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HISTORY OF CANADIAN SURGERY

PRIORITY OF CLINICAL X-RAY REPORTS: A CLASSIC DETHRONED?

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IN GARRISON and Morton's *Medical Bibliography*¹ the second item in the section on diagnostic roentgenology, immediately following Roentgen's communication, is an article by John Cox and R. C. Kirkpatrick of Montreal. This paper, "The New Photography, with Report of a Case in which a Bullet was Photographed in the Leg", appeared in the *Montreal Medical Journal* of March 1896.² Cox was professor of physics at McGill University, and Kirkpatrick was surgeon to The Montreal General Hospital.* Garrison and Morton state that this communication was the "first clinical x-ray report, March 1896".

Recently I acquired a bound volume of the *Montreal Medical Journal* containing this paper. Greatly elated at having, unknowingly, acquired an original copy of a "classic" paper, I began to do some background reading on the discovery of x-rays and their utilization in medicine. I have found that Garrison and Morton appear to be wrong; there are clinical x-ray reports which antedate March 1896.

ROENTGEN'S DISCOVERY: PRECLINICAL APPLICATIONS

Dr. W. C. Roentgen's discovery of x-rays was made public in late December 1895.† It is difficult to imagine how the discovery could have reached the medical profession and the general public more rapidly than was the case. A reprint and photographs were seen by Z. K. Lecher, editor of the *Presse* in Vienna, who ". . . lost no time in exploiting the enormous news value in the story of the rays' discovery. His was

the original contention that the discovery might become of extreme importance in the study of disease, and his enthusiastic article appeared on the front page of the Sunday, January 5, 1896, edition of the *Presse*."⁴ The following extract is from the morning edition of the *Frankfurter Zeitung* for January 7, 1896: "At the present time we wish only to call attention to the importance this discovery would have in the diagnosis of diseases and injuries of bones . . . (the surgeon) could find the position of a foreign body, such as a bullet or a piece of shell . . ."⁵

Roentgen makes no mention of any specific use of the rays. Among the photographs he presented was one of a hand with a ring on the finger. His statement was: "If the hand be held before the fluorescent screen, the shadow shows the bones darkly, with only faint outlines of the surrounding tissues." Nothing more.

The first reference to Roentgen's discovery that I have found in the English-language medical press is in the *British Medical Journal* for January 18, 1896. In this issue there is a communication from Professor Arthur Schuster, a physicist, who writes: "Prof. Roentgen, of Würzburg, announces the discovery of remarkable photographic effects which he ascribes to a new kind of radiation. As the statements which have appeared in most of the daily papers are inaccurate in many respects, a short description of what Prof. Roentgen claims to have accomplished may interest the readers." And after summarizing the discovery, Professor Schuster continues: "As flesh, skin, and cartilage are more transparent than bone, the photograph of a hand gives a complete outline of the bones of the hand and fingers, the outline of the flesh being only faintly marked. It is not necessary to enter into the many possible medical applications which this photograph opens out."⁹

*See addenda for brief biographies.

†According to Sarton,⁷ the basic discovery made by Roentgen took place on November 8, 1895. Dr. Roentgen completed his preliminary communication on December 28, 1895, and this was promptly published in the *Sitzungsberichte der Physikalisch-Medizinischen Gesellschaft in Würzburg*.⁸

Since the middle of January 1896, an ever-increasing flood of articles and notes concerned with Roentgen's rays has appeared in the medical literature. Within the first year of the discovery (1896) no less than 49 books or pamphlets and 1044 papers were published on the subject of Roentgen rays!⁷

CLINICAL APPLICATIONS

On January 25, 1896, an x-ray photograph of a hand* appears in the *British Medical Journal*. This was taken by A. A. C. Swinton and J. C. M. Stanton. It showed the bones of the normal hand; no pathology was present. However, in this discussion we are concerned with priority of publication of a clinical report utilizing x-rays as a diagnostic aid.

The first mention I have found of the diagnostic use of x-rays is in a leading article in the *British Medical Journal* for February 1, 1896.

“. . . Professor Moseitig, of Vienna, has taken photographs which showed with the greatest clearness and precision the injuries caused by the pistol shot in the left hand of the man and the position of the small projectile. In another case the same observer detected the position and nature of a malformation in the left foot of a girl with entire success.

“Professor Lannelongue, of Paris, has also been successful in photographing some of his cases . . . (and) has submitted to the Academy of Sciences several negatives of human limbs. One of them represents a diseased thighbone.”¹⁰

The editor's source of information for these remarks is not recorded.

Mr. Sidney Rowland was commissioned by the *British Medical Journal* to prepare a “Report on the Application of the New Photography to Medicine and Surgery”. The first section of this remarkable report, which continued almost weekly for several

months, appeared on February 8, 1896. From it we learn:

“Some of the earliest endeavours to apply Prof. Roentgen's discovery not only to diagnosis but to treatment are reported from Vienna. Prof. Moseitig was the first to utilize the new method. At the Medical Society he reported two cases in which operative procedures were carried out under the guidance of the exact knowledge of the anatomical conditions obtained by the new radiation . . . The first case is one of deformity of the distal phalanx of the hallux, which appeared to be double.”¹¹

The report includes an excellent photograph showing a supernumerary phalanx.

