11 cases, *Amer. Surg.*, **21:** 130, 1955.
5. Everson, T. C. *et al.*: Partial gastrectomy versus vagotomy with gastroenterostomy in treatment of duodenal ulcer, *A.M.A. Arch. Surg.*, **74:** 547, 1957.
6. Goligher, J. C., Moir, P. J. and Wrigley, J. H.: The Billroth-I and Polya operations for duodenal ulcer: a comparison, *Lancet*, **1:** 220, 1956.
7. Harvey, H. D.: Twenty-four years of experience with elective gastric resection for duodenal ulcer, *Surg. Gynec. Obstet.*, **112:** 203, 1961.
8. MacKenzie, W. C. *et al.*: Islet cell tumours and peptic ulcers. A report of two cases of Zollinger-Ellison syndrome, *Canad. J. Surg.*, **2:** 6, 1958.
9. MacQueen, D. G.: The Belcher gastrectomy for peptic ulcer, *Canad. Med. Ass. J.*, **72:** 666, 1955.
10. Oberhelman, H. A., Jr. *et al.*: Ulcerogenic tumors of the duodenum, *Ann. Surg.*, **153:** 214, 1961.
11. Priestley, J. T. and Gibson, R. H.: Gastrojejunal ulcer; clinical features and late results, *Arch. Surg.*, **56:** 625, 1948.
12. Tanner, N. C.: Surgical aspects of gastric and duodenal ulceration (excluding complications), *Postgrad. Med. J.*, **30:** 124, 1954.
13. Walters, W. and Lynn, T. E.: The Billroth I and Billroth II operations: comparison of results six to ten years after operation for gastric, duodenal and gastrojejunal ulcers, *A.M.A. Arch. Surg.*, **74:** 680, 1957.
14. Weir, J. F. and Bennett, H. S.: Peptic ulcer: a follow-up study after partial gastrectomy, *Proc. Mayo Clin.*, **31:** 632, 1956.

Résumé

Ceci est une étude statistique portant sur 41 malades traités à l'Hôpital de l'Université de l'Alberta, atteints d'ulcère pylorique. Le diagnostic fut confirmé dans tous les cas à l'intervention. La lésion originelle était dans tous les cas, sauf un, un ulcère duodénal. Il n'y avait que deux femmes dans ce groupe. Les auteurs ont essayé de déterminer quelles étaient les relations possibles entre le traitement d'un ulcère primaire et l'apparition

ultérieure d'un ulcère pylorique. L'intervalle de temps entre ces deux évènements variait de quelques jours à 24 ans. Le diagnostic correct put être fait radiologiquement dans 72% des cas. Les interventions précédant l'apparition de l'ulcère pylorique furent: la gastro-entérostomie dans 18 cas, la vagotomie associée à la gastro-entérostomie dans deux cas, et la résection gastrique dans 21. Les symptômes varient, et sont par ordre de fréquence: la douleur, l'hémorragie (massive dans sept cas, la perte de poids, les troubles du transit, la diarrhée, et enfin la perforation. Dans les cas secondaires à une résection gastrique, le type de technique employée est important: l'apparition de l'ulcère pylorique est plus fréquente après une résection type Billroth I qu'après un Billroth II. Dans l'ensemble, il ressort de cette étude que la vagotomie est le traitement de choix de l'affection. Cette vagotomie doit être associée à une résection correcte; au besoin il faudra à nouveau réséquer, si l'intervention première était insuffisante. Les fistules gastro-jéjuno-coliques, s'il en existe, devront être traitées dans le même temps. Comme c'est fréquemment le cas dans ces réinterventions, les manœuvres intra-abdominales peuvent être difficiles et si besoin est, il ne faudra pas hésiter à faire la vagotomie par voie thoracique. Dans les cas de cette série, on rencontre un tiers de malades qui souffrirent de symptômes de "dumping". Il y eut trois décès dûs à une anastomose non étanche, une insuffisance cardiaque et une perforation.

PAPILLARY ADENOMAS OF THE COLON AND RECTUM: CLINICAL AND PATHOLOGICAL BEHAVIOUR*

A Plea for More Conservative Treatment

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THERE IS considerable controversy concerning the entity, papillary adenomas (villous papillomas) of the large intestine. Quain[20] reported the first successful surgical removal of a villous tumour from the rectum in 1855, and believed that such tumours were not cancerous. In 1861, Holmes[18] reported two villous tumours. In 1899 Quénu and Landel[21] published the first comprehensive study of villous tumours with four case reports and pointed out the difference in structure between the villous tumours and adenomas. Until 1934[3] less than 100 cases had been reported in the literature.

On the other hand, reports had been presented[7, 16, 26] emphasizing the close relationship between papillary tumours and adenomas (adenomatous polyps), and suggesting that these were variations in growth, to which all adenomas might be subject. Helwig[17] concluded that all adenomas have a basic resemblance and attached no particular significance to minor variations in structure and cells. The rarity of these lesions, the diversity of observations and opinions, the small size of published series and the meagre experience of any single surgeon or pathologist of this lesion, have all combined to make difficult the evaluation of the biological nature and clinical behaviour of these tumours.

Papillary adenomas of the large intestine are not the same entity as adenomatous polyps. There is a fundamental difference in structure between papillary tumours and adenomas of the large intestine. The normal structure of the epithelium of the mucosa can be divided into two parts: the surface epithelium and the underlying mucus-secreting glands. Though both portions have a similar embryological origin, differences may be noted between the cells of the surface epithelium and cells of the underlying glands. The former tend to be narrower and elongated, as if compressed, and the nucleus tends to occupy the mid-portion of the cell and, less frequently, the base. There is an increased intensity of nuclear staining. On the other hand, in the underlying mucus-secreting glands, the lining is made up almost en-

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tirely of plump mucus-secreting goblet cells, with a small nucleus at the base of each cell.

In 1947, Dukes[10] advanced the explanation that adenomas arise by the proliferation of cells of the underlying mucus-secreting glands in the depths of the mucous membrane. A small nodule of new growth, embedded in the submucosa, results. As growth continues towards the surface, in the direction of least resistance, it elevates the mucosa. With the help of peristalsis, a tumour with an elongated narrow stalk, covered with normal epithelium, is finally produced. On the other hand, Dukes believes that the villous tumour begins with the proliferation of the cells of the surface epithelium (resulting in finger-like projections, having narrow stroma with elongated blood vessels). A striking change from the normal mucosal pattern begins sharply at the edge of the tumour, which, as observed by Quénu and Landel,[21] is the most active site of proliferation. The adenoma is essentially an intramucosal growth with central growth activity.

Clinical Material

Seventy-six cases were collected from the records of patients seen at the Winnipeg General Hospital and the St. Boniface General Hospital between 1944 and 1961. The *tumeurs compeuses* of Bensaude, Cain and Lambling,[1] with malignant change, are not included because carcinoma from the adenomatous element has a different nature and course than carcinoma developing from the papillary element. Excluded also were the cases in which the macroscopic diagnosis was papillary adenoma while microscopically the tumour showed villous and adenomatous characteristics. Patients started on treatment during the year 1962 are also excluded, thus allowing a minimum of one year's observation. None of the lesions was an electrolyte-secreting tumour.

Of the 76 patients, 44 were male (58%) and 32 female (42%). This gives about the same male-female ratio reported in the larger series (Table I). The average age at the time of first treatment was 60.7 years, ranging from five to 91 years. There were three cases in the first decade of life.

TABLE I.—Male-Female Ratio

Males	44 (58%)
Females	32 (42%)
Total	76 (100%)

Case Reports

Case 1.—This 6-year-old-girl, treated in 1957, had two episodes of minor rectal bleeding during the year before operation. During the months before operation she had five episodes of massive hemorrhage. Barium enema and air-contrast studies demonstrated a tumour in the sigmoid colon which was removed by resection of the bowel segment. Pathological examination revealed a benign papillary adenoma, 1.0 x 0.3 x 0.7 cm. in size, with a wide and slightly elongated base. The child has been free of disease since operation.

Case 2.—This 6-year-old boy was treated in 1957 after rectal bleeding of one year's duration. Barium enema revealed a polypoid lesion, 2.5 x 1.5 x 1.2 cm. in size, in the lower sigmoid colon. It was removed by loop resection through the sigmoidoscope, and the pathologist described it as a benign papillary adenoma. He has been well since.

Case 3.—This 6-year-old boy had four episodes of alarming rectal bleeding within three days, associated with colicky pain and anorexia. Rectal digital examination revealed a lesion 0.3 cm. in diameter. This was removed by local excision and reported to be a benign papillary adenoma. There has been no recurrence to date.

Age Incidence

None of the 76 patients was in the second or third decade. There was then a sharp rise to the eighth decade. Twenty-four per cent were between 70 and 79 years of age. This is higher than reported in other series (Fig. 1).

Distribution

Sixty-nine per cent of the 76 lesions occurred in the rectum, 25% in the recto-sigmoid and sigmoid colon and 6% in the rest of the colon. Ninety-four per cent were within reach of the sigmoidoscope (Table II).

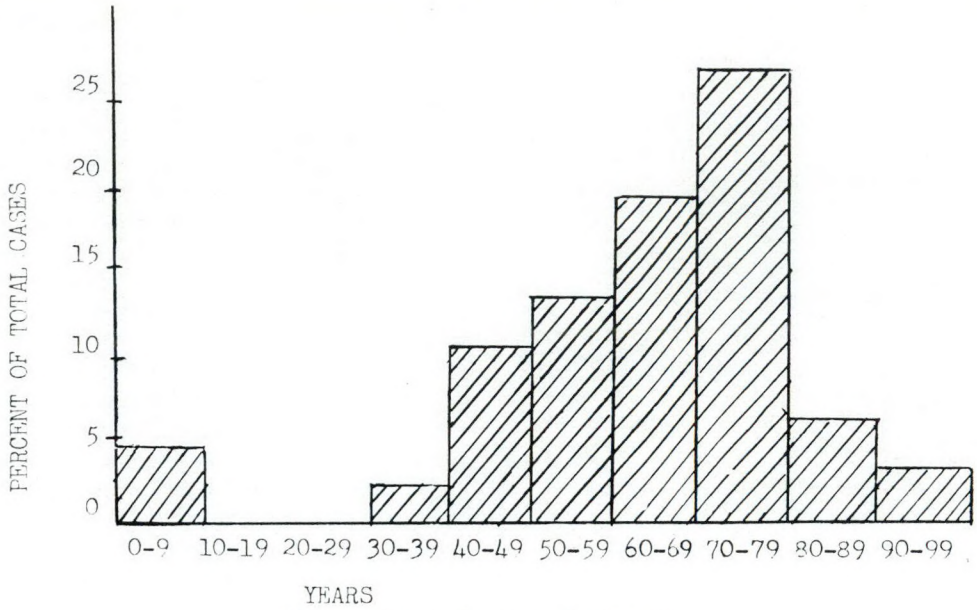

Fig. 1.—Age at the time of operation.

TABLE II.—Distribution of Lesions in Large Bowel

Site of lesions	*No. of patients*
Cecum	1
Ascending colon	3
Transverse colon	1
Sigmoid	15
Rectosigmoid	4
Rectum	52
Total	76

TABLE III.—Presenting Symptoms

Symptoms	*No. of patients*
Bleeding	36
Diarrhea and/or mucous discharge	8
Pain—colic	8
Protrusion of polyp	3
Anemia, weakness and weight loss	3
Incidental discovery	18
Total	76

Presenting Symptoms

Nearly one-half of the patients presented with rectal bleeding, ranging from a few days to 10 years before operation. In 24% of cases, the tumour was discovered incidentally on routine examination and/or on investigation for other disease. Diarrhea and/or mucous discharge was the presenting symptom in eight cases, but many patients presenting with other symptoms also had diarrhea and mucous discharge. Protrusion of a large papillomatous mass was the presenting symptom in three patients in the oldest age group (Table III).

Histopathology

Multiple biopsies and sections were carried out as indicated in each individual tumour. The degree of anaplasia was determined by the criteria of Broders and classified into the following categories: benign, atypical, carcinoma *in situ*, carcinoma Grade I-IV. To determine invasiveness, each specimen was dissected and investigated histologically by Dukes' method into groups A, B, and C. Not a single case in this series had metastasis of papillary adenocarcinoma to lymph node or liver (Table IV).

TABLE IV.—Histopathology (Broders' Classification)

Classification	*No. of patients*	*%*
Benign	36	47
Atypical	4	5
Carcinoma *in situ*	6	8
Grade I	13	17
Grade II	15	20
Grade III	2	3
Total	76	100

TREATMENT

Local excision and/or cautery were carried out in 45 patients with benign and low-grade malignant papillary adenomas where the site and size of the lesion allowed this procedure, either through the sigmoidoscope or by direct exposure (Table V).

TABLE V.—TYPE OF OPERATION

Operations	*No. of patients*
Local excision and/or cautery	45
Segmental resection	14
Right hemicolectomy	3
Anterior resection	3
Abdominoperineal resection	7
Total colectomy with ileostomy	1
Not treated	3
Total	76

Simple segmental or sleeve resection was performed upon 14 patients in whom local excision was not feasible or in whom a more radical operation was not deemed necessary.

Radical procedure with *en bloc* removal of regional lymph nodes was performed upon 15 patients.

Three patients had right hemicolectomy for lesions in the ascending colon. Two of them had Grade II papillary adenocarcinoma and one had Grade III. None of them had metastases to regional lymph nodes or to liver. None of these lesions penetrated through the bowel wall into the pericolic fat. Two patients had no recurrences. The patient with the Grade III lesion developed a palpable mass at the site of the previous tumour two years later. This mass, which when resected measured 8 cm. in diameter, had recurred at the site of the previous anastomosis. The tumour was similar in histological structure and grade of malignancy to the papillary adenocarcinoma removed two years earlier. Again there were no metastases to the liver or regional nodes. It is suggested that since the tumour was resected with more than adequate margins of safety, the recurrence was due to implantation of tumour cells or of fragmented tumour tissue at the suture line. The patient is well now, six years after operation.

Three patients had anterior resections for Grade II papillary adenocarcinoma of the sigmoid colon and upper part of the rectum. None of them had metastases to the liver or lymph nodes, and the lesions were classified as Dukes B. Two patients had local recurrences, one of them dying two years later of unknown cause, the tumour still present. The third was a 51-year-old man who came to hospital with signs of large bowel obstruction and a mass in the left lower quadrant. At laparotomy a large tumour was palpated in the sigmoid colon, surrounded by abundant granulation tissue, anchoring the lesion to the bladder. Resection was deemed impossible, right transverse colostomy was performed and radiotherapy was given. Three months later no mass was palpable and laparotomy was carried out. The granulation tissue had disappeared and no metastases were seen in lymph nodes or liver. The tumour was removed by anterior resection and the colostomy was left open to relieve the suture line. The patient recovered, put on weight and went back to work. He returned 15 months later, in excellent health, for closure of the colostomy. Soon after colostomy closure two small tumours were found in the rectus muscle and were biopsied. The pathologist reported papillary adenocarcinoma of the same grade and structure as the tumour removed by anterior resection two years previously. A barium enema revealed a stenosing lesion at the site of the previous resection. This was biopsied through a sigmoidoscope and a tumour of similar structure and grade was identified on microscopical examination. At laparotomy many implantations in the peritoneal cavity showed the same grade and structure as the original tumour.

Seven patients had abdominoperineal resection.

CASE 1.—A 45-year-old man had intermittent rectal bleeding for a year. Proctoscopy revealed a large papillary adenoma on the posterior wall of the rectum, containing a focus of Grade I papillary adenocarcinoma. The tumour was removed by abdominoperineal resection and was classified Grade I, Dukes A. He died five years later of small bowel obstruction. Autopsy revealed no recurrence.

CASE 2.—A 58-year-old woman had a mucous and watery discharge per rectum for one year. A papillary lesion in the rectum was biopsied and showed Grade I malignant change. The tumour was removed by abdominoperineal resection and was classified as Grade I, Dukes A. The patient is alive and well with no recurrence six years later.

CASE 3.—A 78-year-old man had a benign papillary adenoma removed in 1952. Four years later he had a recurrence and biopsy showed malignant change. An abdominoperineal resection was performed and the specimen revealed Grade II, Dukes A papillary adenocarcinoma. The patient is alive and well six years later.

CASE 4.—A 42-year-old woman was investigated for rectal bleeding and a large papillary tumour was found in the rectum. Biopsy showed evidence of Grade II malignant change. The tumour penetrated into the muscular layer. Regional lymph nodes were clear of tumour. The lesion was classified as Dukes B.

CASE 5.—A 71-year-old man underwent biopsy of a large papillary rectal tumour which revealed Grade II malignancy. The tumour penetrated into the subserosal fat but not into the perirectal fat. The lymph nodes were clear and he is alive without recurrence after five years.

CASE 6.—A 67-year-old man had Grade II, Dukes A papillary adenocarcinoma in a specimen from an abdominoperineal resection. He died seven years later of coronary thrombosis with no evidence of recurrent tumour.

CASE 7.—A 75-year-old woman had rectal bleeding for four years. She had a large papillary tumour in the upper portion of the rectum. A local excision was performed in 1953 and a Grade I papillary adenocarcinoma, confined to the mucosa, was reported. A year later she developed a severe stricture and a colostomy was carried out. Recurrent tumour appeared in 1957, necessitating an abdominoperineal resection. The tumour was classified Grade I, Dukes A. The patient is alive and well with no evidence of recurrence.

One patient had a total colectomy for three carcinomatous lesions, associated with ulcerative colitis of 14 years' duration. She was 32 years of age. The pathologist reported these lesions as follows: adenocarcinoma of the rectum confined to that structure; stenosing adenocarcinoma of the sigmoid colon with metastases to mesosigmoid lymph nodes; papillary adenocarcinoma of the transverse colon, with no penetration into pericolonic fat and no metastases in its regional lymph nodes. Classification was Grade II, Dukes B. The last-mentioned lesion was surrounded by a large friable mass of granulation tissue, anchoring it to the uterus. This was stripped off and the whole colon resected, the patient being left with an ileostomy.

There was a striking similarity between this case and one presented above in the anterior resection series. These two cases may represent an interesting phenomenon. The papillary adenocarcinoma has only a slight tendency to penetrate into extracolonic tissues. When, in rare instances, it prepares to break through the confines of the harbouring organ, it elicits a response similar to that seen in a foreign-body reaction. It may be that this is a defence mechanism invoked by the body when the lesion threatens to break out of its original confines.

CURE RATE

Benign Lesions

Of 40 patients, 27 were alive with no recurrence after one to 18 years. One patient died of coronary occlusion 10 days after operation. Three died of other causes, without recurrence, during the years following operation. Two refused treatment; one was lost to follow-up; the other, who was seen with a large papillary adenoma in 1951, died in the late 1950's. Six patients had 14 benign recurrences, mostly following fulguration, in 0-3 years and were subsequently cured and are alive and free of recurrence. One patient had malignant change in a recurrence and was cured by adequate excision (Table VI).

Malignant Lesions

Of 36 patients who had papillary adenocarcinoma of the colon and rectum, 20 patients are alive with no evidence of recurrence. Five had recurrence in one to three

TABLE VI.—Cure Rate

Benign lesions	*No. of patients*
No recurrence	27
Recurrence within:	
1 year	4
1 - 3 years	2
3 - 5 years	0
Recurred with malignant change	1
Died during postoperative period of coronary occlusion	1
Died of other causes, without recurrence	3
Not treated	2
Total	40

Malignant lesions	*No. of patients*
Free of disease in:	
0 - 3 years	6
3 - 5 years	3
After 5 years	11
Recurrence within:	
1 year	2
1 - 3 years	4
3 - 5 years	0
Died of disease	0
Died of other causes:	
myocardial degeneration 3 yrs. postoperatively, no recurrence	1
asphyxia 6 yrs. postoperatively, no recurrence	1
bowel obstruction 5 yrs. postoperatively, no recurrence	1
adenocarcinoma of sigmoid and rectum with recurrence	1
acute suppurative nephritis 67 days postoperatively, no recurrence	1
hemorrhage, 27 days postoperatively, no recurrence	1
unknown cause, no sign of recurrence	1
septicemia, 17 days postoperatively, no recurrence	1
	8
Died during postoperative period, diffuse enteritis and septicemia	1
Not treated—patient refused treatment	1
Total	36

years, subsequently eradicated. One patient had recurrence with implantation at site of resection, at multiple sites in the peritoneal cavity and in the lower half of the right rectus muscle. This patient is alive and well, with very few ill effects related to his tumours. One patient died of septicemia 10 days after operation. One patient refused treatment and was lost to follow-up. Eight patients died of other causes, seven of them without evidence of recurrence and one with recurrence. No death was directly attributable to papillary adenocarcinoma of the colon or rectum, and none had liver or lymph node metastases. Two deaths in the postoperative period give a mortality of 2.6% for the whole series. Other gastrointestinal pathology found associated with villous adenomas of the colon and rectum is shown in Table VII.

TABLE VII.—Villous Adenomas Associated with Other Gastrointestinal Pathology

Associated conditions	*No. of patients*
Adenocarcinoma	9
Benign adenomatous polyps	3
Ulcerative colitis	2
Diverticulitis	2
Multiple polyposis, stomach, small and large bowel	1
Hemorrhoids	1
Melanosis coli	1
Postoperative stricture	1
Total	20

Discussion

This study led to the conclusion, contrary to reports in the literature, that papillary adenocarcinoma owing to its biological nature is relatively benign, in spite of its histological anaplasia. It does not have a tendency to invade venous and lymphatic routes and neighbouring organs, as do carcinomas arising from adenomas. In the 14 patients who underwent segmental resection for papillary adenocarcinoma and in the 14 who had *en bloc* radical resection of tumour and regional nodes, not a single case had venous or lymphatic metastases. In each case the specimen was subjected to meticulous investigation by the pathologist. According to various reports,[5, 6] one-half to two-thirds of bowel carcinomas arising from adenomas had lymphatic or liver metastases at the time of the intended curative resection. If carcinomas arising in papillary adenomas were essentially the same, lymphatic metastases should have been found in approximately 12 to 18 in our series. This, however, was not the case.

We believe, therefore, that radical *en bloc* resection is indicated only in very rare instances. Abdominoperineal resection may be indicated where the papillary adenoma cannot be eradicated by a more conserva-

tive method, because of the size and location, but not necessarily because of histological malignancy.

We believe that cautery and/or loop resection should not be used in the treatment of these lesions. Adequate excision should be carried out with a scalpel and with safe margins (at least 1 cm. beyond the edge of the tumour in the rectum). Care should be taken not to squeeze and fragment the tumour, thereby increasing the chance of implantation at the site of resection[5] or into the abdominal wall[2] or cavity. Adequate excision with safe margins means at least 1 cm. from macroscopic edge of the lesion in the rectum and the usual segmental resection for lesions in the rest of the colon, with a few centimetres' margin.[5]

The majority of the seven patients who underwent abdominoperineal resection could have been treated more conservatively with preservation of the sphincter. Since these lesions in the rectum are often in old people with advanced degenerative cardiovascular and/or respiratory diseases, the risk of abdominoperineal resection is often greater than the risk of dying from spread of the papillary tumour. Most of these tumours (benign or with malignant change) in the lower half of the rectum can be removed adequately by the method used by one of the authors (C.W.C.). Under general or spinal anesthesia, the patient is placed in the lithotomy position. Retractors are placed in the anus; Duval's lung forceps are introduced, guided by the index finger. The tumour is grasped and delivered through the anus. This intussuscepts the wall of the rectum containing the tumour. Depending on the extent of the base of the tumour, one or more Kelly's forceps are applied to the folded rectal wall, 1 cm. or more beyond the edge of the lesion. The tumour is then cut off along the distal edge of the Kelly's forceps and an intestinal chromic cat-gut suture is run to oversew the forceps. The forceps are then removed, and the suture is tightened and tied. A second layer of suture may be run back if necessary. Applying Kelly's forceps beyond the base of the tumour, the suturing is continued until the whole tumour is encompassed. With this method one can obtain safe margins laterally and also deep to the tumour. One of the authors (C.W.C.) has removed 12 lesions of various sizes by this method with no recurrence.

Summary and Conclusions

Papillary adenomas of the large intestine are an entity distinct from adenomatous polyps because of their origin from different types of cells of the bowel mucosa and their different way of growth. The growth of papillary adenomas is extramucosal (adenomatous polyps are intramucosal) and they are covered with essentially normal bowel mucosa. Papillary adenomas have a great tendency to recur locally and elsewhere by implantation. In spite of the histological anaplasia of the papillary adenocarcinoma, their biological behaviour is relatively benign. They do not tend to cause venous and lymphatic metastases, and they do not tend to penetrate through the bowel wall. Radical resection, widely employed currently in the treatment of papillary adenocarcinomas, is rarely indicated. Conservative adequate excision with safe margins, with care being taken to prevent implantation, is recommended. Papillary adenomas in the lower half of the rectum can be treated adequately by eversion through the anus and excision.

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References

1. Bensaude, R., Cain, A. and Lambling, A.: Les tumeurs villeuses du rectum, *Presse méd.*, **38:** 1713, 1930.
2. Binkley, G. E. and Sunderland, D. A.: Diagnosis and treatment of papillary adenomas of the rectum, *Amer. J. Surg.*, **75:** 365, 1948.
3. Bowman, F. B.: Villous papilloma of the rectum, *Canad. Med. Ass. J.*, **31:** 488, 1934.
4. Castleman, B. and Krickstein, H. I.: Do adenomatous polyps of the colon become malignant? *New Eng. J. Med.*, **367:** 469, 1962.
5. Cole, W. H., Economou, S. and Hunter, J.: Carcinoma of the colon, *Surg. Clin. N. Amer.*, **42:** 519, 1962.

6. Coller, F. A., Ransom, H. K. and Regan, W. J.: Cancer of the colon and rectum, American Cancer Society, New York, 1956.
7. David, V. C.: Papillomata of the large bowel, *Ann. Surg.*, **82:** 109, 1925.
8. Denoix, D. F.: Conclusion de la diversité de certain cancer, Monographie de l'Institut National d'Hygiène, Ministère de la Santé Publique, Paris, 1954, pp. 153-158.
9. Dukes, C. E.: Surgical pathology of rectal cancer; president's address, *Proc. Roy. Soc. Med.*, **37:** 131, 1944.
10. Dukes, C. E.: An explanation of the difference between a papilloma and an adenoma of the rectum, *Proc. Roy. Soc. Med.*, **40:** 829, 1947.
11. Engell, H. C.: Cancer cells in the blood; a five to nine year follow-up study, *Ann. Surg.*, **149:** 457, 1959.
12. Fisher, B. and Fisher, E. R.: Host factors influencing the development of metastases, *Surg. Clin. N. Amer.*, **42:** 335, 1962.
13. Grinnell, R. S.: The spread of carcinoma of the colon and rectum, *Cancer*, **3:** 641, 1950.
14. Grinnell, R. S.: Results in treatment of carcinoma of the colon and rectum; analysis of 2341 cases over 35 year period with five year survival; results in 1667 patients, *Surg. Gynec. Obstet.*, **96:** 31, 1953.
15. Hardy, J. D.: On the cause of death in cancer: systemic effects of nonendocrine tumors, *Surg. Cl n. N. Amer.*, **42:** 305, 1962.
16. Harp, R. A., Waugh, J. M. and Dockerty, M. B.: Non infiltrating villous colonic tumors: partial review of literature and report of 63 cases, *Dis. Colon Rectum*, **5:** 121, 1962.
17. Helwig, E. B.: The evolution of adenomas of the large intestine and their relation to carcinoma, *Surg. Gynec. Obstet.*, **84:** 36, 1947.
18. Holmes, T.: Villous tumours of the rectum, *Trans. Path. Soc. Lond.*, **12:** 120, 1861.
19. Mackie, J. A., Jr., Miller, L. D. and Fitts, W. T., Jr.: Polyps and polypoid lesions of the large bowel; surgical considerations, *Surg. Clin. N. Amer.*, **42:** 1451, 1962.
20. Quain, R.: Diseases of the rectum, 2nd ed.. Walton and Moberly, London, 1855, p. 295.
21. Quénu, E. and Landel, G.: Des tumeurs villeuses ou épithéliomes superficiel végétants du rectum, *Rev. Gynéc.*, **3:** 95, 1899.
22. Southwick, H. W., Harridge, W. H. and Cole, W. H.: Recurrence at the suture line following resection for carcinoma of the colon; incidence following preventive measures, *Amer. J. Surg.*, **103:** 86, 1962.
23. Sunderland, D. A. and Binkley, G. E.: Papillary adenomas of the large intestine; a clinical and morphological study of 48 cases, *Cancer*, **1:** 184, 1948.
24. Swinton, N. W. and Warren, S.: Polyps of the colon and rectum and their relation to malignancy, *J. A. M. A.*, **113:** 1927, 1939.
25. Welch, J. S. and Dockerty, M. B.: Villous carcinoma of the colon, *Dis. Colon Rectum*, **1:** 251, 1958.
26. Wheat, M. W., Jr. and Ackerman, L. V.: Villous adenomas of the large intestine. Clinicopathological evaluation of 50 cases of villous adenomas with emphasis on treatment, *Ann. Surg.*, **147:** 476, 1958.

Résumé

La relation entre les tumeurs adénomateuses de l'intestin et leur malignité est toujours discutée. Histologiquement, il y a une grande différence de structure entre les papillomes et les cancers ou les adénomes. En fait, il y a lieu, à ce point de vue, de faire une distinction entre la couche superficielle et la couche profonde de l'épithélium intestinal. Il a été soutenu que les adénomes naissaient de la prolifération des cellules de la couche profonde, c'est-à-dire des glandes sécrétrices de mucus. Les auteurs procèdent à une étude statistique de 76 cas de ce genre, tirés des archives de deux hôpitaux du Manitoba. Sur ce nombre, il y avait 44 hommes (58%) et 32 femmes (42%); l'âge moyen, au début du traitement, était de 60.7 ans, comprenant des cas entre cinq et 91 ans. Trois malades appartenaient à un groupe de 10 ans ou moins, et leurs histoires sont résumées ici. Il n'y a aucun cas dans les deuxième et troisième décades de la vie, mais par contre, on observe une augmentation considérable de l'incidence autour de 80 ans. Les lésions siègeaient dans le rectum (69%), dans le recto-sigmoïde (25%), ou dans le côlon (6%). Les symptômes le plus fréquents étaient: le saignement rectal, la diarrhée, parfois l'expulsion de glaires muqueuses. Le traitement fut divers: excision locale ou cautérisation, résection segmentaire, résection large. Les resultats éloignés peuvent être résumés comme suit: sur 40 lésions bénignes, on trouva six récidives; dans les lésions histologiquement malignes (36 malades), 20 ne présentèrent aucune récidive. Cette étude permet donc de conclure que, contrairement à ce qui a été rapporté dans la littérature, l'adénocarcinome papillaire du gros intestin est relativement bénin. Il n'a que peu ou pas de tendance à envahir les canaux lymphatiques ou veineux: ceci est bien montré par l'étude des pièces opératoires de 14 malades qui subirent des résections extensives "en bloc", où l'on ne trouva aucune métastatisation.

ELECTIVE USE OF TWO INCISIONS IN MEDIAL MENISCECTOMY

Results of 50 Two-Incision Procedures Compared with 50 Single-Incision Meniscectomies*

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THE DEVELOPMENT of a therapeutic technique depends largely upon the success enjoyed by the main proponents of it. This is particularly true of surgical procedures which lend themselves to many modifications designed to suit the skill and experience of the individual surgeon. Frequently, a different approach is not adopted because basic principles may appear to be at stake. This seems to be the case when the innovation requires that two incisions be used in place of one; the rejection is based on the assumption that two wounds would carry a greater morbidity.

This assumption of increased morbidity has dominated the practice of medial meniscectomy. In most centres, this procedure is carried out through the standard anteromedial approach and the partially dissected meniscus is displaced into the intercondylar fossa before the excision of the posterior horn. The use of the second, posteromedial incision, has been advocated for cases in which difficulties are encountered in the final stages.[1] Undoubtedly, the single-incision approach may be preferable for proficient, experienced orthopedic surgeons and may be time-saving for them.

The second incision brings with it the very real benefit of clear visualization of the posterior portion of the meniscus and makes complete posterior-horn removal certain.[2] A retained portion of the posterior horn is a significant factor in the continuation of the patient's symptoms and frequently makes a second arthrotomy necessary.

For this reason the elective use of the second incision can be recommended for surgeons in training and for any surgeon who performs meniscectomies infrequently. A review of the literature for the last 10 years did not produce evidence of increased morbidity in the two-incision procedure. On the surgical service of the Canadian Forces Hospital in Kingston, Ontario, the elective posteromedial incision has been used for six years under the direction of the senior author (A.C.D.) with very satisfying results.

The initial stages of the double-incision meniscectomy are identical with the standard approach. The first incision is made slightly oblique along the longitudinal axis with the distal end pointing gently laterally. It is therefore an anteromedial parapatellar incision (carried out with the knee flexed to 90°) located about one finger's breadth off the medial border of the patella and reaching about 2½″ above the joint line (Fig. 1).

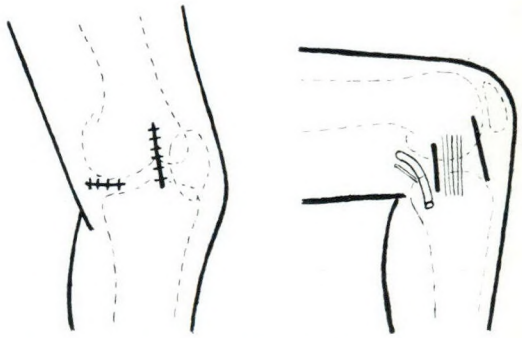

Fig. 1.—Relative position of skin and deep incisions.

After the penetration through the capsule and transection of the attachment of the anterior horn, the dissection is carried out with Smillie's knives along the medial rim of the meniscus, while continuous pull is exerted on a Kocher clamp grasping the anterior horn. When approximately two-thirds of the rim has been dissected, the tip of the clamp is pushed posteromedially into the joint space until the soft tissues of the medial aspect of the knee bulge over it. Abduction of the hip at this stage is help-

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ful. In the presence of "bucket-handle" tears, the displaced "handle" portion should first be returned medially to the condyle.

The posterior incision is then made directly over the tip of the clamp and is located just anterior to the course of the long saphenous vein at the joint-line level. Because of skin tension lines in this area, it has been found more advantageous to make the skin incision transverse, about 1" in length, and incise the deeper layers longitudinally, thus minimizing the chance of injuring the long saphenous vein or saphenous nerve. The clamp holding the anterior horn is exteriorized at this stage, the cartilage grasped by a new clamp and the posterior horn resected under almost continuous direct vision, provided retractors are put to full use.

The advantages of this approach are multiple, the main factor being safety. The possibility of injury to the popliteal structures is almost nil, and blind injury to the articular cartilage, with its dangerous sequelae, is greatly minimized. The greatest advantage, however, is the operator's confidence and the ease of removal of the posterior horn.

TABLE I.—100 Uncomplicated Medial Meniscectomies—1954 - 63

	Single incision	*Double incision*
Number of cases	50	50
Patient's age:		
Average....years	29	26
Range....years	17-41	17-48
Affected knee:		
Right	19	22
Left	31	28
Duration of symptoms extending over:		
Years	16	19
Months	29	22
Days	5	9
Follow-up in % of cases	84%	90%
Average duration..months	16.3	7.1
Range	2 months —10 years	1 month —2 years
Surgical diagnosis:		
Normal	5	7
Bucket-handle tear	16	22
Anterior horn tear	6	3
Posterior horn tear	12	13
Mid-portion tear	1	2
Multiple tears	2	0
Questionable anterior horn	1	0
Questionable posterior horn	1	3
Unspecified tear	6	0
Average days in hospital	37.7	36.0
Average number of post-operative hospital days	29.7	26.3
Average days of sick leave	20.7	24.5
Average duration of light duties....months	8.7	5
Major postoperative complications	10	5
Minor postoperative complications	8	14

In order to carry out a more thorough assessment of the results, 50 cases each of single and double-incision meniscectomies were compared in their various aspects (Table I). Only simple meniscectomies were selected for this review. Cases were eliminated that involved other knee pathology which could affect the functional results or the duration of convalescence, such as multiple injuries to the knee joint, chondromalacia and osteoarthritis. The pathological changes present in these 100 cases were confined to the medial semilunar cartilage; the diagnosis was based on the findings of complete knee exploration at the time of arthrotomy.

Several features of Table I require some elaboration. The patients were in the age group usually involved in active sports but the range in this series is also affected by the age of the military population. By the same token, only one patient was female. The duration of hospitalization, which may appear unduly long in comparison with civilian hospitals, is related to the necessity of retaining the patients in a centre providing supervised active physiotherapy, rather than returning them to a small unit where professional supervision is not feasible, and the usual "home" convalescence is not available in military housing. The duration of "light duties" is a variable feature in the convalescent stage. This period is put to different uses by the individual, and the limited activity which it implies is frequently not adhered to during off-duty hours. However, this designation is necessary for administrative reasons during the surgical follow-up period in order to prevent the posting of the convalescent to areas where he might be under excessive stress.

The use of a second incision did not increase the morbidity; on the contrary, the results obtained with it appear to be more satisfactory (Table I).

The 10 major complications incurred by

patients in the first group involved the readmission to hospital of seven patients; in three, retained posterior horns were removed. In two more, such retention was suspected but no operation was performed. Three patients had recurrent severe intra-articular effusions that required several aspirations and injections with hydrocortisone; one had thrombophlebitis and one had prolonged pain. The eight minor complications consisted of effusions with aspiration and hypoesthesia owing to the interruption of the infrapatellar branch of the saphenous nerve.

The five major complications in the second group required the readmission of three patients, two for extensive physiotherapy because of a limited range of movement and one for removal of the lateral meniscus which was thought to contain the pathological changes responsible for the initial, poorly localized symptoms, not entirely relieved by the first operation.

The last two patients required prolonged hospitalization because of septic arthritis in one and thrombophlebitis in the other. The minor complications were similar to those noted in the first group for seven patients; three other patients developed slight serous discharge from their wounds; two complained of ill-defined aches in the joint, and two of tightness in the periarticular soft tissues.

On the basis of this review, it appears that morbidity does not increase with the second incision and its advantages justify its use electively.

Summary

The morbidity of 50 uncomplicated medial meniscectomies performed through two incisions was compared with the morbidity of 50 single-incision meniscectomies and was found to be smaller. The elective use of the second posteromedial incision appears desirable in order to be certain that the posterior horn of the medial semilunar cartilage is removed completely.

References

1. Smillie, I. S.: Injuries of the knee joint, 3rd ed., E. & S. Livingstone, Ltd., Edinburgh, 1962.
2. Scharf, R. F.: A survey of knee surgery at the National Defence Medical Centre, *Med. Serv. J. Canada,* **19:** 659, 1963.

Résumé

Les auteurs décrivent ici une variation dans la technique de la méniscectomie et rapportent leurs résultats personnels. Fréquemment, il est difficile, à l'aide d'une seule incision, d'atteindre la corne postérieure du ménisque. C'est la raison pour laquelle on recommande ici d'aborder l'articulation par une incision légèrement oblique par rapport à l'axe du membre, antéro-interne, passant à une largeur de doigt du bord de la rotule. On pénètre dans la capsule, et la partie antérieure du ménisque est disséquée en s'aidant d'une traction à la pince. Pour atteindre la région postérieure, on incise les parties molles à la face postéro-interne de l'articulation sur cette même pince; l'incision cutanée sera transversale et l'incision profonde longitudinale, de façon à éviter la veine saphène et le nerf. On a ainsi une bien meilleure vue sur la corne postérieure du ménisque, et on réduit ainsi le danger d'une excision incomplète. Les auteurs étudient les résultats obtenus chez deux groupes de 50 malades chacun; le premier fut opéré avec une seule incision et le deuxième avec deux incisions. D'après les chiffres fournis, il est certain que ce dernier procédé n'augmente ni la mortalité, ni les complications post-opératoires. Les résultats d'ensemble sont plus satisfaisants.

A SYSTEM OF ORTHOPAEDICS AND FRACTURES. 2nd ed. A. Graham Apley. 393 pp. Butterworth & Co. (Canada) Ltd., Toronto, 1963. $14.75.

The second edition of this useful text maintains the high standard achieved in the first edition published four years ago. The fact that a second edition was required in such a relatively short time is an indication that there is need for this sort of text.

The book is aimed primarily at the needs of Fellowship candidates and attempts to summarize briefly the present concepts of diagnosis and treatment in the broad field of musculoskeletal disorders. No attempt is made to go into great detail and controversial aspects are avoided completely. The new edition contains a very useful new chapter on the management of major accidents. It includes management of injuries at the scene of the accident, the management of specific problems such as shock, concussion, respiratory obstruction, and so on in the accident department, and also describes the organization of an accident unit.

Although the book emphasizes the treatment methods in vogue in Great Britain and is, therefore, somewhat conservative by North American standards, it is a really useful book for Fellowship and American Board candidates on this continent as well and is highly recommended to them for "bedside reading" during the agonizing last few weeks before the examinations.

THE TREATMENT OF ILIOFEMORAL VEIN THROMBOSIS (PHLEGMASIA DOLENS) BY THROMBECTOMY*

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ILIOFEMORAL venous thrombosis is described in the literature under such descriptive titles as "milk leg", phlegmasia alba dolens, and phlegmasia cerulea dolens. The serious complications and the considerable chronic morbidity that result from this condition have led to dissatisfaction with the established conservative management of iliofemoral vein thrombosis and to the advocacy of thrombectomy in its treatment.[1-3] Reconstructive venous surgery was first advocated by Leriche in 1928.[1] Subsequent work by Haller, Fontaine and Mahorner confirmed the efficacy of thrombectomy in reducing chronic morbidity following iliofemoral venous thrombosis.[4] We initially applied this procedure in the management of cases of iliofemoral vein thrombosis with complications, many of which are potentially fatal. The following case reports illustrate this use.

CASE REPORTS

CASE 1.—J.S., a 74-year-old man, was admitted to St. Michael's Hospital with a typical picture of phlegmasia alba dolens involving his right lower limb. The onset of this condition occurred during sleep and the patient awakened with a feeling of intense weight and weakness in his right leg. He was unable to walk and swelling increased rapidly. Tenderness, lymphadenopathy and considerable induration over the right femoral vessels were noted in the groin. The patient complained of considerable pain in the right calf, associated with some deep tenderness. Initially, the swollen leg was quite warm with superficial venous prominence (Fig. 1a). A venogram demonstrated the typical pattern of femoral vein obstruction (Fig. 1b). This patient had had recurrent episodes of arteriosclerotic coronary occlusion and previous difficulty from benign enlargement of the prostate with urinary retention and infection.

Intravenous heparin therapy, repeated administrations of fibrinolysin and elevation of the lower limbs failed to control the swelling. After seven days of the above program, signs of arterial inflow embarrassment developed with increasing coldness of the leg, increasing muscular weakness, numbness in the foot and diminishing pedal pulses.

On the tenth day of conservative management, the femoral vein was explored on the right side under epidural anesthesia. A well-organized thrombus was present in the common femoral vein and related superficial femoral vein. Extensive anterograde and retrograde clotting was present in the iliac vein, common and superficial femoral and long saphenous veins. A considerable amount of lymphadenopathy and inflammatory reaction surrounded the thrombophlebitis. An incision was made at the saphenofemoral junction with removal of thrombus and clot. Excellent anterograde and retrograde flow was obtained from all tributaries and the venotomy was repaired with 5-0 Mersilene suture.

Relief from pain and calf tenderness occurred immediately after the operation and within two days the swelling had effectively subsided. The patient was walking on the fifth postoperative day. Anticoagulant therapy was maintained with intramuscular heparin initially, and was continued as a long-term program, in view of the coronary artery disease, with warfarin sodium (Coumadin). Pelvic infection related to recurrent episodes of cystitis with prostatic urinary obstruction was considered a precipitating factor in the development of this thrombosis.

The patient was free of symptoms in his right lower extremity, which was of normal size and showed no tendency to swelling, some three months after thrombectomy. At this time he was readmitted with a similar phlegmasia condition in the left lower limb. He had gross urinary retention and infection, extreme mental confusion and a blood urea nitrogen level of 72 mg. %. Exploration of the left femoral vein was performed on the fifth day of hospital admission and a localized thrombus was removed from the junction of the external iliac and common femoral veins.

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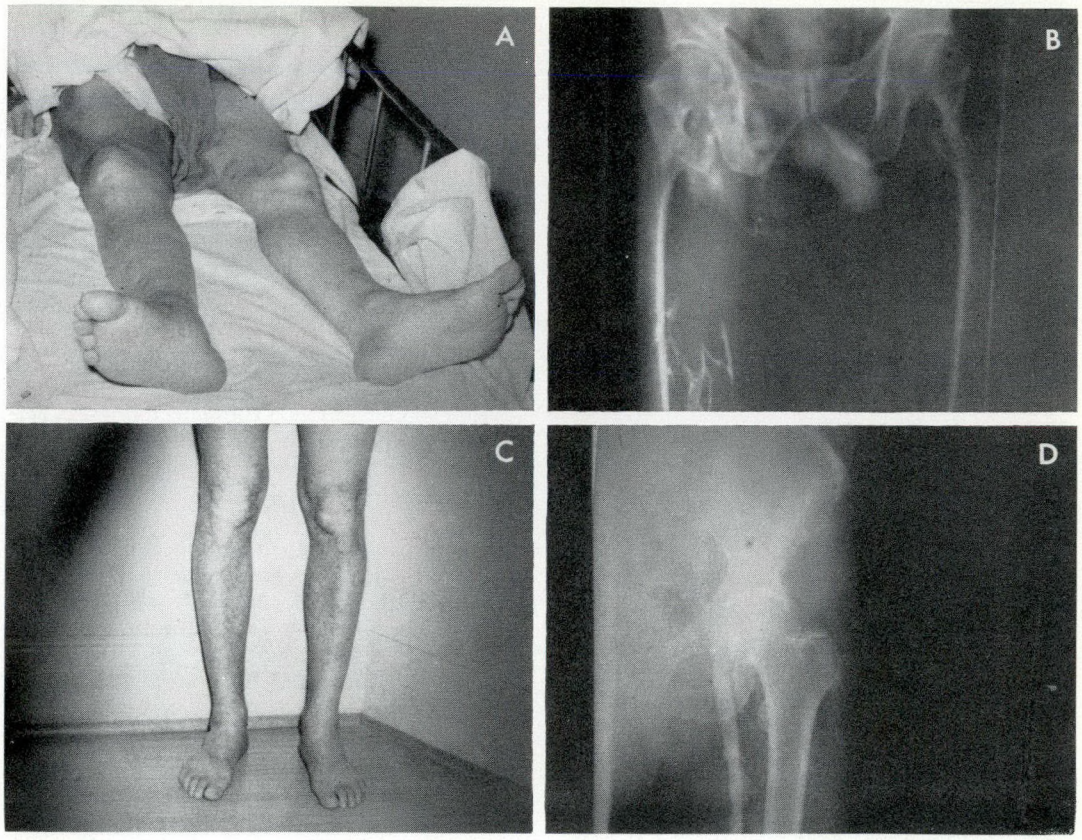

Fig. 1.—Appearance of limbs and venograms in phlegmasia alba dolens. A. Swelling extends from toes to groin of right leg in patient J.S. with phlegmasia dolens. B. The venogram shows obstruction to flow at the mid-thigh level in all venous channels, excepting collateral. C. Normal appearance of lower limbs, M.D., six months after thrombectomy. D. Venogram demonstrates normal flow and valve function six months after thrombectomy in C.P.

The response to operation was excellent with immediate alleviation of the pain and tenderness and effective control of the swelling within two days. The patient was ambulatory at this time, and the mental confusion and disorientation subsided promptly. The urinary tract infection was treated in the usual manner with catheter drainage and antibiotics.

Three weeks after operation, the patient developed a left epididymo-orchitis and a flare-up of the cystitis which rapidly progressed to anuria. A diuretic response following the usual conservative management of this complication occurred one week after its onset. Five days later signs of pneumonia developed in the right lung; this precipitated a second period of renal shutdown. Congestive cardiac failure developed from which the patient failed to recover. Permission for an autopsy could not be obtained.

CASE 2.—M.D., a 35-year-old man, was admitted to hospital with hemoptysis, right pleuritic chest pain, and a radiologically visualized infiltration of the right lower lung field. A history was obtained of recurrent painful swelling of the right lower limb for a period of approximately 18 months. This swelling generally occurred below the knee but occasionally extended to the groin. Swelling was again present before the onset of the pulmonary symptoms for 38 hours before this admission. With development of chest pain, reduction of the lower limb swelling occurred. Systemic review was negative except for moderate non-specific dyspepsia.

Anticoagulant therapy with both heparin and warfarin sodium was begun on admission to hospital. Effective blood levels were obtained and some degree of melena and hematemesis occurred. Despite anticoagulant therapy, episodes of bilateral pulmonary embol-

ism recurred, the fourth of which was associated with marked clinical shock some 20 hours after hospital admission. At this time the only clinical sign in the lower limbs was moderate tenderness, localized to the right common femoral vein region. In view of recurrent pulmonary embolism, bilateral femoral vein ligation was planned.

Common femoral veins, with their related tributaries, were exposed bilaterally under epidural anesthesia. On the right side, a partially organized thrombus was present at the confluence of the superficial femoral and profunda femoris veins. Considerable anterograde and retrograde clotting was present in the common femoral, iliac, saphenous and superficial femoral veins. The thrombus was removed through an overlying incision and the clot aspirated. Excellent flow was obtained from all tributaries. A considerable amount of clot could be aspirated by retrograde catheterization of the right superficial femoral vein. The superficial femoral veins were interrupted bilaterally at their junction with the profunda femoris veins. Heparinization, commenced before operation and supplemented during the operation, was maintained for three weeks postoperatively.

This man has remained well without further pulmonary embolism or venous insufficiency of his lower limbs for six months after operation (Fig. 1c).

Case 3.—C.P., a 78-year-old woman, was admitted to St. Michael's Hospital with a history of sudden onset of pain, warmth and swelling in the left lower limb. This developed quite spontaneously while she was sitting in a chair watching television. There was no history of previous vascular disturbances in her lower limbs. Three normal pregnancies were not associated with venous complications of any kind. Although rather obese, the patient had led an active life until the onset of her present symptoms which left her unable to walk. She complained of a feeling of weight in the left lower limb, described as a sensation of lameness and paralysis as much as of pain. A normal arterial supply was present on examination of the lower limbs. Gross swelling extended from the foot to the groin in the left leg. This swelling was warm, tender and pitting, with a reddish discolouration and superficial venous distension. There was an increase of 4" in girth of the thigh compared with the right side. Tenderness was particularly marked along the femoral vessels but was also present in the left calf. The patient complained of severe pain in the calf muscles.

Following the diagnosis of acute phlegmasia alba dolens in this elderly woman, control of the condition with anticoagulation therapy was attempted. Adequate blood coagulation levels on intravenous heparin were maintained with difficulty. In addition, the patient developed signs of basal pneumonitis after 24 hours of rest with the foot of the bed elevated. The leg failed to show any reduction in size and the effects of cardiac decompensation became apparent with increasing pulmonary congestion and the development of sacral and dependent edema of the trunk.

Left iliofemoral vein thrombectomy was performed 48 hours after hospital admission. The procedure was carried out under epidural anesthesia, supplemented by local infiltration with 1% lidocaine (Xylocaine). Full heparinization was maintained during the procedure and for three weeks subsequently. A partially organized thrombus was present in the common femoral vein extending into the distal segment of the external iliac vein. Retrograde clotting had occurred in the long saphenous vein and to a limited extent in the superficial femoral vein. Thrombus and clot were removed through an incision at the saphenofemoral junction with restoration of good anterograde and retrograde flow from all tributaries. After repair of the venotomy, the long saphenous vein was divided. The patient experienced relief from pain immediately after the operation. Within five days, the swelling had completely resolved and the patient was ambulatory, with elastic bandages to her lower legs. Six months after operation, the patient was symptom-free, having returned to her preoperative activity level, and, wearing a light-duty elastic stocking support, had no evidence of venous insufficiency to her lower limbs. A venogram performed at this time demonstrated a normal deep venous system in the left leg with intact common femoral vein valves (Fig. 1d).

Discussion

The etiology of iliofemoral venous thrombosis has classically been linked with pregnancy in the complication known as "milk leg". This has been attributed to changes in pelvic venous drainage associated with the development and abruption of the placenta. The obstruction to venous drainage by a pelvic mass has also been indicted. The association of iliofemoral thrombosis with occult abdominal carci-

noma, particularly pancreatic, has long been noted.[4] It is of interest that in none of our patients was there a history of previous vascular insufficiency or of a relation to pregancy. A history of pelvic infection was obtained in one patient (J.S.). In two patients the iliofemoral thrombosis apparently occurred spontaneously, following a prolonged period of sitting with the hip and knee joints flexed, suggesting that stasis with kinking of the vein is an important factor in the development of iliofemoral venous thrombosis, as it is in arterial atherothrombosis.

Clinical features of iliofemoral venous thrombosis are generally clear-cut. Gross pitting edema involves the entire limb from toes to groin (Fig. 1a). Such a limb is painful, particularly in the calf muscles. However, a dull throbbing pain may be present in the entire limb which at the same time feels heavy, useless and weak. Skin colour varies with the extent of arterial insufficiency. A warm leg with rubor and superficial venous distension may occur in the early stages. Pallor may occur once the leg is elevated. We have not found Homan's sign of deep calf tenderness to be a striking feature. Tenderness is elicited with deep palpation in the groin and femoral triangle regions. Inguinal lymphadenopathy may be quite marked. A pelvic or rectal examination may reveal a boggy fullness of the pelvic wall in relation to the inflammatory periphlebitic reaction and the collateral venous congestion.

A venogram performed via a tributary of the saphenous vein confirms the diagnosis. A typical pattern is illustrated in Fig. 1b. Abrupt cut-off of the major venous channels from the lower limb occurs at a relatively uniform level in the thigh, with small collaterals establishing drainage.

The complications and morbidity occurring with iliofemoral vein thrombosis have been emphasized in recent reports. Of serious consequence is pulmonary embolism, which can be fatal or, with recurrence, cause chronic pulmonary vascular insufficiency.[5] Progression to cerulea dolens with arterial inflow occlusion carries the risk of limb loss and a systemic reaction for which treatment is unsatisfactory and which is related to a distinct mortality rate.[6, 7] The after-effects of extensive deep venous thrombophlebitis are seen in the post-phlebitic syndrome where incompetent, recannulated venous channels leave the leg chronically swollen and painful. The limb becomes the seat of recurring episodes of thrombophlebitis and ulceration. The swelling of the post-phlebitic syndrome is difficult to control with elastic support and tends to be self-aggravating, establishing a vicious circle which can, with development of lymph stasis, culminate in a condition of elephantiasis.[8]

Our concept of the pathogenesis of phlegmasia alba dolens and its complications is based on the operative findings during thrombectomy and on the clinical histories of these patients. In each case, a relatively well-organized thrombotic segment is present in the common femoral vein related to one or more of its major tributaries. Extending in retrograde and anterograde fashion from this thrombus is a recently formed gelatinous clot. Depending on the extent of this clot and its occlusion of tributaries draining the limb, the amount of edema present and of arterial inflow obstruction occurring will vary. We feel, too, that it is the recently formed gelatinous and poorly adherent anterograde clot that breaks off to lodge in the lungs. This source of emboli is likely to develop at sites of entrance of large tributaries, such as the internal hypogastric vein, and accounts for the relief in leg swelling often associated with embolic episodes. It possibly accounts for recurrent pulmonary embolism, which may result in chronic obstructive pulmonary hypertension. The operative findings and clinical history of the patient (M.D.) illustrate this event and it occurred in other patients in whom femoral vein division was performed for control of pulmonary embolism.

We attribute the occurrence of cerulea dolens to extension of the thrombotic process to involve more and more of the venous drainage of the leg causing, eventually, passive arterial inflow obstruction.[6] The leg then becomes mottled and pulseless with signs of neurological deficit and

myositic changes. Frank gangrene with a definite mortality rate has been ascribed to this stage.[7]

The conservative management of iliofemoral vein thrombosis is based on control of swelling with elevation of the lower limbs and limitation of thrombus progression by anticoagulant therapy. The initiation of effective anticoagulant therapy, particularly with heparin, has reduced the incidence of complications, such as pulmonary embolism, and limited the extension of the thrombotic process that causes arterial inflow embarrassment. However, the debility associated with an established cerulea dolens and the incidence of the post-phlebitic syndrome appears to be little altered by effective heparinization. Our limited experience with thrombolytic agents, such as the fibrinolysins and streptokinase, has been discouraging. The results of the use of sympathetic blocks and of continuous epidural anesthesia have been equivocal.[5] Interruption of pathways for recurrent pulmonary embolism, such as ligation of the vena cava or of the femoral veins, has resulted in a significant incidence of debilitating disturbances involving the venous drainage of the lower limbs, particularly where the latter are the seat of extensive pre-existing thrombosis.[9]

Thrombectomy was initially proposed by Leriche in 1928 to prevent pulmonary embolism. In 1957, Fontaine[1] and Mahorner, Castleberry and Coleman[2] reported thrombectomy in an attempt to reopen thrombosed veins as treatment for the post-phlebitic syndrome. Haller and Abrams[10] advised this procedure for the treatment of the acute obstructive condition and have indicated a direct relationship between the efficacy of surgical removal of thrombus and the duration of disease symptoms. We employed thrombectomy in the treatment and management of the complications of phlegmasia alba dolens—the prevention of recurrent embolism, the prevention of extension of thrombosis and arterial embarrassment—and where continued conservative management was for some reason not possible, as in Case 3. Our results tend to support the use of this technique in the treatment of acute uncomplicated iliofemoral thrombosis.

The operation is performed under local or epidural anesthesia with systemic heparinization using 1 mg. of heparin intravenously per kg. body weight. The common femoral vein and its related tributaries are gently exposed and circumscribed with umbilical tapes. The presence of thrombosis is immediately apparent on inspection of the vein (Fig. 2). A considerable degree of inflammatory lymphadenitis is generally present. We do not expose the iliac veins or inferior vena cava unless both limbs are involved in the edematous process. An incision is made at the saphenofemoral junction. Recently formed gelatinous anterograde and retrograde clot is readily removed. This is facilitated by the use of a transparent tube connected to strong suction and with the patient performing a Valsalva maneuver. A segment of fairly well-organized thrombus will usually be recognized in the common femoral vein and can be extracted with the suction tip or a curved clamp. Retrograde catheterization of the profunda femoris and superficial femoral veins is performed to insure that no residual clot is present which may be a source of recurrent thrombosis or of pulmonary embolism. If any doubt exists as to the presence of extensive clotting in these tributaries, they are interrupted. The saphenous vein is generally divided and the venotomy repaired with 5-0 Mersilene suture. The foot of the bed is elevated for two to three days following operation to hasten resorption of edema fluid. The patient is allowed up on the second or third day with elastic bandage supports to the lower legs. Heparinization is maintained by the intramuscular route for a further two to three weeks.

The ease with which the clot can be aspirated makes pulmonary embolism unlikely during thrombectomy. Haller, in extensive use of this technique, has not found pulmonary embolism to be a hazard, and we not not expose the iliac vein–vena cava region unless bilateral limb edema indicates that clot already extends to this level.

Results

The results of thrombectomy in the

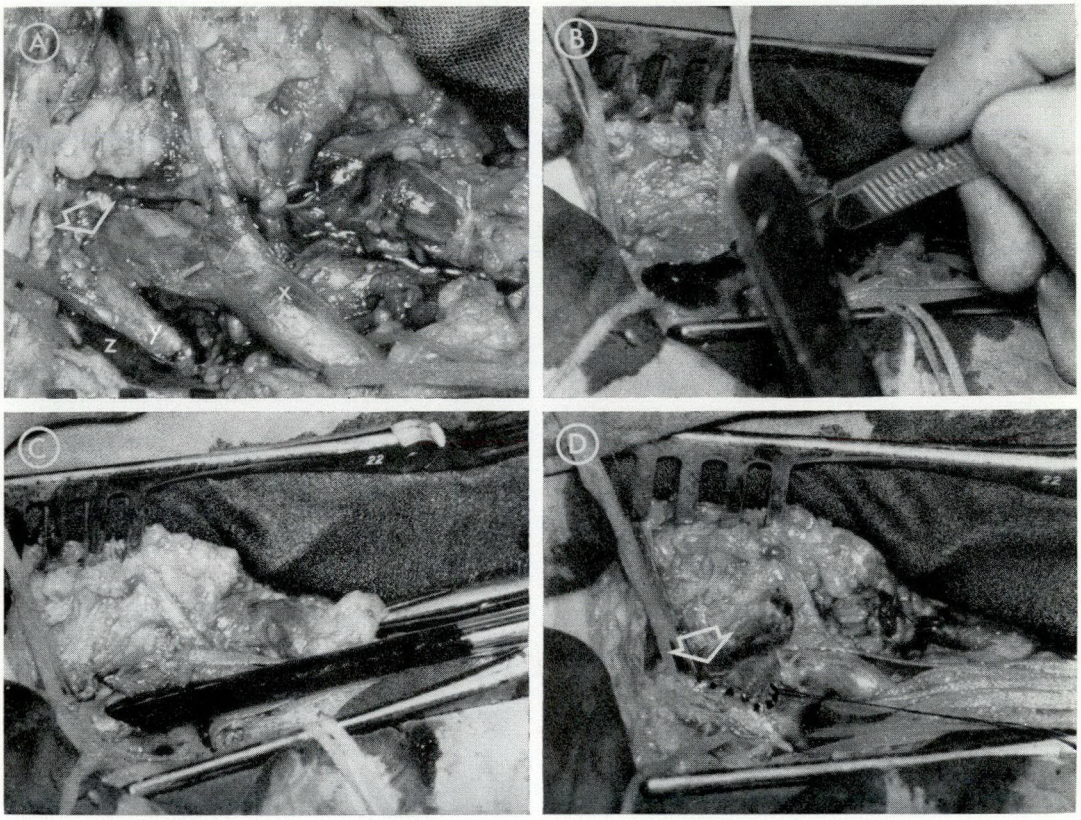

Fig. 2.—Right iliofemoral venous thrombectomy. A. Dissection shows long saphenous vein (x) joining common femoral vein (y) at the arrow. The common femoral artery (z) is retracted laterally. The veins are tense and distended by thrombus. B. Clot is extruded through a venotomy during Valsalva maneuver. C. Clot removal continued with transparent suction tube gently introduced into the vein. D. Normal blood flow, without vessel distension, is established after vein repair.

treatment of complications of iliofemoral vein thrombosis have been encouraging in the four instances described above. We were able to reverse a tendency to arterial inflow obstruction of serious proportion in one patient, and in another patient, to effectively control recurrent pulmonary embolism. In a third elderly patient, early ambulation following operation facilitated the control of congestive cardiac failure symptoms. Even more gratifying was the complete absence of the usual postphlebitic signs in patients followed up four months and longer after operation (Figs. 1c and d). One patient died approximately four months after operation on the right femoral vein and one month after operation for a recurrent episode involving the opposite limb. This death occurred during anuria associated with a genitourinary infection. Although an autopsy was not performed, it was felt that femoral vein thrombectomies were not directly contributory to this patient's death.

Summary

The application of iliofemoral vein thrombectomy to the treatment of four episodes of complicated phlegmasia alba dolens in three patients is described. The clinical features and complications of acute iliofemoral vein thrombosis are outlined. A discussion of the pathophysiology of iliofemoral vein thrombosis and its complications is presented. The results obtained support the use of this procedure in the management of acute uncomplicated iliofemoral vein thrombosis.

References

1. Fontaine, R.: Remarks concerning venous thrombosis and its sequelae, *Surgery*, **41:** 6, 1957.
2. Mahorner, H., Castleberry, J. W. and Coleman, W. O.: Attempts to restore function in major veins which are the site of massive thrombosis, *Ann. Surg.*, **146:** 510, 1957.
3. Haller, J. A., Jr.: Thrombectomy for acute iliofemoral venous thrombosis in the postpartum period, *Surg. Gynec. Obstet.*, **112:** 75, 1961.
4. Hubay, C. A. and Holden, W. A.: Venous thrombosis, necrosis, and neoplasia, *Surg. Gynec. Obstet.*, **98:** 309, 1954.
5. Allen, E. V., Barker, N. W. and Hines, E. A.: Peripheral vascular diseases, 3rd ed., W. B. Saunders Company, Philadelphia, 1962, p. 569.
6. Savage, J. P.: Role of reflex spasm in the pathogenesis of venous ischemia, *Surg. Gynec. Obstet.*, **113:** 47, 1961.
7. Haimovici, H.: Gangrene of the extremities of venous origin; review of literature with case reports, *Circulation*, **1:** 225, 1950.
8. De Takats, G.: Vascular surgery, W. B. Saunders Company, Philadelphia, 1959, p. 339.
9. Anlyan, W. G. *et al.*: Pulmonary embolism following venous ligation, *A.M.A. Arch. Surg.*, **64:** 200, 1952.
10. Haller, J. A., Jr. and Abrams, B. L.: Use of thrombectomy in the treatment of acute iliofemoral venous thrombosis in forty-five patients, *Ann. Surg.*, **158:** 561, 1963.

Résumé

La thrombose de la veine ilio-fémorale est décrite dans de nombreux articles sous des désignations diverses: jambe laiteuse "milk leg", phlegmasia alba dolens et phlegmasia cerulea dolens. Le traitement conservateur n'est guère satisfaisant dans cette affection, et des complications graves ou une morbidité chronique importante lui font généralement suite. La thérapeutique chirurgicale reconstructrice a été avancée en tout premier lieu par Leriche, suivi par ses élèves. Les auteurs rapportent ici trois histoires de cas qui sont démonstratives. Le premier cas est celui d'un homme de 74 ans, admis à l'hôpital pour un état bien classique de phlegmasia alba dolens. Ce tableau s'était apparemment établi sans cause particulière. On institua tout d'abord un traitement conservateur avec élévation du membre et administration d'héparine et de fibrinolysine, ce qui n'apporta aucune amélioration. Dix jours plus tard, une exploration fut effectuée sous anesthésie épidurale. On trouva alors un thrombus bien organisé, siégeant dans la veine fémorale commune et ses branches superficielles. Des phénomènes de lymphadénite étaient aussi présents. On procéda à une thrombectomie à travers une incision de la jonction saphéno-fémorale, ce qui rétablit immédiatement un très fort courant sanguin. La douleur et l'enflure disparurent rapidement après l'intervention, et le malade fut capable de marcher cinq jours plus tard. Le deuxième cas est celui d'un homme de 35 ans, admis à l'hôpital pour hémoptysie, douleur de pleurite du côté droit avec existence d'une opacité radiologique dans la même region. Dans son passé, on découvrit une histoire d'enflure de la jambe droite qui dura pendant 18 mois; chose curieuse, ces troubles avaient cédé en même temps qu'apparaissait le syndrome pulmonaire. Le malade fut soumis à un traitement par anticoagulants, héparine et warfarine sodique. Malgré cela, on assista à des épisodes nouveaux d'embolisation pulmonaire; localement, au niveau du membre inférieur, les signes cliniques étaient très discrets. On procéda à une exploration sous anesthesie épidurale. Les veines fémorales communes furent disséquées des deux côtés. A droite, on trouva un thrombus partiellement organisé à la confluence des veines fémorales superficielles et profondes, dont on fit l'ablation. Un flot sanguin satisfaisant se rétablit immédiatement, et l'intervention fut complétée par une cathétérisation aspiratrice de la veine fémorale superficielle. Ceci arrêta les épisodes d'embolisation et le malade peut maintenant être considéré comme guéri. Troisième cas.—Une femme de 78 ans est admise pour l'apparition subite d'une enflure accompagnée de douleur dans son membre inférieur gauche. Ceci était apparu très subitement, sans cause apparente, alors qu'elle était assise regardant la télévision. La malade n'a aucun antécédent vasculaire. A l'examen, le membre inférieur était considérablement enflé, du pied jusqu'à la racine de la cuisse; cette enflure était chaude à la palpation et l'on nota une distension des veines superficielles. Le traitement conservateur fut institué, mais devant l'installation d'un syndrome pulmonaire de la base, on décida d'explorer. Toujours sous anesthésie épidurale, on procéda à l'ablation d'un thrombus ilio-fémoral gauche, par une incision de la jonction saphéno-fémorale. Les symptômes retrocédèrent dans les cinq jours suivants, et la malade put être levée. Les auteurs estiment que le traitement conservateur des thromboses des veines des membres inférieurs n'est justifié que dans les cas bénins. L'héparine n'a qu'une action limitée et les fibrinolytiques ou la streptokinase ne donnent que des résultats décourageants. Lors de l'intervention, avec dissection soignée, le thrombus est facile à localiser, puis à extraire. Les résultats éloignés sont très satisfaisants.

THE SURGICAL SIGNIFICANCE OF RADIATION INJURIES TO BOWEL*

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COMPLICATIONS of radiotherapy for pelvic malignancy may include radiation injury to the intestine, which by virtue of its potentially lethal result is of major concern to the surgeon, both in respect of diagnosis and management. Since the first descriptions of this injury 67 years ago,[1] a number of reports have stressed the importance of recognition of this lesion, especially since its manifestations so often mimic recurrent malignancy.

Despite the newer sources and techniques of radiation therapy, such complications continue to occur. With the hope of improving our management of these, we have reviewed the literature and studied the records of 54 patients with radiation injury to bowel treated at the Toronto General Hospital. An attempt has been made to discover the most satisfactory means of management of the more serious aspects of this problem, especially those that require surgical intervention.

INCIDENCE

The incidence of radiation damage to bowel has been reported to be between 2% and 5% in patients receiving pelvic radiation.[2, 3] It has also been reported that 17% of those who sustained injury develop strictures[4] and between 50% and 75% have some permanent residual rectal change.[5] Damage to the ileum following pelvic radiation has occurred in 0.6% to 1.5% of patients.[3, 6, 7] In a study of rectal and bladder injuries sustained during radiation of the uterine cervix, Kottmeier and Gray[8] reported injury in 10% of patients receiving standard dosage, while 15% developed symptoms of such injury with more intensive therapy.

ETIOLOGY AND PATHOGENESIS

Todd's Hunterian lecture in 1938[2] is still the classic paper with respect to description and classification of the lesion which he termed "factitious proctitis". Radiation injury of the sigmoid colon and rectum produces two different pathological states. The first is the intrinsic reaction that occurs within the rectal or bowel wall and consists of hyperemia and edema within days of radiation. In three to four weeks, granulomatous inflammation and ulceration develop. Fistulas may occur later. Delayed healing, characterized by fibrosis, leads to stenosis after a variable period.

The second form is an extrinsic reaction which occurs in the perirectal connective tissues. Fibrosis with resultant extrinsic compression, and endarteritis with resultant ischemia, affect the bowel wall secondarily. The connective-tissue mass so formed may suggest the presence of diffusely recurrent malignant disease throughout the pelvis.

Although the entire gastrointestinal epithelium is vulnerable to radiation, the small bowel mucosa appears to be most sensitive. However, the ileum is mobile and infrequently fixed by pelvic adhesions, which tends to protect it from more common injury. Requarth and Roberts[3] reported four patients who sustained damage to ileum; three presented with small bowel obstruction and, of these, two had ileum fixed within the pelvis.

It would appear that an excessive or a too concentrated course of radiation is the most important cause of injury.[9] Other etiological factors may be errors in technique of administration such as dislodgment of radium applicators,[10] a retroverted uterus, or pre-existing pelvic inflammatory disease.[2] There remains a group of patients whose tissues appear to react excessively to a standard and properly applied course of radiation.

The most extensive study correlating radiation dosage and its pathological effects on the rectum was carried out in Stockholm by Kottmeier and Gray,[8] who

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followed up 500 consecutive patients treated radiologically for carcinoma of the cervix. Mild mucosal changes were noted in 14% and more advanced lesions, such as necrosis, ulceration and moderate stenosis, occurred in 7%. Only 1% developed more severe stenoses or fistulas requiring operative intervention. A rectal dose below 4000 r. resulted in significant damage in 1.6%. As the dosage increased above 5000 r., an increased incidence of complications occurred. When external radiation was added to interstitial radium, no rectal lesions were noted if the total rectal dose remained below 4000 r. but became appreciable if it was increased to 6000 r. or more.

Time of Onset

Todd[2] noted that the onset of acute proctitis coincided with the termination of treatment or occurred in the following two weeks. Late rectal reactions followed at an average time of six months after the completion of radiotherapy with a range of one month to several years. Aune and White[10] found the onset of proctosigmoiditis was usually within the first few months, whereas the development of mechanical obstruction was rare before five months and not unusual up to several years. Simpson and Spaulding[11] reported a patient with bowel obstruction due to radiation stricture 14 years after radiation, and Abrahamson,[12] an instance occurring 19 years after treatment.

Clinical Manifestations

Radiation injury to bowel may present as proctosigmoiditis with or without obstruction or as ileitis with or without obstructive symptoms.[13] In the colon and rectum, sigmoidoscopy in the early stages reveals redness, edema and friability of the mucous membrane. The pathological changes are usually concentrated on the anterior rectal wall at the level of the cervix in those patients whose treatment is centred in that structure.

With progression of the disease, atrophy, telangiectasia, scarring, ulceration and contracture supervene. The ulcers may be discrete, single or multiple. The majority of ulcers will heal but those which are intractable present a challenge to the clinician in both diagnosis and treatment. They may closely simulate an ulcerative type of malignancy.

The symptoms associated with the pathological findings follow in logical sequence and are tenesmus, rectal bleeding, diarrhea, increased secretion of mucus and rectal pain, both with and also independent of defecation.

The extrinsic lesion described by Todd manifests itself as diffuse induration and thickening of the rectal wall and pelvis simulating the "frozen pelvis". Rectal biopsy, although helpful, may fail to establish an accurate diagnosis. Among 200 patients referred to the Mayo Clinic with the diagnosis of recurrent carcinoma, 9.5% had radiation changes without evidence of tumour.[14]

The development of strictures of the ileum, sigmoid colon or rectum is associated with the symptoms of partial or complete bowel obstruction. This is seen most commonly in the sigmoid in 47%, rectum in 28%, rectosigmoid in 14% and ileum in 9%.[15]

In acute radiation ileitis, the manifestations include weight loss, anemia, hemorrhage and perforation. The late effects include malabsorption and obstruction.[12] Six of nine patients with radiation ileitis described by Wiley and Sugarbaker[6] developed obstruction. Of the six patients presented by Warren and Friedman,[16] three had fistulas and three stenosis.

Treatment

Surgical measures in the treatment of severe complications of radiation ileitis, colitis and proctitis are the subject of controversy. Reported series are small and give no more than an indication of the ideal treatment. There is general agreement that the early manifestations may be temporary and self-limiting and can be adequately managed by a regimen of bland diet, antispasmodics, antibiotics and sedation. Colcock and Hume[13] recommend hospitalization if the symptoms have not subsided within two weeks. In hospital they add bed rest, general supportive measures,

transfusion if dictated by anemia, and hydrocortisone enemas. They also recommend colostomy if, after two weeks of hospital treatment, proctosigmoiditis remains severe and uncontrolled.

The indications for surgical intervention in chronic radiation proctosigmoiditis include persistent severe pain, bleeding, obstruction, incipient perforation and diversion of the fecal stream from non-healing ulcers and fistulas.[10]

The conservative treatment of patients with obstructive symptoms due to radiation strictures, as described by McIntosh and Hutton,[17] is not without danger. White and Finn[9] report unfortunate results in four patients treated in this manner. Of 26 patients managed by supportive but non-operative means, two died of massive hemorrhage and two of perforation. These authors recommend wide local excision with primary end-to-end anastomosis (with or without colostomy if the involved area is in the colon), and colostomy alone if resection is not feasible.

Wiley and Sugarbaker[6] and Graham and Villalba[7] recommend bypass without excision and state that, "Heavily irradiated tissues heal poorly and are notoriously vulnerable to infection. For this reason, resection of the intestine is rarely indicated. It is required for massive hemorrhage, but for obstruction or fistula formation a bypass procedure is much preferred." They report two patients who died after primary resection and anastomosis owing to leakage at the suture line. Only one of three patients treated by resection survived. Four patients survived when the involved segment of ileum was bypassed and an end-to-side ileocolostomy was performed, with the distal end of the divided ileum brought out as a mucous fistula.

Operative treatment used at the University of Illinois was reported by Requarth and Roberts,[3] who presented 12 surgically treated cases. They also stressed the necessity of complete excision of diseased bowel. They did not recommend resection of the rectum or rectosigmoid because of the technical difficulty experienced. Smith *et al.*[18] recommended colostomy and late resection of rectal strictures that failed to respond to dilatation.

Toronto General Hospital Series

Since 1940, 54 patients with radiation injuries to bowel were admitted for treatment at the Toronto General Hospital. A much larger number of patients were successfully managed as outpatients. Of those admitted, 47 were women and seven, men. The average age was 51 years and the range was from 23 to 78 years.

TABLE I.—Site of Primary Tumour Receiving Radiation

Lesions	*No. of patients*
Carcinoma, cervix	38
Carcinoma, cervix and endometrium	2
Carcinoma, ovary	2
Carcinoma, vagina	2
Carcinoma, testis	2
Carcinoma, rectum	2
Carcinoma, endometrium	1
Chondrosarcoma, ileum	1
Ewing's tumour, ileum	1
Lymphosarcoma, cecum	1
Malignant melanoma, rectum	1
Abdominal tumour, primary site unknown	1

Carcinoma of the cervix was the most common primary tumour and with the addition of tumours of the uterus, ovary and vagina resulted in a great female preponderance. The proximity of the cervix and rectum resulted in damage to the rectum in the event of a mishap. Two patients with carcinoma of the rectum and one with malignant melanoma of the rectum were included because the radiation injury occurred in the sigmoid colon or small intestine.

TABLE II.—Form of Application of Radiotherapy

	No. of patients
External radiation only	9
Interstitial radium only	4
Combined external and interstitial radiation	41
Repeat course of radiation	8

Onset of Symptoms

The first symptoms of radiation injury experienced by 11 patients coincided with the administration of radiation or occurred within 30 days of its termination. Since each of these 11 patients sustained serious injury requiring hospitalization and in some cases operative intervention, it can

be said that the early reaction is not always benign and care must be exercised in management of these problems, with greater emphasis on the degree of pathological change observed and the symptoms experienced than on the time of onset.

In the remaining 43 patients, the onset of symptoms was delayed and the average interval between termination of radiotherapy and onset was 17.3 months. The greatest delay in onset was 13 years.

TABLE III.—Clinical Manifestations

		No. of patients
Rectal bleeding		30
Incomplete rectal or sigmoid obstruction		29
Anemia of a severity requiring transfusion		14
Diarrhea		13
Rectal pain		13
Fistulas		11
rectovaginal	5	
vesicovaginal	2	
enterocutaneous	2	
enterocolic	1	
enteroenteric	1	
Passage of mucus in stool		7
Complete small bowel obstruction		5
Incomplete small bowel obstruction		4
Ureteral strictures		4
Perforation of colon		3
Complete colon obstruction		2

The most prominent clinical feature in this group of patients was obstruction, which played a dominant role in 40 of the 54 patients. In some patients, especially those with lower rectal strictures, the symptoms were managed conservatively by adjusting diet and by the use of laxatives. In a few, dilatation was necessary.

Rectal bleeding was a common finding but generally was not severe. Bleeding proved to be sufficiently massive and persistent to warrant colostomy in only one patient, a 43-year-old woman; this occurred two years after radiation for carcinoma of the cervix. However, she developed a paranoid psychosis and operation was deferred. This patient is still in hospital and requires frequent blood transfusions.

Survival Following Radiation

Nineteen patients lived five years or more, and eight, 10 years or more. Thirty-five patients are still alive but for a period of less than five years. There were 19 deaths, the causes of which are given in Table IV.

TABLE IV.—Causes of Death

	No. of patients
Recurrent tumour	9
Recurrent tumour and effects of radiation	5
Radiation effects	4
Unrelated cause	1

In Table IV it will be noted that in nine patients death was attributed to the effects of radiation; in four, to such effects in the absence of malignant disease, and in five to these effects in the presence of co-existing malignant disease.

In four of the 19 patients who died, death can be ascribed to the effects of radiation on the small or large bowel. The average age of these four at the time of death was 51.7 years and the average survival from the last treatment was 20.4 months. Three patients died as a result of perforation of necrotic bowel and one from the effects of an intestinal-vaginal fistula.

In five patients, although the presence of metastatic disease was verified at operation, at autopsy or was obvious clinically, the direct cause of death was thought to be the effects of radiation. The average age of these five patients was 40.2 years and the average time from last treatment was 30.2 months. All of them died of bowel obstruction or its sequelae and in only one was the metastatic disease at an advanced stage.

Surgical Treatment

In 28 of the 54 patients, operative intervention was required because of complications of radiation injury to the intestine. More than one operative procedure was necessary in 11 and a total of 47 operations was performed.

Results of Surgical Treatment

Colon resection with end-to-end anastomosis or abdominoperineal resection was performed in seven patients with no operative mortality. One patient died 2½ years after resection because of small

TABLE V.—Results of Conservative Treatment

	No. of patients
Total treated conservatively	26
Alive at last follow-up	13
Average follow-up 7.8 years	
Range in follow-up 10 months to 14 years	
Died	13
Cause of death—recurrent tumour	8
—effects of radiation	3
—other causes	2

bowel obstruction due to a radiation stricture, which was treated by a bypass procedure. Six patients are alive and have survived for periods of up to 14 years.

In three patients, small bowel resection was carried out with no operative mortality. One patient is alive one month after operation but has disseminated lymphosarcoma. Another is alive and well more than one year after operation. The third in whom resection was carried out following a radiation perforation and peritonitis, died of recurrent tumour three months after operation.

Small bowel bypass (enteroenterostomy and ileocolostomy) was performed upon five patients. Four of these patients died in the postoperative period of peritonitis owing to either perforation of the retained pathological segment or to leakage at the site of anastomosis. Because of small bowel damage, the fifth patient underwent a bypass procedure in addition to a sigmoid colostomy; the latter was carried out because of pelvic recurrence and radiation proctosigmoiditis. After a stormy postoperative course, she passed the bypassed segment of ileum per colostomy. The patient subsequently died of recurrent tumour.

Colostomy was performed upon 19 patients, only four of whom survived free of malignant disease. Two of these colostomies were subsequently closed. Three patients died within three months of metastatic carcinoma or the effects of associated operations. Two patients with sigmoid colostomies developed small bowel obstruction which proved fatal in both instances. Three patients required further bowel resection. Six patients were lost to follow-up study.

TABLE VI.—Types of Operation

1. Colostomy—sigmoid colon	17
2. Colostomy—transverse colon	2
3. Closure of colostomy	3
4. Revision of colostomy	2
5. Colon resection—primary resection and anastomosis of sigmoid colon	3
—anterior resection of rectum	2
—abdominoperineal resection	2
6. Primary small bowel resection	3
7. Bypass procedures—enteroenterostomy	3
—ileotransverse colostomy	2
8. Plastic repair of small bowel stricture	1
9. Miscellaneous—ureteroplasty	2
—division of adhesions	1
—drainage of abscess	1
—pain-tract section	3

Discussion

The high incidence of radiation injury in women reflects the frequent use of radiation in the treatment of gynecological cancer. Although the total number of patients treated for radiation injuries is not known, the majority are managed in a satisfactory manner by conservative means without hospital admission, and with symptomatic recovery. If the symptoms are sufficiently severe to require hospitalization, the incidence of serious complications is high.

In this group, the mortality directly attributable to radionecrosis of bowel was 17%. Of these, four patients were apparently free of malignant disease at the time of death. The five patients in whom metastatic disease was present but in whom the cause of death was radiation injury, died of the effects of bowel obstruction, despite surgical intervention in some cases.

None of the deaths was due to hemorrhage, although anemia was a prominent feature in nearly one-quarter of the patients.

Analysis of the treatment and its results led to some interesting impressions. Of the 13 out of 26 patients who were treated conservatively and survived, most did remarkably well as evidenced by the average survival of nearly eight years. It appears that the effects of radiation in these patients were self-limiting and the response of the tumour to treatment was satisfactory. However, a note of caution must be interjected. Complications of radiation, sufficiently severe to cause death, occurred in three of the 26 patients in this group.

A by-pass procedure is not recommended as the operation of choice in radiation ileitis. Four of the five patients in whom damaged bowel was by-passed died of peritonitis owing to leakage from the area of radiation injury or from the anastomosis. The fifth patient survived but had a complicated postoperative course culminating with the passage of the by-passed loop per colostomy. We recommend that this procedure be reserved for those cases in which mobilization of the bowel is technically difficult or hazardous.

We have had greater success with resection of diseased small or large bowel and primary end-to-end anastomosis. Ten patients treated in this manner survived operation even though in one patient, resection was performed in the presence of generalized peritonitis owing to perforation of the ileum. Two patients in this group died of malignant disease, one after three months and one after 30 months, but eight patients are alive and well for periods up to 14 years.

A colostomy, preferably a sigmoid colostomy, is frequently the only procedure possible because of the presence of a low-level stenosis, associated radiation injury and pelvic malignancy, or extensive recto-vaginal fistulas. A sigmoid colostomy is functionally superior to one placed in the transverse colon. However, a wide resection of the radiated bowel is preferred. Anterior resection, abdominoperineal resection and sigmoid colon resections were all feasible and were carried out successfully in the small group of patients reported here.

Summary

Radiation injuries of small bowel, colon and rectum occur in 2% to 5% of patients receiving pelvic radiation, most commonly for carcinoma of the cervix.

The effects of radiation may clinically mimic recurrent malignant disease and the treatment of a complication amenable to cure may be neglected for this reason.

If technically feasible, a wide resection of the damaged small or large bowel is advised. Bypass, in our experience, has been unsatisfactory, whereas primary resection has given good results.