The first American reference which I have been able to locate is in an editorial, entitled “X-Rays”, in the *Boston Medical Journal* of February 13, 1896.¹² Accompanying the usual résumé of Roentgen's discovery is a photograph of an x-ray of a normal hand.

On February 15, Mr. Sidney Rowland reported that copies of x-rays taken by Professor Roentgen had been received.¹³ These included one of a fracture of the forearm with much displacement. On this same date a brief editorial note on “The Roentgen Rays” appeared in the *Journal of the American Medical Association*,¹⁴ the first mention of the subject in that journal.

“Rare Anomalies of the Phalanges Shown by the Roentgen Process” is the title of an editorial in the *Boston Medical Journal* of February 20, 1896.¹⁵ This article includes a photograph of a hand showing a case of a suppressed and rudimentary phalanx. No case history was given. “The picture is taken from a patient at the Boston City Hospital by the kind cooperation of the Department of Physics at the Massachusetts Institute of Technology with gentlemen connected with the hospital.”

Finally, in the *Lancet* for February 22, 1896, there appears a communication entitled: “The Discovery of a Bullet Lost in the Wrist by Means of the Roentgen Rays”, by Robert Jones and Oliver Lodge.¹⁶ This article includes a clear photograph showing the bullet in the wrist. The case and x-ray were presented at a meeting of the Liverpool Medical Institution on February 13, 1896. This paper is also reported, briefly,

*As an indication of the marked interest in the phenomenon of x-rays, a notice appeared in the *British Medical Journal* one week later stating that Mr. Swinton had received so many requests for copies of his photograph of the hand that he had arranged for the Swan Electrical Engraving Co. to handle and supply them.

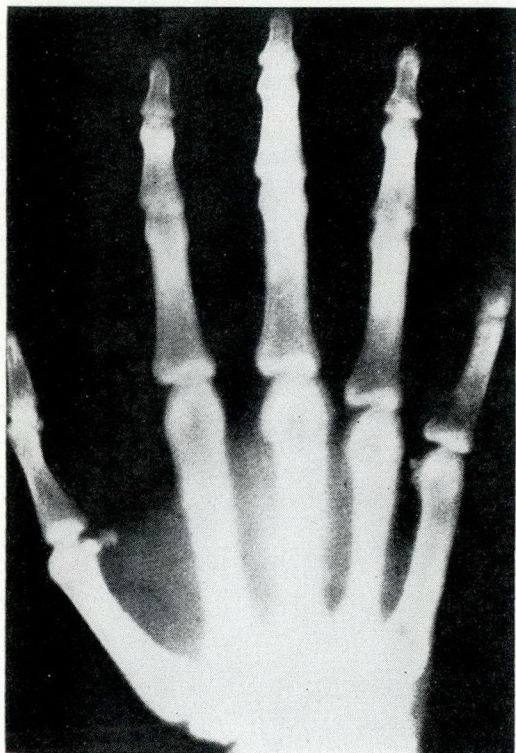


Fig. 1.—Photograph of living hand showing bones; used to illustrate Cox and Kirkpatrick's article (*Montreal Med. J.*, 24: 661, 1896). All three radiographs were made with a Puluj tube containing a brilliant fluorescing screen and called the "Schirm-Lampe". This tube was excited directly from the secondary of a large Kuekenkorff coil (10" spark) fed with 4 amperes at 8 volts on the primary. This particular radiograph was taken by Messrs. King and Pitcher, of the McDonald Physics Building, on the evening of February 7, 1896. The exposure in this case was 30 minutes.

in the *British Medical Journal* for the same date, and appears to fulfill all the criteria as the first published case history *per se* wherein x-rays were utilized diagnostically.

By the end of February, Roentgen ray photographs* had been taken of dislocations, fractures, a variety of foreign bodies, arthritis and tuberculosis of the bone. The vessels of the hand and of the kidney had been injected and photographed post mortem.

*The names Roentgen rays and x-rays, which have survived, were applied early to the phenomenon. The picture obtained on film was less easy to name, and the following early suggestions are representative: rotograph, X-graph, shadow-type, shade picture, scotograph, skiograph, actinograph and kathograph.



Fig. 2.—The x-ray showing the bullet in the patient's leg. The original to this photograph has been lost; this picture, made from a copy kindly supplied by the Osler Library at McGill University, is greatly superior to the reproduction shown in the original article in the *Montreal Medical Journal*. Exposure 45 minutes.