References

1. Walsh, D.: Deep tissue traumatism from roentgen ray exposure, *Brit. Med. J.*, **2:** 272, 1897.
2. Todd, T. F.: Rectal ulceration following irradiation treatment of carcinoma of cervix uteri; pseudo-carcinoma of rectum (Hunterian lecture), *Surg. Gynec. Obstet.*, **67:** 617, 1938.
3. Requarth, W. and Roberts, S.: Intestinal injuries following irradiation of pelvic viscera for malignancy, *A.M.A. Arch. Surg.*, **73:** 682, 1956.
4. Aldridge, A. H.: Intestinal injuries resulting from irradiation treatment of uterine carcinoma, *Amer. J. Obstet. Gynec.*, **44:** 833, 1942.
5. Maas, J. M.: Intestinal changes secondary to irradiation of pelvic malignancies, *Amer. J. Obstet. Gynec.*, **56:** 249, 1948.
6. Wiley, H. M. and Sugarbaker, E. D.: Roentgenotherapeutic changes in the small intestine; surgical aspects, *Cancer*, **3:** 629, 1950.
7. Graham, J. B. and Villalba, R. J.: Damage to small intestine by radiotherapy, *Surg. Gynec. Obstet.*, **116:** 665, 1963.
8. Kottmeier, H. L. and Gray, M. J.: Rectal and bladder injuries in relation to radiation dosage in carcinoma of the cervix; a 5 year follow-up, *Amer. J. Obstet. Gynec.*, **82:** 74, 1961.
9. White, W. C. and Finn, F. W.: Late complications following irradiation of pelvic viscera, *Amer. J. Obstet. Gynec.*, **62:** 65, 1951.
10. Aune, E. F. and White, B. V.: Gastrointestinal complications of irradiation for carcinoma of the uterine cervix, *J. A. M. A.*, **147:** 831, 1951.
11. Simpson, W. J. and Spaulding, W. B.: Long-delayed bowel complications of radiotherapy, *Canad. Med. Ass. J.*, **80:** 810, 1959.
12. Abrahamson, R. H.: Radiation ileitis, *A.M.A. Arch. Surg.*, **81:** 553, 1960.
13. Colcock, B. P. and Hume, A.: Radiation injury to sigmoid and rectum, *Surg. Gynec. Obstet.*, **108:** 306, 1959.
14. Craig, M. S., Jr. and Buie, L. A.: Factitial (irradiation) proctitis; clinico-pathologic study of 200 cases, *Surgery*, **25:** 472, 1949.
15. Pessell, J. F.: Quoted by Aune, E. F. and White, B. V., Gastrointestinal complications of irradiation for carcinoma of the uterine cervix, *J. A. M. A.*, **147:** 831, 1951.
16. Warren, S. and Friedman, N. B.: Pathology and pathologic diagnosis of radiation lesions in the gastro-intestinal tract, *Amer. J. Path.*, **18:** 499, 1942.
17. McIntosh, H. C. and Hutton, J. E.: Clinical and roentgen aspects of irradiation stricture of rectum and sigmoid; its course and treatment, *Amer. J. Roentgen.*, **52:** 647, 1944.

18. SMITH, L. M. C. *et al.*: Radiation injury to rectum and sigmoid colon, *Amer. Surg.*, **27:** 660, 1961.

RÉSUMÉ

Parmi les complications de la radiothérapie profonde pour lésions cancéreuses du bassin, il y a lieu de considérer les blessures de l'intestin. Leur gravité est grande. Les auteurs ont étudié statistiquement 54 cas de ce genre traités au "Toronto General Hospital". Il ressort que la fréquence de ces lésions varie entre 2% et 5% des cas soumis à la radiothérapie. Les types de cancer qui avaient nécessité le traitement étaient: cancer du col utérin, cancer du corps utérin, cancer de l'ovaire, cancer du vagin, cancer du testicule, cancer du rectum, cancer de l'iléon ou du cæcum. Les symptômes apparurent en moyenne une trentaine de jours après la cessation de la thérapie. Ils consistaient en saignement rectal, obstruction partielle anémie sévère nécessitant des transfusions, diarrhée, douleur rectale, excrétion de glaires muqueuses, perforation côlique. Dans cette série, il y eut neuf cas de mort qui peuvent être attribués directement aux complications de l'irradiation. Vingt-huit malades durent être soumis à des ré-interventions qui étaient: colostomies principalement sur le sigmoïde, résections côliques, résections du grêle, entéro-entérostomies, colostomies iléo-transverses, traitement de rétrécissements du grêle, plasties urétèrale, sections de brides adhérentielles et enfin drainages d'abcès. Du point de vue histopathologique, on sait que les radiations causent tout d'abord une réaction dans la paroi intestinale, se traduisant par une hyperhémie et un œdème; secondairement, un état inflammatoire accompagné de la formation de tissu granulomateux s'installe. C'est ainsi que naissent les ulcérations, les fistules et les rétrécissements. Le tissu conjonctif péri-rectal réagit par une fibrose; les petits vaisseaux montrent souvent des phénomènes d'endartérite qui expliquent les troubles ischémiques. Les auteurs attirent l'attention sur le fait que ces lésions par irradiation peuvent facilement être confondues avec une métastatisation ou une généralisation du cancer primaire. Ce diagnostic doit être fait.

A PRACTICAL MANUAL FOR THE TREATMENT OF BURNS. Eli Rush Crews, with a foreword by Sidney Schiffer. 119 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1964. $8.00.

This book, dedicated to enlightenment of the surgical resident and practising surgeon, joins a rapidly increasing literature on the care of the burn wound. The author's treatment of the subject from first aid through early management to the healing phase is cursory. The teaching regarding local wound care with bacteriostatic agents and the emphasis on preoperative fluid balance is praiseworthy; for the novice, the instruction as to ascertaining the depth of burn and the management of nutritional balance is deficient and the conservative management of deep circumferential limb burns without immediate fasciotomy is questionable. The style throughout is pleasantly conversational but the audience to which the book is directed will wish for more precise and condensed details of the initial phases; no schedules for the administration of narcotic, tranquillizer, digitalis, or even blood in the management of the extensive deep burn are included.

TEXTBOOK OF THE FUNDUS OF THE EYE. Arthur J. Ballantyne and Isaac C. Michaelson. 520 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1962. $25.20.

Although this text is designed primarily to record the appearance of the normal and diseased fundus it consists of much more than a collection of fundus drawings. Wherever possible appropriate pathological preparations have been employed to illustrate disease states and this permits a more accurate correlation of visible ophthalmoscopic signs with structural change. In addition the authors have frequently employed visual field records to demonstrate the effects of fundus lesions on vision. Discussions of symptoms, prognosis and treatment are included. The book describes methods of fundus examination, the appearance of the normal fundus, changes with vascular disease, inflammations, degenerations, tumours and disease of the choroid and optic nerve. The many coloured illustrations, drawings and photographs are of a very high quality. The book is not a definitive reference work on eye disease but does make possible a better understanding of the significance of ophthalmoscopic findings.

REVIEW ARTICLE

CANCER OF THE BLADDER

Biochemical Factors in Its Etiology

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THE search for the cause of cancer has led investigators into the many diverse fields of biochemistry, virology, biometrics and statistics, cytological biochemistry, genetics and immunology.

There are a number of reasons why research into the etiology of cancer of the bladder has concentrated on its biochemical aspects. Such a relationship was first suggested in 1895 by Rehn,[1] who reported three patients with bladder tumour in a dye-works in Germany employing a total of 45 workers. So firm became this association that it was termed "aniline workers' cancer".[2-4] Today it is recognized that tumours of the bladder are an occupational hazard, not only in the dye industry, but, more recently, also in the synthetic rubber and plastics industries. By 1946, tumours of the bladder became a specified disease in the Industrial Injuries Act of Great Britain.[5]

Apart from industrial exposure, there is a geographical distribution of the disease which has so far defied analysis. In the large urban centres in North America, Great Britain, Denmark and Australia, the incidence at the age of 75 is approximately 130 per 100,000 living population. The incidence in the urban areas of Japan, Norway, Sweden and New Zealand and in the rural areas of the countries listed above is about half of this, or 40 to 65 per 100,000 living population at the age of 75. Moreover, in the high-incidence countries, the incidence has doubled in the past 20 years.[6, 7]

In the Middle East and Africa, where bilharzial infestation is endemic, there is a definite relationship between this disease and cancer of the bladder.[8] Turkish cattle have a higher incidence than North American cattle,[9] and cigarette smokers are more prone to it than non-smokers.[7]

These well-known and diverse etiological factors beg for a common biochemical explanation. The first attempts at biochemical investigation were directed toward the relationship of industrial factors to cancer of the bladder.

Although initial investigations implied that aniline itself was the carcinogen, it soon became evident that certain intermediaries in its manufacture were responsible. The most commonly implicated compound was 2-naphthylamine (Fig. 1); the others,

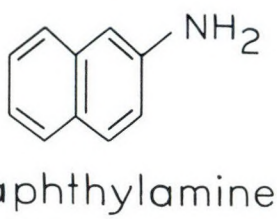

Fig. 1.—2-naphthylamine, a compound which belongs to the general class of aromatic amines because it contains a benzene ring to which an amino group is attached.

for example, benzidine and paraxenylamine, shared with naphthylamine the same structural features in that they were all aromatic amines. Since the major concepts in this field developed around 2-naphthylamine, the subsequent discussion concerns this compound to the exclusion of the others.

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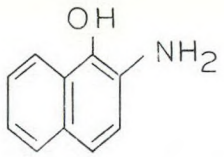


2-amino-1-naphthol

Fig. 2.—2-amino-1-naphthol. Note that the hydroxyl group is adjacent to the amino group.

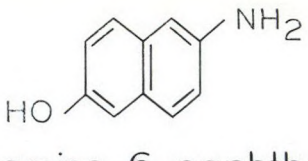
In 1938, Hueper, Wiley and Wolfe[10] demonstrated that the oral administration of 2-naphthylamine to dogs for periods as long as two years produced cancer of the bladder in over 80% of the animals so treated. However, similar attempts in rabbits and mice met with failure and so did direct instillation of 2-naphthylamine into the bladder.[11]

Scott and Boyd[12] demonstrated that if 2-naphthylamine was fed to dogs in whom the urinary stream had been diverted to the sigmoid colon, bladder cancer did not develop, although carcinoma of the upper urinary tract did. This was confirmed by McDonald and Lund,[13] who fed 2-naphthylamine to dogs in whom the dome of the bladder had been isolated from the bladder proper. Carcinogenesis occurred in the bladder but spared the isolated dome.

Whatever the final carcinogen, it seemed to exert its effect through direct contact with the urothelium, and was carried to this point of contact by the urinary stream.

Since 2-naphthylamine itself in direct contact with the bladder epithelium failed to produce bladder cancer, a search was begun for its metabolic products. From this search evolved our present formulation of bladder oncogenesis. Wiley[14] found that a large proportion of 2-naphthylamine administered to dogs was hydroxylated in the ortho-amino position to 2-amino-1-naphthol (Fig. 2), whereas other investigators noted that in rabbits and mice, which seemed immune to the carcinogenic effects of 2-naphthylamine, hydroxylation took place on the opposite ring (Fig. 3).[15, 16]

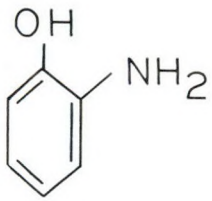
The fundamental concept arose that the *carcinogenic aromatic amines had to be metabolized to their ortho-aminophenol derivatives first, and then excreted in the urine, where, by direct contact with the urothelium, carcinogenesis was stimulated.*



2-amino-6-naphthol

Fig. 3.—2-amino-6-naphthol. Note that the hydroxyl group is remote from the amino group.

Bonser and associates[17-19] confirmed this concept by demonstrating that paraffin pellets impregnated with the aromatic amines were far less carcinogenic when instilled directly into the mouse bladder than when these same pellets were impregnated with the ortho-aminophenol derivatives of the aromatic amines (Fig. 4).



O-aminophenol

Fig. 4.—Ortho-aminophenol. In this basic configuration there is a benzene ring to which an amino group and a hydroxyl group, immediately adjacent to each other, are attached.

This last group of experiments completed the classical requirements for establishing the etiology of any disease. Exposure to the agent had been demonstrated. Its metabolites had been recovered from the urine of patients, and, finally, exposure of experimental animals to the agent orally or to its metabolites topically reproduced the disease.

Beta-Glucuronidase

The ortho-aminophenols related to industrial bladder cancer and those to be discussed in relation to spontaneous bladder cancer are found in the urine partly as free compounds, and partly as conjugates with sulphuric and glucuronic acids. It is conceivable that urinary aryl-sulfatase and beta-glucuronidase could convert these harmless conjugates to free and active

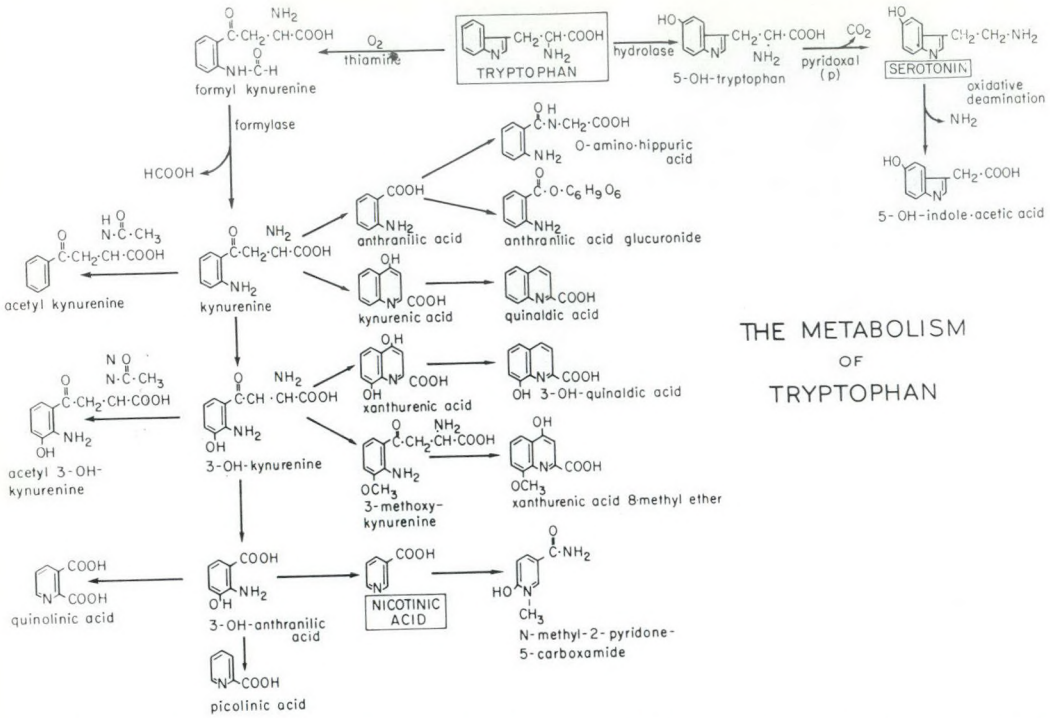


Fig. 5.—The metabolism of tryptophan. Note that all the ortho-aminophenols occur in the pathway that leads to nicotinamide via kynurenine.

carcinogens. Both enzymes were found in greater than normal amounts in the urines of patients with bladder cancer. [20-22]

However, other urinary tract diseases[22] and even surgical procedures[23] were also associated with elevations of urinary glucuronidase. Moreover, the administration of 1-4 saccharolactone, a known glucuronidase inhibitor, failed to modify the carcinogenic activity of the aromatic amines in experimental animals[24] and failed to alter the natural history of the disease in man.[25] Removal of the bladder containing tumour resulted in a return of previously elevated glucuronidase levels to normal, and it appears that the elevated urinary glucuronidase seen in bladder tumour patients is the result of tumour metabolism.[23] Even the normal bladder is a significant source of urinary glucuronidase.[26] At the present writing, the role of beta-glucuronidase is in doubt, but is by no means disproved. If this enzyme does participate in carcinogenesis, it would suggest that the tumour, through the elaboration of beta-glucuronidase, enhances its own growth.

Spontaneous Bladder Cancer

The biochemical findings in industrial bladder cancer patients led investigators to search for *endogenous* sources of ortho-aminophenols in spontaneous bladder cancer patients. A prominent source was tryptophan, an essential amino acid. Besides being incorporated into the body proteins, it is also broken down to many products (Fig. 5), such as certain ortho-aminophenols; for example 3-hydroxykynurenine, 2 amino-3-hydroxyacetophenone, and 3-hydroxyanthranilic acid. Xanthurenic acid and xanthurenic acid 8-methyl ether are also ortho-aminophenols, but in the former, the amino group, and in the latter, both the amino group and the hydroxyl group, are substituted.

Once again, direct implantation of tryptophan and its metabolites in cholesterol and paraffin pellets into the mouse bladder confirmed that the ortho-aminophenol products were carcinogenic and that 3-hydroxyanthranilic acid was the chief offender.[27] Independent investigators con-

firmed that patients with cancer of the bladder did in fact excrete larger amounts of 3-hydroxyanthranilic acid than did normal subjects.[28-30] It is an accepted principle that chemical carcinogenesis requires prolonged exposure to the carcinogen,[31] and in the specific case of bladder tumours in man this period may be as long as 15 years.[32] The metabolic pattern in these patients before the onset of tumour is not known. Abul-Fadl and Khalafallah[33] note that bilharzial infestation alone is associated with an increased urinary excretion of 3-hydroxyanthranilic acid. Perhaps in this small select group of patients we may be permitted to assume the presence of an increased amount of ortho-aminophenols in the urine which precedes the onset of tumour.

In 1962, Kerr *et al.*[34] noted that in a patient with renal cell carcinoma, the affected kidney excreted twice as much ortho-aminophenol carcinogens as the contralateral normal kidney, although, in other respects, the function was equal on the two sides. This led to the investigation of the role of the urinary tract in ortho-aminophenol production. It was observed that the normothermic perfused isolated dog's kidney was capable of metabolizing tryptophan along its carcinogenic pathway, as was an isolated human bladder containing tumour.[35] It was concluded that the urinary tract, or the urinary tract containing tumour, was a significant source of kynurenine, a metabolite which while not itself a carcinogen is nevertheless a precursor of the carcinogenic ortho-aminophenols. Although it is assumed that the liver is a major anatomic site of tryptophan metabolism, the role of other sites such as the prolific flora of the intestinal tract has not been explored fully.

In order to elucidate further the biochemical abnormality in bladder cancer patients, Kerr, Barkin and associates have used a tryptophan tolerance test. Tryptophan metabolites are determined in successive 24-hour urine collections before and after the administration of L-tryptophan. The metabolites are grouped together into the four major steps leading to nicotinamide. The basic biochemical abnormality in patients with bladder tumours appears to

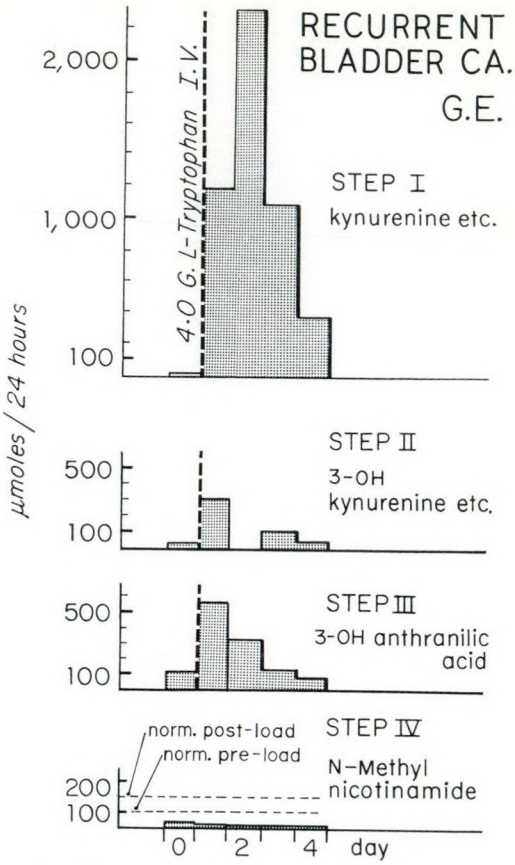


Fig. 6.—Tryptophan tolerance test in a patient with multiple recurrences of bladder tumours. The metabolites grouped together in each bar graph are indicated on the right. Following tryptophan administration there is an increased excretion of all metabolites except nicotinamide, indicating a block in the conversion of 3-OH anthranilic acid to nicotinamide.

be an inability to convert 3-hydroxyanthranilic acid to nicotinamide (Fig. 6). This results in an accumulation proximally of ortho-aminophenol as well as other metabolites of tryptophan.

Quagliariello and associates[36] reported that large doses of pyridoxine (vitamin B_6) will restore the biochemical abnormality in tryptophan metabolism seen in patients with cancer of the bladder. This has been confirmed by Brown *et al.*[30] and in our own laboratory. However, clinical trials with pyridoxine have, as yet, failed to alter the natural history of the disease in these patients.

The ultimate proof of the role of tryptophan in the genesis of spontaneous bladder

cancer would be the demonstration of these abnormalities predating the onset of bladder cancer. In order to do this one would have to measure the pattern of tryptophan metabolism in a vast number of normal young subjects and follow them up for several decades in order to determine whether an abnormal pattern is accompanied by a significant increase in the incidence of cancer of the bladder. This is neither practical nor feasible. Therefore, present lines of research are directed toward the investigation of the role of the tumour in the production of tryptophan metabolites. Patients with bladder tumour are being investigated before and after cystectomy or transurethral resection in order to determine whether the biochemical abnormality persists after the removal of the tumour. If it does, then we shall have reliable proof of a co-existing biochemical abnormality which is independent from the tumour.

SUMMARY

The investigation of industrial bladder tumours led to the observation that aromatic amines are absorbed and metabolized to their ortho-aminophenol derivatives. It is these compounds which, when excreted in the urine, come into contact with the urothelium and stimulate the onset of tumour. There is doubt concerning the importance of beta-glucuronidase in liberating the free ortho-aminophenols from the inactive conjugated forms in which they are, to a certain extent, excreted.

A search for endogenous ortho-aminophenols in relation to spontaneous bladder cancer led to the investigation of tryptophan and its metabolites. Implantation experiments confirmed that certain of its ortho-aminophenol products are carcinogenic, and these have been found in excessive amounts in patients with bladder tumour.

Although it is assumed that the liver is the chief site of tryptophan metabolism, evidence has been presented to show that the urinary tract and the urinary tract containing tumour are sources of ortho-aminophenol precursors derived from tryptophan.

Although there is considerable evidence that a derangement in the metabolism of tryptophan is the biochemical basis for carcinogenesis in the bladder, no definite conclusion can be reached until it has been demonstrated that the abnormality in tryptophan metabolism observed in these patients precedes the onset of tumour formation or, at least, that it is not the result of the tumour.

Therefore, further investigation continues into the relationship between tumour metabolism and the abnormal products of tryptophan breakdown found in patients with carcinoma of the bladder.

REFERENCES

1. REHN, L.: Blasengeschwülste bei Fuchsin-Arbeitern, *Langenbecks Arch. Kin. Chir.*, **50:** 588, 1895.
2. WIGNALL, T. H.: Incidence of disease of the bladder in workers in certain chemicals, *Brit. Med. J.*, **2:** 291, 1929.
3. BILLIARD-DUCHESNE, J. L.: Les amino tumeurs de la vessie (tumeurs dites aniliniques), *J. Urol. Méd. Chir.*, **53:** 401, 1947.
4. FERGUSON, R. S.: Symposium on aniline tumors of the bladder; introduction, *J. Urol.*, **31:** 121, 1934.
5. GREAT BRITAIN, LAWS, STATUTES, ETC.: Industrial Injuries Act, 1946, Geo. 6, His Majesty's Stationery Office, London, 1946.
6. CASE, R. A. M.: The mortality from cancer of the urinary bladder in England and Wales, *In:* Tumours of the bladder. ed ted by D. M. Wallace, E. & S. Livingstone, Ltd., London, 1959, p. 3.
7. LOCKWOOD, K.: On the etiology of bladder tumours in København-Frederiksberg; an inquiry of 369 patients and 369 controls, *Acta Path. Microbiol. Scand.*, 51: (Suppl. 145): 1, 1961.
8. MUSTACCHI, P. AND SHIMKIN, M. B.: Cancer of the bladder and infestation with Schistosoma hematobium, *J. Nat. Cancer Inst.*, **20:** 825, 1958.
9. PAMUKCU, A. M., BROWN, R. R. AND PRICE, J. M.: Trytophan metabolites in the urine of Turkish cows with urinary bladder cancer, *Cancer Res.*, 19: 321, 1959.
10. HUEPER, W. C., WILEY, F. H. AND WOLFE, H. D.: Experimental production of bladder tumors in dogs by the administration of beta-naphthylamine, *J. Industr. Hyg.*, **20:** 46, 1938.
11. BONSER, G. M. *et al.*: The carcinogenic properties of 2-amino-1-naphthol hydrochloride and its parent amine, 2-naphthylamine, *Brit. J. Cancer*, 6: 412, 1952.
12. SCOTT, W. W. AND BOYD, H. L.: Study of the carcinogenic effect of beta-naphthylamine on normal and substituted isolated sigmoid loop bladder of dogs, *J. Urol.*, **70:** 914, 1953.
13. MCDONALD, D. F. AND LUND, R. R.: The role of the urine in vesical neoplasm: I. experimental confirmation of the urogenous

theory of pathogenesis, *J. Urol.*, **71:** 560, 1954.
14. Wiley, F. H.: The metabolism of beta-naphthylamine, *J. Biol. Chem.*, **124:** 627, 1938.
15. Dobriner, K., Hofmann, K. and Rhoads, C. P.: The metabolism of beta-naphthylamine by rats, rabbits and monkeys, *Science*, **93:** 600, 1941.
16. Boyland, E. and Weigert, F.: The metabolism of carcinogenic compounds, *Brit. Med. Bull.*, **4:** 354, 1947.
17. Bonser, G. M. *et al.*: The induction of tumours of the bladder epithelium in rats by the implantation of paraffin wax pellets, *Brit. J. Cancer*, **7:** 456, 1953.
18. Bonser, G. M. *et al.*: The carcinogenic activity of 2-naphthylamine, *Brit. J. Cancer*, **10:** 533, 1956.
19. Bonser, G. M. *et al.*: Induction of epithelial neoplasms in the urinary bladder of the dog by intravesical injection of a chemical carcinogen, *J. Path. Bact.*, 68: 561, 1954.
20. Boyland, E., Wallace, D. M. and Williams, D. C.: The activity of the enzymes sulphatase and beta-glucuronidase in the urine serum and bladder tissue, *Brit. J. Cancer*, **9:** 62, 1955.
21. Boyland, E., Gasson, J. E. and Williams, D. C.: Enzyme activity in relation to cancer; the urinary beta-glucuronidase activity of patients suffering from malignant disease, *Brit. J. Cancer*, **11:** 120, 1957.
22. Melicow, M. M., Uson, A. C. and Lipton, R.: Beta-glucuronidase activity in the urine of patients with bladder cancer and other conditions, *J. Urol.*, **86:** 89, 1961.
23. Kerr, W. K. *et al.*: Biochemical factors in the etiology of carcinoma of the bladder, *Cancer*, **16:** 633, 1963.
24. Bradley, H. J., Jr.: The effect of beta-glucuronidase inhibitor and methylcholantrene on the induction of bladder tumors in rats, *J. Urol.*, **88:** 626. 1962.
25. Boyland, E.: The biochemistry of bladder cancer, Charles C Thomas, Springfield, Ill., 1963, p. 73.
26. Kerr, W. K. *et al.*: Observations on the movement of ions and water across the wall of the human bladder and ureter, *J. Urol.*, **89:** 812, 1963.
27. Allen, M. J. *et al.*: Cancer of the urinary bladder induced in mice with metabolites of the aromatic amines and tryptophan, *Brit. J. Cancer*, **11:** 212, 1957.
28. Boyland, E. and Williams, D. C.: The metabolism of tryptophan, 2. metabolism of tryptophan in patients suffering from cancer of the bladder, *Biochem. J.*, **64:** 578, 1956.
29. Tompsett, S. L.: The determination in urine of some metabolites of tryptophan: kynurenine, anthranilic acid, and 3-hydroxy anthranilic acid and reference to the presence of o-aminophenol in urine, *Clin. Chim. Acta*, **4:** 411, 1959.
30. Brown, R. R. *et al.*: The metabolism of tryptophan in patients with bladder cancer, *Acta Un. Int. Cancr.*, **16:** 299, 1960.
31. Yamagawa, K. and Ichikawa, K.: Experimentelle Studie über die Pathogenese der Epithelialgeschwülste, *Mitt. a d. Med. Fakult. a.k. Tokyo*, **15:** 295, 1915.
32. Scott, T. S.: The incidence of bladder tumours in a dyestuffs factory, *Brit. J. Industr. Med.*, **9:** 127, 1952.
33. Abul-Fadl, M. A. M. and Khalafallah, A. S.: Studies on the urinary excretion of certain tryptophan metabolites in bilharziasis and its possible relation to bladder cancer in Egypt, *Brit. J. Cancer*, **15:** 479, 1961.
34. Kerr, W. K. *et al.*: A hypernephroma associated with elevated levels of bladder carcinogens in the urine; case report, *Brit. J. Urol.*, **35:** 263, 1963.
35. Kerr, W. K., Barkin, M. and Menczyk, Z.: Biochemical factors in the etiology of cancer of the bladder: II. the metabolism of tryptophan along its carcinogenic pathway in the urinary tract. To be published.
36. Quagliariello, E. *et al.*: Tryptophan-nicotinic acid metabolism in patients with tumours of the bladder: changes in the excretory products after treatment with nicotinamide and vitamin B_6, *Brit. J. Cancer*, **15:** 367, 1961.

Résumé

Il y a de nombreuses raisons qui ont fait suspecter une relation possible entre le cancer de la vessie et divers produits chimiques. Ainsi, en 1898 déjà, Rehn avait noté trois cas de ce genre chez un groupe de 45 ouvriers employés dans la fabrication de colorants synthétiques. On parla même alors de "cancer des ouvriers de l'aniline". De nos jours, on s'accorde à reconnaître que effectivement, les tumeurs de la vessie sont un danger professionnel, non seulement dans l'industrie des colorants mais aussi dans certaines branches de l'industrie du caoutchouc. En outre, dans les pays où la bilharziose sévit, on note une nette augmentation de ces cancers. Il semble donc qu'on puisse leur trouver un facteur étiologique commun, peut-être une substance chimique. Expérimentalement, on a commencé à étudier l'action des amines aromatiques. L'aniline est cancérigène, mais certains composés intermédiaires le sont également. C'est ainsi qu'on a pu provoquer le cancer vésical avec 80% d'incidence, chez des chiens recevant oralement de la 2-naphtylamine pendant deux années; de plus, si l'on provoque une dérivation du flot urinaire vers le côlon sigmoïde, la vessie se trouve épargnée. Il est donc certain qu'il s'agit là d'une action directe de la drogue (ou d'un de ses produits de dégradation) sur l'épithélium vésical. La 2-naphtylamine n'est pas excrétée telle quelle, mais transformée en 2-aminonaphtol. On a avancé que cette transformation pourrait peut-être s'effectuer sous l'influence de la beta-glucuronidase, mais la question de savoir si cette enzyme est produite par la muqueuse vésicale ou par la tumeur n'est pas clarifiée. Les auteurs ont cherché si de tels ortho-aminophénols ne seraient pas d'origine endogène, et ceci les a mené à étudier en détail le métabolisme du tryptophane et de ses métabolites. Le siège principal de ce métabolisme est le foie, mais le tractus urinaire semble y participer également à l'état normal. En conclusion, il y a, selon les auteurs, de bonnes raisons de penser que les troubles du métabolisme du tryptophane sont reliés à la carcinogénèse vésicale, ceci ne pourra être définitivement prouvé que lorsqu'on pourra démontrer que ces troubles précèdent réellement l'apparition de la tumeur.

CASE REPORTS

CONGENITAL SOLITARY KIDNEY WITH CROSSED ECTOPIA*

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Crossed renal ectopia involving a congenital solitary kidney is an extremely rare anomaly of the urinary tract. Only eight such cases have been reported in the urological literature to date. In a series of 364 cases of renal agenesis and dysgenesis from the Armed Forces Institute of Pathology, Ashley and Mostofi[1] reported 232 cases of unilateral agenesis and did not encounter a single case of crossed ectopia among them. Crossed ectopia itself is an unusual anomaly. Abeshouse[10] was able to collect 337 cases from the literature, and added four of his own. In the majority of these, the two kidneys are fused. Wilmer[2] found the incidence of unfused crossed renal ectopia to be 14.5% of all forms of crossed ectopia. The case of crossed ectopia of a solitary kidney presented here is believed to be the ninth in the literature, and the first having an associated retrocaval ureter.

Case Report

J. McM., a 25-year-old white woman, was admitted to the Ottawa Civic Hospital on July 3, 1963. She had been born after a normal full-term delivery and had had no significant illnesses until the age of 9. At that time a left inguinal herniorrhaphy was performed, when it was recorded that a structure encountered was thought to be the left ovary and was returned to the peritoneal cavity. At age 13, she was seen by her family phsyician because of delayed menarche. She was referred to a gynecologist who discovered that the vagina and uterus were absent. At age 19, she was admitted to hospital in British Columbia with an acute urinary tract infection. An intravenous pyelogram showed a solitary kidney on the right side with some degree of hydronephrosis. The infection responded to treatment with antibacterial drugs. No further investigation was carried out at that time.

After another acute infection at the age of 20, she was sent to Vancouver where a cystoscopy and retrograde pyelograms were carried out. It was noted that there was a solitary kidney with crossed ectopia and some obstruction at the ureterovesical junction. An attempt was made to dilate the ureterovesical junction endoscopically. The possibility of plastic surgery to construct a vagina was considered, but the procedure was deferred. Since that time she has not had any further urological complaints. She was married at the age of 22 and despite her genital anomalies, has been happy and well adjusted. Before her referral for urological assessment in June of 1963, she had undergone a medical examination required before adopting a child, and was found to have mild pyuria and proteinuria. She was then admitted to hospital for complete urological investigation.

General physical examination was unremarkable aside from the genital tract. She was a well-developed young woman with normal body build and secondary sex characteristics. Blood pressure was 120/78 mm. Hg. A kidney was felt in the right renal fossa. It was not palpably enlarged and was not tender. There were no other masses or areas of tenderness in the abdomen. Pelvic examination was deferred.

Urinalysis disclosed an occasional white blood cell, no casts and a one-plus proteinuria. The leukocyte count was 8100/c.mm. with normal differential. Hemoglobin was 12 g., hematocrit 37%, sedimentation rate 15 mm. in 1 hour, and the total protein 5.7 g. with normal albumin/globulin ratio and electrophoretic pattern. Blood urea nitrogen (BUN) was 18 mg. % and creatinine 1.1 mg. %. An intravenous pyelogram was carried out which showed a solitary functioning left kidney with crossed ectopia. There was a moderate dilatation of the ureter and pelvis, suggesting obstruction at the ureterovesical junction and the possibility of a retrocaval ureter. A second renal outline could not be seen. Cystoscopy revealed a hemitrigone and a normal left ureteral orifice. There was no evidence of urethral or

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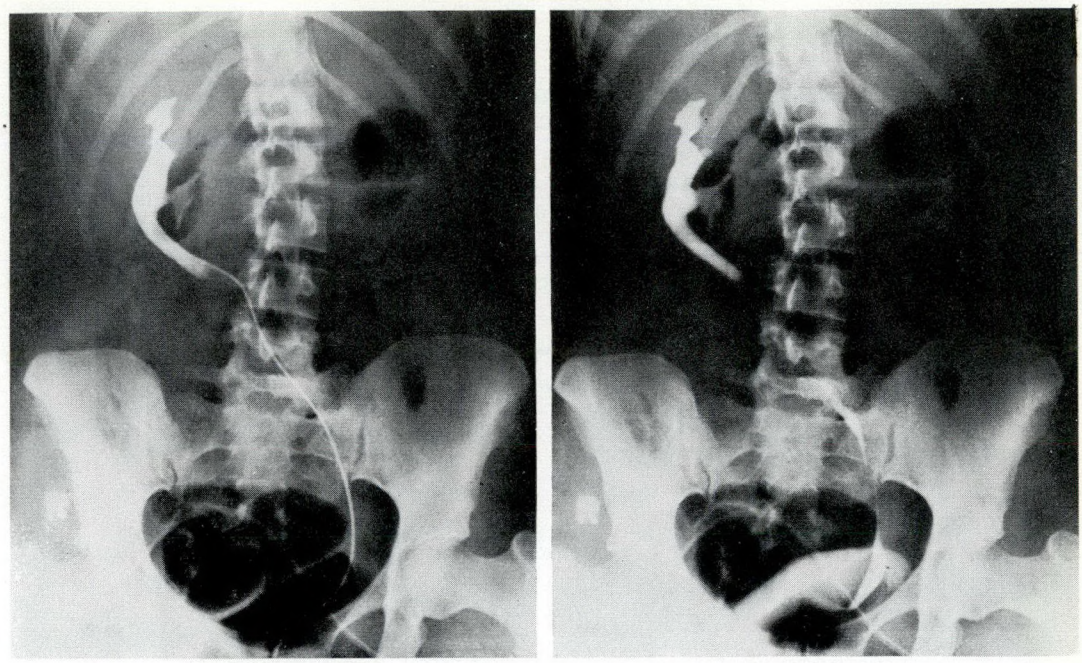

Fig. 1.—Retrograde pyelogram before operation. Solitary left kidney with crossed ectopia and malrotation is shown. (a) Obstruction due to the retrocaval course of the ureter can be seen. (b) As the catheter is withdrawn, the dilatation of the lower ureter became evident.

bladder neck obstruction. A bladder specimen of urine was taken for culture and no growth was obtained. A No. 5 F. ureteral catheter was easily passed up to the left renal pelvis and a retrograde pyelogram was obtained. These films confirmed the diagnosis of crossed ectopia of a solitary kidney with obstruction at the ureterovesical junction (Fig. 1). Again the possibility of a retrocaval ureter was suggested. The labia were well formed. The urethral orifice was rather patulous. The vagina was represented by a shallow depression posterior to the urethral meatus. On rectal examination under anesthesia the uterus could not be felt, but a normal-sized ovary was easily palpable on each side.

A decision was made to explore the ureter with a view to reimplanting it in the bladder to relieve the ureterovesical obstruction. The peritoneal cavity was opened through a midline suprapubic incision which was extended superiorly to a point above the umbilicus. The uterus was absent. The ovaries were present and normal in size. There were rudimentary fallopian tubes on each side. These consisted of the ampulla and fimbriae which were slightly smaller than normal. The tubes then tapered medially to the fine cord-like structures which disappeared after about 5 cm. There was no right kidney. The left kidney lay in the right renal fossa and its ureter crossed the midline to enter the left side of the bladder. The ureter was considerably more dilated than had been apparent in the pyelograms. The posterior parietal peritoneum was incised and the retrocaval course of the ureter became apparent. Since both ureterovesical and retrocaval obstructions required correction, the ureter was transected where it entered the bladder, dissected off the posterior wall of the inferior vena cava and drawn proximally from under the vena cava, so that it lay to the right side of the great vessels. A retroperitoneal tunnel was made down to the right posterolateral wall of the bladder and the ureter placed in it. All peritoneal openings were then closed. Working extraperitoneally and through the bladder, the ureter was reimplanted on the right posterolateral wall of the bladder. An oblique muscular and submucosal tunnel was made and the cut edge of the ureteral wall was everted to form a cuff, after about 5 cm. of redundant ureter had been excised. The bladder was closed in two layers and drained with an indwelling urethral catheter. A Penrose drain was left in the retroperitoneal space and brought out through the suprapubic incision which was closed in layers.

Her postoperative course was satisfactory despite a low-grade fever which lasted for

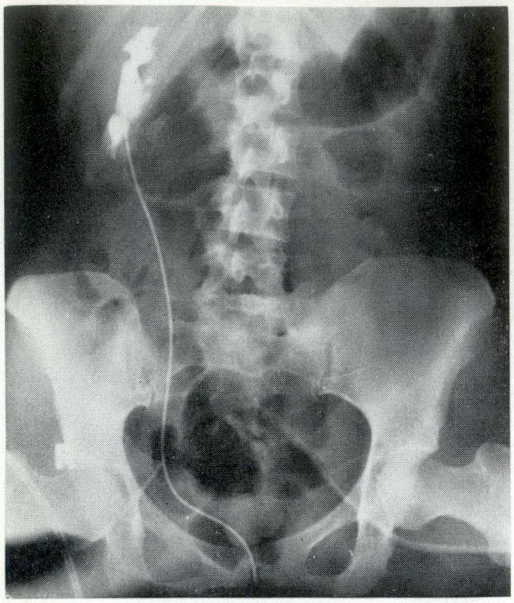

Fig. 2.—Retrograde pyelogram taken in the early postoperative period. The new course of the reimplanted ureter is seen. The ureter has not been filled with dye.

one week. This was attributed to urinary tract infection, although there was no direct evidence to support this. Antibiotic therapy was instituted and the fever gradually subsided. Repeat urine cultures had shown no growth. Postoperatively the BUN was 18 mg. % and urine output was normal. The Penrose drain was removed in one week and the catheter in 12 days. At that time cystoscopy and retrograde pyelograms were repeated. The nipple of the reimplanted ureter was covered with a loose flocculant exudate which made its viability difficult to assess. However, an efflux of clear urine was noted. A ureteral catheter was easily introduced. These early films showed the new course of the ureter and the degree of dilatation to be about the same (Fig. 2). She was discharged from hospital afebrile, voiding freely and without discomfort.

Discussion

Congenital solitary kidney is an uncommon anomaly. In 51,880 autopsies, Campbell[3] found 94 cases of renal agenesis, a ratio of 1:552. He noted that this abnormality was frequently accompanied by anomalies of the lower urinary tract or of other systems. Shumacker[4] collected 28 cases of unilateral renal agenesis accompanied by true unicornuate uterus and other anomalies of the female genital tract, such as isolateral kidney and ovary, round ligament, broad ligament, bicornuate, septate, solid or arcuate uterus, double vagina and other malformations. Of the anomalies of position involving the upper urinary tract, crossed ectopia is probably the least common. In the majority of these (85.5%) the two kidneys are present in a fused form, the remainder being unfused. Ashley and Mostofi[1] reviewed 245,000 autopsy protocols taken from the Armed Forces Institute of Pathology in which they found eight cases of crossed renal ectopia, all of the fused type. There were no cases of solitary crossed renal ectopia. Crossed ectopia involving a congenital solitary kidney is exceedingly rare, only eight having appeared in the literature before this report.[5-9] In all but two of these, there have been associated anomalies involving the genital tract and this has been true with the present case as well. In fact, it has been our experience in this hospital that in all cases of congenital solitary kidney, where there has been an absence of the trigone on the side involved, anomalies of the genital tract have been present.

There is no general agreement as to whether the ureter alone crosses the midline to unite with the metanephric tubules of the opposite side, or whether the kidney and ureter cross together. The latter is perhaps more widely accepted.

Most of the cases to date have presented with upper urinary tract obstruction, infection or both. In the present case there was a past history of pyelonephritis, but no evidence of active infection was obtained during our examination. The cause of the ureterovesical obstruction was not apparent. Bladder function was normal and pathological examination of the excised lower ureteral segment was unremarkable. However, the hydroureter and delayed emptying on intravenous pyelography were quite definite. Had this been the only site of obstruction, a simple reimplantation likely would have been our approach to the problem. With a second point of obstruction due to the retrocaval course of the ureter, it was necessary to attempt

to overcome both impediments and so the operation described above was performed. To date she remains well and free from symptoms referable to the urinary tract.

Summary

The ninth case of crossed renal ectopia with a solitary kidney is reported. Management of the associated ureterovesical and retrocaval obstruction is described.

References

1. Ashley, D. J. B. and Mostofi, F. K.: Renal agenesis and dysgenesis, *J. Urol.*, **83:** 211, 1960.
2. Wilmer, H. A.: Unilateral fused kidney: report of five cases and review of the literature, *J. Urol.*, **40:** 551, 1938.
3. Campbell, M. F., editor: Urology, Vol. 1, W. B. Saunders Company, Philadelphia, 1954, p. 240.
4. Shumacker, H. B., Jr.: Congenital anomalies of the genitalia associated with unilateral renal agenesis, with particular reference to true unicornuate uterus; report of cases and review of literature, *Arch. Surg.*, **37:** 586, 1938.
5. Magri, J.: Solitary crossed ectopic kidney, *Brit. J. Urol.*, **33:** 152, 1961.
6. Day, R. V.: Some rare anomalies of the kidney and ureter with case reports, *Surg. Gynec. Obstet.*, **38:** 51, 1924.
7. Alexander, J. C., King, K. B. and Fromm, C. S.: Congenital solitary kidney with crossed ureter, *J. Urol.*, **64:** 230, 1950.
8. Brancato, G.: Rene solitario in distopia crociata, *Chirurgia (Milano)*, **9:** 388, 1954.
9. Purpon, I.: Crossed renal ectopy with solitary kidney; a review of the literature, *J. Urol.*, **90:** 13, 1963.
10. Abeshouse, B. S.: Crossed ectopia with fusion: review of literature and report of four cases, *Amer. J. Surg.*, **73:** 658, 1947.

Résumé

L'ectopie croisée d'un rein unique est un status très rare dont on ne trouve que huit cas décrits dans la littérature; les auteurs en rapportent ici un neuvième. Il s'agit d'une femme de 25 ans, admise le 3 juillet 1963 au "Ottawa Civic Hospital". Dans ses antécédents, on trouve une histoire de hernie inguinale gauche opérée à l'âge de 9 ans, dont le sac contenait une structure curieuse que le chirurgien pensa alors être l'ovaire. A l'âge de 13 ans, comme elle n'avait pas de règles, elle fut examinée par un gynécologiste qui découvrit une absence de vagin et d'utérus. A l'âge de 19 ans, elle souffrit d'une crise infectieuse urinaire aiguë et un pyélogramme intraveineux qui fut pratiqué montra un rein unique droit avec un léger degré d'hydronéphrose; cependant, l'affection répondit bien au traitement antiseptique. Une année plus tard, on pratiqua une cystoscopie et un pyélogramme par voie rétrograde, qui fit découvrir un rein unique en position croisée, ce qui causait un certain degré d'obstruction à la jonction urétéro-vésicale. Lors de l'admission dans le service des auteurs, la malade souffrait de pyurie et d'albuminurie; elle était dans un état général satisfaisant et normalement développée, à part ses anomalies génitales. L'analyse des urines permit de trouver une albuminurie modérée et quelques leucocytes. Une laparotomie fut faite: l'utérus était absent, mais les ovaires étaient normaux; il existait aussi deux trompes utérines rudimentaires. Il n'y avait pas de rein à droite; le rein gauche était situé dans la fosse rénale droite, et son uretère traversait la ligne médiane pour s'insérer sur la moitié gauche de la vessie. Par une incision rétropéritonéale, on put disséquer l'uretère, qui était passablement dilaté, et passait en arrière de la veine cave inférieure. On le sectionna à son insertion vésicale et le ramena sur le côté droit des gros vaisseaux; un tunnel rétropéritonéal fut pratiqué dans la paroi postéro-latérale droite de la vessie, de façon à le ré-insérer. La vessie fut suturée en deux plans et toutes les incisions péritonéales soigneusement refermées. Un drainage fut laissé en place. Les suites opératoires furent satisfaisantes; le drain fut enlevé au bout d'une semaine; les contrôles bactériologiques des urines se révèlèrent stériles. La malade put être renvoyée à domicile.

AORTIC ARCH ANOMALY WITH AORTIC DIVERTICULUM CAUSING ESOPHAGEAL OBSTRUCTION IN THE ADULT

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SINCE the first successful attack on vascular compression of the trachea and esophagus by Gross[1] in 1945, the numerous anomalies resulting from faulty development of the fourth branchial arches and their surgical significance have been gradually clarified. A review of this fascinating subject has recently been published from this clinic.[2] Except in childhood, vascular compression of the esophagus or trachea, or both, has been generally considered a medical rarity, although the first case published in 1789 by Bayford[3] was that of a woman who died of starvation as a result of this malformation.

Diverticula of the aorta in association with aortic arch anomalies have been reported in adults. Arkin[4, 5] in 1926 and again in 1936 reported autopsy findings in cases of double aortic arch, partial stenosis of the left arch and diverticulum formation at the left dorsal root. Kommerell[6] in 1936 and Roche, Steinberg and Robb[7] in 1941 have described diverticula of the aorta at the origin of an anomalous subclavian artery. Brombart[8] has emphasized the frequent association of a diverticulum at the root of the descending aorta which displaced the esophagus anteriorly in 12 out of 17 cases of right-sided aortic arch (Brombart's Type II). It has generally been accepted that diverticula which occur at the same level represent vestiges of the left or right embryonic fourth branchial arch. The mature arch configuration is said to be completed between the third and sixth week of embryonic life. Ordinarily, the left fourth arch persists as the aortic arch. When the right arch assumes this major contribution, the left fourth branchial arch may persist as a complete though smaller vessel, as a band, or as a diverticulum at the level of the left dorsal root.

Blackford[9] and Arkin[5] postulated that when stenosis of the left aortic isthmus occurs before regression of the right branchial arch, the latter persists with a varying degree of retention of the left arch, as described above. It may be significant, however, that despite extensive experience with arch anomalies in childhood, Gross[10] and others[11-13] make no mention of aortic diverticula or that the effect of increasing age on the aortic wall together with a traction effect exerted by attached vestigial bands or anomalous vessels may contribute in adults to the formation of aortic diverticula and ultimately to obstruction.

In those cases in which a ductus Botalli communicates with the retained left component arch of a doubled aortic arch, a functional requirement for the left arch remains until birth. With closure of the ductus and subsequent regression of the

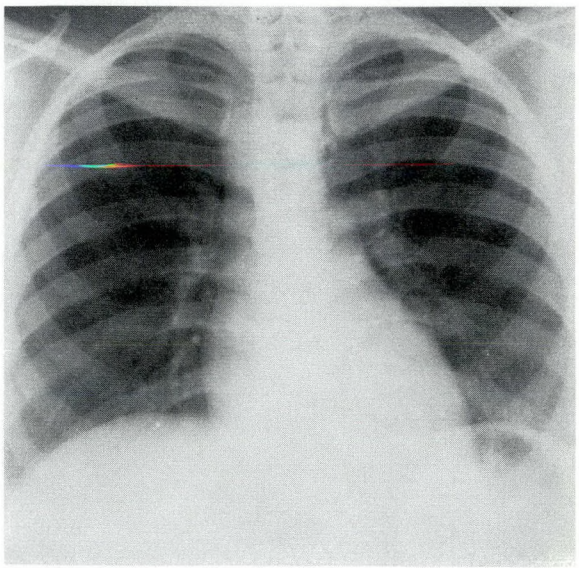

Fig. 1.—Routine posteroanterior radiograph of the chest showing normal lung fields. The heart is not enlarged. The aortic knob is absent on the left and there is evidence of an aortic knob or arch projecting to the right at the level of the fourth and fifth thoracic segments.

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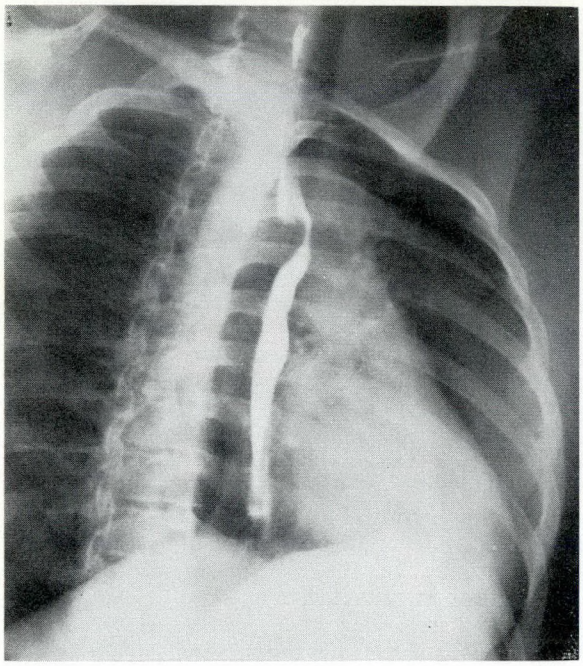

Fig. 2.—Right anterior oblique film (14 x 17) shows deviation of the upper third of the esophagus to the left with a sharp indentation of the posterior right lateral aspect of the esophagus.

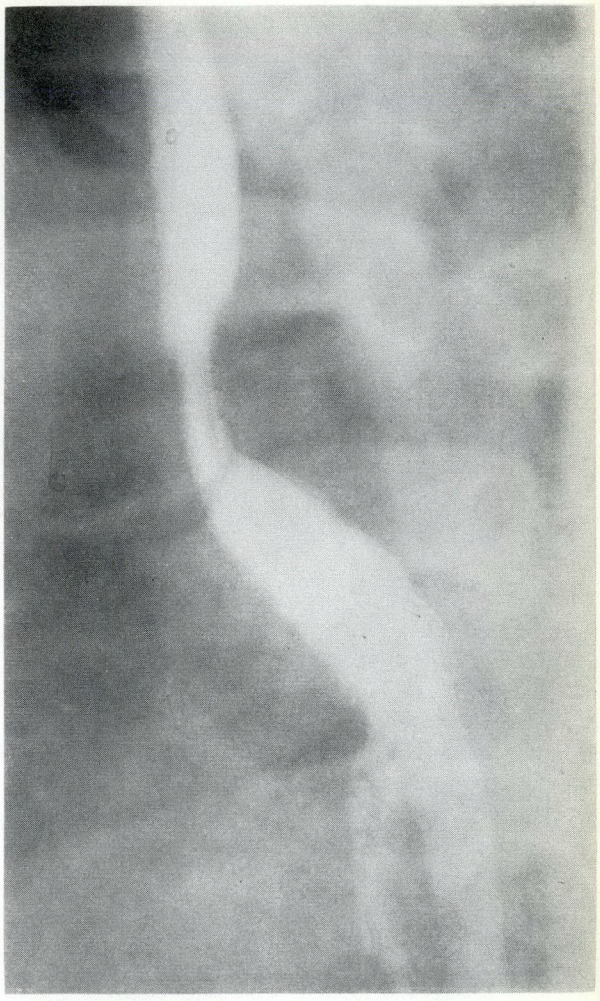

Fig. 3.—Spot film in left anterior oblique position shows anterior deviation of the esophagus above the level of the bifurcation of the trachea.

distal left arch, continued and increasing traction may be exerted at the point of attachment to the growing aorta. Diverticula of the aorta formed in this manner may not reach significant size until adult life.

It has long been known that changes in position and contour of the esophagus occur secondarily to vascular anomalies. It is also well known that these changes may be detected by fluoroscopy and radiography of the barium-filled esophagus. Probably the most common and best known of these is the oblique indentation of the upper part of the esophagus produced by an aberrant right subclavian artery. It is also well known that angiocardiography will frequently outline such anomalies with precision. Simultaneous combination of the two methods, however, provides an extraordinarily graphic demonstration of the relationship of a vascular anomaly to the esophageal defect. Since it is the practice at this institution and in most others to perform angiocardiography without general anesthesia, it is a simple matter for a co-operative patient to swallow thick barium paste immediately before the contrast medium is injected. Usually barium will remain in the esophagus for the duration of the angiocardiogram. It has been our experience that this technique may aid in the precise definition of the anomaly responsible for the esophageal defect and the associated dysphagia.

The following case is described because it is an unusual form of esophageal obstruction and illustrates the application of new developments in contrast radiography. It is to be expected that with wider application of modern diagnostic techniques and with increased clinical awareness of these

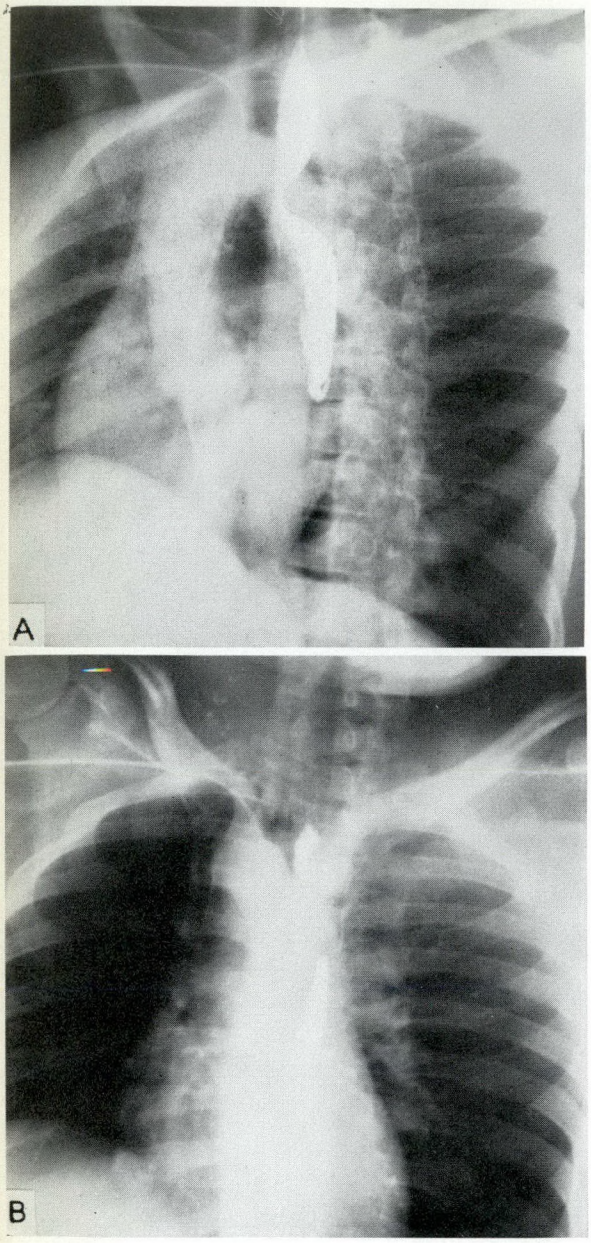

Fig. 4.—Angiocardiogram. **A.** A No. 8 N.I.H. catheter has been passed into the left ventricle. Film made in full right posterior oblique position shows good visualization of the aorta with deviation of the esophagus at the level of the proximal descending portion of the aorta. We believe that this was produced by diverticulum. **B.** Film made with minimal right posterior oblique rotation demonstrates a right aortic arch. Note bulge of the aorta in the proximal descending portion on the left lateral aspect, corresponding to the defect in the column of barium. This represents the defect produced by the diverticulum of the aorta. A swallow of thick barium paste had been given before each injection.

anomalies, these obscure but significant causes of dysphagia in the adult will be brought to light and treated satisfactorily. This case also suggests a possible etiology of dysphagia lusoria appearing at a period late in childhood or in adult life; namely, the development of a traction diverticulum of the aorta with increasing esophageal compression.

Case Report

A 28-year-old Negro woman was first seen at the Lahey Clinic because of fatigue after an episode of influenza. She also described a sensation of food "sticking" in her throat over the 18-month period before her clinic visit. This difficulty in swallowing had become very troublesome during the last few weeks of this period. A posteroanterior radiograph of the chest revealed an abnormal silhouette (Fig. 1). An upper gastrointestinal x-ray examination with barium revealed a filling defect at the junction of the middle and upper thirds of the esophagus (Figs. 2 and 3).

On admission to the hospital on December 11, 1962, the patient was moderately obese and in no distress. Physical findings were within normal limits. Esophagoscopy was performed and revealed a narrowing of the esophagus at 23 cm. associated with a submucosal ridge pulsating posteriorly.

A transbrachial aortogram using a No. 8 National Institutes of Health (N.I.H.) catheter was obtained simultaneously with an esophagogram. These films revealed an anomalous aortic arch associated with esophageal obstruction (Fig. 4).

On December 19, 1962, utilizing a left lateral approach, thoracotomy was carried out. At operation the aorta was found to descend just to the left of the midline. A normally developed right aortic arch was present. However, the esophagus and trachea were anomalously placed to its left. There was a left innominate artery which was retracted downward into the exposed posterior mediastinum by a narrow contracted vessel. At the point of attachment of this small vessel to the descending aorta, a diverticulum, measuring 3 cm. x 3 cm., was present. This diverticulum appeared to be pulled onto the posterolateral surface of the esophagus (Figs. 5 and 6). A long, taut ligamentum arteriosum joined the above vessel in its midportion. It was the surgeon's impression that the ligamentum arteriosum and a distal left arch had atrophied together and, with shortening and traction,

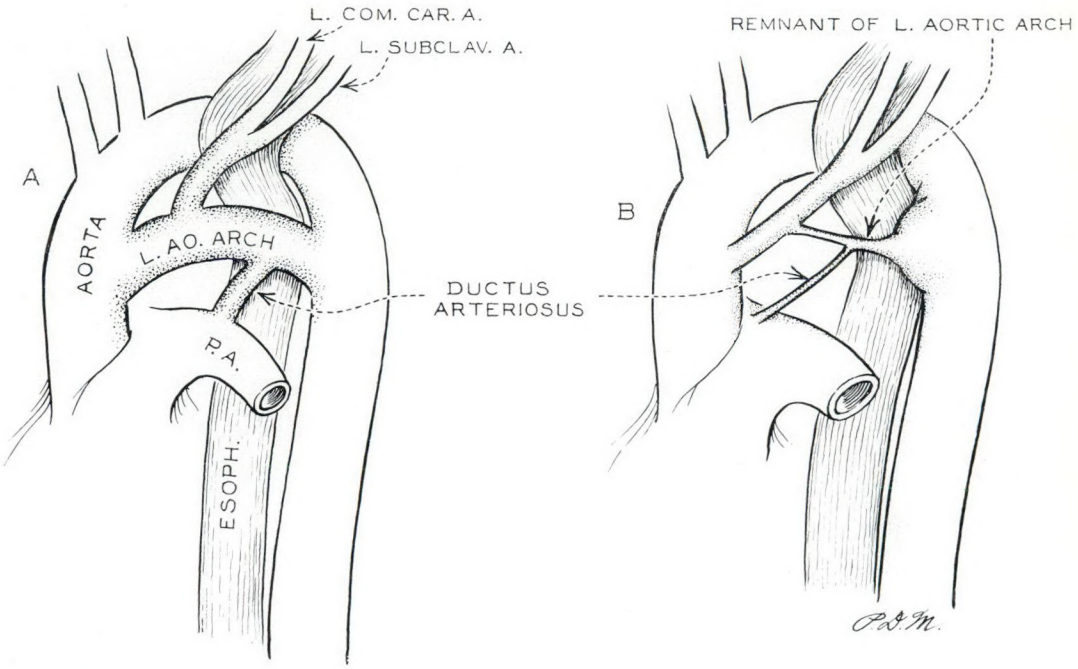

Fig. 5.—A. Common type of dyphagia lusoria due to left innominate or subclavian artery had double aortic arch. **B.** Diagrammatic representation of finding in case reported.

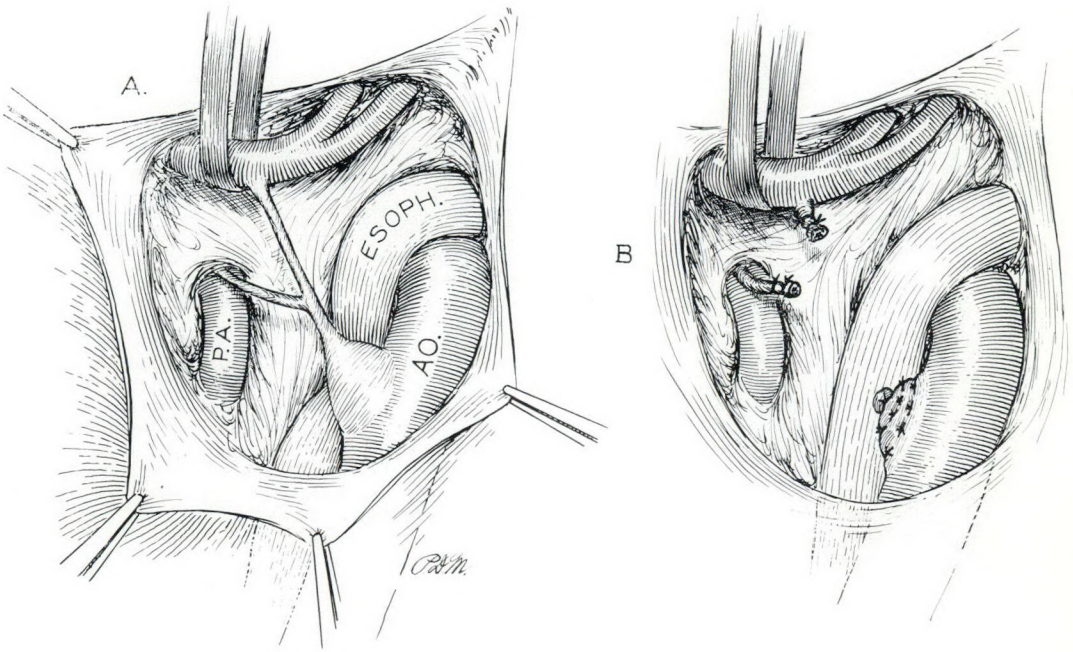

Fig. 6.—A. Artist's drawing of actual findings as seen at operation. Attention is drawn to the possible part played by an enlarging diverticulum in older patients. **B.** The completed operation.

had produced a diverticulum of the aorta. This diverticulum rather than the vascular ring produced the esophageal obstruction but without tracheal compression.

The vestigial distal left arch and the ligamentum arteriosum were divided. The aortic diverticulum was clamped at its broad base and oversewn. The esophagus was mobilized and found to be free.

The patient's postoperative course was smooth and at the time of her discharge nine days after thoracotomy, she enjoyed standard hospital meals without difficulty.

Conclusions

A case of vestigial left aortic arch with esophageal compression is presented with appropriate drawings and angiograms. The simultaneous use of a thick barium paste esophagogram and intra-aortic contrast study is described.

A possible explanation for the late development of clinical symptoms is offered.

References

1. Gross, R. E.: Surgical relief for tracheal obstruction from vascular ring, *New Eng. J. Med.*, **233:** 586, 1945.
2. Watkins, E., Jr. and Hering, A. C.: Compression of the trachea and esophagus by anomalous great vessels: diagnosis and treatment, 1761-1961, *Surg. Clin. N. Amer.*, **41:** 821, 1961.
3. Bayford, D.: An account of a singular case of obstructed deglutition, *In*: Memoirs of the Medical Society of London, Vol. 2, Charles Dilly, London, 1789, p. 271.
4. Arkin, A.: Total Persistenz des rechten Aortenbogens im Röntgenbild, *Wien. Arch. Inn. Med.*, **12:** 385, 1926.
5. Arkin, A.: Double aortic arch with total persistence of the right and isthmus stenosis of the left arch: a new clinical and x-ray picture; report of six cases in adults, *Amer. Heart J.*, **11:** 444, 1936.
6. Kommerell, B.: Verlagerung des Oesophagus durch eine abnorm verlaufende Arteria subclavia dextra (Arteria lusoria), *Fortschr. Roentgenstr.*, **54:** 590, 1936.
7. Roche, U. J., Steinberg, I. and Robb, G. P.: Right-sided aorta with descending aorta simulating aneurysm, *Arch. Intern. Med. (Chicago)*, **67:** 995, 1941.
8. Brombart, M.: La radiologie clinique de l'œsophage, Masson & Cie, Paris, 1956.
9. Blackford, L. M.: Coarctation of the aorta, *Arch. Intern. Med. (Chicago)*, **41:** 702, 1928.
10. Gross, R. E.: The surgery of infancy and childhood: its principles and techniques, W. B. Saunders Company, Philadelphia, 1953.
11. Blumenthal, S. and Ravitch, M. M.: Seminar on aortic vascular rings and other anomalies of the aortic arch, *Pediatrics*, **20:** 896, 1957.
12. Lasher, E. P.: Types of tracheal and esophageal constriction due to arterial anomalies of the aortic arch, with suggestions as to treatment, *Amer. J. Surg.*, **96:** 228, 1958.
13. Taussig, H. B.: Congenital malformations of the heart, The Commonwealth Fund, London, 1947.

Résumé

Histoire d'un cas.—Une femme de race noire, âgée de 28 ans, est vue à la clinique Lahey (Boston, Mass.) pour fatigue générale suivant un épisode grippal. Elle se plaint aussi d'un léger degré de dysphagie, existant depuis 18 mois. Effectivement, un examen baryté, montre un défaut de remplissage au niveau de la jonction du tiers supérieur et du tiers moyen de l'œsophage. Elle est alors hospitalisée en décembre 1962. A l'examen général, elle présente une obésité moyenne, mais rien d'anormal. L'œsophagoscopie montre une stricture siégeant à 23 cm. de la bouche. On pratique un aortogramme simultané avec un œsophagogramme; on met ainsi en évidence un arc aortique anormal comprimant l'œsophage. Une thoracotomie gauche est faite: l'aorte descend à gauche de la ligne médiane; l'arc aortique droit est présent et normalement développé; l'œsophage et la trachée sont anormalement placés sur sa gauche; enfin, il existe une artère innominnée avec un diverticule rélié à une formation ligamentaire (ligament artériel) provoquant la compression œsophagienne. Ces structures sont libérées et sectionnées et le diverticule excisé. Les suites opératoires furent très satisfaisantes, et la malade put être renvoyée à domicile neuf jours plus tard. Les auteurs résument les données embryologiques de ce problème. Diverses anomalies peuvent provoquer ce syndrome de compression œsophagienne. Les anomalies œsophagiennes, sont d'une façon générale, secondaires aux anomalies vasculaires. Un diagnostic exact est important. Celui-ci peut être grandement facilité par la combinaison simultanée de l'angiogramme et de l'œsophagogramme; l'anesthésie générale n'est pas nécessaire et on demande simplement au malade d'avaler une gorgée de bouillie barytée juste avant d'injecter le liquide de contraste vasculaire. Des images très précises peuvent ainsi être obtenues.

ESOPHAGEAL DUPLICATION PRESENTING AS A "GOITRE" IN A 64-YEAR-OLD WOMAN

I. H. KOVEN, B.A., M.D., C.M., F.R.C.S.[C], F.A.C.S.* and
M. I. STEINHARDT, M.A., M.D.,† *Toronto*

THE entity, esophageal cyst, has been well documented in the literature. Most cases reported are found in infancy or childhood, and represent a congenital anomaly which can occur anywhere in the mediastinum. The clinical manifestations associated with this anomaly depend on its size and the site where it occurs. In many cases the presenting symptoms are associated with the pressure effects secondary to the esophageal cyst.

Since in the literature most cases are discovered in the younger age groups, the finding of such an anomaly presenting clinically for the first time in a 64-year-old woman is considered worthy of report.

CASE REPORT

Mrs. T.C., a 64-year-old woman, was in good general health until three months before her admission to hospital. At that time, after an episode of viral upper respiratory infection, she began to be bothered by increasing dyspnea. This was worse at night in the supine position, and also during the day if she changed position rapidly. She also noted an associated slight dysphagia, particularly to solid and semi-solid foods. The dyspnea continued to increase in severity until April 2, 1961, when she was admitted to hospital because of marked shortness of breath and an audible stridor.

The pertinent point in her past history was that she had been told by her mother that at the age of five she had had a "goitre", and she had noted a swelling in the anterior part of her neck since that time. This had become progressively larger over the years.

On admission to hospital, she was in some respiratory distress. She was of stocky build and slightly obese. She had noted a weight loss of approximately 3 lb. to 4 lb. in the two weeks before admission. There was no associated heat intolerance, tremor, nervousness or diarrhea. She had had no previous medical treatment for goitre.

The pertinent findings on physical examination were confined to the neck, where there was a large obvious "goitre" present, more to the right of the midline and disappearing behind the sternum. The trachea was shifted to the left, and the mass moved on swallowing. There was no audible bruit. The chest was clear to auscultation and percussion, except for an audible inspiratory stridor. Examination of the ear, nose and throat was negative. The vocal cords moved equally. Examination of the tongue was negative. The blood pressure was 140/80 mm. Hg and the pulse was 80 per minute with a regular rhythm.

Laboratory Investigations

The pertinent findings were a blood sugar of 110 mg. %; serum proteins, 7.36 g. %; albumin, 4.04 and globulin, 3.32; the A/G ratio, 1:2; and protein-bound iodine, 7.4 mg. Blood Wassermann was negative. The venous pressure was reported as 230 mm. of water. The electrocardiogram was within normal limits, and on pulmonary function studies the vital capacity was within normal limits.

Radiographic examination revealed the presence of a large retrosternal mass in the upper mediastinum displacing the trachea towards the left and somewhat anteriorly (Fig. 1). A barium swallow was carried out and again it was noted that there was a large retrosternal mass present on the right side; it displaced the trachea to the left, and the esophagus was displaced slightly anteriorly and to the left as well (Fig. 2).

On April 15, 1961, the patient was taken to the operating-room with a preoperative diagnosis of retrosternal goitre. Once exposure had been obtained and the strap muscles of the neck divided, it was found that the thyroid gland itself was completely normal. It was displaced anteriorly and to the left by a large saccular mass lying to the right of the trachea and esophagus and extending into the superior mediastinum, behind the sternum. By blunt and sharp dissection, it was possible to separ-

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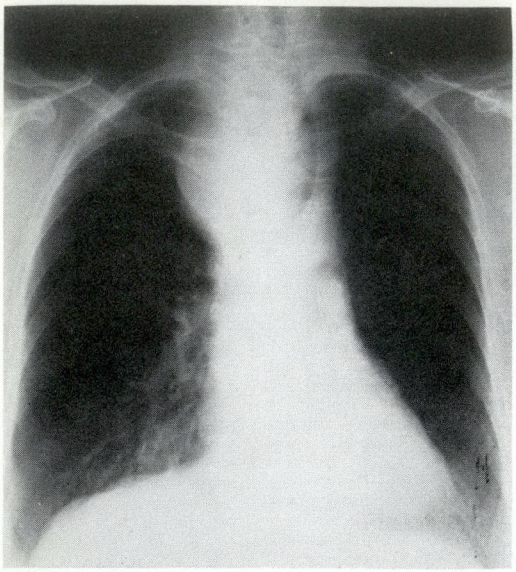


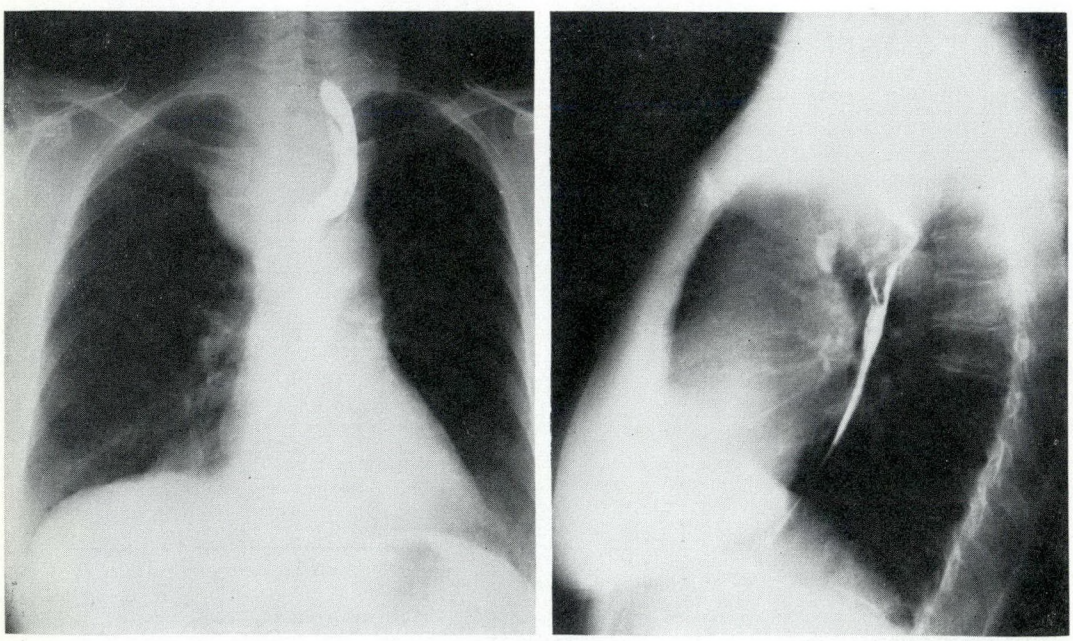
Fig. 1.—Radiograph of the chest showing deviation of trachea by a soft tissue mass.

ate the carotid sheath and recurrent laryngeal nerve from the mass after division of the inferior thyroid artery on the right side. At this point, the mass, which was cystic, was entered with a trocar and approximately 150 c.c. of opaque whitish fluid was obtained. Although no communication between this mass and the esophagus had been demonstrated on the radiograph, in order to rule out this possibility a Levin tube was passed into the pharynx and methylene blue dye was allowed to run into the esophagus. No dye appeared in the contents of the sac. As the dissection progressed, it was found that the saccular structure was intimately associated with the lateral wall of the upper third of the esophagus, and as one approached the esophagus, it was noted that the muscular walls of both structures were intimately associated. A plane of cleavage was established and the entire sac was removed. Examination of the esophagus after this produced no evidence of any communication with or perforation of the esophagus.

Pathological Findings

On pathological examination the specimen consisted of a membranous-like firm portion of tissue, which measured approximately 11.5 cm. in length and 5.5 cm. in diameter. Microscopical section showed an irregular layer of stratified squamous epithelium lying on a layer of smooth muscle tissue. The final pathological report was enterogenous cyst (esophageal) (Fig. 3).

The patient's postoperative course was quite smooth, with complete amelioration of symptoms and disappearance of the presenting mass in the anterior portion of the right side of the neck.



a b

Fig. 2—(**a**) Radiograph of a barium swallow; anteroposterior view demonstrating displacement of esophagus; (**b**) in a lateral projection.

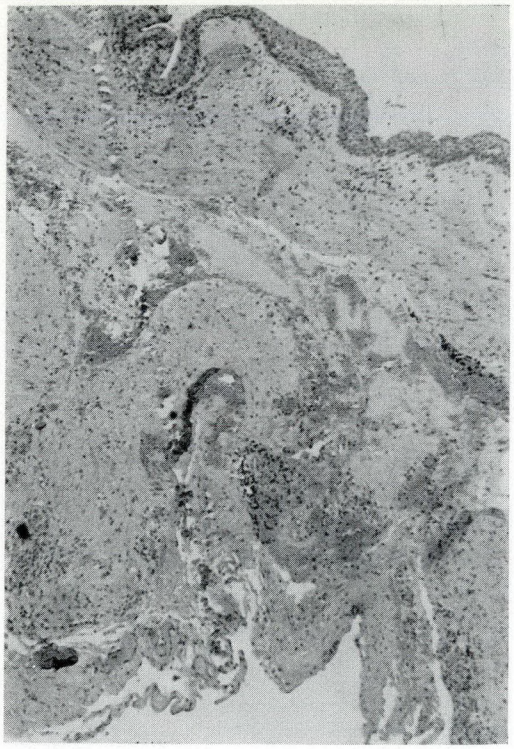


Fig. 3.—Low-power photomicrograph showing cyst wall with stratified squamous epithelium.

Discussion

Gross,[1] in his review of cases of esophageal duplication, noted that 65% occur within the first year of life, followed by 9% in the second year and 8% in the third year. Nese[2] reports 10 cases of benign tumours and cysts of the esophagus, in which only one case of esophageal cyst is included. In this instance, the cyst occurred at the lower end of the esophagus in a woman, aged 44 years. Borrie[3] defines esophageal duplication as a triad of (1) intimate attachment to the alimentary tract, (2) a lining of mucous membrane similar to some part of the alimentary tract, and (3) possession of a smooth muscle coat.

Esophageal cyst has been well documented in the literature.[1, 4-6] so a further review here would be redundant. However, the fact that this congenital anomaly is most frequently reported as manifesting itself in the younger age groups might lead the physician to fail to consider this entity in the differential diagnosis of a presenting mass in the neck, as was the case in this patient.

Summary

A case of esophageal duplication, first discovered in a woman 64 years of age, is presented. The clinical and operative findings are reported in detail, as well as the final pathological findings. The pertinent literature is reviewed to show that this anomaly is rarely found in the older age groups, and to substantiate the clinical and pathological findings of this case.

The authors wish to express their appreciation to Drs. D. Bohnen, B. Willinsky and A. M. Morrow, for their assistance in the management and presentation of this case.

References

1. Gross, R. E.: The surgery of infancy and and childhood; its principles and techniques, W. B. Saunders Company, Philadelphia, 1953, p. 221.
2. Nese, G.: Benign tumors and cysts of the esophagus, *Acta Chir. Scand.*, **114:** 165, 1958.
3. Borrie, J.: Duplication of the oesophagus; review and description of two cases, *Brit. J. Surg.*, **48:** 611, 1961.
4. Bremer, J. L.: Diverticula and duplications of the intestinal tract, *Arch. Path. (Chicago)*, **38:** 132, 1944.
5. Gross, R. E., Neuhauser, E. B. D. and Longino, L. A.: Thoracic diverticula which originate from the intestine, *Ann. Surg.*, **131:** 363, 1950.
6. Lewis, F. T. and Thyng, F. W.: The regular occurrence of intestinal diverticula in embryos of the pig, rabbit, and man, *Amer. J. Anat.*, **7:** 505, 1907.

Résumé

De nombreux cas de kystes œsophagiens ont été rapportés dans la littérature, spécialement chez les jeunes enfants. Les symptômes sont variables, selon la taille et la localisation du kyste, mais se ramènent généralement à des troubles de compression. La découverte de cette affection chez un malade âgé est une éventualité rare et c'est la raison pour laquelle les auteurs décrivent le cas suivant. Il s'agit d'une femme de 64 ans, hospitalisée en avril 1961. Les troubles dont elle souffre remontent à trois mois auparavant: elle présente une dyspnée importante, surtout en position couchée, et un certain degré de dysphagie pour les aliments solides. On ne trouve rien de particulier dans ses antécédents. A l'examen général on trouve dans la région du cou une tuméfaction qui semble, à première vue, être un goître de grosse taille, s'étendant surtout à droite de la ligne médiane et plongeant derrière le sternum. Cette tuméfaction repousse la trachée vers la gauche, et est mobile à la déglutition. Les divers examens de laboratoire se trouvent dans les limites normales. La radiographie confirme l'existence d'une tumeur rétrosternale. On décide alors d'intervenir avec le diagnostic pré-opératoire de goître. A l'opération, on trouve cependant une thyroïde

tout à fait normale, mais par contre une grosse masse kystique est évidente: on la dissèque, puis la ponctionne, ce qui permet de ramener environ 150 ml. de liquide trouble. Tandis que la dissection progresse, on découvre un point d'attachement à la paroi œsophagienne dans son tiers supérieur; il se trouve même que les musculatures des deux structures sont en étroite association. On trouve un plan de clivage qui permet l'extraction totale sans perforation de l'œsophage. Les suites opératoires furent satisfaisantes, et les symptômes disparurent. L'histopathologie confirma qu'il s'agissait bien d'un kyste d'origine œsophagienne, la paroi en étant formée d'un épithélium aplati stratifié reposant sur une couche musculaire lisse.

CLINICAL NEUROSURGERY. Proceedings of the Congress of Neurological Surgeons, Houston, Texas, 1962. Vol. 10. 411 pp. Illust. The Williams & Wilkins Company, Baltimore, Md.; Burns & MacEachern, Ltd., Toronto, 1964. $16.00.

The tenth volume of "Clinical Neurosurgery" contains the edited proceedings of the Twelfth Annual Meeting of the Congress of Neurological Surgeons held in Houston, Texas, in the fall of 1962. Each year the meeting honours an oustanding senior neurosurgeon, and on this occasion it was Dr. Bronson S. Ray. The introduction contains a biographical sketch and his bibliography. The first three chapters were written by Dr. Ray and cover Surgery of Recurrent Intracranial Tumours, Surgical Treatment of Acromegaly, and Trends in Neurological Surgery.

This book contains 14 additional chapters on a variety of neurological subjects by recognized authorities. Five papers are related to the hypophysis and six to neuroradiological presentations. Noteworthy among the latter is one by Giovanni Di Chiro entitled "The Reliability of Neuroradiology". He has achieved an accuracy of 92% in the detection and localization of intracranial space-occupying lesions and of 64% in assessing their nature. It is his opinion that, since interpretation and technique are so intimately related in this field, both should be the direct responsibility of the neuroradiologist.

In a chapter entitled "The Use of Steroids for Control of Cerebral Edema", Lyle A. French and Joseph H. Galicich report their experience with dexamethasone, a synthetic glucocorticoid, and conclude that it is a highly effective agent.

The article by James C. White, "Aneurysms Mistaken for Hypophyseal Tumours", is very much worth while. He reported three personal cases and also reviewed 33 cases from the literature.

One of the highlights of this book is the chapter by Michael DeBakey on "Concepts Underlying Surgical Treatment of Cerebrovascular Insufficiency". The author's vast experience and the concise presentation of this subject make this paper an important one for anyone interested in this complex problem.

This volume also contains the ten-year cumulative index of the Proceedings of the Congress of Neurological Surgeons, which is well worth having.

JOINT PAIN. Diagnosis and Treatment Using Manipulative Techniques. John McM. Mennell. 178 pp. Illust. Little, Brown and Company, Boston; J. B. Lippincott Company of Canada Ltd., Montreal, 1964. $9.75.

This monograph summarizes the author's personal experience and philosophy regarding joint pain and its treatment. The introductory chapters are concerned with his own views and ideas, as well as general considerations of joint disease. The final chapters include techniques of joint manipulations, and a short chapter on osteoarthritis. By far the greater bulk of the book is concerned with examination of joint mobility. The book is well illustrated, making good use of the double-exposure prints to project a range of motion in a joint.

The work could be more appropriately entitled "Joint Motion" or "Joint Stiffness" rather than "Joint Pain". Other than speculations and hypotheses, there is little material of scientific nature in the book which would explain the mechanism of joint pain. It is rather a comprehensive study of a clinical entity involving loss of a specific joint motion, called by the author "joint dysfunction". This refers to the loss of joint-play movements; that is, the involuntary movements present in all synovial joints. This involuntary joint-play must be restored at the appropriate phase of the joint disease by manipulative technique before normal voluntary joint motion can occur. Undoubtedly, loss of motion and joint pain are intimately related, but not necessarily as cause and effect, nor is it relieved as easily or simply as this book suggests.

As well as the lack of scientific data, no mention is made of specific results of treatment, a very precarious combination when manipulative therapy is under discussion.

Those interested in the fine points of manipulative techniques will have considerable interest in the author's ideas.

SURGICAL TECHNIQUE

THE FUSION OF INTERPHALANGEAL JOINTS*

D. C. ROBERTSON, M.D.,† *Toronto*

I HAVE been impressed by the fact that arthrodesis of interphalangeal joints is often very badly done. Failures are common and the result is nearly always worse than the preoperative state. Postoperative non-union is nothing more than a traumatic arthritis, which is perhaps more disabling than the condition for which the operation was undertaken. A complication such as atrophy of the terminal pulp of the finger, produced by Kirschner wires inserted through it for immobilization, results in a permanent and irretrievable disability. Fusion in poor position because of imperfect preparation of the bone ends or because of inadequate fixation detracts from a result that could have been excellent. Yet arthrodesis of these small joints is widely considered to be a simple operation, to be followed by a three-week period of rather imperfect immobilization.

This paper outlines a technique of precision mitring and skeletal fixation which I have found extremely satisfactory and which, so far as I have been able to discover, is original. This report is based upon the successful arthrodesis of 64 interphalangeal joints in 52 patients. There were no failures. While a discussion of the indications for fusion is not intended, it may be said that most of the 64 fusions were carried out because of traumatic arthritis or flexor profundus division with an intact sublimis, and most were fusions of the distal interphalangeal joint. A small number (11) required fusion of the proximal interphalangeal joint and the usual indication in these cases was traumatic arthritis or irreparable extensor apparatus injury.

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Presented at the Annual Meeting of The American Society for Surgery of the Hand, Chicago, January 1964.
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As in any operation on the hand requiring precise dissection, a tourniquet is required. For this reason it is necessary to do an axillary block, brachial plexus block, or use general anesthesia.

TECHNIQUE

The approach to the distal interphalangeal joint is through a U-shaped incision with the proximally based flap made over the dorsum of the joint. The flap is turned up and the extensor tendon divided transversely. A wide exposure of the whole dorsal aspect of the joint is obtained (Fig. 1). The capsule is cleared away and this includes the fibrous plate which is the flexor portion of the joint capsule. The approach to the proximal interphalangeal joint may be either through a similar incision or through a longitudinal midline dorsal incision centred over the joint. The

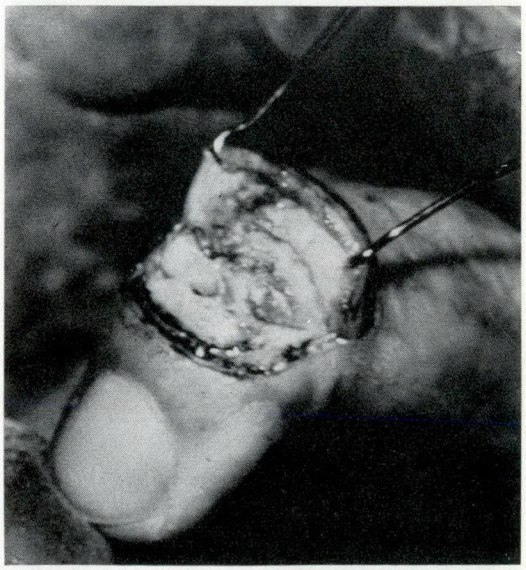

Fig. 1.—The approach. The dorsum of the joint is widely exposed.

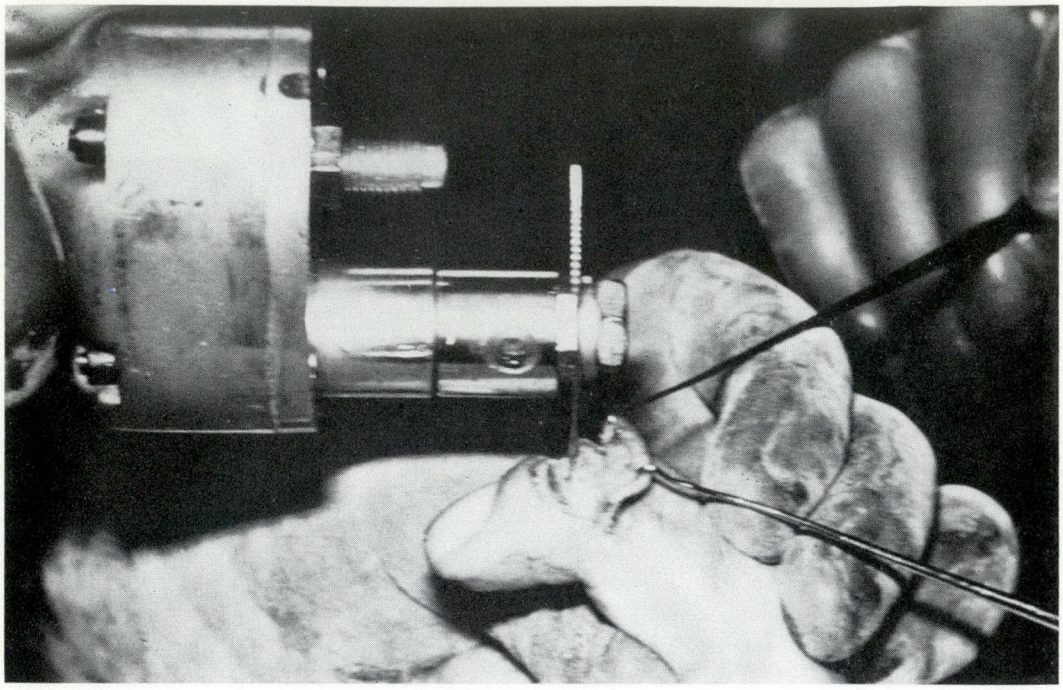

Fig. 2.—The excision of the joint and the mitring of the bones.

skin flaps are easily retracted to give a wide dorsal exposure.

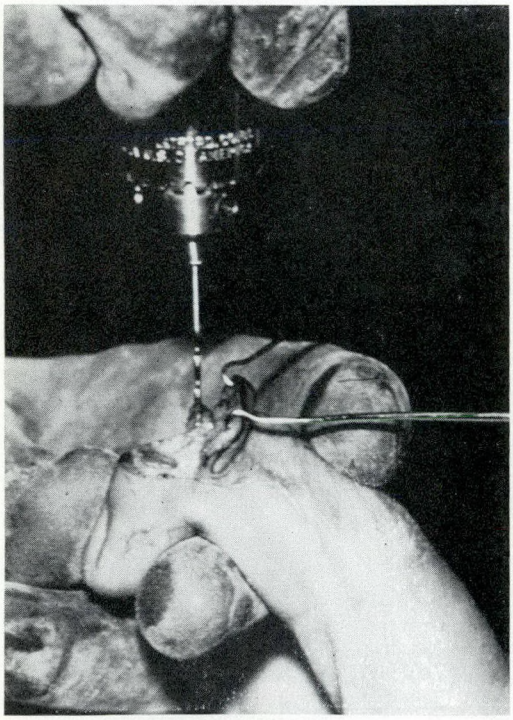

Fig. 3.—The drilling of the four holes for wiring.

A Stryker saw with a narrow blade is used to cut the bone ends, and with this instrument a perfect cut can be made at whatever angle is required to correct deformity and obtain the desired angle of fusion (Fig. 2). This is one of the keys to success. Removal of the joint surfaces with a chisel or rongeurs simply does not leave perfectly flat surfaces to oppose each other. A high-speed burr had been suggested for this purpose, but these instruments are so light in the operator's hand that the cut surface turns out to be less than perfectly flat and smooth. The fixation of these matched bone ends must now be perfectly made. It has been my experience that crossed Kirschner wires prevent rotation in only one direction and that they tend to hold the cut surfaces apart rather than together. Wire-loop fixation is definitely preferable. Two vertical drill holes are made in each bone opposite to each other (Fig. 3). A length of No. 28 stainless-steel wire is passed through each pair (Fig. 3). The cut surfaces are approximated and the wires are twisted tight (Fig. 4). Because of the perfect cuts made by the saw, the line of fusion is almost invisible when the wires

Fig. 4.—The wires are passed and the mitred bone ends approximated.

have been tightened. Furthermore, the twisting-up of the wires applies the cut surfaces of the bone tightly together and indeed compresses them together (Fig. 5). The twisted ends are cut and turned out of the way and the extensor tendon, if present, is closed over them and the skin flap is replaced and closed. For skin closure, I have used 6-0 chromic catgut.

A plaster splint is applied. Only a finger splint is required for distal interphalangeal joint fusions, but it is necessary to include the wrist for proximal interphalangeal joint fusions and for interphalangeal joint fusions of the thumb. Where stiffness of the remaining joint of the digit is not a problem the splint should remain in place for six weeks. Occasionally there may be pressing reasons for reducing the duration of immobilization in the fingers. In such cases the splint can be removed at three weeks and gentle movement of the finger permitted. A splint should be supplied for use when the finger is not being exercised.

The optimum angle of fusion varies with each joint in each finger. About 50° of flexion at the distal interphalangeal joint

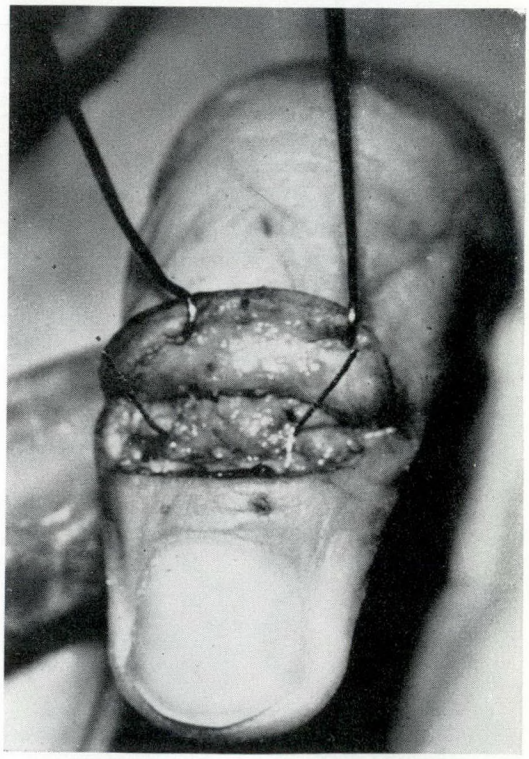

Fig. 5.—The wires are tightened and the cut surfaces of the bone are held firmly together.

Fig. 6.—The end result of the fusion of index and middle finger distal interphalangeal joints.

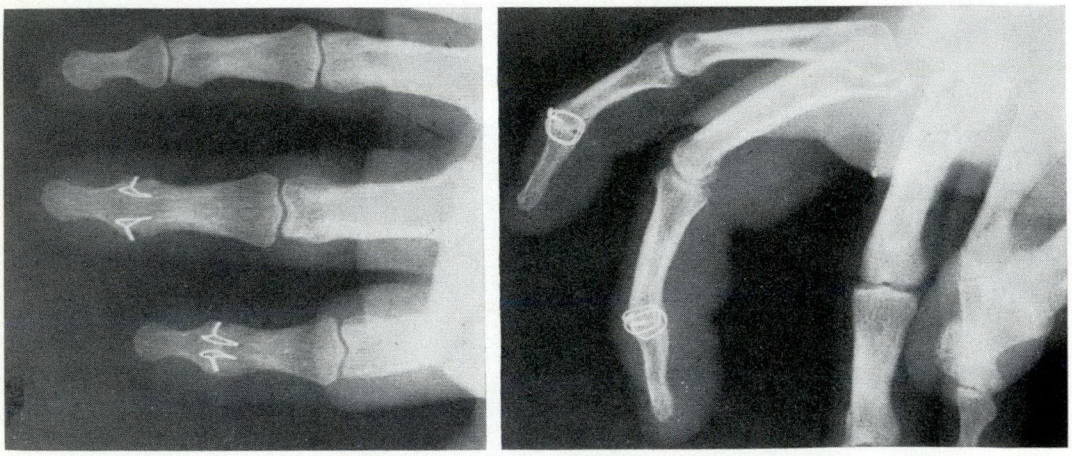

Fig. 7.—Radiographic views of the same case as in Fig. 6.

and 75° of flexion at the proximal interphalangeal joint is desirable in an index finger. Variations in these angles for other fingers will depend upon the patient's preference and perhaps upon his occupation as well (Figs. 6 and 7).

It is not unusual to find that a joint which requires fusion has a dorsal cover of thick unstable scar quite unsuitable to a surgical approach. In such cases the scar may be excised and the fusion carried out in the usual way. At the conclusion of the operation the defect may be covered with a free full-thickness skin graft. The line of fusion is so fine that it does not affect the take of the graft; indeed the fusion improves the bed on which the graft is to be placed. I have modified the procedure only by placing one 26-gauge stainless-steel loop transversely instead of using two vertical wire loops of 28-gauge. This provides good fixation but it is not as effective as the vertical loops. However, it removes all wire from the bed of the graft.

Many of these patients have a damaged and deformed finger-nail and require a fusion of the distal interphalangeal joint. It has been my practice to excise the nail and

nail bed and replace it with a free full-thickness skin graft. Three months later the fusion can be carried out through the usual approach.

I have had two patients in whom part of the flap became necrotic because of old scarring. With these I have been stubbornly conservative and fusion has proceeded normally. The necrotic skin sloughs and the area heals just as it would if there were no fusion beneath it. The ensuing scar may or may not require later operative repair.

I have seen many complications and failures of fusions of interphalangeal joints following an extraordinary variety of procedures. I recommend this approach as precise, adaptable and productive of excellent results.

SUMMARY

A new technique for fusion of interphalangeal joints is described. The importance of adequate dorsal exposure and precise fitting of the bone ends is emphasized. In addition to skeletal fixation by wire loops, a plaster cast is required.

RÉSUMÉ

L'auteur a eu l'occasion de rencontrer dans sa pratique un nombre considérable d'arthrodèses interphalangiennes mal faites, ce qui mène à un résultat souvent plus mauvais que l'état pré-opératoire. En fait, lorsqu'il y a échec, on se trouve en présence d'une forme spéciale d'arthrite traumatique. Pour cette raison, l'auteur a été amené à mettre au point une technique précise visant à obtenir une immobilisation parfaite de l'arthrodèse. Il présente également une étude statistique de 64 cas de ce genre observés chez 52 patients. Il n'y eut aucun échec dans cette série. L'incision cutanée pour arthrodèse interphalangienne distale sera en forme de U, faite sur le dos de l'articulation. Pour les arthrodèses proximales on peut utiliser une incision semblable ou encore une incision longitudinale sur la ligne dorso médiane. Il est important que les extrémités osseuses soient coupées très franchement et présentent une surface parfaitement plate; ceci peut être fait avec une scie de Stryker. La fixation des extrémités osseuses ne peut être parfaite avec des broches de Kirschner croisées, car celles-ci tendent à écarter les surfaces. Il est préférable de recourir à une fixation par anse métallique passant dans des trous faits dans chaque os. Si l'opération a été faite correctement, la ligne de jonction entre les deux surfaces devient pratiquement invisible. Après l'intervention, on devra appliquer une atelle plâtrée pour six semaines. En ce qui concerne les angles de section à adopter, l'auteur recommande les chiffres suivants: 50° en flexion pour les arthrodèses distales, et 75° pour les proximales; ces chiffres ne sont pas absolus et peuvent varier selon les cas, parfois peut-être selon le métier du malade. Chez les patients où l'ongle a été antérieurement blessé et endommagé, il sera bon de faire une excision unguéale totale avec greffe de peau libre dans un premier temps; dans un deuxième temps, on pourra procéder à l'arthrodèse requise.

ANATOMIE PATHOLOGIQUE, GYNECOLOGIQUE ET OBSTETRICALE. Corrélations anatomo-cliniques. Claude Gompel. Avec la collaboration de Paul Wilkin. 736 pp. Illust. Librairie Maloine S.A., 27, rue de l'Ecole de Médecine, Paris VIe, 1963. 160 NF. $32.00 (approx.).

Ce précis s'adresse aux pathologistes et aussi aux cliniciens. L'auteur fait une synthèse des connaissances actuelles de l'anatomie pathologique, gynécologique et obstétricale, en ayant soin d'y associer les notions d'étiologie et de pathogénie et les éléments cliniques indispensables à la compréhension des données morphologiques. La conception de l'ouvrage rappelle celle des manuels américains. L'iconographie est considérable et le choix des illustrations est excellent. Leur reproduction, malheureusement, laisse souvent à désirer.

Une centaine de pages sont consacrées à la pathologie du placenta et des annexes fœtales. Cette partie de l'ouvrage, une contribution de P. Wilkin, constitue un apport précieux dans un des domaines les plus mal connus et les plus négligés de la pathologie.

Une matière très étendue et variée est couverte dans les neuf chapitres de cet ouvrage et, forcément, plusieurs sujets y sont traités d'une façon un peu schématique. A bien des endroits le lecteur aurait souhaité trouver un peu plus de détails. A titre d'exemple, les quelques lignes, page 591, sur les caractères microscopiques de la môle disséquante, nous semblent insuffisantes pour l'analyse histologique de cette lésion et sa différentiation du choriocarcinome. Chaque chapitre est suivi d'une bibliographie abondante contenant des références choisies, récentes et de provenance internationale.

Dans son ensemble, le précis du docteur Gompel doit être hautement recommandé et on doit souhaiter la publication prochaine de volumes en français de même valeur sur d'autres aspects de l'anatomie pathologique.

EXPERIMENTAL SURGERY

HEMODILUTION DURING EXTRACORPOREAL CIRCULATION: A PRELIMINARY REPORT OF ITS EFFECT ON HEMOLYSIS

JOHN C. COLES, M.D.,* JORGE R. BUTTIGLIERO, M.D.† and JOHN AUST,‡
London, Ont.

FLUIDS other than blood have been used as diluents or complete blood substitutes in the priming of heart-lung machines. The use of various diluents has been proposed in order to counteract certain specific undesirable effects encountered during extracorporeal circulation; these include tris buffer, trishydroxyaminomethane (THAM), for metabolic acidosis;[1, 2] mannitol for renal failure;[3] and low-molecular-weight dextran (Rheomacrodex) for inadequate peripheral blood flow.[3, 4]

Aside from their specific properties, the addition of diluents reduces the amount of donor blood exchanged with the patient's own during extracorporeal circulation. This appears to be important in the prevention of post-perfusion sequestration of blood.[5-7]

Our experience with the use of hemodilution in 120 patients who underwent extracorporeal circulation suggested that the degree of hemolysis was influenced by the type of diluent.

During cardiopulmonary bypass, mechanical trauma always causes hemolysis but many variables in the apparatus itself may influence the amount of hemolysis that occurs. The variability of the factors in each case makes difficult a correct evaluation of the role played by the diluent in the production of hemolysis. For this reason, we set out to investigate experimentally the effect of different diluents upon hemolysis, using an apparatus of our own design in which conditions similar to those of cardiopulmonary bypass were produced but in which the factor of mechanical trauma to the red cells was standardized.

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METHOD

The diluents used were: (1) 0.3 molar tris buffer (THAM); (2) 5% glucose in water; (3) 5% glucose in ¼-strength normal saline; (4) 10% low-molecular-weight dextran (Rheomacrodex), and (5) 5% mannitol. These diluents were used in concentrations of 10% and 20% of the total priming volume of the perfusion apparatus. The remaining volume was made up of whole blood. The types of blood used were: (1) 24-hour-old heparinized dog blood; (2) 24-hour-old heparinized human blood, and (3) 30-day-old citrated human blood.

The apparatus employed (Fig. 1) consisted of an oxygenator reservoir to and from which the blood was propelled in a circle by a roller pump. The disc-type oxygenator was run at 100 revolutions per minute with an oxygen flow of 3 litres per

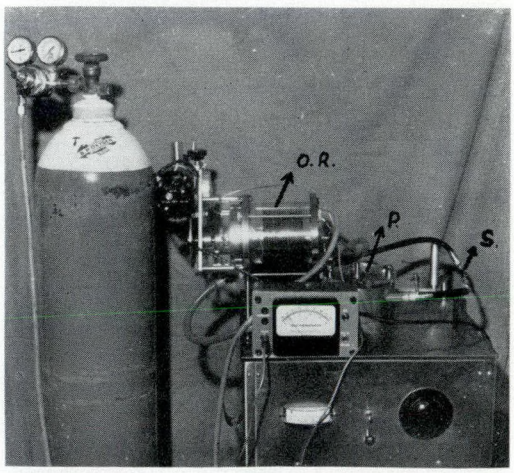

Fig. 1.—Apparatus designed to mimic conditions encountered in extracorporeal circulation while standardizing mechanical trauma to the blood. Blood is pumped in a circle, in and out of an oxygenator reservoir (O.R.) by a roller pump (P). A stricture (S) in the tubing creates a high-pressure gradient, eliciting a high degree of hemolysis.

minute. The pump was a completely occlusive DeBakey roller type, standardized at 1 litre per minute. A point of high resistance, designed to elicit a high degree of hemolysis in a short time, was created by interposing an infant-sized femoral-artery cannula (1/16″ in diameter) in the circuit. Two hundred millilitres of blood or blood-diluent mixture (enough to cover one-half of the radius of the discs in the oxygenator) were used in each experiment.

The first experiments were of two hours' duration, but, as the hemolysis was excessive, this was later reduced to one hour. The blood and the diluents were warmed to 20° C. to avoid temperature-induced changes in viscosity which could affect the results. Continuous readings of temperature during the pump run, by means of a telethermometer, showed variations of less than 1° C. between the different experiments. Hemolysis was measured by the benzidine method, modified by Crosby and Furth, and expressed in milligrams of hemoglobin per 100 ml. of plasma.

Results

Table I shows the results of two experiments with dog's blood. In both, complete hemolysis occurred when tris buffer was used as a diluent. This did not occur in experiments conducted with human blood, and the use of dog's blood in this study was therefore discontinued.

The results of four experiments using 24-hour-old heparinized human blood are shown in Table II.

The degree of hemolysis varied with each experiment. In order to facilitate the evaluation of the results, the amount of plasma hemoglobin in each experiment in which whole blood was used was taken as a unit, and the degree of hemolysis with each diluent was expressed as a percentage of this unit (Fig. 2).

Table III and Fig. 3 present the results of four experiments conducted with 30-day-old citrated human blood. In all of the experiments with human blood, the results were similar.

The addition of 5% glucose in water and 5% glucose in normal saline did not significantly alter the degree of hemolysis, compared with that obtained with whole blood.

Addition of tris buffer produced a considerable increase in hemolysis.

Addition of mannitol and low-molecular-weight dextran produced a marked decrease in hemolysis. This decrease was more marked with mannitol.

TABLE I.—Results of Two Experiments Using Dog's Blood

24-hour-old heparinized dog blood—2-hour pump run hemolysis expressed in plasma hemogloblin mg.%

	Diluent concentration 20%	
	Exp. No. 1	*Exp. No. 2*
Whole blood	150	200
THAM	Total hemolysis	Total hemolysis
5% glucose in water	129	144
Low-molecular-weight dextran	117	115
Mannitol	96	121

Note complete hemolysis obtained with THAM.

TABLE II.—Results of Four Experiments Using Fresh Human Blood

24-hour-old heparinized human blood hemolysis expressed in plasma hemoglobin mg.%
Exp. No. 1—2 hours; Exp. Nos. 2, 3 and 4—1 hour

	Diluent concentration 20%		*Diluent concentration 10%*	
	Exp. No. 1 2 hrs.	*Exp. No. 2 1 hr.*	*Exp. No. 3 1 hr.*	*Exp. No. 4 1 hr.*
Whole blood	280	105	92	98
THAM	450	125	118	126
5% glucose in water	360	107	79	96
5% glucose in 1/4 normal saline		102	75	98
Low-molecular-weight dextran	240	93	64	54
Mannitol	160	61	40	47

In Experiment No. 1, of 2-hour duration, the degree of hemolysis was excessive. As a consequence, further experiments were of 1-hour duration.

TABLE III.—Results of Four Experiments Conducted with Citrated Bank Blood

30-day-old citrated bank blood hemolysis expressed in plasma hemoglobin mg.% pump run—1 hour

	Diluent concentration 20%		*Diluent concentration 10%*	
	Exp. No. 1	*Exp. No. 2*	*Exp. No. 3*	*Exp. No. 4*
Whole blood	324	290	308	266
THAM	540	420	487	458
5% glucose in water	372	310	282	260
5% glucose in 1/4 normal saline	344	286	288	247
Low-molecular-weight dextran	228	194	205	174
Mannitol	168	172	146	168

The degree of hemolysis is higher than in experiments utilizing fresh hepari ized human blood.

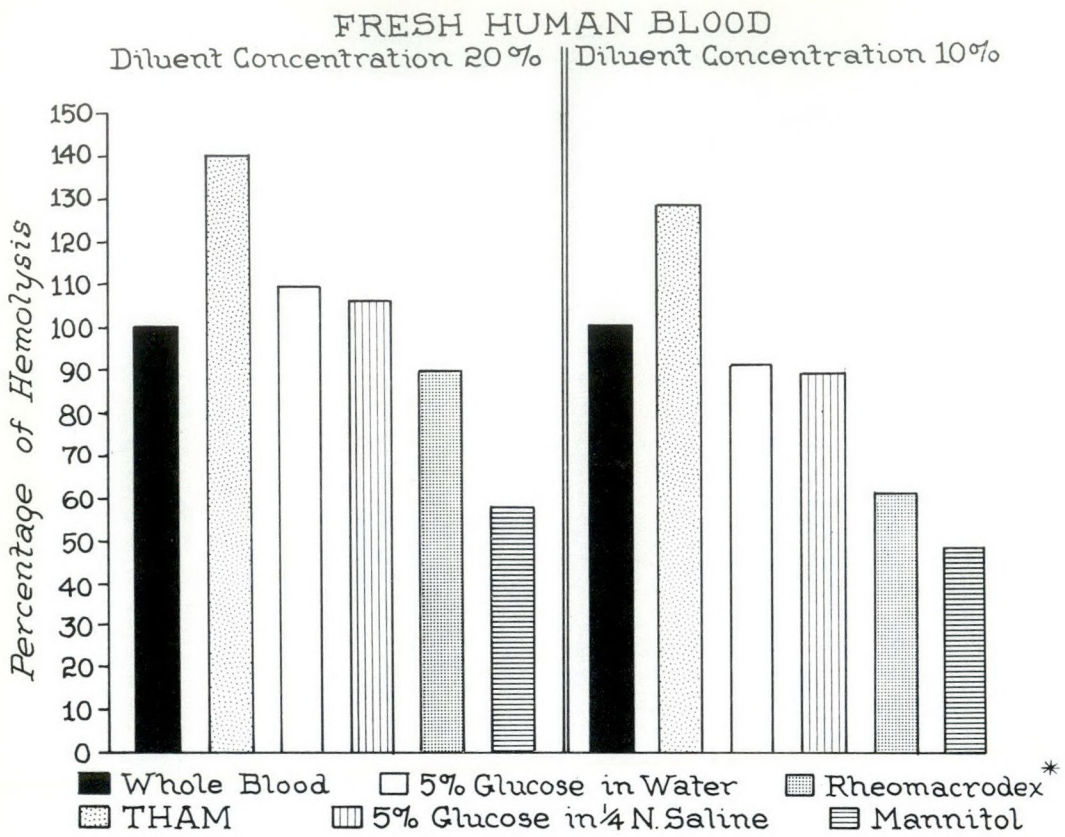

Fig. 2.—In four experiments conducted with fresh heparinized human blood, the hemolysis obtained with whole blood was taken as a unit; the hemolysis with each diluent is expressed as a percentage of this unit.

Addition of tris buffer produced a considerable increase in hemolysis. This increase was accentuated when used in 20% concentration, that is, 20% of the total volume of the perfusion apparatus.

Five per cent glucose in water and in ¼-strength normal saline showed no significant difference when compared with whole blood, slightly more hemolysis with 20% concentration and slightly less with 10% concentration.

Low-molecular-weight dextran (Rheomacrodex*) showed a marked decrease in hemolysis with 20% concentration and a further decrease with 10% concentration.

Hemolysis was considerably reduced when mannitol was used as a diluent. This reduction was slightly greater when used in a 10% concentration.

Discussion

We are aware that addition of diluents produced a relative decrease in the hematocrit value, with dilution of plasma hemoglobin. However, this decrease was not corrected as it is in extracorporeal circulation; the level of plasma hemoglobin is, in itself, the important factor.

The problem of sequestration of blood in visceral capillaries during and after total body perfusion has been analyzed recently by Litwak, Slonim and Gadboys.[6, 7] These authors have pointed out the direct relationship between the total amount of homologous blood exchanged and sequestration, and have suggested two methods for decreasing its magnitude: (1) hemodilution, as a means of reducing the total amount of blood exchanged while maintaining the same flow rate, and (2) return to the pump-oxygenator of the maximum possible amount of blood lost during the procedure.

The latter procedure implies an increase in hemolysis, since Osborn and his associates[8] have shown that during extracorporeal circulation, most of the hemolysis occurs in the coronary sinus suction system.

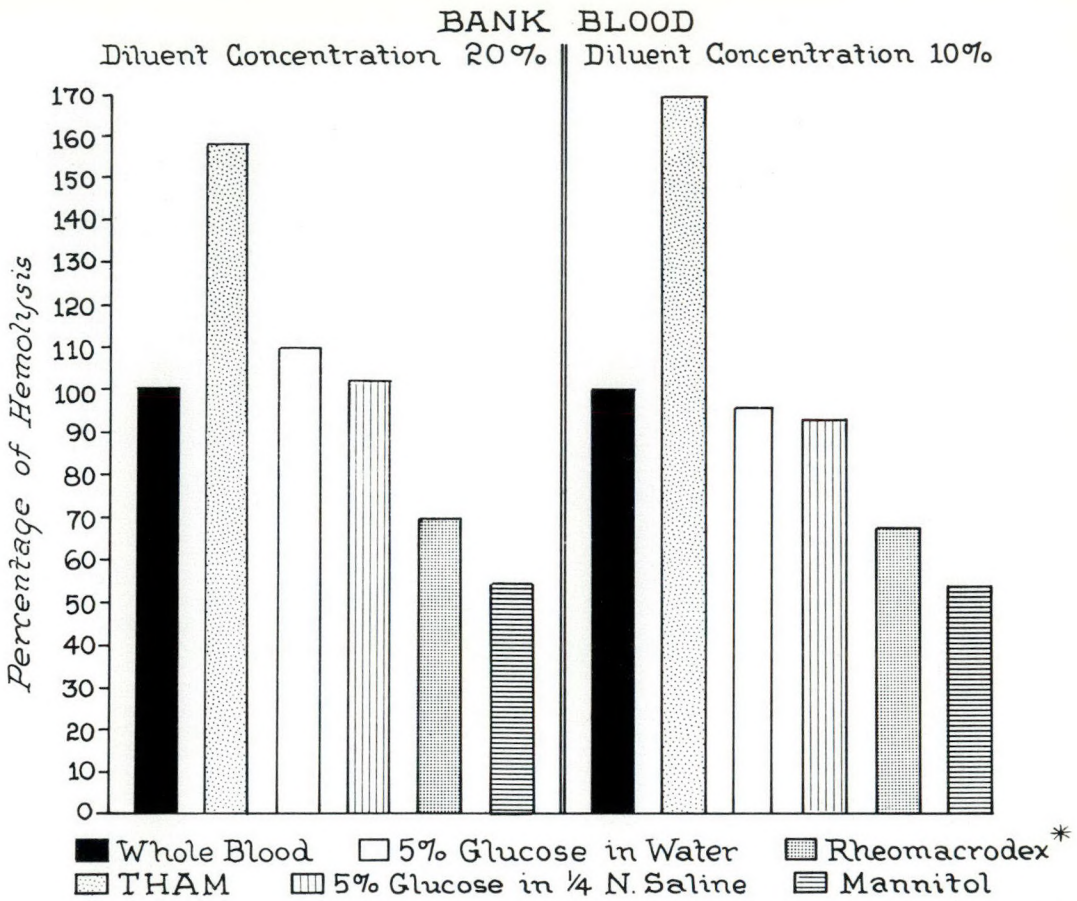

Fig. 3.—In four experiments conducted with citrated bank blood, the hemolysis with each diluent is expressed as a percentage of the hemolysis encountered in the experiments with whole blood. The results are consistent with those obtained with fresh heparinized human blood.

*Low-molecular-weight dextran.

In view of these findings, the use of mannitol as a diluent appears to be indicated, not only to attempt to prevent renal tubular damage by eliciting osmotic diuresis, but also, as our results tend to indicate, as a means of achieving a significant reduction in hemolysis.

The consistent decrease in hemolysis achieved when low-molecular-weight dextran is used as a diluent appears to be a further recommendation for the use of this agent, in addition to its favourable effects in the microcirculation.

Summary

The hemolysis which results from mechanical trauma of a pump-oxygenator can be influenced by the use of blood diluents. An apparatus simulating extracorporeal circulation was employed to determine the effect of several diluents on the degree of hemolysis.

The results of this investigation indicate that a marked decrease in hemolysis is achieved by the addition of either mannitol or low-molecular-weight dextran. This decrease is more marked with mannitol. The addition of 5% glucose in water or in ¼-strength normal saline does not significantly alter the degree of hemolysis. The addition of tris buffer causes a definite increase in hemolysis.

The technical assistance of Mr. T. Walko is gratefully acknowledged.

REFERENCES

1. PEIRCE, E. C., 2nd: Effects of 2-amino-1-hydroxy methyl-1, 3-propanediol (tris) during cardiac bypass procedures, *Ann. N.Y. Acad. Sci.*, **92:** 765, 1961.
2. MOORE, D. AND BERNHARD, W. F.: Efficacy of 2-amino-2-hydroxymethyl-1, 3 propanediol (tris buffer) in the management of metabolic lacticacidosis accompanying prolonged hypothermic perfusions, *Surgery*, **52:** 905, 1962.
3. MOORE, F. D.: Tris buffer, mannitol and low viscous dextran: three new solutions for old problems, *Surg. Clin. N. Amer.*, **43:** 577, 1963.
4. GELIN, L. E. AND INGELMAN, B.: Rheomacrodex — a new dextran solution for rheological treatment of impaired capillary flow, *Acta chir. scand.*, **122:** 294, 1961.
5. LITWAK, R. S. *et al.*: Alterations in blood volume during normovolemic total body perfusion, *J. Thorac. Cardiov. Surg.*, **42:** 477, 1961.
6. GADBOYS, H. L., SLONIM, R. AND LITWAK, R. S:. Homologous blood syndrome; I. preliminary observations on its relationships to clinical cardiopulmonary bypass, *Ann. Surg.*, **156:** 793, 1962.
7. LITWAK, R. S. *et al.*: Homologous-blood syndrome during extracorporeal circulation in man; II. phenomena of sequestration and desequestration, *New Eng. J. Med.*, **268:** 1377, 1963.
8. OSBORN, J. J. *et al.*: Hemolysis during perfusion: sources and means of reduction, *J. Thorac. Cardiov. Surg.*, **43:** 459, 1962.

RÉSUMÉ

On a proposé, dans les techniques de circulation extra-corporéale, divers liquides comme remplaçants ou comme diluants du sang. Ceci permet évidemment de réduire la quantité de sang à prélever des donneurs. L'inconvénient que l'on rencontre alors est un degré variable d'hémolyse. Cette hémolyse est due en partie au traumatisme mécanique du passage du sang dans l'appareil et aussi aux diluants utilisés. Les auteurs ont étudié expérimentalement ces divers facteurs. L'appareillage utilisé consistait en un réservoir d'oxygène auquel le sang était connecté; l'oxygénateur était du type à disque, tournant à 100 tours par minute; la pompe était du type DeBakey, ajustée à un débit constant d'un litre par minute. La quantité de sang utilisée était de 200 ml. Un point de résistance, destiné à provoquer un degré constant d'hémolyse mécanique, fut créé par l'introduction dans le circuit d'une canule artérielle de 1/16 de pouce de diamètre. Les qualités de sang employées furent: (1) du sang de chien héparinisé vieux de 24 heures; (2) du sang humain héparinisé également vieux de 24 heures; et (3) du sang humain citraté datant de 30 jours. Les diluants essayés furent: (1) une solution 0.3 molaire de tampon tris (THAM); (2) une solution de 5% de glucose dans l'eau; (3) une solution de glucose à 5% dans un soluté physiologique dilué au quart; (4) du dextran à 10% (Rheomacrodex); et finalement (5) une solution à 5% de mannitol. Le degré d'hemolyse produit était mesuré par un test à la benzidine. La témperature de l'ensemble était soigneusement controllée et maintenue à 20° C. Les résultats peuvent être résumés comme suit. Avec le sang de chien, une hémolyse totale se produisit avec le tampon tris, ce qui n'arriva pas avec le sang humain; pour cette raison, l'emploi du sang de chien fut abandonné dans les expériences ultérieures. Les produits qui causent le moins de dommage sont par ordre: le mannitol et le dextran, et il semble que le mannitol soit capable de protéger les cellules sanguines. Le soluté glucosé ne montre aucune action significative. Le tris augmente nettement l'hémolyse.

ANATOMY FOR THE ANESTHESIOLOGIST. A Stereoscopic Atlas. William H. L. Dornette. 389 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1963. $15.00.

The well-versed anesthetist must be a clinical anatomist as well as a clinical physiologist and pharmacologist. Until now he has not had access to a textbook of anatomy designed specifically to meet his requirements. Dornette's attractive book has much to recommend it, but, alas, does not quite fulfill this reviewer's hopes. For an anatomy textbook, courses and distribution of peripheral nerves and their relation to other structures are not described with sufficient detail. The following, taken from page 43, is a pertinent example of the general lack of essential detail: "the iris is a delicate washer-shaped structure located behind the cornea".

Long an enthusiastic teacher of anesthesiology, Dr. Dornette had been particularly interested in the development of devices that could aid in teaching. In this book, he employs stereoscopy to give the reader three-dimensional illustrations. Considerable difficulty was encountered by this reviewer and several other volunteers before they could obtain a three-dimensional view and it was felt that the space devoted to the paired pictures would have been better used for more two-dimensional pictures. On the other hand, the stereoscopic device proved to be very effective for those who found how to use it quickly.

Sections of the book, especially Chapters 2 and 10, contain excellent material on pharmacology, physiology and clinical anesthesiology which are of considerable practical value but do not belong in a textbook of anatomy.

For its fine anatomical pictures and for a quick reference textbook, it does belong in the anesthesiologist's bookshelf.

ETUDE EXPERIMENTALE DE L'HYPOTHERMIE PROFONDE A L'AIDE DE L'ALCOOL INTRAVEINEUX ET DE L'ADRENALINE*

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L'HYPOTHERMIE modérée mise au point par Bigelow, Callaghan, et Hopps[1] a été de 1950 à 1954 le procédé de choix en chirurgie à cœur-ouvert. Mais l'excitabilité du myocarde entraînant la fibrillation ventriculaire limitait le temps intra-cardiaque. Aussi cette technique quoique toujours employée fut remplacée par la technique d'oxygénation extra-corporelle en normothermie. En 1959 Drew et Anderson[2] redonnaient à l'hypothermie profonde un regain de faveur. Toutefois les complications diverses, en particulier cérébrales, de cette méthode lui font préférer aujourd'hui la circulation extra-corporelle associée à l'hypothermie modérée. S'inspirant des travaux de Bigelow[3] sur l'emploi de l'alcool au cours de l'hypothermie, nous avons entrepris une série d'expériences. L'alcool protège le myocarde au cours de l'hypothermie profonde et probablement d'autres organes, tel le cerveau. La mise au point d'une méthode sûre d'abaissement de la température corporelle permettant un arrêt circulatoire total, suffisamment prolongé pour l'application de techniques chirurgicales cardiaques ou extra-cardiaques, est de la plus grande importance. Le cœur-poumon artificiel, en dépit de ses perfectionnements demeure un fardeau pour le chirurgien. Actuellement, la température peut être abaissée à 18° ou 20°C. d'une façon pratiquement sûre sans adjonction de circulation extra-corporelle ou de chambre hyperbarique. Les expériences préliminaires exposées ici ont été faites en vue d'éliminer l'obstacle de la fibrillation ventriculaire en hypothermie profonde par administrations intraveineuse d'alcool et d'adrénaline. Ces expériences ont porté avant tout sur le cœur, mais des informations ont été aussi obtenues sur les autres systèmes. Trois techniques d'hypothermie profonde ont été utilisées: (1) L'hypothermie à l'aide de la circulation extra-corporelle. (2) L'hypothermie à l'aide du bain glacé. (3) L'hypothermie à l'aide de la chambre froide.

MATÉRIEL ET MÉTHODES

Vingt-huit chiens bâtards en bonne santé ont été employés. Leur poids variait de 5 à 33 kg. (moyenne 17 kg.). Après prémédication à la morphine-atropine, ils furent anesthésiés au pentho-barbital sodique (25 à 30 mg./kg. en moyenne). Le nembutal intraveineux à la dose de 25 mg./kg. fut utilisé dans trois cas d'hypothermie de surface. Puis l'intubation endo-trachéale fut pratiquée; la respiration fut assistée manuellement à l'oxygène pur sauf dans les cas d'hypothermie en chambre froide où l'on employa un respirateur mécanique à l'air comprimé.

Le Tableau I résume les cas d'hypothermie profonde, classés en cinq groupes. Dans les trois premier groupes l'hypothermie fut obtenue à l'aide de la circulation extra-corporelle. Le cœur-poumon artificiel utilisé est une modification de l'appareil Dewall-Lillehei-Zudhi. Les échangeurs thermiques sont montrés à la Fig. 1, comprenant la spirale de Zudhi et la chambre de démoussage où circule l'eau froide ou chaude. Le quatrième groupe correspond aux cas d'hypothermie par bain glacé et le cinquième d'hypothermie par chambre froide.

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*Travail effectué dans le service de chirurgie expérimentale de l'Hôtel-Dieu St-Vallier de Chicoutimi, Qué.

Présenté à la 33ème réunion annuelle du Collège Royal des Médecins et Chirurgiens du Canada, Québec, janvier 1964.

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TABLEAU I.—Résumé des cinq groupes d'hypothermie

Groupes	*Méthode*	*"Priming volume"*	*Administration intraveineuse*	*Température moyenne en fibrillation ventriculaire*
1 (11)	Cœur poumon artificiel Dewall-Lillehei-Zudhi	Sang (1000 à 2000 c.c.)		30° C.
2 (4)	Cœur poumon artificiel Dewall-Lillehei-Zudhi	Soluté glucosé 5% *vs.* Rhéomacrodex (250 à 500 c.c.)		29° C.
3 (8)	Cœur poumon artificiel Dewall-Lillehei-Zudhi	Soluté glucosé 5% *vs.* Rhéomacrodex (250 à 500 c.c.)	Alcool éthylique et adrénaline	18° C.
4 (3)	Bain glacé		Alcool éthylique et adrénaline	Pas de fibrillation
5 (2)	Chambre froide		Alcool éthylique et adrénaline	20° C.

Groupe 1

Il comprend 11 chiens où l'hypothermie a été obtenue par circulation extra-corporelle. Le cœur-poumon artificiel a été amorcé avec du sang d'un autre chien. Le "priming volume" a varié de 1000 c.c. à 2000 c.c.

Groupe 2

Ce groupe est formé de quatre chiens.

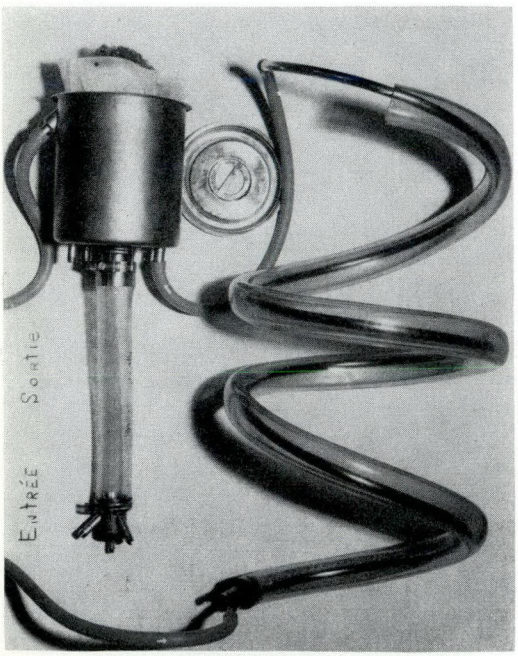

Fig. 1.—Echangeurs thermiques.

L'hypothermie fut obtenue ici par hémodilution provoquée soit avec un soluté de glucose à 5%, soit avec un type spécial de dextran (Rhéomacrodex*). Le "priming volume" varia entre 250 et 500 c.c.

Groupe 3

Il comprend huit chiens. La méthode d'hémodilution fut également utilisée, soit par soluté glucosé à 5% soit par le dextran spécial. Le "priming volume" a également varié de 250 c.c. à 500 c.c. Dans ce groupe du glucose à 5% avec 15% d'alcool éthilique fut administré dans une patte antérieure avant l'hypothermie. Chaque chien reçut une dose empirique de 1.5 g. d'alcool éthilique par kilogramme. Nous regrettons ici de ne pouvoir fournir l'alcoolémie. D'autre part un soluté glucosé à 5% a été installé contenant de l'adrénaline. Cette drogue fut injectée à la dose d'un γ/kg./min. quand la température atteignit 30° C.

La Fig. 2 montre la préparation de l'animal avant l'hypothermie. Les températures rectale, œsophagienne, cérebrale, tympanique et musculaire sont mesurées ainsi que l'EEG et l'ECG. Une aiguille installée dans le canal rachidien permet de mesurer la pression ou de prélever du liquide céphalo-rachidien. La pression fémorale est enregistrée sur bande de papier à l'aide d'un appareil Sanborn. Un cathéter est installé dans l'urètre pour prélèvement des urines.

*Pharmacia Laboratories, Inc., New York.

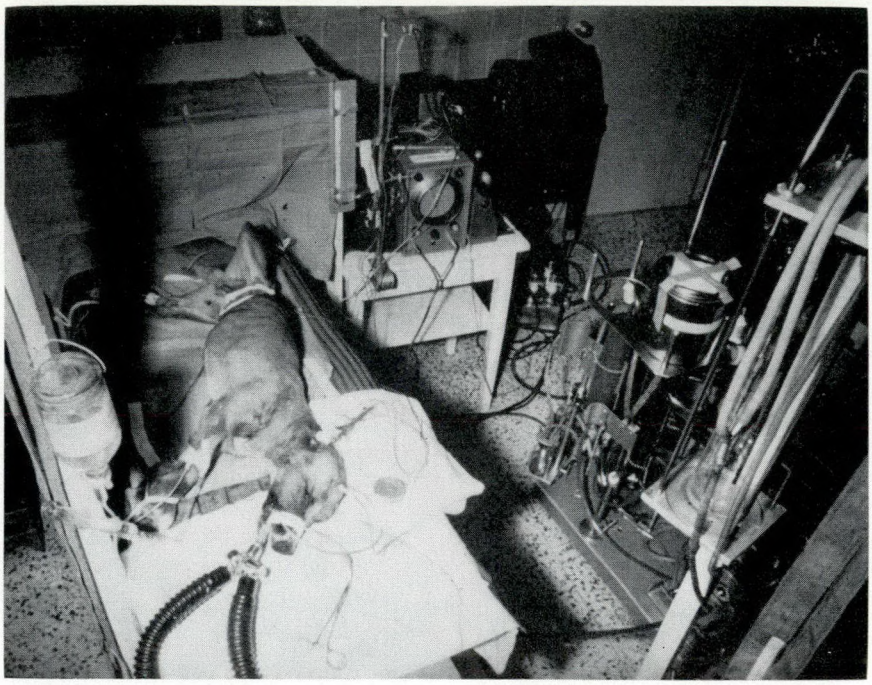

Fig. 2.—Installation du chien avant l'hypothermie.

Pendant ce temps le cœur-poumon artificiel est amorcé avec du soluté glucosé à 5% à raison de 20 c.c./kg. ou du dextran à raison de 12 c.c./kg. Quand l'un ou l'autre de ces solutés n'atteint pas le minimum de 250 c.c. de "priming volume" ils sont ajoutés l'un à l'autre. Le débit du cœur-poumon artificiel est réglé suivant la charte de Gollan (Fig. 3) mais en étant beaucoup plus généreux dans le débit que Gollan. La température de l'eau circulant dans la machine à trois compartiments de Kimray* est la plus basse à —5° C. et —12° C. et la plus élevée à 46° C.

*Kimray, Inc., Oklahoma City 18, Oklahoma, U.S.A.

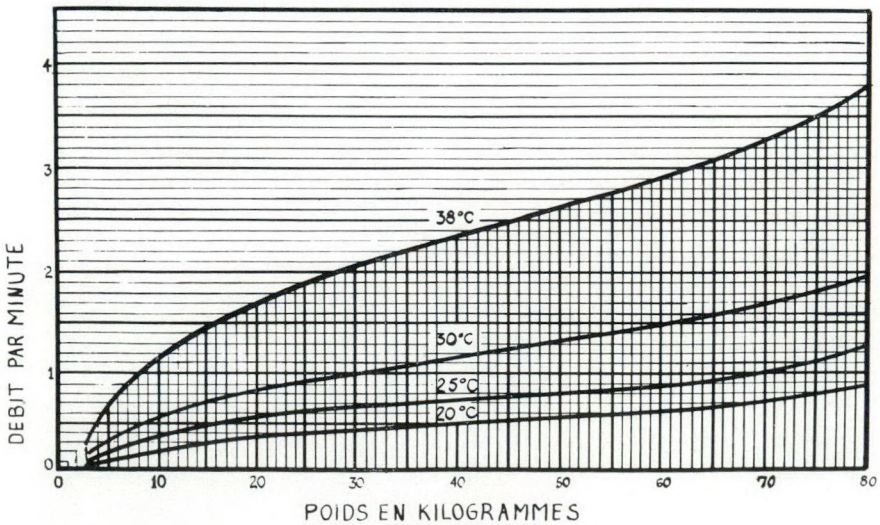

Fig. 3.—Charte de Gollan

Groupe 4

Il comprend trois chiens. Une installation semblable à celle du groupe 3 est faite avant l'hypothermie. La température intra-cardiaque est prise ici grâce à un cathéter placé dans la veine jugulaire ou la veine fémorale. Le chien est ensuite plongé dans un bain d'eau glacée variant de —5° C. à —12° C. Cette température a été obtenue en mettant de l'alcool éthylique et du sel marin dans l'eau. (L'alcool éthylique est administré à la dose de 1.5 g./kg. avant l'hypothermie et l'adrénaline à la dose de 1 γ/kg./min. quand la température atteint 30° C.) Sous hypothermie par bain glacé deux chiens ont subi une thoracotomie à 20° C. pour installer un pacemaker destiné à l'excitation directe du myocarde pour abaisser la température. Dans ces deux cas, le pace-maker n'a pas pris le contrôle ventriculaire.

Groupe 5

Il comprend deux chiens. Ces chiens furent préparés comme ceux des groupes 3 et 4; ils furent placés dans un réfrigérateur construit par la "Gervett Refrigerator Co. Buffalo, N.Y.", utilisé originellement pour la conservation des cadavres. Grâce à un orifice dans le plafond, il est possible de passer les tubes de perfusion contenant l'alcool et l'adrénaline, les lignes de l'ECG et de l'EEG, les cathéters pour la pression artérielle et la température et enfin le tube du respirateur artificiel. Cette technique d'hypothermie profonde par chambre froide serait confortable pour le sujet et le médecin, et nous paraît la plus pratique. Cette méthode serait sous la responsabilité de l'anesthésiste; le malade pourrait ainsi être refroidi lentement pendant la nuit et le chirurgien l'opérerait tranquillement le matin suivant. Il est connu qu'un individu ayant ingurgité de fortes doses d'alcool et tombant dans la neige la nuit, se retrouve le plus souvent vivant le matin, avec une température rectale ou buccale parfois au-dessous de 60° F.; dans le même cas un sujet à jeun mourrait avant d'atteindre cette température.

RESULTATS

Groupe 1

Dans 10 des 11 cas étudiés la fibrillation ventriculaire apparut lorsque la température œsophagienne était aux environs de 29° C. Dans un cas cependant, la fibrillation ventriculaire n'est survenue qu'à 15° C. Ces expériences n'avaient pas pour but d'étudier la tolérance du myocarde au froid mais plus simplement d'obtenir de basses températures avec survie de l'animal. La température œsophagienne la plus basse à été de 10° C. avec une moyenne de 14° C. Le temps de refroidissement a varié de neuf à 39 minutes avec une moyenne de 19 minutes. L'arrêt circulatoire fut réalisé chez 10 chiens entre 10 et 40 minutes avec une moyenne de 26 minutes. La durée de la circulation extra-corporelle a varié de 46 à 96 minutes (avec une moyenne de 70 minutes), et la pression artérielle au cours des perfusions de 45 à 100 mm. Hg. La défibrillation ventriculaire a été obtenue dans neuf cas dont une fois spontanément, mais toujours aux environs de 29° C. et 30° C. Dans les deux autres cas, la défibrillation fut impossible. Quatre cas furent facilement défibrillés avec un seul choc de 1/10 de seconde à 60 volts. Dans les quatre autres cas, la défibrillation a été plus difficile et il fallut employer tout l'arsenal de la réanimation cardiaque et des chocs électriques de plus en plus intenses et répétés. Trois chiens ont survécu à l'intervention à long terme, soit 27%. Trois chiens sont morts sur la table d'opération, soit 27%. Cinq chiens sont mort dans les 24 heures, (y compris une transplantation du cœur qui a survécu 24 heures 25 minutes) soit 46%. La mortalité a donc été de 73%. Dans cinq cas, la mort fut causée par hémorragie ou œdème aigu du poumon, dans un cas par coma acidosique, dans un cas par incompatibilité sanguine et dans un cas par erreur technique.

Groupe 2

C'est également un groupe de contrôle pratiqué avec la méthode d'hémodilution à l'aide du soluté glucosé à 5% ou du dextran. Au cours de ces expériences la fibrillation ventriculaire s'est toujours pro-

duite autour de 27° à 28° C. (température œsophagienne). La température la plus basse a été de 23° C. Il n'y a pas eu d'arrêt circulatoire. La pression artérielle au cours de la perfusion a varié de 45 à 70 mm. Hg. Dans les quatre cas (dont deux transplantations cardiaques), la défibrillation a été obtenue facilement avec un seul choc autour de 30° C. Le temps de circulation extra-corporelle a varié de 38 à 134 minutes. Les deux cas de transplantation cardiaque sont morts dans les heures suivantes. Un chien porteur d'une valvule aortique de Starr-Edwards est mort neuf jours plus tard par obstruction de l'ostium de l'artère coronaire gauche. Un cas de greffe de l'aorte ascendante est mort d'hémorragie en cours d'opération. Les examens hématologiques et biochimiques étaient sensiblement normaux.

Groupe 3

Dans ce groupe l'hypothermie a été pratiquée à l'aide de la circulation extra-corporelle, l'hémodilution avec le glucose à 5% à raison de 20 c.c. kg./min. ou le dextran à raison de 12 c.c./kg., l'alcool intraveineux et l'adrénaline. Les huit animaux de ce groupe ont reçu 1.5 g. d'alcool éthylique à 95% dans un soluté glucosé à 5% par voie intraveineuse avant l'hypothermie. Quatre d'entre eux reçurent de l'adrénaline à la dose de 1 γ/kg./min. lorsque la température œsophagienne atteignit 30° C. Dans six cas, l'arrêt cardiaque par fibrillation ventriculaire est survenue au-dessous de 20° C. (température œsophagienne), soit: deux cas à 17° C., deux cas à 18° C., un cas à 14° C. et un cas à 9° C. Dans un autre cas, la fibrillation ventriculaire est apparue à 22° C.; le massage cardiaque simple a permis de rétablir des battements énergiques jusqu'à 17° C. Dans le dernier cas, le cœur s'est arrêté dès la mise en route de la circulation extra-corporelle à 30° C. mais un seul choc électrique l'a défibrillé et les battements persistèrent jusqu'à 17° C. (Fig. 4). On peut donc constater que le refroidissement est plus rapide chez les chiens qui reçoivent de l'adrénaline (40 minutes en moyenne) que chez ceux qui n'en reçoivent pas 52 minutes

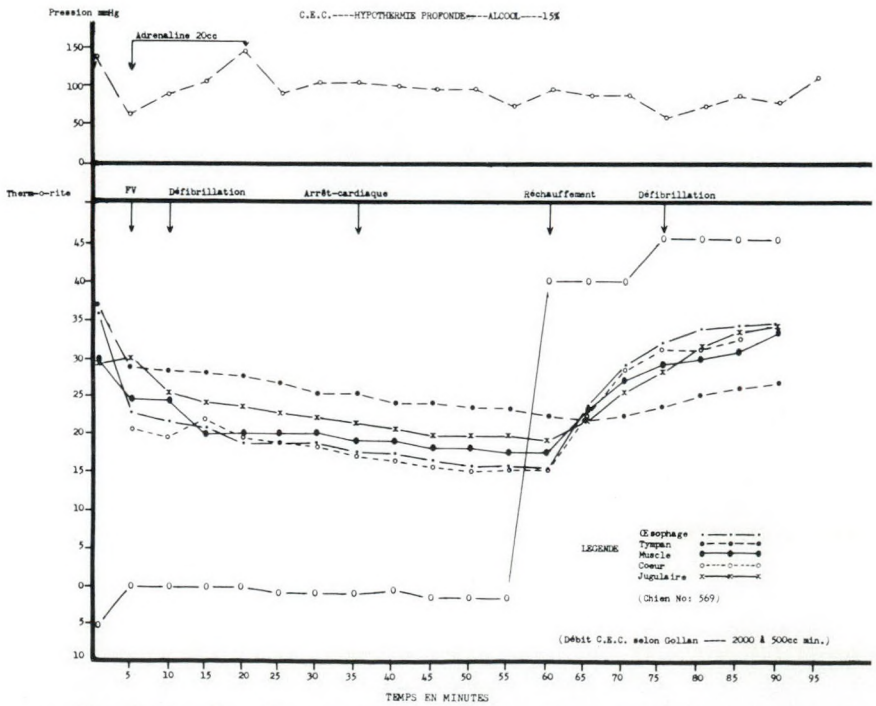

Fig. 4.—Courbes de température et de pression enregistrées au cours de l'hypothermie par circulation extra-corporelle chez le chien no. 569.

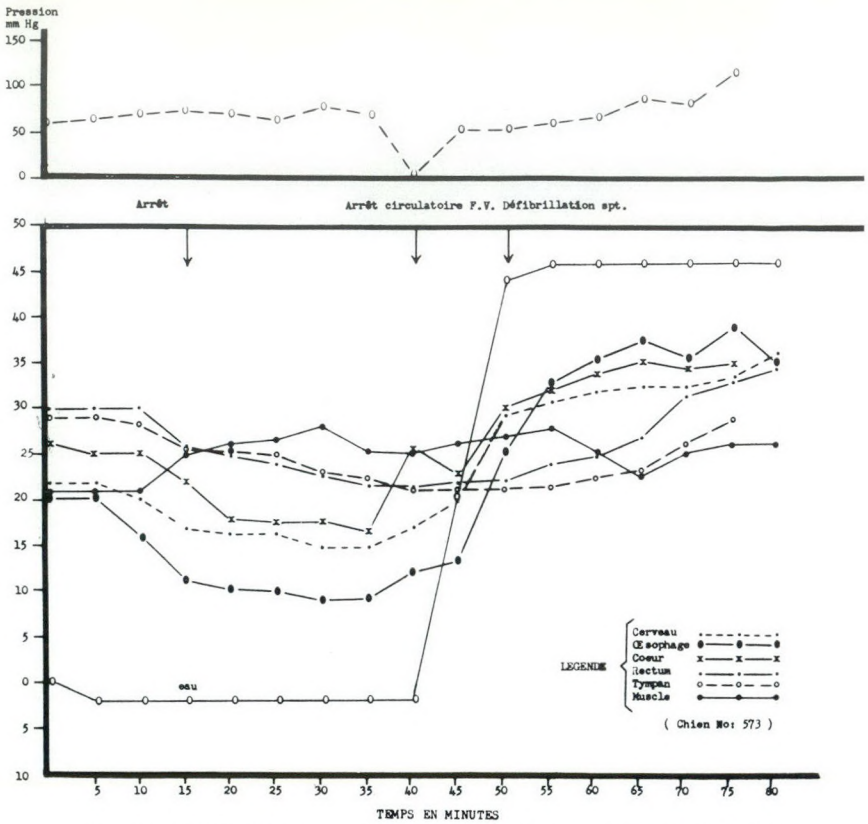

Fig. 5.—Défibrillation spontanée à la température cérébrale de 21°C.

en moyenne). La durée du refroidissement a varié de 30 à 60 minutes. La température la plus basse enregistrée a été de 9° C. avec une moyenne de 11° C. (œsophage). Le chien montré à la Fig. 5 a défibrillé spontanément à la température cérébrale de 21° C. au début du réchauffement. Dans un cas le cœur a été défibrillé électriquement par un seul choc à la température œsophagienne de 23° C. au début du réchauffement. Dans les autres cas, la défibrillation électrique a été pratiquée aux environs de 30° C. Un choc a suffi pour faire repartir le cœur, qui a conservé un bon tonus, et un aspect rosé. Le débit de la circulation extra-corporelle a oscillé entre 60 et 100 c.c./kg./min. (moyenne de 80 c.c./kg./min.). La pression de perfusion la plus basse a été de 60 mm. Hg et la plus haute de 110 mm. Hg, avec une moyenne de 75 mm. Hg; tandis que chez les chiens non adrénalisés, la pression moyenne a été de 68 mm. Hg. La durée de la circulation extra-corporelle a varié de 58 à 100 minutes (moyenne 82 minutes). La durée du réchauffement a été sensiblement la même avec ou sans adrénaline. Trois chiens ont survécu à l'intervention avec des suites, opératoires excellentes. Un de ces chiens est mort sept jours plus tard par pyo-pneumothorax. La survie a donc été de 37.5%. Trois chiens sont morts d'hémorragie dans les 24 heures post-opératoires. Le sang n'a jamais été utilisé au cours de ces expériences et n'a jamais été remplacé dans les suites post-opératoires. Un chien est mort d'hémorragie cérébrale causée par la trépanation et l'aiguille du thermocouple. Un chien est mort de coma diabétique, malgré le traitement, 48 heures après l'intervention.

Les examens hématologiques et biochimiques, avant et après hypothermie ne montrent pas de changements appréciables dans les groupes 1 et 2. Toutefois le magnésium est très diminué dans le groupe 3.

TABLEAU II.—Examens biochimiques dans les différents groupes

	No.	Na			K			Cl			Mg			HCO^3-			pH			pCO_2	
		Avant	Pendant	Après	Avant	Pendant	Après	Avant	Pendant	Après	Avant	Pendant	Après	Avant	Pendant	Après	Avant	Pendant	Après	Avant	Après
Groupe de contrôle sans alcool	2	145		138	3.8		4.0	116		110	2.2		2.7	23.0		13.6					
Groupe en circulation extra-corporelle avec sang	9	140		130	3.7		3.5	109		101				23.2		16.0					
Groupe en circulation extra-corporelle avec alcool et adrénaline	7	145	135	135	3.9	4.4	2.9	110	109	109	2.2	0.45	1.65	25.0	22.0	18.0	7.2	7.3	7.5	35	23
Groupe hypothermie de surface bain glacé	3	138	145	134	3.1	3.8	2.6	108	104	104	2.0	1.1		24.4	25.0	13.0	7.25	7.24	7.3	56	58
Groupe hypothermie en chambre froide	1	150	130		3.5	3.0		112.2						29.0	12.7				7.23		

Les prélèvements faits à la fin du refroidissement montrent une diminution à 0.45 mEq., (taux normal 2.2 mEq.) (Tableau II). L'abaissement du taux de mg.++ a aussi été observé au cours de l'hypothermie par bain glacé. Au cours du réchauffement ce taux redevient normal. L'électrocardiogramme montre un rythme sinusal à 60 à des températures jugulaires de 20° C. La pression systolique est à 100 mm. Hg à cette température (Fig. 6). Au cours de ces hypothermies avec alcool intraveineux un phénomène inusité est apparu à une température d'environ 20° C.: l'exophtalmie des globes oculaires avec mydriase totale (Fig. 7). A cette température, la pression du liquide céphalo-rachidien est cependant basse. Nous pensons être ici en présence d'une sorte de glaucome aigu dû à l'alcool. Au cours du réchauffement, les globes oculaires redeviennent rapidement normaux. Un chien n'a pas présenté d'exophtalmie; il avait reçu une dose d'alcool plus faible, soit 1 g./kg.

Groupe 4

Un des trois chiens soumis au bain glacé a reçu du nembutal intraveineux et les deux autres du pentotal. La température du bain a été maintenue entre —5° C. à —12° C. Ces trois chiens ont reçu de l'alcool éthylique à raison de 1.5 g. dans du soluté glucosé à 5%. L'adrénaline a été administrée à la dose de 1 γ/kg./min.

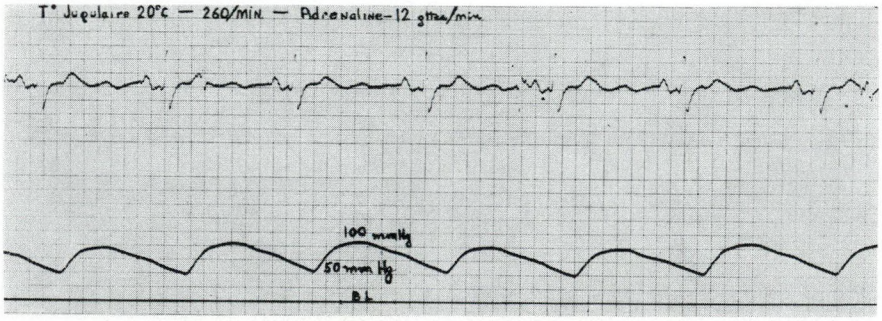

Fig. 6.—Electrocardiogramme et pression systémique à la température jugulaire de 20° C.

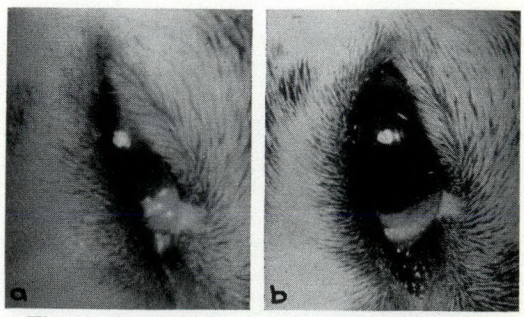

Fig. 7.—(a) Oeil du chien à la température de 25° C. et (b) œil du chien à la température de 20° C.

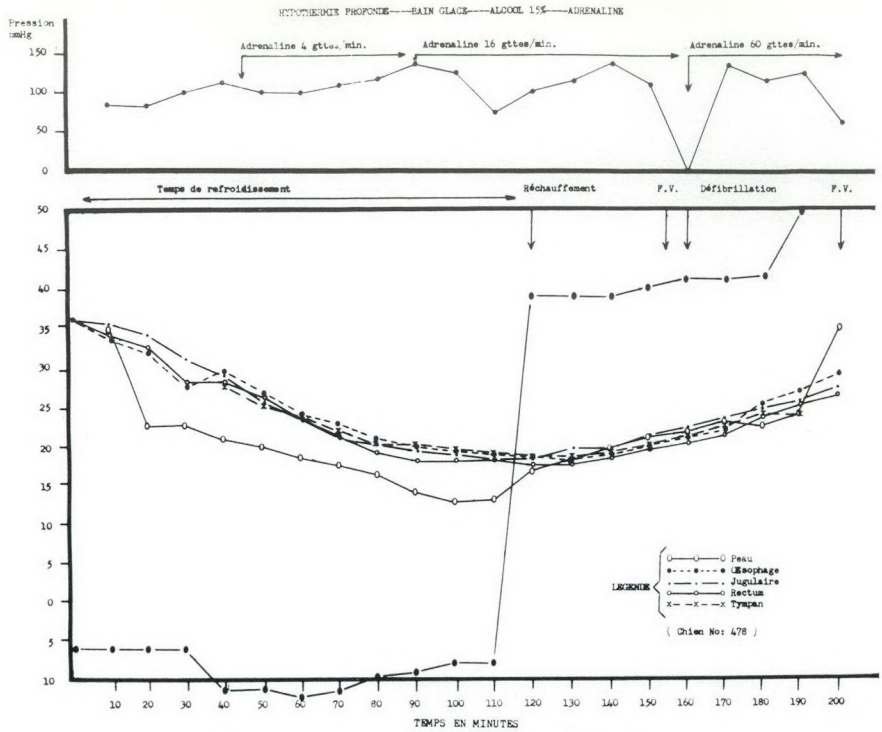

Fig. 8.—Hypothermie de surface par bain glacé.

D'après la durée de l'expérience ces chiens ont reçu respectivement 3800 γ d'adrénaline pour un poids de 20 kg., 4750 γ d'adrénaline pour un poids de 15 kg., 6300 γ pour un poids de 22 kg.

La durée du refroidissement a varié de 110 à 215 minutes. Les chiens ont été retirés du bain froid à la température jugulaire de 18° C., 20° C et 19° C. A la sortie du bain glacé, les températures descendent encore d'un degré et ceci même au début du réchauffement. Ce réchauffement (Fig. 8) a été commencé avec le matelas therm-o-rite, mais la température ne s'élevant que de 1° C. par heure, il a été continué dans un bain d'eau chaude. Avant ce bain, la pression artérielle était de 100 mm. Hg, mais subitement une fibrillation ventriculaire apparut. Une thoracotomie permit de constater que le cœur avait un bon tonus, le massage cardiaque fait remonter la pression artérielle à 110 mm. Hg, et un choc électrique rétablit les battements cardiaques. Après la fermeture de la thoracotomie le chien fut plongé dans un bain d'eau chaude et les diverses températures remontèrent très rapidement et uniformément. La diurèse fut de 35 c.c./heure pendant toute l'expérience, l'aspect et l'examen des urines étant normaux. Les examens de sang montrent une hémoconcentration et une polyglobulie, ainsi qu'une baisse du potassium et du magnésium. L'hypertension des globes oculaires très manifeste aux environs de 20° C., disparaît très rapidement au cours du réchauffement. Sur deux chiens on a installé un pace-maker dans le but de prolonger l'hypothermie; celui-ci n'a cependant jamais pris le contrôle des contractions ventriculaires.

Groupe 5

Les deux chiens de ce groupe ont été placés dans une chambre froide qui ne présentait pas toutes les commodités souhaitable pour obtenir des résultats valables. Une fois fermée, la chambre ne permet pas de contrôler directement l'animal; il en est de même quant à divers appareils tels que les tubes de respiration, de perfusion, et l'enregistrement électrique. Nous avons seulement obtenu un aperçu de la progression du refoidissement en am-

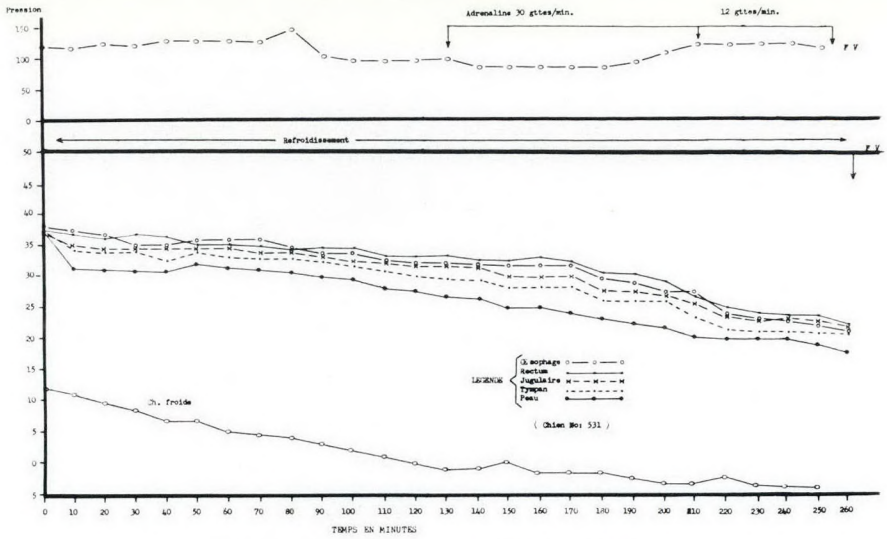

Fig. 9.—Hypothermie par chambre froide.

biance froide, avec emploi d'alcool et d'adrénaline (Fig. 9). La fibrillation ventriculaire est survenue à la température de 20° C. (œsophage, jugulaire et rectum). Les deux chiens ont reçu comme dans les groupes précédents de l'alcool et de l'adrénaline. La pression artérielle et le pouls se sont toujours maintenus normaux. L'hypertension des globes oculaires est apparue, comme dans les cas précédents, à la température de 20° C. Il est frappant de voir que les courbes des diverses températures sont pratiquement identiques (Fig 9).

Discussion

L'hypothermie thérapeutique provoque des modifications biologiques en relation avec plusieurs fonctions organiques, telles qu'endocriniennes, enzymatiques, énergétiques, cérébrales, biochimiques, hémodynamiques, etc.; beaucoup de ces facteurs échappent encore aujourd'hui à notre connaissance même chez l'individu en normothermie. Pourtant, le clinicien, un peu à l'encontre du physiologiste ou du chercheur pur, a déjà obtenu des résultats encourageants dans l'utilisation pratique de l'hypothermie. Depuis une dizaine d'années la circulation extracorporelle en normothermie avait détrôné l'hypothermie modérée; depuis ces techniques sont utilisées en association dans la plupart des centres de chirurgie cardio-vasculaire. Toutefois certains chirurgiens maîtrisant les techniques de corrections de nombreuses malformations cardiaques à l'aide du cœur-poumon artificiel ont délibérément abandonné l'étude de l'hypothermie profonde. Il faut cependant admettre que le cœur-poumon artificiel demeure une complication pour le chirurgien, malgré l'entraînement constant et progressif des techniciens et le perfectionnement des appareils; la circulation extra-corporelle en normothermie, ou associée à l'hypothermie modérée, est loin d'être toujours sans danger. Une circulation extra-corporelle durant plus de 150 minutes est certainement dangereuse. L'hypothermie profonde obtenue à l'aide de moyens naturels ou même pharmaceutiques offrirait une plus grande sécurité. La découverte de la ou des substances hormonales qui provoquent l'hibernation chez certain animaux tels la marmotte et l'ours sera sans doute le progrès de l'avenir.

Néanmoins plusieurs auteurs tels que Malmejac,[4] Yonezawa et Okamura,[5] Meyne *et al.*[6] et Benichoux *et al.*[7] ont obtenu des résultats intéressants, tendant à supprimer la barrière conventionnelle de l'arrêt circulatoire par fibrillation ventriculaire en hypothermie aux environs de 28° C. Malmejac[4] insiste sur l'hyperventilation et la perfusion à dose physiologique de l'adrénaline pour maintenir la

fonction myocardique. Nous pouvons confirmer les travaux de Malmejac sur le dosage physiologique de l'adrénaline: le chien en hypothermie a un comportement circulatoire normal. Malmejac a utilisé les mêmes doses d'adrénaline que nous-mêmes.

L'hypocapnée n'a pas été systématiquement recherché dans ces expériences mais dans deux observations, le pCO_2 était au-dessous de 25 mm. Hg, et dans trois autres observations le pCO_2 était normal. Dans une expérience du Groupe 4, un chien a présenté une acidose respiratoire décompensée avec pH à 7.19 et pCO_2 à 63 mm. Hg dès le commencement de l'expérience. A la fin de l'hypothermie le pH était à 7.1 et le pCO_2 à 92 mm. Hg. Cependant le chien a eu un bon comportement hémodynamique et la défibrillation s'est faite aisément.

Yonezawa et Okamura[5] favorisent l'anesthésie profonde au cours de l'hypothermie. En 1961, ils avaient déjà opéré sous hypothermie de surface variant entre 26° C. et 17° C., 53 cardiopathies (15 communications interventriculaires, 11 insuffisances mitrales, trois tétralogies, quatre pentalogies, 14 communications inter-auriculaires, une sténose pulmonaire, un canal auriculoventriculaire commun, une sténose aortique) avec 42 survies en bonne santé. Les arrêts circulatoires avaient duré de 6 à 45 minutes. Meyne *et al.*[6] provoquent l'hypothermie profonde à l'aide de la chambre hyperbarique. La description qu'ils donnent de la fibrillation ventriculaire à 20° C. du tonus cardiaque et de la défibrillation facile, est semblable à nos observations en hypothermie au-dessous de 20° C. avec alcool et adrénaline intraveineux. L'hyperkaliémie observée à trois atmosphères n'a pas été dans nos expériences. Il semble que Benichoux *et al.*[7] réussissent à corriger l'acidose extra-cellulaire et intra-cellulaire avec le THAM. L'acidose intra-cellulaire est sans doute la plus importante à éviter au cours de l'hypothermie profonde pour retarder la fibrillation ventriculaire. Dans nos observations le bicarbonate de soude s'est avéré satisfaisant; le THAM sera essayé lors d'expériences ultérieures.

Les observations préliminaires sur l'hypothermie profonde avec alcool intraveineux montrent que l'alcool a un effet protecteur sur le myocarde; ceci est en opposition des conclusions de Degerli et Webb.[8]

Conclusions

L'alcool éthylique à la dose de 1.5 g./kg. permet d'obtenir d'une façon constante la conservation des battements cardiaques en hypothermie au-dessous de 20° C. Le cœur entre en fibrillation ventriculaire lorsque la température descend au-dessous de 20° C. à 17° C. Toutefois, chez un chien, le cœur a continué à battre jusqu'à 9° C. La défibrillation est toujours facile aux environs de 20° C. à 25° C. La température cérébrale suit la température œsophagienne en hypothermie par circulation extra-corporelle et est pratiquement la même que celle des cavités cardiaques en hypothermie de surface; c'est-à-dire qu'une hypothermie à 20° C. permettrait un arrêt circulatoire d'au moins 60 minutes sans lésions cérébrales.[9] L'hypothermie profonde de surface peut être conduite de façon sûre au moyen de l'alcool intraveineux et facilitée par la perfusion continue d'adrénaline à la dose d'un γ/kg./min. au cours du refroidissement et du réchauffement. L'hypothermie de surface en chambre froide malgré sa lenteur apparaît la plus satisfaisante. Des techniques compliquées et onéreuses telles que le cœur-poumon artificiel, la chambre hyperbarique ont été résolues. Une chambre de refroidissement et de réchauffement pourrait être réalisée à beaucoup moins de frais. En chirurgie cardiaque, le temps opératoire serait grandement facilité, les canulations éliminées et surtout les traumatismes sanguins et cellulaires évités.

Le mode d'action de l'alcool demeure hypothétique, mais l'on peut supposer qu'il a un effet cataboliseur sur la cellule myocardique à basse température. La chute du taux du magnésium au cours de l'hypothermie profonde reste à éclaircir, ainsi que l'hypertension des globes oculaires sans hypertension du liquide céphalo-rachidien.

Mademoiselle Jacqueline Gilbert infirmière responsable du département, et Monsieur Marcel Bouchard et Monsieur Marc Buteau, techniciens, ont été d'un précieux secours au cours de ces expériences. Les photos et les schémas ont été réalisés par Monsieur Gaetan Jeanrie, chef du département de photographie et d'art médical.

Bibliographie

1. Bigelow, W. G., Callaghan, J. C. et Hopps, J. A.: General hypothermia for experimental intracardiac surgery; use of electrophrenic respirations, an artificial pacemaker for cardiac standstill, and radiofrequency rewarming in general hypothermia, *Ann. Surg.*, **132:** 531, 1950.
2. Drew, C. E. et Anderson, I. M.: Profound hypothermia in cardiac surgery; report of three cases, *Lancet,* **1:** 748, 1959.
3. Bigelow, W. G.: Communication personnelle.
4. Malmejac, J.: Hypothermie profonde sans circulation extra-corporelle. *In*: Proceedings of Symposium International: L'hypothermie profonde en chirurgie cardiaque et extra-cardiaque, 1961, Paris, UNESCO, Paris, 1962, p. 57.
5. Yonezawa, T. et Okamura, H.: Clinical deep hypothermia for intracardiac surgery (26° C.- 17° C. by surface cooling), *In*: Procedings of Symposium International: L'hypothermie profonde en chirurgie cardiaque et extra-cardiaque, 1961, Paris, UNESCO, Paris, 1962, p. 64.
6. Meyne, N. G. *et al.*: Deep hypothermia under high pressure without extracorporeal circulation, *In*: Proceedings of Symposium International: L'hypothermie profonde en chirurgie cardiaque et extra-cardiaque 1961, Paris, UNESCO, Paris, 1962, p. 66.
7. Benichoux, R. *et al.*: Arrêt circulatoire hypothermique sans circulation extra-corporelle avec perfusion de THAM, *In*: Proceedings of Symposium International: L'hypothermie profonde en chirurgie cardiaque et extra-cardiaque, 1961, Paris, UNESCO, Paris, 1962, p. 72.
8. Dergerli, I. U. et Webb, W. R.: Alcohol; cardiac function and coronary flow, *Surg. Forum,* **14:** 252, 1963.
9. Connolly, J. E. et Boyd, R. S.: The effects of hypothermia on the brain, *In*: Proceedings of Symposium International: L'hypothermie profonde en chirurgie cardiaque et extra-cardiaque, 1961, Paris, UNESCO, Paris, 1962, p. 267.

Summary

In a dog experiment it has been found that in all cases, ethyl alcohol at the dosage of 1.5 g./kg. (empirically chosen) will maintain heart beats during hypothermia below 20° C. to 17° C. In one dog, however, the heart kept on beating until 9° C. Defibrillation is always easy around 20° C. to 25° C. Cerebral temperature follows closely on esophageal temperature in extracorporeal circulation hypothermia; it is almost identical to that of the cardiac chambers in surface hypothermia. This implies that a 20° C. hypothermia would allow a circulatory arrest of at least 60 minutes without giving rise to cerebral damage. Deep surface hypothermia may be carried out safely with the help of intravenous alcohol. It is facilitated by the use of a continuous adrenaline drip at the dosage of one γ/kg./min. during the cooling and the rewarming periods. Surface hypothermia in refrigerated rooms, in spite of its slowness, seems to be the most satisfactory method of all. Considering that complicated and costly techniques such as heart-lung apparatus and hyperbaric oxygen chambers have been built and are now accepted, there is no reason why a cooling and a rewarming room could not be devised (at much lower cost) and commonly used in hypothermia. Operating time in cardiac surgery could be greatly shortened; cumbersome connections and cannulas could be dispensed with; blood and tissues could be spared damaging trauma.

The mechanism of action of alcohol still remains to be elucidated but it may be hypothesized that ethanol exerts a catabolic effect on the myocardial cells at low temperatures. The drop in blood magnesium, and also the intra-ocular hypertension without a corresponding rise in CSF pressure are as yet unexplained.

HISTOCHEMICAL STUDIES OF THE FATE OF AUTOLOGOUS DIGITAL FLEXOR TENDON GRAFTS IN THE CHICKEN

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THE histological events which take place in the healing digital flexor tendon are still a matter of controversy. Lindsay and McDougall[1] concluded their article on the fate of autologous digital flexor tendon grafts with the following statement: ". . . Histological studies indicate that the graft as a whole survives, and is reconstructed by a process of 'repair'—by an increase in number of mature fibroblasts, a revascularization of the graft and a gradual reconstitution or replacement of the original collagen. At the sutured or injured ends, however, union is accomplished by a process of 'regeneration': the collagen fibres of the acellular tissue are lysed and the spaces so formed are filled in with new vascular fibrogenic tissue which later becomes orientated and mature."

The purpose of the present study was to further clarify these healing processes by the use of histochemical stains which differentiate between old and new collagenic fibres.

MATERIAL AND METHOD

The digital flexor mechanisms of 20 healthy adult hens were used for the reasons stated by Lindsay and Thomson.[2] Preoperative preparation was similar to that which they described. Autologous, nonsutured, free profundus tendon grafts were taken from the middle toe of each foot and transferred to the middle toe of the opposite foot (Fig. 1). The graft and sheath were minimally traumatized by this procedure, except for the suture holes left in the proximal end of the graft and the tearing of the vinculum longus. The chickens were sacrificed eight weeks after operation, because previous investigations[3] had revealed that all types of healing were histologically demonstrable at this time. The healing toes were opened immediately after sacrifice and the tendon grafts were examined grossly. The graft and tendon stump were then removed, fixed in 10% formalin, embedded in paraffin, and sectioned as shown in Fig. 2. The proximal profundus stump was separately sectioned when it had retracted away from the graft.

The sections were stained with hematoxylin and eosin, hematoxylin and periodic acid-Schiff (H and PAS), alcian blue, toluidine blue, hematoxylin and eosin azure (HEA), and pinacyanol erythrosinate (PE). This communication will discuss only the results of the H and PAS stain of the proximal end of the graft and of the proximal stump. The results of alcian-blue staining will not be discussed because it gave similar results to the H and PAS-stained sections. The toluidine blue, HEA, and PE material also will not be described because these stains were not uniformly successful. Only the longitudinal sections of Zone 1 will be discussed because the cross sections, although they yielded interesting information, were technically too poor for photography, and the longitudinal sections of Zone 4 added nothing to the results of Zone 1.

RESULTS AND DISCUSSION

Hematoxylin and periodic acid-Schiff staining[4] was found to be applicable to a study of tendon repair, because it distinguishes between old collagenic fibres which stain light pink (PAS-negative), and new collagenic fibres which stain purplish-red (PAS-positive). This may be due to the fact that the more mature and differentiated fibres contain fewer unbound glycols available for the Schiff reaction.

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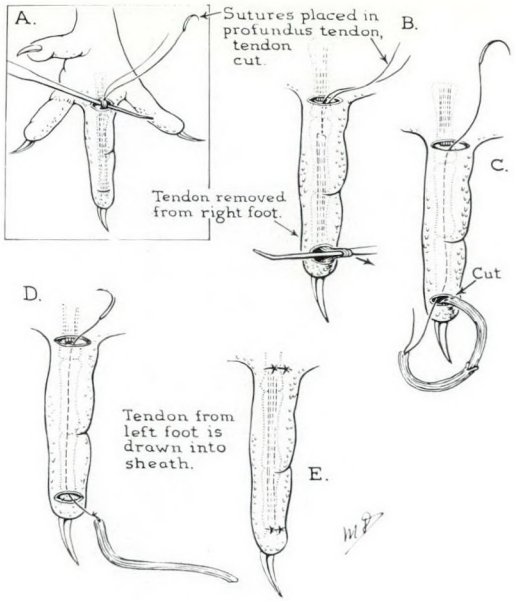

Fig. 1.—Autologous tendon graft operation. Only the right foot is shown. A, B and C show a graft being cut from it, and D and E show a graft from the left foot being substituted. The same procedure is also carried out on the left foot.

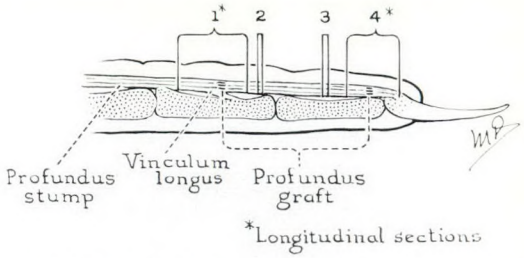

Fig. 2.—Method of sectioning postoperative profundus tendon graft and stump material. Cross sections were taken in Zones 2 and 3.

A. Normal Tendon

Normal tendon stained with H and PAS was found to have light pink collagenic fibres[5] and dark purplish-blue nuclei. The cytoplasm of the fibroblasts was usually indistinguishable, but sometimes stained a bright PAS-positive. PAS-positive cytoplasmic staining may indicate the cytoplasmic storage of the precursors of ground substance or cementing substance.[6] The epitenon and endotenon stained bright purplish-red. Fig. 3 shows a photomicrograph of a longitudinal section of normal tendon stained with H and PAS.

B. Incidental Findings

Fibrocartilage is normally found in digi-

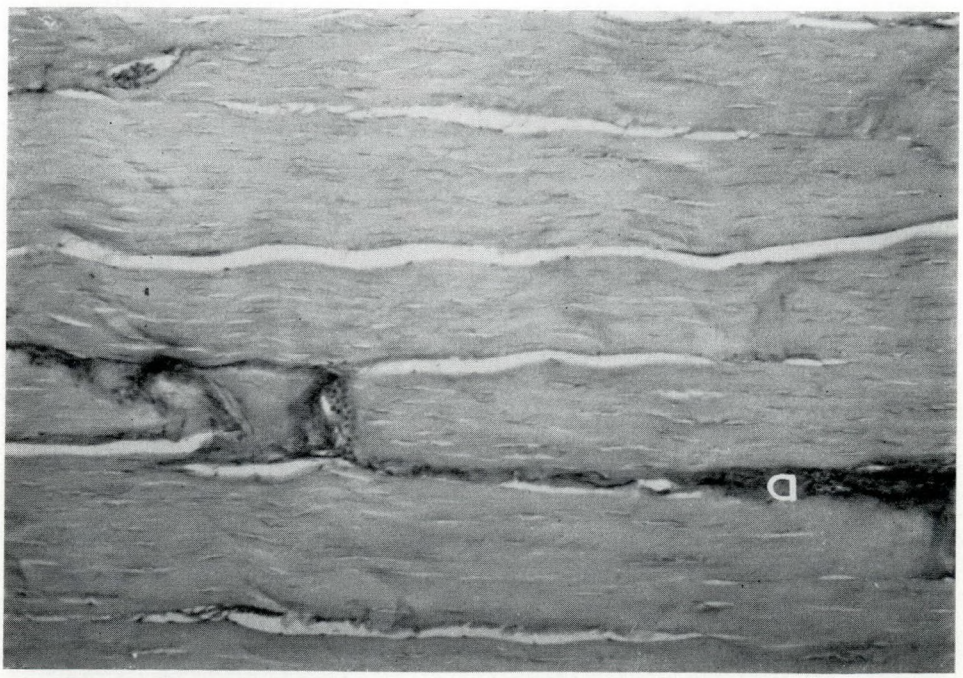

Fig. 3.—Photomicrograph of normal tendon showing dark hematoxylin-stained nuclei and (a) PAS-positive endotenon. The collagenic fibres are light.

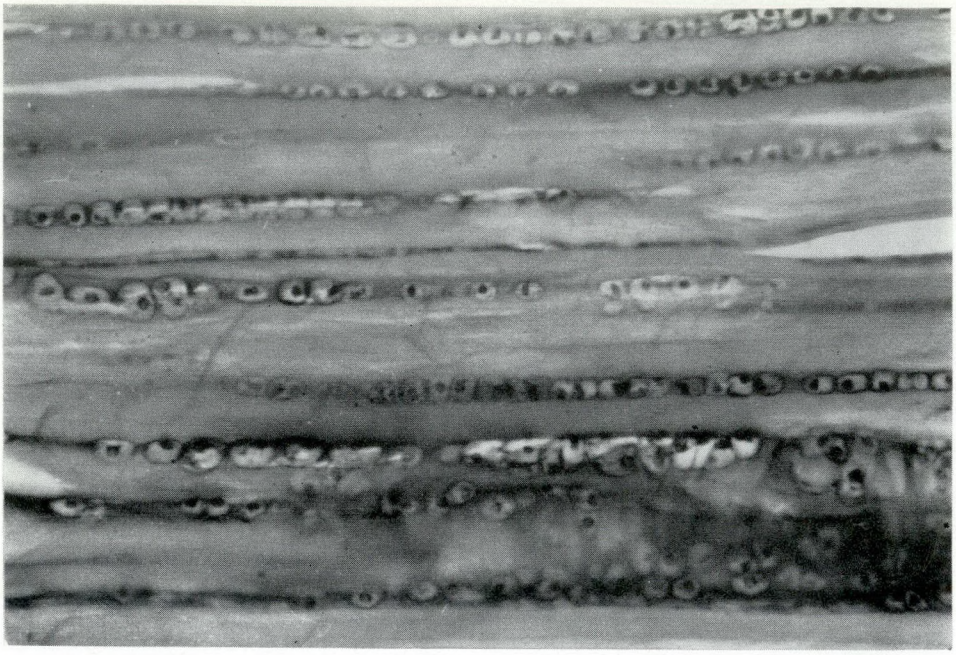

Fig. 4.—Fibrocartilage present in a tendon which has not been operated upon.

tal flexor tendons at points of excessive stress and strain. In these zones of fibrocartilage, chondrocytes are arranged in a random fashion. Fibrocartilage of a slightly different appearance comprised a large part of some specimens of the profundus tendon in the digital sheath area. Fig. 4 shows such an area of fibrocartilage with its long parallel rows of small dark nuclei each surrounded by a halo of PAS-positive material. Fibrocartilage is also found in the profundus tendon after healing. Buck[7] describes fibrocartilage and bone formation in the healing Achilles tendons of rats. It is possible that zones of fibrocartilage, which appear in areas where excessive

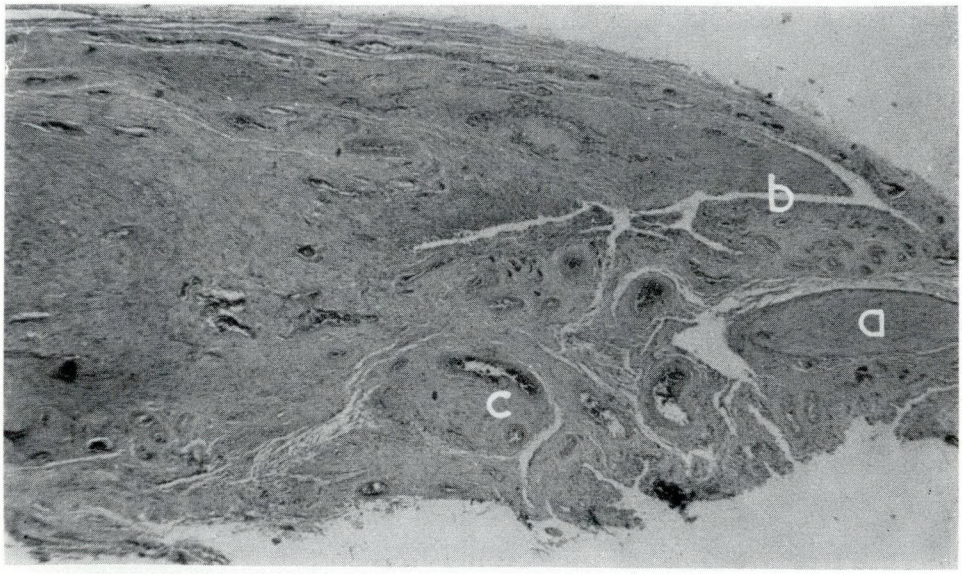

Fig. 5.—(a) Vinculum, (b) sheath and (c) vascular peritendinous connective tissue incorporated into the gap area.

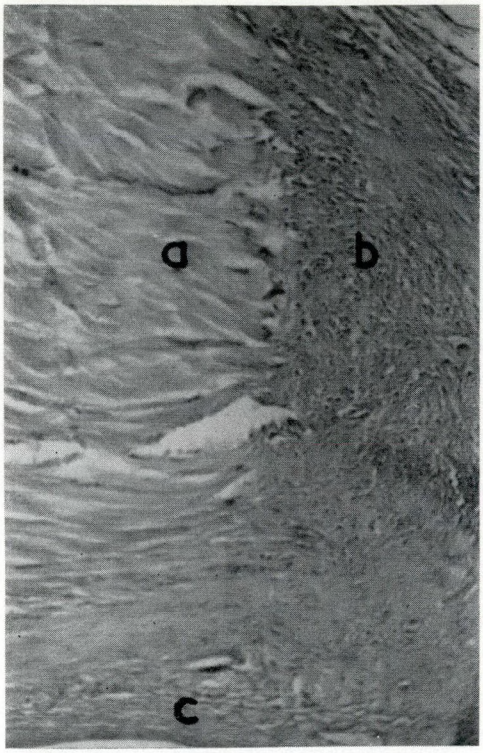

Fig. 6.—Junction between proximal stump (a) and gap (b); only the epitenon (c) is fused with the gap.

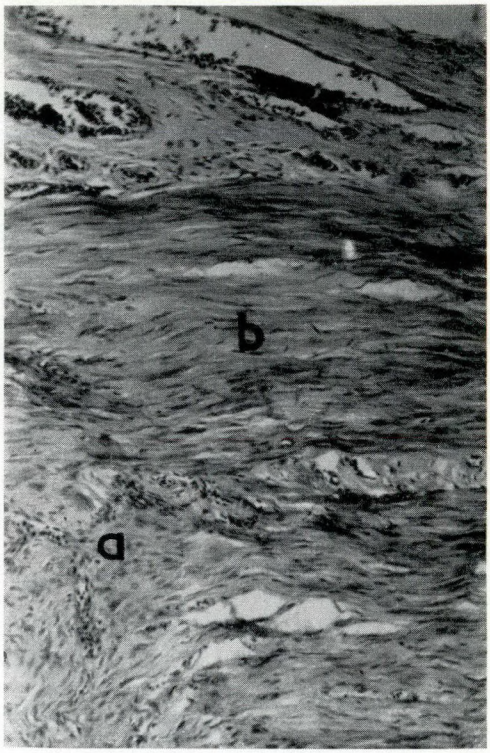

Fig. 7.—Junction between gap (a) and graft (b).

stress and strain does not occur or in areas of tendon injury and repair, may be the result of marginal nutrition. Marginal nutrition, although it allows the fibroblast to survive, may result in its conversion to a less metabolically active cell-form, the chondrocyte.

A gap was usually present between the proximal profundus stump and the proximal end of the graft. This gap area was filled with young proliferating fibroblasts and fine disoriented collagenic fibres. Pieces of vinculum, sheath and peritendinous connective tissue rich in vessels and fat cells were often found in the gap tissue into which they had probably been incorporated after collapsing into the gap area (Fig. 5). Studies in chickens sacrificed much later than eight weeks after operation have revealed that these structures, incorporated in the gap area, are gradually invaded by capillaries and fibroblasts, eventually lose their architectural distinctiveness and become part of the granulation tissue characteristic of the gap area.

The junction between the fibroblastic connective tissue of the gap area and the proximal profundus stump was characterized by a distinct line of demarcation between old tendon and new gap tissue. Epitenon was fused with the proliferating gap tissue, but the fibre bundles of the stump showed little union with the fine gap fibres (Fig. 6).

The junction between the gap tissue and the proximal end of the graft was not so distinct (Fig. 7). Gap tissue and epitenon merged as in the proximal stump-gap junction, but in addition to this there was invasion of proliferating gap tissue between the collagenic fibre bundles. The fibre bundles themselves were hypercellular and appeared to fuse with the fine gap fibres.

C. Types of Repair

Tendon injury may be due either to direct trauma or to nutritional deficiency as in the case of the free graft when all vessels have been severed. The histological events which were observed in

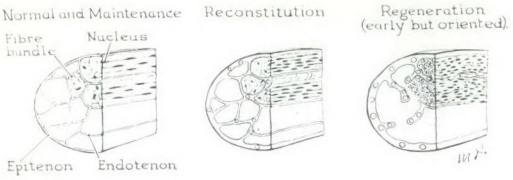

Fig. 8.—Diagrammatic schemes of maintenance, reconstitution and regeneration. Maintenance resembles normal tendon. Reconstitution is characterized by fine slightly PAS-positive fibres, vascular and slightly thickened epitenon and endotenon, and frequently by a change in the number of nuclei. Regeneration is characterized by very fine PAS-positive fibres, disrupted epitenal and endotenal patterns, and an increase in the number of vessels and nuclei.

healing free tendon grafts have led us to postulate that tendon may react to this injury in any one or combination of three different ways. We have called these responses to injury "maintenance", "reconstitution" and "regeneration" (Fig. 8). By analogy the tendon fibres may be compared with a factory and the fibroblasts with its workmen. Maintenance is analogous to the repair of a damaged factory in which the damage has been slight enough to make it possible for the workmen already present to complete the repair without reinforcements or new parts. Reconstitution is analogous to the repair of a factory in which some workmen have been killed and some parts of the factory destroyed. It is therefore necessary to call in some new workmen and to produce some new parts. Regeneration is analogous to the repair of a factory which has been so severely damaged that all the workmen have been killed and the factory destroyed. An entirely new group of workmen must be called in and the factory must be totally rebuilt. The collagen fibrils of tendon respond to injury in only two ways: they either survive or degenerate. In an area of maintenance, they all survive; in an area of regeneration, they all degenerate; and in an area of reconstitution, some survive and some degenerate.

Maintenance may be defined as the repair of injured tendon by the fibroblasts already present in that tendon, without the invasion of new fibroblasts. This type of repair is a response to very minimal injury and is not demonstrable microscopically. Tendon being "maintained" would appear normal. Maintenance probably occurs in the zones of normal appearance that border zones of more obvious injury in the

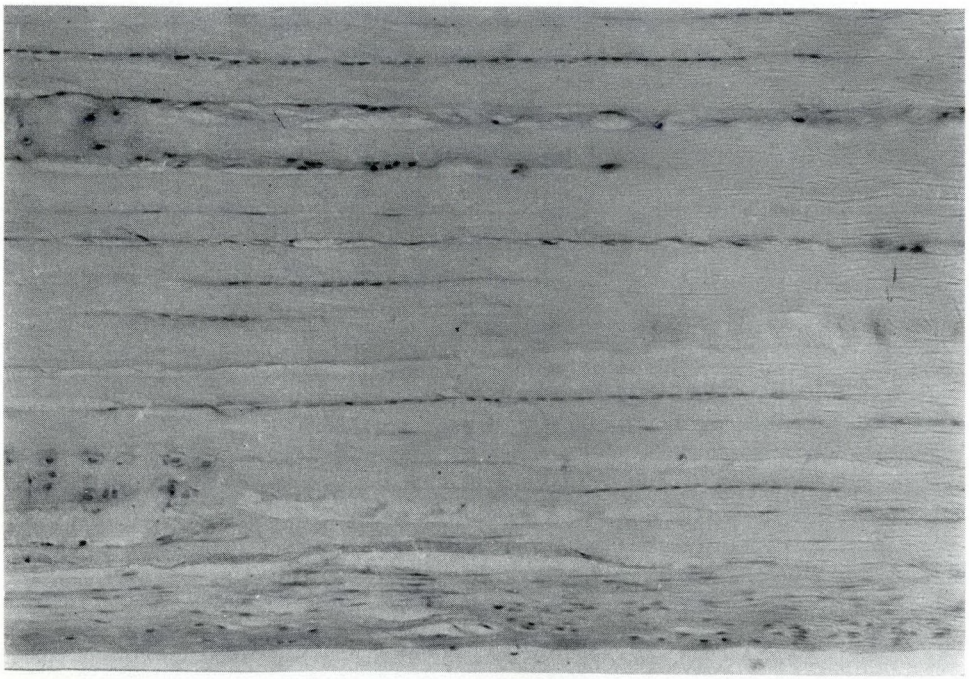

Fig. 9.—Early stage of reconstitution in a tendon graft.

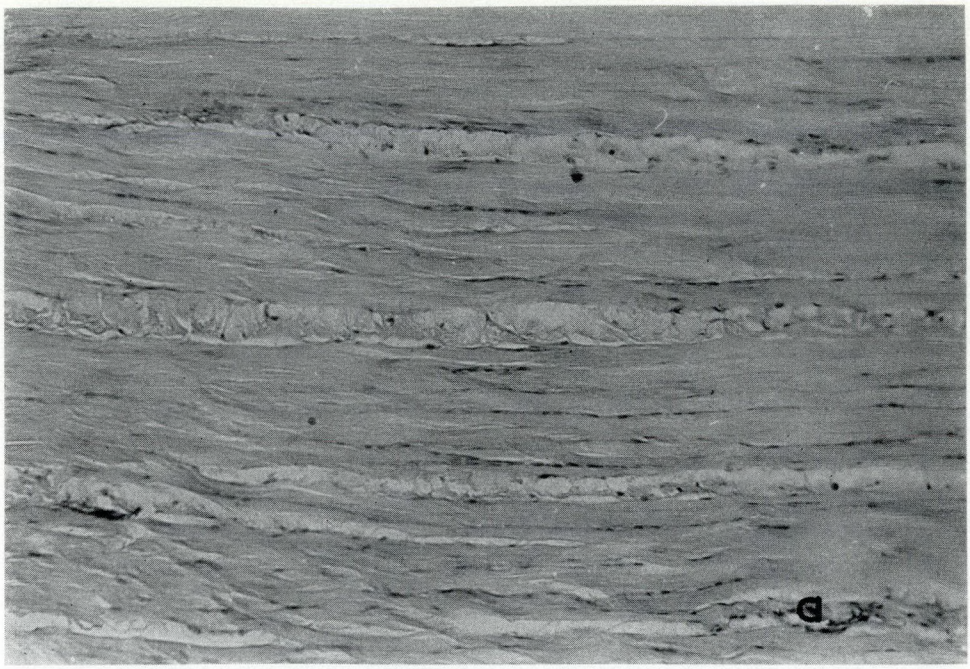

Fig. 10.—Later stage of reconstitution in a tendon graft. (a) Capillaries have invaded the graft.

profundus stump. Maintenance may occasionally occur in the central part of the graft, but in this location it is difficult to distinguish from the early stages of reconstitution.

Reconstitution may be defined as the repair of injured tendon by the invasion of new fibroblasts to augment the old surviving fibroblasts, and by the deposition of new collagenic fibrils or possibly cementing substance around old surviving collagenic fibrils. An area which appears to be undergoing early reconstitution is shown in Fig. 9. Endotenon and parallel collagenic fibre bundles are still present, but the number of nuclei is reduced in some areas. The collagenic fibres remain light pink (PAS-negative), but there are PAS-positive halos or streaks extending out from a few of the nuclei. Fig. 10 shows a slightly later

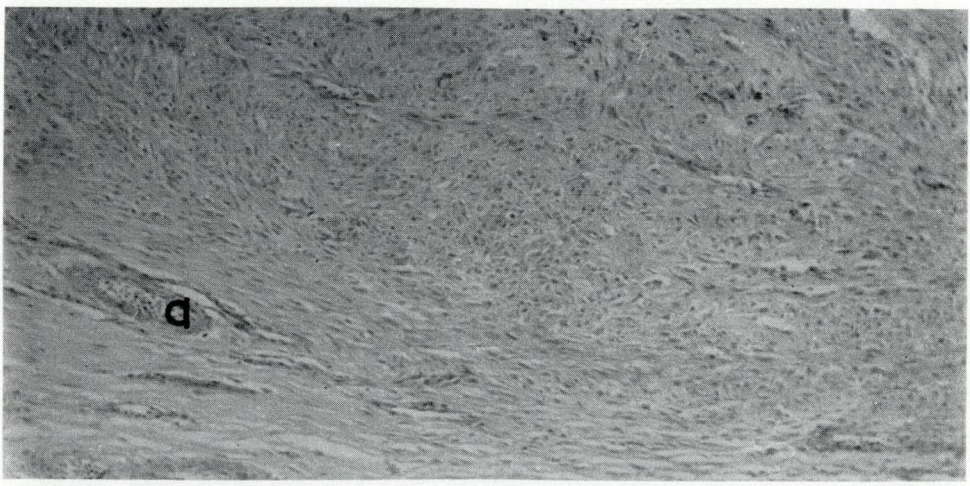

Fig. 11.—Early stage of regeneration in a tendon graft. (a) Capillaries are already present.

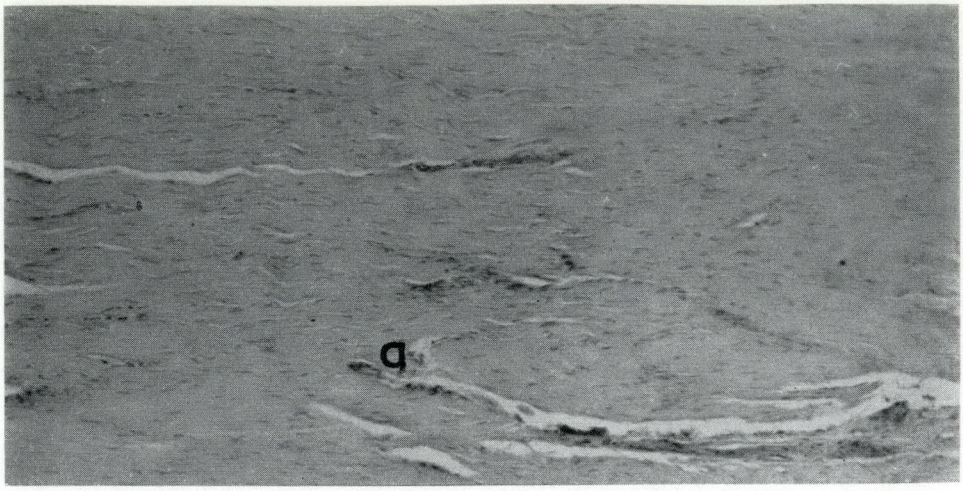

Fig. 12.—Later stage of regeneration in a tendon graft. (a) Capillaries are still present.

stage of reconstitution. Small blood vessels have invaded the endotenon, which has become slightly thickened. Epitenon, which is not shown in Fig. 10, also became thickened and vascular. The tendon fibres have become slightly finer and more PAS-positive, indicating that some of the old fibrils have degenerated and that some new fibrils have been deposited. There has been a slight increase in the number of cells in the fibre bundles owing to the invasion of young fibroblasts through adhesions and from the cut tendon ends. These new fibroblasts are frequently rounder and more fluffy than the dark flat nuclei of surviving cells. As the reconstituted area matured, its appearance gradually became more like normal tendon. Its fibres became thicker and less PAS-positive and its cells more sparse. Reconstitution was most frequently seen in the central portion of a minimally traumatized free graft. It also occasionally occurred between the zones of regeneration and maintenance in the profundus stump.

Regeneration may be defined as the repair of injured tendon by the total replacement of its fibroblasts and fibres by invading granulation tissue. An area of early regeneration is shown in Fig. 11. Endotenal and epitenal architecture have been lost. The elongated fibroblasts and dense collagenic fibre bundles have completely disappeared. Their place has been taken by plump ovoid fibroblasts with PAS-negative cytoplasm, and fine new PAS-positive collagenic fibres nourished by a rich capillary network. Regeneration is preceded by a defect such as the gap area or by complete tendon degeneration,[8] which progresses through a stage of swollen fibres and decreased fibroblasts to eventual lysis. Regeneration is the reaction to severe injury and is always found in the gap area adhesions and usually at both ends of the graft. A severely traumatized graft or proximal stump may regenerate throughout. The regeneration tissue of the gap area is continuous with the epitenon of the stump and graft and occasionally extends into the cut tendon ends between the tendon bundles as already described (Fig. 7).

The disorganized arrangement of regeneration tissue changes to a parallel orientation of fibres and fibroblasts as the tissue matures (Fig. 12). The fibres gradually thicken and the fibroblasts become elongated and less numerous. Epitenon regenerates and sheath may reform.[2, 9] Capillaries also decrease in number, and there is an attempt to re-form endotenal compartments. However, even in relatively mature regeneration tissue, the reversal toward normal is never complete and the regenerated area remains less organized and more vascular. Regeneration was seen first in the region of the gap and only later in the graft. However, it was observed that even at eight weeks

postoperatively, the regeneration tissue of the graft appeared more differentiated and mature than that of the gap. This was probably due to the fact that in the gap area, regenerating tissue first developed in an unorganized fashion, while in the graft, regenerating tissue was aided in orientation by the remaining though degenerating structure of the old tendon. The disoriented new fibres of the gap were probably broken down to be resynthesized in an oriented fashion, but in the regenerating tissue of the graft area no breakdown and resynthesis were necessary since orientation was already present.

Areas of maintenance, reconstitution, and regeneration may intermingle with each other, making it difficult to determine which type of repair is taking place. Reconstitution may vary from almost complete maintenance to almost complete replacement. As reconstituting and regenerating tissues mature, they become more alike and may eventually become indistinguishable.

Lindsay and McDougall[1] studied the fate of the free digital flexor tendon graft using standard hematoxylin and eosin stains. Their findings have in the main been confirmed by this study using histochemical methods.

Other methods of studying free tendon graft healing have supported the findings of Lindsay and McDougall[1] and those of this study. Fibroblasts involved in free tendon graft healing were radioactively tagged and were found to migrate from the peritendinous tissues into the gap areas and graft ends. They appeared to completely replace these areas, with a resulting complete change in graft architecture (regeneration). The central portion of the graft was invaded by very few new fibroblasts and underwent very little change (reconstitution).[10] Newly formed collagen has also been radioactively tagged in healing free tendon grafts. Biochemical tendon analysis revealed a heavy deposit of new labelled collagen in the graft and stump ends, and a scanty deposit in the central graft area. These findings also suggest regeneration in the gap areas and graft ends, and reconstitution in the graft centre.[11]

SUMMARY

Digital flexor tendons appear to respond to injury by maintenance, reconstitution, or regeneration.

Maintenance, the response to very minimal injury, is repair by fibroblasts already in the injured area. Reconstitution, the response to moderate injury, is repair by invading fibroblasts and new collagenic fibrils which augment the surviving cells and fibrils. Regeneration, the response to severe injury, is repair by complete replacement of the old tendon elements by new fibroblasts and fibres.

The authors wish to express their gratitude to Dr. Sylvia H. Bensley, University of Toronto, for her guidance and assistance in the preparation of this article.

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REFERENCES

1. LINDSAY, W. K. AND MCDOUGALL, E. P.: Digital flexor tendons: an experimental study; Part II. The fate of autogenous digital flexor tendon grafts, *Brit. J. Plast. Surg.*, **13:** 293, 1961.
2. LINDSAY, W. K. AND THOMSON, H. G.: Digital flexor tendons: an experimental study; Part I. The significance of each component of the flexor mechanism in tendon healing, *Brit. J. Plast. Surg.*, **12:** 289, 1960.
3. SOROKOLIT, W.: Unpublished data.
4. PEARSE, A. G. E.: Histochemistry; theoretical and applied, J. & A. Churchill, Ltd., London, 1953, p. 134.
5. PUCHTLER, H. AND SWEAT, F.: Some comments on the Ninhydrin-Schiff reaction, *J. Histochem. Cytochem.*, **10:** 365, 1962.
6. MANCINI, R. E. *et al.*: A histochemical and radioautographic study of the participation of fibroblasts in the production of mucopolysaccharides in connective tissue, *J. Histochem. Cytochem.*, **9:** 278, 1961.
7. BUCK, R. C.: Regeneration of tendon, *J. Path. Bact.*, **66:** 1, 1953.
8. WALKER, F. G., BENSLEY, S. H. AND LINDSAY, W. K.: The effects of an antihistamine (Promethazine) on the reaction of tendons to trauma—a histological study, *Canad. J. Biochem. Physiol.*, **39:** 89, 1961.
9. POTENZA, A. D.: Tendon healing within the flexor digital sheath in the dog, *J. Bone Joint Surg.* [*Amer.*], **44A:** 49, 1962.
10. LINDSAY, W. K. AND BIRCH, J. R.: The fibroblast in flexor tendon healing, *Plast. & Reconstruct. Surg.*, To be published.
11. LINDSAY, W. K. AND BIRDSELL, D. C.: Collagen deposition in flexor tendon healing. Unpublished data.

Résumé

Le mode de guérison des tendons fléchisseurs des doigts est, du point de vue histologique, mal connu. Les auteurs ont procédé à une série d'expériences en vue d'élucider ce problème. Vingt coqs adultes furent utilisés; des greffons tendineux furent prélevés au niveau du doigt médian d'une patte, puis transférés au même niveau à la patte opposée. On évita, aussi soigneusement que possible de traumatiser le tendon ou sa gaine. Les coqs furent sacrifiés huit semaines plus tard; les parties greffées furent examinées macroscopiquement, puis prélevées, fixées dans une solution de formol à 10%, incluses en paraffine et sectionées pour la microscopie. Ces coupes furent colorées à l'aide de différentes techniques, pour comparaison. Ces expériences montrent que les tendons répondent de diverses manières au traumatisme. Selon les cas, on observe soit une simple survie du tissu, ou bien une reconstitution ou encore une régénération complète. La survie simple existe dans les cas où le traumatisme a été très léger; il s'agit d'une réparation effectuée par les cellules conjonctives présentes. La reconstitution s'observe dans les cas où le tramatisme est d'importance moyenne; le région greffée est le siège d'une invasion de cellules conjonctives venant augmenter le nombre des cellules en place. La régénération vraie, réponse au traumatisme grave, est un remplacement complet des cellules mortes et des fibres collagènes par de nouveaux éléments.

LES SUTURES DE L'AORTE THORACIQUE. Etude clinique et expérimentale. Fernand Lantin. Préface par F. d'Allaines. 171 pp. Illust. Editions Arscia S.A., Bruxelles, 1963. 350 FB. $7.00 (approx.).

Cette publication arrive à point car elle apporte une solution scientifique et pratique à un problème devenu sérieux depuis que les chirurgiens cardiaques attaquent routinièrement les lésions de valvule aortique.

L'aortotomie de l'aorte ascendante, exigée par les techniques de correction, se complique trop souvent de formations anévrysmales au niveau de la ligne de suture.

Pour prévenir ces difficultés, l'auteur mentionne les principes de base de toute chirurgie vasculaire. Cependant, il en ajoute un autre à savoir la nécessité de conserver l'intégrité de l'adventice. Le traumatisme et surtout la résection de cette membrane tendent à éliminer les vaso-vasorum qui sont les vaisseaux nourriciers de la paroi. Ceci invite à la nécrose, à la déhiscence de la suture et enfin à l'anévrysme. L'auteur démontre clairement par ses travaux chez l'animal et des résultats cliniques la grande supériorité d'une technique qui respecte scrupuleusement l'adventice.

Enfin au niveau de l'aorte ascendante, l'auteur préconise l'aortotomie transversale de préférence à une aortotomie longitudinale en raison d'une tension réduite sur les fils de suture.

Notre expérience corrobore pleinement les conclusions du Docteur Lantin.

Bien que l'aorte ascendante ait été le principal segment vasculaire étudié, ce travail intéressera surement tout chirurgien vasculaire ou cardique.

Ce livre est bien ordonné. Il est remarquable par sa clarté et sa précision. Tout milieu chirurgical devrait en posséder un exemplaire.

A PORTFOLIO OF CHEST RADIOGRAPHS. For Undergraduate and Postgraduate Students. B. T. Le Roux and T. C. Dodds. Foreword by Andrew Logan. 367 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1964. $10.75.

This is an excellent book. The reader is shown a series of chest radiographs which have been selected to illustrate "the common radiographic opacities". In the 367 pages of the work, there are 300 figures, many consisting of several separate reproductions. A brief text lucidly explains what should be seen in each illustration; and in addition presents in a few words a wealth of clinical material. The photographs are adequate for their purpose.

Part I of the book deals with "Radiographic Anatomy", Part II with "The Chest Wall, Lungs and Pleura", and Part III with "The Mediastinum".

The authors have succeeded in synthesizing clinical, pathological, surgical and radiographic findings into a well-proportioned presentation, and the reader's interest never flags. The book will be of particular interest to postgraduate students of chest disease, but also to any others who wish to look intelligently at radiographs and not only the radiologist's reports. In some ways it is a series of "proved case" conferences, and is an innovation in the textbook teaching of chest radiography. The only point of strong disagreement concerns the value of bronchography in the diagnosis of bronchial carcinoma; the reviewer has found that bronchography is sometimes the only means, short of tissue resection, of disclosing bronchial obstruction in early questionable cases. One can feel no hesitation in recommending this book to all who would become familiar with the common radiographic opacities of the chest.

EXPERIMENTAL ANASTOMOSIS OF THE LEFT INTERNAL MAMMARY ARTERY TO THE DIVIDED CIRCUMFLEX CORONARY ARTERY USING THE NRC-VOGELFANGER STAPLING DEVICE*

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THE Mark-4 model of the stapling device, designed and built by the National Research Council upon the suggestion of Dr. I. J. Vogelfanger, will suture end-to-end anastomoses of vessels from 2 mm. to 5 mm. in external diameter.[17, 19] Anastomosis of the rabbit's abdominal aorta with this instrument compared with manual suture has been demonstrated to have a shorter occlusion time, a higher patency rate and a lower mortality rate. Coronary artery anastomosis was undertaken in this laboratory in order to provide a crucial test of this method of vascular anastomosis.

This apparatus was used to accomplish end-to-end anastomosis of the left internal mammary artery to the divided circumflex branch of the left coronary artery in the dog (Fig. 1). Circumflex ligation at this level is lethal in about 50% anesthetized dogs and in about 90% of conscious dogs.[12, 18] Temporary occlusion beyond two minutes carries a high risk of ventricular fibrillation.[5, 9] Comparable procedures, using various techniques, have been associated with a mortality rate of about 50%, although Hall, Khouri and Gregg[9] achieved a considerably lower figure.[6-8, 11, 13] The

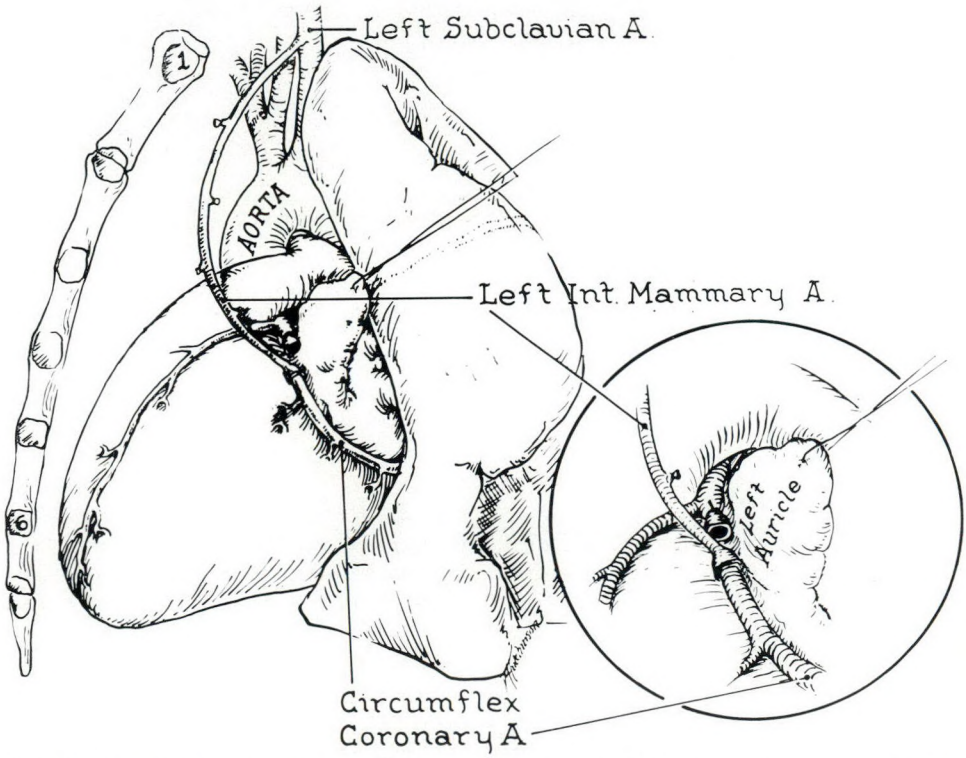

Fig. 1.—Diagram of experimental procedure; viewed from the left side with the anastomosis inset.

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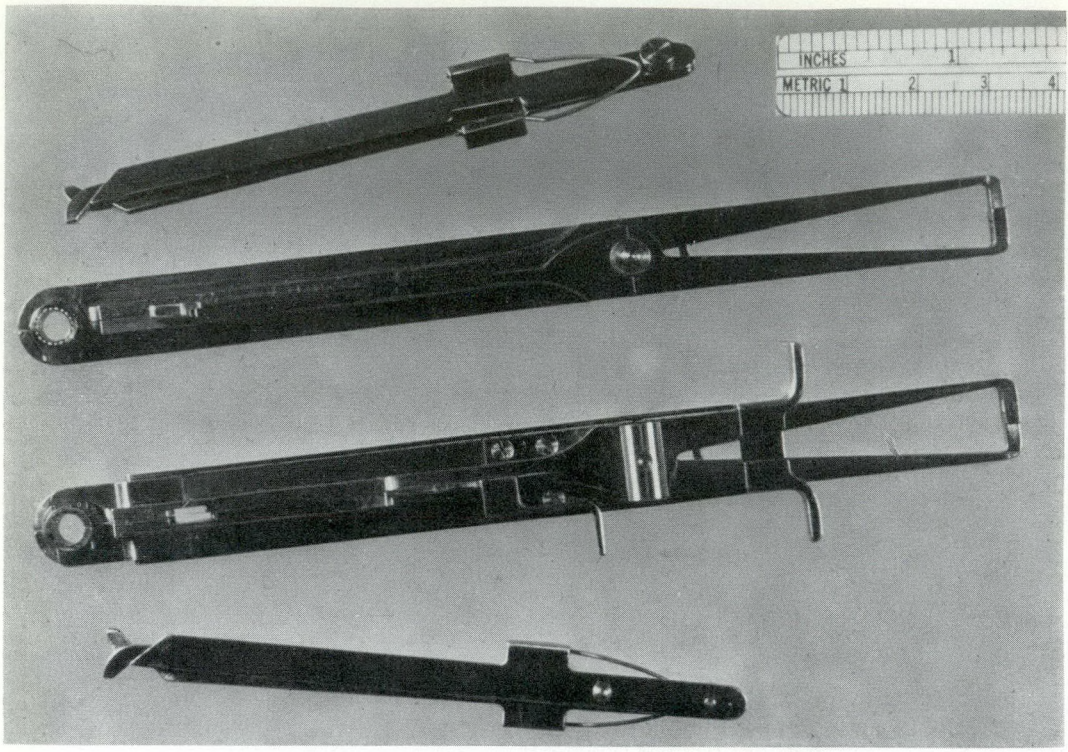

Fig. 2.—The NRC-Vogelfanger stapling device dissembled with hemostatic clamps. The "anvil" bushing is above, the "driver" bushing below. The locking and driving devices are incorporated in the handle of the "driver" bushing. These hemostatic clamps were not used in this experiment.

clinical application of this procedure will be discussed later in this communication.

Material and Methods

Mongrel dogs were anesthetized with pentobarbital, intubated and ventilated with room air. In order to obtain vessels at least 2 mm. in external diameter, dogs weighing at least 11 kg. were required. Under surgically clean conditions, the left pleural space was opened through the bed of the fourth rib. The left internal mammary artery was mobilized from its origin to the fifth rib. The pericardium was opened anterior to the phrenic nerve and the left atrial appendage was retracted. Dissection of the proximal 2 cm. of the circumflex branch usually required sacrifice of one atrial and one small ventricular branch. The internal mammary artery was occluded, ligated distally and divided. The "driver" bushing (Fig. 2) was applied proximally with the end everted over the staples. The following steps were then taken in fairly rapid sequence. The circumflex branch was ligated close to its origin and divided. The distal end of this vessel was everted over the "anvil" bushing. Both open ends were irrigated with heparinized saline and then united by locking the handles of the instrument. At this point, the hemostatic clamps were released and flow was restored. This minor alteration in the original procedure,[17, 19] in which the staples were driven and the bushings removed before restoration of flow, minimized the time of coronary occlusion. Light pressure with dry gauze supplemented hemostasis. Fifteen experimental animals were compared with 14 control animals in which the circumflex branch had been ligated at the same level under anesthesia.

Mortality rates were compared with a second control group undergoing acute coronary occlusion without anesthesia, 24 hours after a tie had been placed loosely around the circumflex coronary artery.[12]

The size of the anastomosis was measured by comparing the external diameter

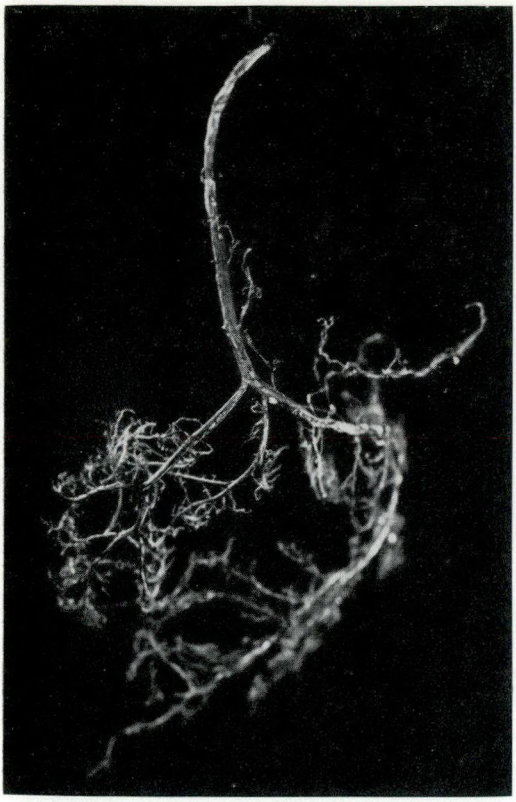

Fig. 3.—A vinyl cast. The circumflex system has filled through the internal mammary artery. This cast was prepared by Dr. D. Busby.

of the internal mammary artery to sizing rods, thus determining the bushing to be used. The duration of vascular occlusion was noted. Lead II of the electrocardiogram was recorded before and after circumflex ligation. Mortality rates were assessed upon the basis of 24-hour survival. Patency of the anastomosis was determined by cineangiography in four living animals, by vinyl casting in three sacrificed animals (Fig. 3) and by postmortem angiograms in three animals (Fig. 4). Gross and histological sections of the anastomoses and the myocardium were examined by an independent observer (Fig. 5). The position of the ligature was measured from the bifurcation of the left coronary artery using calipers. All of the dogs used for this experiment were included except one animal in which the procedure was carried out for production of a coloured cine film.

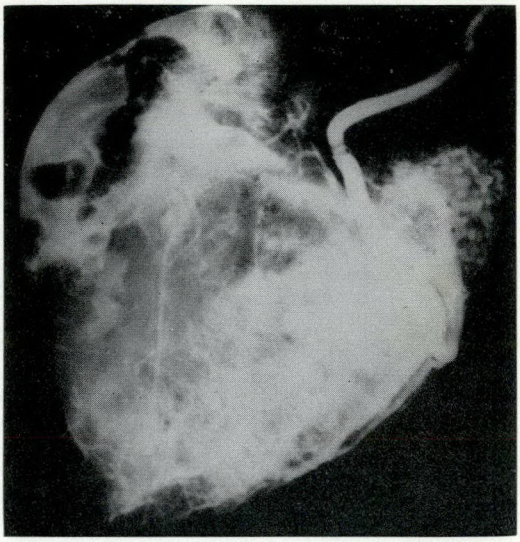

Fig. 4.—A postmortem angiogram. There is slight constriction at the anastomosis, marked by the staples. The contrast medium penetrates into the myocardium and fills the anterior descending artery.

Results

There were 10 male dogs in the stapled group and three in the control group. The mean weight was 20 kg. in the stapled group and 11 kg. in the control group. These differences were not considered significant.

The sizes of these vessels are listed in Table I. Thrombosis was more frequent in the smaller vessels. Technical difficulties led to prolonged periods of interruption of coronary perfusion in two dogs with 2.0 mm. vessels, resulting in ventricular fibrillation.

TABLE I.—Size of Anastomoses

External diameter in mm.	*Number of dogs*	*Patent anastomosis*
2.0	4	1*
2.5	5	4
3.0	5	4†
3.5	1	1

Mean external diameter = 2.7 mm.
Patency rate = 10/13 (77%).

*Ventricular fibrillation occurred during two procedures and patency could not be assessed. One dog died about 20 hours later with thrombosis of the anastomosis and myocardial infarction. The fourth dog survived one month with a patent vessel, yet had a myocardial infarction.

†One dog had a patent vessel but with myocardial infarction.

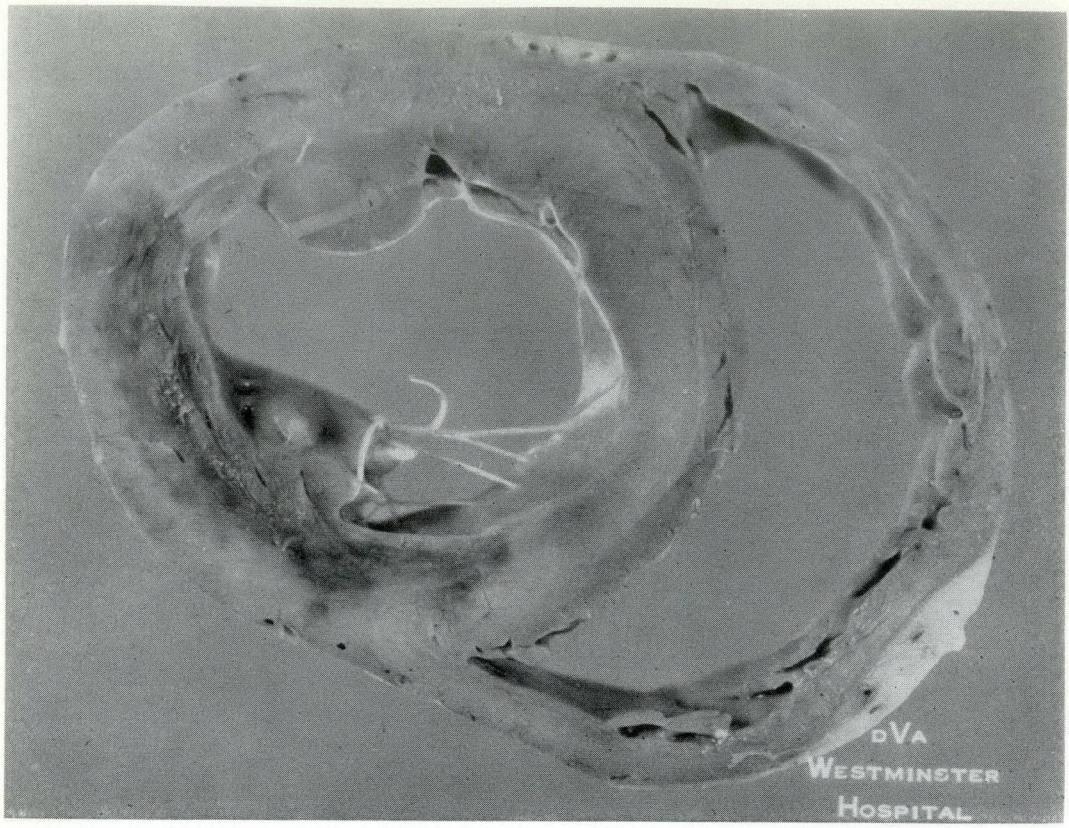

Fig. 5.—Infarction of the posterior wall of the left ventricle in cross-section. This extensive infarct occurred although the anastomosis remained patent.

In the stapled group, the ligatures were 1.5 to 8 mm. from the bifurcation of the left coronary artery, with a mean distance of 4.4 mm. For the control series, the range was 1 to 5 mm., with a mean distance of 3.1 mm. This difference was not significant ($P > .05$).

Lead II of the electrocardiogram was recorded as in Fig. 6. Typical changes consisted of deepening of the Q-waves, elevation of the S-T segment and later inversion of the T-wave, signifying ischemic changes. Two dogs in the stapled group, both presenting technical problems that necessitated prolonged coronary artery occlusion, developed ventricular fibrillation.

The electrocardiographic (ECG) findings were less marked and tended to revert towards normal in the stapled dogs, except

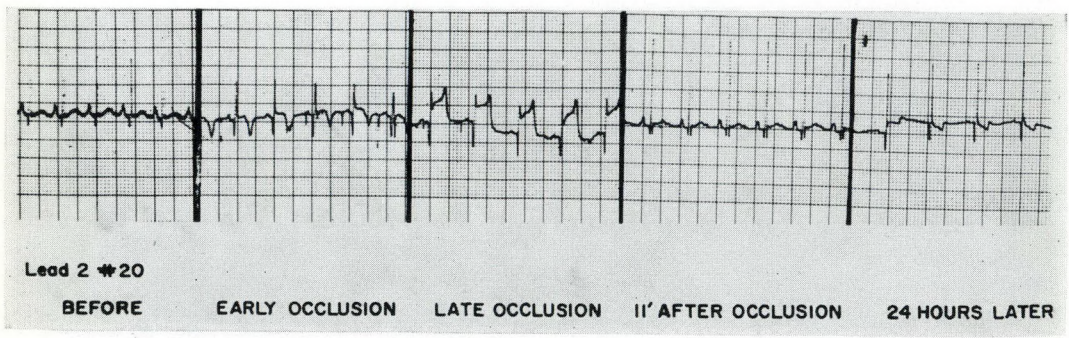

Fig. 6.—Electrocardiographic changes (Lead II) before occlusion of the circumflex branch of the coronary artery in the dog, during early occlusion, during late occlusion, 11 hours and 24 hours after occlusion.

in three that had infarcts. Ligation under anesthesia produced more marked and permanent ECG changes; seven of 14 dogs developed ventricular fibrillation. Defibrillation was not attempted in either group.

The 24-hour mortality rates shown in Table II paralleled the one-hour mortality rates. There was no statistical difference[14] between the dogs with coronary artery stapling and those with ligation under anesthesia. Ligation of the circumflex artery at the same level, carried out without anesthesia 24 hours after the chest had been opened, had a significantly greater mortality rate. As detailed in the footnote to Table I, three deaths occurred in the group with the smallest (2 mm.) anastomoses. These deaths were associated with prolonged interruption of coronary artery flow owing to technical problems. There were four late deaths, two due to atelectasis and pneumonia. Three dogs were maintained for long-term survival — one, that had a myocardial infarct, was sacrificed at four weeks; the second, at six weeks; and the third, that had a normal myocardium, at three months. All three had patent vessels.

TABLE II.—24-Hour Mortality Rates

Stapled group	4/15 = 27%
Control group with anesthesia	8/14 = 57%
Control group without anesthesia	12/13 = 92%

These figures were compared by the chi-square test with Yates' modification.[10, 14] The mortality rate in the stapled group is significantly lower than in the control group having ligation without anesthesia (chi-square = 6.96), but not significantly different from the control group having ligation under anesthesia (chi-square = 2.99).

Patency of the anastomosis was assessed in 13 dogs that survived for more than one hour. Nine were patent (69%).

Myocardial infarction occurred in six out of 13 dogs (Fig. 5) that underwent stapling and survived one hour. The anastomosis was thrombosed in four of these animals, yet in two of them the anastomosis was patent. Of seven control dogs that survived one hour, three had myocardial infarcts.

Discussion

The observed mortality rates for the two control groups undergoing acute occlusion of the proximal circumflex coronary artery, with and without anesthesia, are representative of those in the literature.[7, 12, 18] The relatively low mortality rate in the stapled group, significantly lower than acute ligation in conscious dogs by chi-square analysis, also compares favourably with mortality rates quoted for coronary anastomosis by various techniques.[7, 9, 20] Measures which improve the chance of survival after experimental coronary occlusion, such as oxygen inhalation, hypothermia and quinidine administration, might improve these results. The use of heparin and antibiotics and closer postoperative pulmonary supervision might also lower the mortality rate.

Hall, Khouri and Gregg[9] noted that the incidence of ventricular fibrillation increased when the coronary circulation was interrupted for more than 150 seconds.[21] In these experiments both dogs that developed ventricular fibrillation had interruption of coronary blood flow for more than two minutes. Three dogs with subsequent myocardial infarction also had interruption of coronary flow for more than two minutes. The NRC-Vogelfanger stapler made it possible to complete an anastomosis within this time limit in seven out of 12 experiments in which the occlusion time was recorded.

The tendency for small vessels to thrombose at the site of anastomosis is well known.[20] It is apparent from Table I that prolonged occlusion, early ventricular fibrillation and later thrombosis were more common in animals in which anastomosis of the smallest vessels was carried out. As the series progressed, only larger dogs were used for the stapling procedure. Regional or systemic administration of heparin or fibrinolysin might improve these results. The observation that some of these small vessels remained patent demonstrated the value of this mechanical device.

Three considerations limit the clinical application of this procedure. As previously observed by Murray *et al.*,[15] myocardial infarction may occur although the coronary artery anastomosis remains patent (Fig. 5). Atherosclerotic lesions of the coronary arteries in man are frequently multiple and widespread, so that probably less than

10% of patients with angina pectoris are suitable for any form of direct arterial surgery.[2, 4] Eversion of the ends of the vessels is required for this method and this maneuver may be impossible in many arteriosclerotic arteries.

SUMMARY

The NRC-Vogelfanger stapling device facilitated end-to-end anastomosis of the left internal mammary artery to the divided circumflex of the left coronary artery in 15 dogs. A slight modification of the original technique allowed minimal occlusion time.

Although this procedure is technically feasible, the incidence of myocardial infarction remains appreciable. Application to direct coronary artery surgery is expected to be restricted, although it may prove suitable for the treatment of an anomalous coronary artery arising from the pulmonary trunk.

The author wishes to express his appreciation to the following persons: Mr. S. H. G. Connock, Section Head, Division of Mechanical Engineering at the National Research Laboratories, for cooperation and assistance; Dr. J. C. Paterson, Director of Laboratories, Westminster D.V.A. Hospital, London, for review of the pathological material; Dr. G. C. Copestake, Head of the Department of Radiology, Victoria Hospital, London, for selective angiography; Dr. E. Meads, Fellow in Surgery, and Mr. H. Fitzpatrick, Westminster D.V.A. Hospital, London, for technical assistance; and Messrs. D. Pulham and S. Hueston, Department of Photography, Westminster D.V.A. Hospital, London, for illustrations.

REFERENCES

1. ALLEN, J. B. AND LAADT, J. R.: The effect of the level of the ligature on mortality following ligation of the circumflex coronary artery in the dog, *Amer. Heart J.*, **39:** 273, 1950.
2. BIGELOW, W. G., BASIAN, H. AND TRUSLER, G. A.: Internal mammary artery implantation for coronary heart disease: a clinical follow-up study one to eight years after operation, *J. Thorac. Cardiov. Surg.*, **45:** 67, 1963.
3. CARROLL, S. E.: Anastomosis of the rabbit's abdominal aorta using the NRC-Vogelfanger stapling device. To be published.
4. CHATTERJEE, K. N., WARREN, R. AND LITTMANN, D.: Selection of patients for coronary artery reconstruction, *Arch. Surg. (Chicago)*, **84:** 108, 1962.
5. DAY, S. B. AND LILLEHEI, C. W.: Experimental basis for a new operation for coronary artery disease; a left atrial-pulmonary artery shunt to encourage the development of interarterial intercoronary anastomoses, *Surgery*, **45:** 487, 1959.
6. FINEBERG, C., CAMISHION, R. C. AND HERING, N.: Revascularization of the dog myocardium. 3. The development of collateral blood supply in the dog heart after thrombosis of synthetic grafts, *Arch. Surg. (Chicago)*, **85:** 882, 1962.
7. FINEBERG, C., FORIS, N. AND CAMISHION, R. C.: Revascularization of the dog myocardium. 2. Acute ligation of the left circumflex coronary artery with and without hypothermia, *Arch. Surg. (Chicago)*, **85:** 717, 1962.
8. GOETZ, R. H. *et al.*: Internal mammary-coronary artery anastomosis: a non-suture method employing tantalum rings, *J. Thorac. Surg.*, **41:** 378, 1961.
9. HALL, R. J., KHOURI, E. M. AND GREGG, D. E.: Coronary-internal mammary artery anastomosis in dogs, *Surgery*, **50:** 560, 1961.
10. MAINLAND, D.: Statistical methods in medical research; qualitative statistics (enumeration data), *Canad. J. Res., E*, **26:** 1, 1948.
11. MAMIYA, R. T. *et al.*: Distal relocation of the origin of the left coronary artery by subclavian-coronary artery anastomosis, *Surg. Forum*, **12:** 227, 1961.
12. MANNING, G. W., MCEACHERN, C. G. AND HALL, G. E.: Reflex coronary artery spasm following sudden occlusion of other coronary branches, *Arch. Intern. Med. (Chicago)*, **64:** 661, 1939.
13. MILLER, E. W., KOLFF, W. F. AND GROVES, L. K.: Experimental coronary artery surgery in dogs employing a pump-oxygenator, *Surgery*, **45:** 1005, 1959.
14. MORONEY, M. J.: Facts from figures, 3rd ed., Penguin Books, Inc., Baltimore, 1957.
15. MURRAY, G. *et al.*: Anastomosis of a systemic artery to the coronary, *Canad. Med. Ass. J.*, **71:** 954, 1954.
16. PHIBBS, C. M., VAN TYN, R. A. AND MACLEAN, L. D.: Vulnerability of the dog heart to ventricular fibrillation: a comparative study of chronic ischemia and three myocardial revascularization procedures, *J. Thorac. Cardiov. Surg.*, **42:** 228, 1961.
17. SCOBIE, D. H., SCOBIE, T. K. AND VOGELFANGER, I. J.: Venous autografts, *Canad. J. Surg.*, **5:** 471, 1962.
18. SKELTON, R. B. *et al.*: Mortality studies in experimental coronary occlusion, *J. Thorac. Cardiov. Surg.*, **44:** 90, 1962.
19. SMIALOWSKI, A. J. AND CONNOCK, S. H. G.: A vascular suturing instrument, National Research Council of Canada, Mechanical Engineering Report No. M1-827, Ottawa 1962.
20. SPENCER, F. C. *et al.*: Coronary artery patch graft: experiment with cardiopulmonary bypass and hypothermia, *Arch. Surg. (Chicago)*, **86:** 81, 1963.
21. THAL, A. P. *et al.*: Direct suture anastomosis of the coronary arteries in the dog, *Surgery*, **40:** 1023, 1956.

RÉSUMÉ

Cet article décrit les résultats d'expérimentations faites sur le chien en vue d'établir une anastomose entre l'artère mammaire interne gauche et la branche circonflexe de l'artère coronaire gauche. On sait classiquement que la ligature

de la circonflexe à ce niveau est mortelle dans 50% des cas chez le chien sous anesthésie, et dans 90% des cas chez les chiens à l'état conscient. L'occlusion temporaire de cette même artère au-delà de deux minutes entraîne presque infailliblement la fibrillation ventriculaire. Ici, les chiens furent anesthésiés au pentobarbital et intubés. La voie d'accès était une thoracotomie au niveau de la quatrième côte gauche; l'artère mammaire interne gauche était disséquée depuis son origine jusqu'à la hauteur de la cinquième côte; le péricarde était alors ouvert en avant du nerf phrénique, et la branche circonflexe de l'artère coronaire était soigneusement préparée sur une longueur de 2 cm. L'artère mammaire interne était ligaturée distalement, puis sectionée. Tout ceci étant prêt, on procédait alors rapidement aux temps suivants: ligature de l'artère circonflexe à son origine, puis anastomose de la mammaire interne et de la circonflexe; cette anastomose était effectuée grâce à l'agrafeuse construite par le Conseil National de la Recherche. Un groupe de 15 chiens fut ainsi opéré; un second groupe de 14 animaux, servant de témoins, fut opéré de la même façon, mais ne subit aucune anastomose. La mortalité fut, après 24 heures, de 27% dans le premier groupe et de 57% dans le second. La fréquence des infarctus graves demeure donc relativement élevée, et il est douteux que cette intervention se justifie en clinique humaine, excepté peut-être dans les cas d'anomalie congénitale où l'artère coronaire naît du tronc pulmonaire.

SCHAUTA-AMREICH'S RADICAL VAGINAL OPERATION OF CANCER OF THE CERVIX. Modified by Hans Högler, with a Foreword by Julius Amreich. 86 pp. Illust. Charles C Thomas, Springfield, Ill.; the Ryerson Press, Toronto, 1963. $7.75.

The effective treatment of carcinoma of the cervix has always been a complex problem. In this modern era, with improvements in surgical techniques and anesthesia and with a better understanding of physiology, the radical surgical approach to the treatment of cervical carcinoma has again regained its rightful place as part of the armamentarium of the cancer therapist.

There is no doubt that the well-trained gynecological surgeon who must face these problems must also be prepared to use all available approaches for the effective treatment of carcinoma of the cervix, whether it be radiotherapy or the radical abdominal or vaginal operations. The radical vaginal operation, which has enjoyed long-standing popularity in Europe, is now gaining recognition in North America as an important technique for the treatment of cervical carcinoma.

Dr. Hans Högler describes well his modification of the radical vaginal operation. The operative technique is well illustrated by comprehensive diagrams. The particular value of this book lies in Dr. Högler's excellent demonstration of an easy and safe procedure for dissecting the ureters by using preoperative cystoscopy for orientation. With this orientation in mind, he describes the paracervical sites of the ureters and the surgical approach to the safe dissection of these structures in their abnormal medial site, or their medial or lateral sites. This feature of the operative technique completes the procedures which have also been described by Navratil and van Bouwdijk Bastianse.

Dr. Högler also treats of the complications which occur during the handling of the cardinal ligaments and stresses that "proper selection for operation should ensure avoidance of exaggerated radicality" and further that "the art probably consists in the right proportion between feasible radicality and unnecessary risk".

Although these modifications are the major contribution of this book, Dr. Högler supports the impressions of the other above-mentioned authors, stresses the advantages of this procedure over the abdominal approach and describes his indications with the advantages which this entails. One should note, however, that his survival rate, when this vaginal approach is used for stage III invasive carcinoma, is not good, and many authors may question the usefulness of the vaginal operation when the disease is so extensive. All have been quick to recognize the weakness of the operation, namely the inability to remove the lymph nodes, and this is particularly applicable with the more advanced stages of the disease. The radical vaginal hysterectomy and extraperitoneal lymphadenectomy advocated by Mitra seem to have little advantage over the radical abdominal hysterectomy.

It would seem, however, that every surgeon should have a working knowledge of this operation and of its modifications proposed by Högler, since at times it would seem to offer significant advantages.

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EDITORIAL

THE RETAINED BILE DUCT STONE—A ROLE FOR CHOLEDOCHODUODENOSTOMY

On occasion, the most careful and experienced surgeon will unwittingly leave a stone in the common bile duct. Operative cholangiography and refinements in operative technique have reduced the incidence of retained stone but have not solved the problem. It seems unwise to subject all patients who require cholecystectomy to a procedure which could increase the risk for all, at the price of avoiding this complication in the few. However, an effective procedure which would avoid the effects of this complication would be of considerable interest if it could be added safely to the standard procedures used in those patients known to be most likely to harbour a missed stone.

Complete clearance of stones is difficult from a dilated common bile duct which contains multiple stones and "biliary mud", whether it is encountered during the primary operation or at re-exploration. The undetected stone may also be hidden, either in the hepatic radicals or at the ampulla. In these circumstances additional drainage to the duct can be provided by external choledochoduodenostomy or by sphincteroplasty. Although sphincteroplasty may allow the subsequent passage of small stones, it will not ensure the passage of stones of the size usually encountered at secondary operations. Transduodenal exploration of the duct and sphincteroplasty have been reserved in most instances for use in those cases in which contrast medium or a probe do not pass readily into the duodenum, or when a filling defect at the ampulla is suggested by operative cholangiography.

Although Riedel described the procedure of choledochoduodenostomy over 70 years ago, it has had variable popularity and has not been widely utilized. This may be due to the misconception that following this operation the ducts would be vulnerable to infection because of the presence of an anastomosis to the duodenum, which is not guarded by a sphincter. However, the passage of duodenal contents into the bile ducts, whether through a choledochoduodenostomy or a sphincteroplasty, will not produce cholangitis. Here, as elsewhere in the body, the essential factor is the adequacy of drainage. If the opening is properly placed and of sufficient size to ensure drainage, infection will not occur. Also the operation is said to be difficult and to predispose to the development of a biliary fistula. However, neither of these fears is justified if the proper indications for the operation are observed. Finsterer,[1] Sanders,[2] Capper[3] and others with large series of cases have all been favourably impressed with its value.

Largely due to the advocacy of Professor Robert Janes, choledochoduodenostomy has been accepted at the Toronto General Hospital as a safe and effective operation. It has been reserved for those cases in which the common bile duct is dilated and contains multiple stones and "biliary mud", whether at the primary or secondary operation. It is especially indicated in the elderly or debilitated patient. The technique used is that of Finsterer and need not be described in detail. A prerequisite of the operation is a dilated duct, and an essential factor in its success is a stoma of at least 2.5 cm. in length, placed in the lowest accessible portion of the duct. The duodenum should be mobilized sufficiently to avoid tension at the anastomosis. Continued patency of the opening can be demonstrated radiologically, and the patient can be expected to remain free of biliary complications. In the experience at this institution, additional operations have not been required when choledochoduodenostomy has been used as an adjuvant to the exploration of the common bile duct. Choledochoduodenostomy, an effective and relatively simple operation, is worthy of more frequent consideration.

John A. Palmer

References

1. Finsterer, H.: *Mém. Acad. Chir. (Paris)*, **78:** 499, 1952.
2. Sanders, R. L.: *Ann. Surg.*, **123:** 847, 1946.
3. Capper, W. M.: *Brit. J. Surg.*, **49:** 292, 1961.

The Royal College of Physicians and Surgeons of Canada

NEWSLETTER

1. REGIONAL MEETING–VANCOUVER

Fellows and Certificated Specialists are reminded that the 1964 Regional Meeting of the College is being held at the Bayshore Inn, Vancouver, on Friday and Saturday, October 23 and 24 (registration on Thursday evening, October 22).

Programs for this meeting have already been mailed to all Fellows and Certificated Specialists in British Columbia and Alberta. Fellows and Certificants from other parts of Canada will be welcomed and may obtain a copy of the program by writing to: Dr. A. D. McKenzie, Chairman, Committee on Arrangements, Department of Surgery, Faculty of Medicine, Vancouver General Hospital, Vancouver, B.C.

2. THE 1965 ANNUAL MEETING

The 1965 Annual Meeting of the College will be held at the Royal York Hotel, Toronto, January 21, 22 and 23.

Plans for the scientific program of the meeting are already well advanced and promise continued maintenance of the high standard of recent College meetings. The program will feature the following outstanding guest lecturers:

The Royal College Lecturer in Medicine: Dr. William B. Castle, Francis Weld Peabody Professor of Medicine, Harvard University, Boston, Massachusetts. Title: "Polycythemias".

The Royal College Lecturer in Surgery: Dr. Joseph E. Murray, Peter Bent Brigham Hospital, Boston, Massachusetts. Title: "Organ Transplants: a Type of Reconstructive Surgery".

The Royal College Lecturer in Obstetrics: Sir John Peel, K.C.V.O., F.R.C.S., Professor of Obstetrics and Gynaecology, Kings College Hospital, London, England. (Title to be announced.)

For the past several years the Friday and Saturday morning combined sessions have featured symposium-type presentations of wide interest and drawing essentially on the personnel and resources of the local medical school and teaching hospitals. These will be continued in 1965. The surgical symposium will deal with "Diseases of the Esophagus" and will be chaired by Dr. F. G. Kergin. Dr. K. J. R. Wightman will chair the medical symposium on the subject of "'Curable Hypertension".

Through the courtesy of Smith Kline & French Inter-American Corporation, closed-circuit colour television, which proved so successful and popular at the 1963 meeting in Edmonton but was not possible because of space limitations at the 1964 meeting, will again be a feature of the Toronto meeting. A Television Committee, under the chairmanship of Dr. James Key, has been at work for several months on the meticulous planning necessary to ensure the success of this aspect of the program. The following subjects will be dealt with in the television programs: "The Respiratory Unit"; Chairman—Dr. C. C. Gray. "Chromosomes and Disease"; Chairman – Dr. W. B. Spaulding. "Endocrinological Problems in Obstetrics and Gynecology"; Chairman – Dr. Joslyn Rogers. "Vagotomy and Pyloroplasty"; Chairman–Dr. Bruce Tovee. "Cardiac Pacemaking"; Chairman–Dr. Donald Wilson.

The Committee on Arrangements is conscious of the advantages inherent in the multidisciplinary make-up of the College and is anxious that the Annual Meeting should attempt to attract the interest and active participation of as many as possible in the various specialties. To this end a special effort has been made this year to encourage the submission of papers from the neurology and neurosurgical group to permit a sectional session of broad general interest on problems in these areas. Depending on the success of this attempt, similar efforts may be made in other specialty areas for future meetings.

3. INVITATION TO CERTIFICATED SPECIALISTS OF THE COLLEGE TO ATTEND THE 1965 ANNUAL MEETING

Once again the Council of the College wishes to extend a cordial invitation to all Certificated Specialists of the College to attend the Annual Meeting and to participate fully in the scientific sessions. Those desiring to attend are asked to complete and return the registration application form opposite as soon as possible. A copy of the program will be sent about mid-December to all those who have registered in advance.

The Secretary,
The Royal College of Physicians and Surgeons of Canada,
74 Stanley Avenue,
Ottawa 2, Ontario.

I desire to register to attend the Scientific Sessions of the Annual Meeting of The Royal College of Physicians and Surgeons of Canada to be held at the Royal York Hotel, Toronto, January 21, 22 and 23, 1965.

Enclosed is a cheque/money order in the amount of $15.00 in payment of the registration fee.

Name of Certificant .....

Address .....

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Name of Specialty .....

(please print)

Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Chirurgische Operationen. Ein Atlas für die Praxis. Band II: Bauch, Urologie, Wirbelsäule, Nervensystem. Horst-Eberhard Grewe and Karl Kremer. 705 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1964. DM. 98.–. $26.50 (approx.).

Correctable Renal Hypertension. Chester C. Winter. 190 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1964. $8.25.

Creative Minds in Medicine. Scientific, Humanistic, and Cultural Contributions by Physicians. William Carleton Gibson. With a foreword by Paul Dudley White. 238 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1963. $8.10.

Diagnostic Urology. Edited by James F. Glenn. 415 pp. Illust. Hoeber Medical Division, Harper & Row, Publishers, Inc., New York, N.Y., 1964. $13.50.

Human Reproduction and Sexual Behavior. Edited by Charles W. Lloyd. 564 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1964. $13.75.

Le Pancréas. Sous la direction de Guy Albot et Félix Poilleux. 310 pp. Illust. Masson & Cie, Paris, 1964. 76 F. ($15.20 approx.).

Modern Trends in Orthopaedics 4: Science of Fractures. Edited by J. M. P. Clark. 254 pp. Illust. Butterworth & Co. (Canada) Ltd., Toronto, 1964. $13.50.

Pediatric Ophthalmology. Edited by L. Byerly Holt. 403 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1964. $13.25.

Saint Bartholomew's Hospital Reports (New Series). Vol. I. Cancer Report 1948-1952. Edited by A. W. Franklin and M. P. Curwen, with a Preface by Sir James Paterson Ross, Bart. 158 pp. Illust. Published for the Treasurer and Governors of St. Bartholomew's Hospital by E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1963. $5.40.

Shock. Edited by S. G. Hershey. 308 pp. Illust. Little, Brown and Company, Boston; J. B. Lippincott Company of Canada Ltd., Montreal, 1964. $12.50.

Surgical Clinicopathological Conferences of the Massachusetts General Hospital. Edited by Benjamin Castleman and John F. Burke. 249 pp. Illust. Little, Brown and Company, Boston; J. B. Lippincott Company of Canada Ltd., Montreal, 1964. $13.50.

The Temporomandibular Joint. 2nd ed. Edited by Bernard G. Sarnat. 260 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1964. $15.00.

Traitement Chirurgical des Malformations Luxantes de la Hanche chez l'Adulte. R. Merle d'Aubigné, J. Evrard, A. Flores, B. Juteau, B. Maudhuit, M. Postel, J.-O. Ramadier, D. Simonin et J.-M. Vaillant. 106 pp. Illust. Masson & Cie, Paris, 1963. 20 F. ($4.00 approx.).

Traitement Chirurgical des Prolapsus Génitaux. R. Merger, J. Lévy, J. Melchior et J. Barrat. 74 pp. Illust. Masson & Cie, Paris, 1964. 26 F. ($5.20 approx.).

Tropical Splenomegaly. A. K. Basu and B. K. Aikat. 195 pp. Illust. Butterworth & Co. (Canada) Ltd., Toronto, 1963. $11.25.

BOOK REVIEWS

(See also pages 399, 413, 432, 437, 442, 463, and 469)

THE SCIENCE OF SURGERY. (Blakiston Outline Series.) Edward H. Storer, James W. Pate and Roger T. Sherman. 540 pp. Illust. McGraw-Hill Company of Canada Limited, Toronto, 1964. $8.65.

The authors divide the teaching of surgery into three parts—science, technique and art. Their volume consists of a concise outline of the science of surgery and makes no pretense of covering the technical aspects such as would interest the young surgeon undergoing postgraduate training. The book is designed purely for the undergraduate student and consists of excellent chapters based on lectures and demonstrations given at the University of Tennessee.

Surgical subspecialties are not generally included with the exception of cardiovascular and thoracic surgery which is dealt with in reasonable proportion to the rest of the field. Fractures are not included, but the last two chapters deal with multiple-system injuries and mass casualties. The book is the latest addition to the Blakiston Outline Series.

Those responsible for the teaching of surgery in faculties of medicine would do well to study this book as a possible addition to the curriculum. The presentation is extremely condensed, but very readable and entirely modern in outlook and approach. The volume is sparsely illustrated with line drawings of considerable ingenuity and teaching value. This book is one of the most attractive of the short outlines available and may well prove very popular with the undergraduate student of surgery.

SIDE EFFECTS OF DRUGS. 4th ed. Edited by L. Meyler. 356 pp. Excerpta Medica Foundation, 119-123 Herengracht, Amsterdam, The Netherlands, 1963. $7.50.

A new edition of this volume, derived from the medical literature of the world, makes a welcome and valuable addition to the library of any surgeon. The book is not large or bulky and could be placed on hospital wards, in the emergency department, the operating room, or wherever emergency drug reactions might be encountered.

The main value of the book to the practising surgeon is as a reference. The enormous range of newer agents frequently encountered in the management of surgical patients renders the pharmacological teaching which most surgeons recall from their undergraduate days completely obsolete. One has only to mention headings such as muscle relaxants, hypotensive agents, antibacterial agents, hormones and synthetic substitutes, anticoagulants, immunological agents, and radioactive isotopes to realize the importance of having such a volume nearby.

THROMBOPHLEBITIS. A Treatise on Its Etiology, Diagnosis and Treatment. J. Earle Estes. 66 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1964. $5.50.

This small book, a treatise on the etiology, diagnosis and treatment of thrombophlebitis, is, as is stated in the preface, "the author's personal comprehension of the problem of thrombophlebitis". This book will be of value to students and physicians in practice and is not intended to be an encyclopedia on venous thrombosis. The author's discussion of definition, etiology and clinical aspects of thrombophlebitis is excellent. The 14 pages used for discussion of the medical treatment of the disease are very well done. Two pages are devoted to the surgical treatment. Many authorities will disagree with some of his views, particularly on the value of inferior vena-caval ligation in repeated pulmonary emboli and thrombectomy in severe ilio-femoral thrombosis in that, whenever surgery is carried out for this problem, it surely should be combined with medical treatment. Most surgeons will agree that femoral vein ligation is a poor operation but ligation of the long saphenous in ascending thrombosis of that vein may be life-saving.

MANAGEMENT OF ORAL EMERGENCIES. Daniel M. Laskin. With a Foreword by Bernard G. Sarnat. 107 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1964. $6.50.

This short monograph attempts to cover the emergencies arising in the dental patient. The sections on Admitting, Operative and Postoperative Emergencies contain brief discussions of the diagnosis and treatment of common conditions of the head and neck, with particular emphasis on the dental problems. The section on Emergencies Associated with Use of Local Anesthesia covers the three categories of reactions, namely, allergic, toxic and hypersensitivity.

The book is concisely written and well illustrated and should be of particular interest to the dentist. It could have a place in the emergency department of hospitals but has little to offer most medical practitioners.

NOUVELLE PRATIQUE CHIRURGICALE ILLUSTREE. Fascicules XXI et XXII (New Surgical Practice Illustrated, Fascicles XXI and XXII). Edited by Jean Quénu. 279 and 280 pp. Illust. Editions Doin, Deren & Cie, Paris, 1963. Fascicule XXI, 50 NF. ($10.00 approx.); Fascicule XXII, 54 NF. ($10.80 approx.).

Cette nouvelle pratique chirurgicale illustrée publiée sous la direction du professeur Jean Quénu fait suite à la pratique chirurgicale il-

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lustrée de Victor Pauchet. Ce travail est très bien connu et nous pouvons dire un classique parmi tous les chirurgiens de langue française.

Il s'agit d'un atlas de chirurgie contenant à chaque page une illustration et avec quelques lignes de texte explicatif au bas de la page. De plus, au début de chaque chapître, l'auteur donne quelques aspects du diagnostic et la conduite à tenir dans les soins pré- et post-opératoires.

Les volumes 21 et 22 suivent en somme la marche qui avait été établie dans les éditions précédentes avec cette différence que les techniques modernes y ont été ajoutées. C'est un volume que nous pouvons recommander à tous les chirurgiens et en particulier aux résidents en chirurgie.

Le seul reproche que nous ayons à faire à cet ouvrage est son manque de classification, comme dans les autres ouvrages du même genre. En effet, dans un même fascicule, on peut trouver des techniques se rapportant à la chirurgie du colon, à la neuro-chirurgie ou à la chirurgie thoracique. Ceci n'a cependant d'inconvénient en ce qu'il faut posséder tous les volumes si l'on désire avoir les techniques se rapportant à un seul sujet.

HANDBOOK OF HISTOPATHOLOGICAL TECHNIQUES. 2nd ed. C. F. A. Culling. 579 pp. Illust. Butterworth & Co. (Canada) Ltd., Toronto, 1963. $14.75.

The second edition of this book has grown by approximately 100 pages of text. This growth reflects the incorporation of much new information, especially in Chapter 1, The Cell, and Chapter 2, Methods of Examination of Tissues and Cells. In Chapter 2, cryostat and fluorescent antigen-antibody techniques are introduced. Comparable additions appear throughout.

The list of appropriate references is augmented and updated. Several of the illustrations portray types of equipment not commonly used in North America.

This handbook deserves a place in the histological and histopathological laboratory, particularly so if a technology training program is in operation. The presentation is clear, straightforward and in good sequence. It is an excellent textbook for medical laboratory technology students as an introduction and in preparation for more advanced registration.

INDICATIONS AND TECHNIQUES IN ARTERIAL SURGERY. Edited by Peter Martin. 112 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1963. $5.50.

This is a useful little book of 112 pages, clearly printed and clearly illustrated. It consists of eight chapters and covers the arteries of the leg, the pelvic vessels, the carotid and vertebral arteries, the superior mesenteric and celiac axis arteries. It also deals with renal artery stenosis, aneurysms, and arterial embolism. Six well-known British vascular surgeons have contributed to this book. In general there is little to disagree with in either the techniques propounded or in the indications for surgery. Useful tips in technique have been presented in a number of cases. There is a good preliminary chapter on the whole subject of peripheral ischemia.

Mr. Mavor contributes the chapter on peripheral artery grafting and agrees with the currently held view that the by-pass graft, using the long saphenous vein, is preferable for femoral obliterative arterial disease. The reviewer would not agree with him that the handling of the vein graft is more difficult than the handling of synthetic graft, nor would he agree that it is necessary to turn the patient and make a midline incision to get at the popliteal artery. The reviewer feels that the leg bent and rotated externally gives excellent access to the popliteal artery through the medial approach.

Mr. Cockett contributes the chapter on endarterectomy. He is a well-known proponent of the "rebore" operation for femoral artery block. Most vascular surgeons nowadays feel that this is less satisfactory than the by-pass graft. Eastcott's contribution deals with the external cerebral vascular system and the surgery of this. The reviewer would not agree with him that local anesthesia is preferred. On this continent general anesthesia with maintenance of perfusion by raising the systolic blood pressure would appear to be the preferred method. He says little about the clearance of the vertebral artery. There is a good chapter on renal artery stenosis and also a good chapter on the treatment of aneurysm. This describes a method of dealing with the aneurysm without excision of the whole aneurysm and leaving the posterior wall *in situ*, which is to be commended.

Chapter 8, contributed by Mr. Tibbs, is clearly written. However, the reviewer would not agree with him that general anesthesia is the preferred form. The vast majority of embolectomies can be performed very satisfactorily under local anesthesia with much less danger to the patient. Furthermore, the use of the Fogarty catheter has revolutionized the method of embolectomy. It is no longer necessary to do the retrograde flush or to make various arteriotomies. Furthermore, most saddle emboli can be cleared through the femorals by this surprisingly effective technique. The principles outlined in Chapter 8 on peripheral arterial embolism are sound. However, as already stated, the latest techniques have obviated much of what is said in this chapter.

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INTENSE O.B. ANALGESIA WITH LIGHT ANAESTHESIA: PENTHRANE*

METHOXYFLURANE

Low concentrations are effective in labor and childbirth

Excellent analgesia is a prime quality of Penthrane in obstetrics. Thus Boisvert and Hudon, studying Penthrane in 500 deliveries,[1] cite as an outstanding feature its high level of analgesia under a light plane of anaesthesia.

In their study they report: "The intensity and rapidity of onset of analgesia is remarkable, occurring within the first two minutes of Penthrane inhalation. It seems evident that anaesthesia is obtained much faster in obstetrical cases than surgical cases. It is also obtained with much lower—indeed minimal—concentrations."

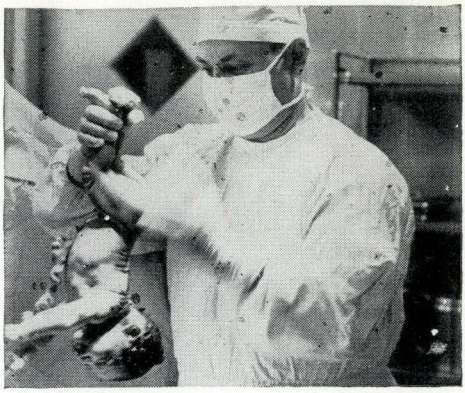
Persistent analgesia

Similarly Romagnoli and Korman, studying 645 deliveries,[2] comment on how "the analgesic effect lingered between pains." This is in keeping with observations of analgesia persisting during the recovery period following surgery.[3,4,5] The obstetrical investigators managed labor pains with much lower amounts of Penthrane than are used in surgery. Vapor concentrations of only 1% suffice for anaesthesia, and 0.42% for analgesia. They considered their results "most gratifying."

Called a drug of choice in obstetrical anaesthesia

Penthrane is a unique type of ether (a halogenated ethyl methyl ether). It is *non*flammable, and virtually free of delirium and vomiting during induction. It permits extremely stable cardiac function. It yields easily controlled anaesthesia, with excellent safety margins.

Boisvert and Hudon state, *"In our opinion, it is the drug of choice in obstetrical anaesthesia."*[1] In evidence, they cite its rapid induction, high level of analgesia under light anaesthesia, very low incidence of vomiting, minimal depression of uterine contractions, minimal respiratory depression of the fetus, and the quiet and rapid recovery.



Effect of Penthrane on respiration of the newborn has been minimal. Most infants cry within the first minute.

LABOR NOT IMPEDED

The studies cited confirm that at these light dosage levels, Penthrane does not interfere with labor.

The first group[1] reported: "It cannot be overemphasized that light Penthrane anaesthesia does not stop or depress uterine contraction. Actually, it often seems to stimulate and accelerate contractions..."

The other group[2] commented: "The obstetricians as well as the nursing staff felt that labor was never arrested or even delayed..."

Prompt induction, recovery

The obstetric patient can be induced rather quickly, reaching a plane deep enough for use of forceps within several minutes. Induction is smooth and pleasant. There is no coughing or struggling.

Unless the procedure has been long, recovery is also short, with the mother awake on the delivery table within several minutes. Anaesthetic is generally discontinued when suturing of the episiotomy begins.

Any modern ether vaporizer is suitable, Self-administration with the Cyprane Trilene inhaler has also been successfully used.

1. Boisvert, M., and Hudon, F., Can. Anaes. Soc. J., 9:325, July, 1962. 2. Romagnoli, A., and Korman, D., Can. Anaes. Soc. J., 9:414, Sept., 1962. 3. Kaveny, R. E., and Wasmuth, C. E., Cleve. Clin. Qt., 29:148, July, 1962. 4. Thomasen, R., et al., Anaesth. & Analg. C. R., 41:225, March, 1962. 5. Artusio, J. F., et al., Anaesthesiology, 21:512, Sept., 1960.

*TRADE MARK REGISTERED

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This small book will be very useful to all vascular surgeons, particularly to those starting out on careers in vascular surgery.

TECHNIQUES AND PROCEDURES OF ANESTHESIA. 3rd ed. John Adriani. 647 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1964. $12.50.

The third edition of this classic text, first published in 1947, will surely be welcomed by all students of the art and science of anesthesiology. So intimate is the relationship between the anesthetist and the surgeon that it would be well if all operating surgeons were to spend some time in the study of the problems faced by their colleagues in maintaining the patient in optimal condition. As in the previous editions, this revised version is principally a condensed outline of detailed techniques, but the explanations given throw considerable light upon the basic physiological considerations which have to be understood both in the operating room and in the recovery room. The detail on the use of equipment designed to assist ventilation is of great interest and well illustrated. The book should be in every surgical library.

WOUND HEALING AND MANAGEMENT. A Monograph for Surgeons. D. M. Douglas. 175 pp. Illust. E. & S. Livingstone Ltd., Edinburgh & London; The Macmillan Company of Canada Limited, Toronto, 1963. $10.75.

This monograph is directed to the surgeon. It aims, in concise form, to outline the biology of wound healing and to discuss some aspects of the management of the surgically incised wound. It is not a detailed review of wound healing or its important ramifications that so greatly affect the surgeon.

Divided into two section, the first, on the pathology of the healing wound, discusses the subject in a superficial fashion. The histology, pathology and biochemistry are outlined in a manner that stimulates the interest but avoids detail. The subject of systemic influences of wound healing, including the role of protein and ascorbic acid deficiency, is incomplete and adds nothing to the same material presented in more standard works on this subject.

The use of the tensiometer in the measurement of the tensile strength of wounds is discussed, including the author's own work in this field. The comparison of the tensile strength of the aponeurosis of the abdominal wall is of considerable interest. The section dealing with bone healing is a synopsis of the work of Ham and Harris.

The second section of the book deals with certain aspects of wound management, especially the prophylaxis of infection. A chapter on operating-room design, based on the arrangements at the Dundee Teaching Hospital, has much merit. This is followed by a good review of sterilization techniques, including the advantages and disadvantages of the use of ionizing radiation in the sterilization of surgical materials.

Whereas the subject of skin preparation, soaps and suture materials is presented in some detail, the discussion of wound dehiscence and incisional hernia is too brief to be of value.

The book fulfils its aim of presenting concisely some of the important aspects of wound healing. It is easy to read and, in many areas, of great interest, but in general this monograph is too superficial to be of real value.

CANCER. Progress Volume 1963. Edited by Ronald W. Raven. 254 pp. Illust. Butterworth & Co. (Canada) Ltd., Toronto, 1963. $13.50.

This volume is a selective study of the more significant advances in cancer research and treatment in the past decade. It deals succinctly with a varied group of topics such as tumour virology, tumour epidemiology, radiation and chemotherapy. Each synopsis is accompanied by an extensive bibliography of the recent contributions to the literature, yet makes no attempt to review completely the subject concerned. The contributors include prominent international investigators and clinicians.

The chapter on tumour virology, by R. J. C. Harris, records the electron microscopy, nucleic-acid chemistry and epidemiology of the known and suspected oncogenic viruses.

A discussion by E. H. Mercer of the role of electron microscopy in tumour study is included.

The epidemiology and geographic distribution of cancer are dealt with in some detail and the work of Dr. Burkitt, on the geographical distribution of lymphoma in African children, will be of interest to anyone not familiar with this subject. The relationship of air pollution and lung cancer is discussed, as is the relationship of soil chemistry to carcinoma of the stomach.

Dealing with circulating cancer cell, Goldblatt and Nadel outline the techniques of cell isolation, concentration and slide preparation. They record the sources of error and compare the findings of investigators using different techniques.

Of interest to the practising surgeon is the section on the biological approach to cancer surgery which deals with the known factors concerning tumour growth, dissemination and biological activity as related to surgical treatment.

This monograph will be disappointing to the reader in search of a comprehensive review of the subject of cancer but will be valuable to the investigator seeking a synopsis and bibliography of any of the subjects discussed.