COX AND KIRKPATRICK'S ARTICLE

In the *Montreal Medical Journal* for February 1896, the editorial page, at the conclusion of a brief mention of Roentgen's discovery, carried this note: "Prof. Cox, of McGill University, has already photographed a hand in a manner that brings out clearly the outlines of the bones of which it is formed, and we hope in our next issue to be able to give our readers some photographs of medical and surgical conditions that will illustrate the scope and utility of this new discovery."¹⁷

The promised article appeared in the March issue; even if priority is denied, it is of great interest. Published as the lead article, there are five pages of written material and three photographs. One is of a normal hand, and is only a fair reproduction (Fig. 1). Another, purportedly showing the bullet in the patient's leg, reproduced very poorly (Fig. 2). The original plate, which is not extant, apparently showed the bullet *in situ*; it was demon-

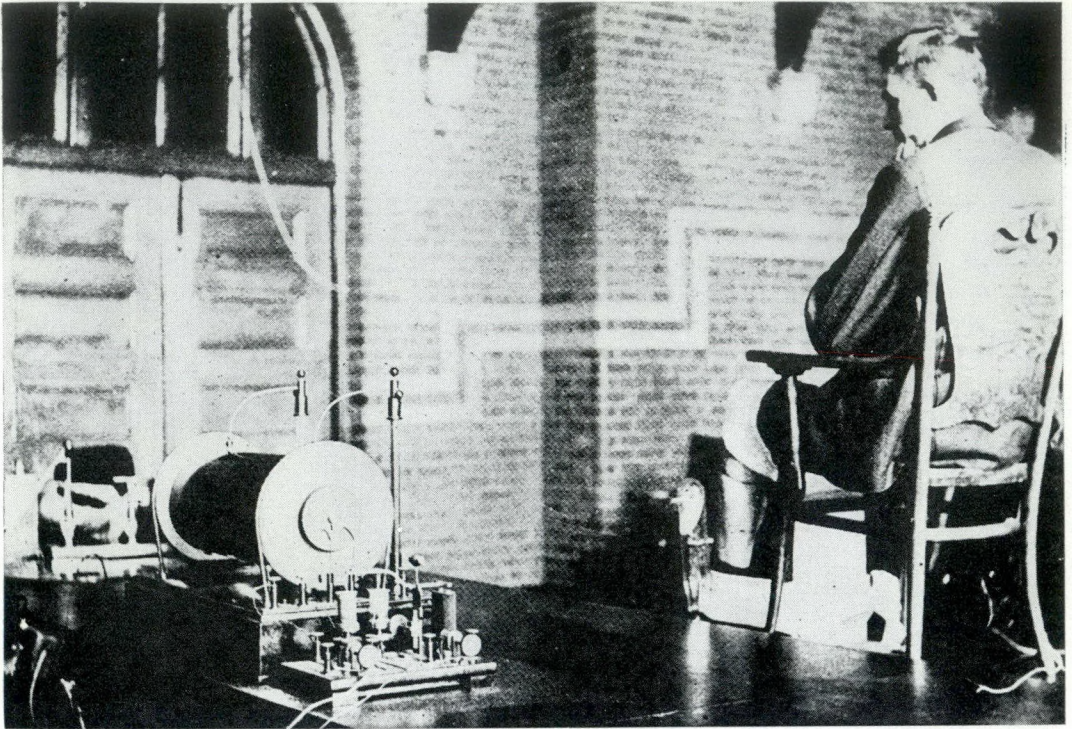


Fig. 3.—A photograph showing the arrangements in the Physics Lecture Theatre, where the radiograph was taken. This illustration also appeared in the March 1896 issue of the *Montreal Medical Journal* (24: 661, 1896). It is not made clear in the article whether the subject shown was the patient whose case is reported, or whether the photograph was made at a later date.

strated before the Montreal Medico-Chirurgical Society on February 7, 1896. The third photograph showed the laboratory arrangement used for making the plates (Fig. 3).

The first three and a half pages of the article are a recapitulation of the theory involved in producing x-rays. Then comes the following:

“What will mainly interest your society is that within four days of our first attempt we have made two trials of the process as applied to surgery. On Wednesday Dr. Armstrong kindly brought me a case of injury to the hip; but I am sorry to say that after one hour’s exposure we obtained not a trace upon the plate (22 in. x 18 in.). I am inclined to attribute this failure to the presence of lead in the black paint of the dark slide kindly loaned by Messrs. Notman, as lead even in a pigment has been found to obstruct the rays.”

This paragraph exemplifies some of the many problems which had to be overcome in this early period.

“This morning (February 7th) Dr. Kirkpatrick was good enough to give me the opportunity of trying to locate a bullet which had begun to cause trouble in the leg of a patient. As this is probably one of the earliest cases of the successful applications of Roentgen’s rays, especially in penetrating such a thickness of flesh, the negative, which clearly shows the flattened bullet lying between the tibia and the fibula, will be seen with interest. The plate was a Stanley . . . and the exposure 45 minutes. It is clearly underexposed, and should have had at least an hour and a half.”

The patient was operated upon on February 8; the bullet was found where it was expected, and removed, and the patient was discharged well in 10 days.

Two months after this publication the editors* stated: “Two months ago we pub-

*At this time the editors of the *Montreal Medical Journal* were Drs. Thomas G. Roddick, James Stewart, A. D. Blackader, J. George Adami, George E. Armstrong and R. C. Kirkpatrick.

lished some of the early results which were obtained in this connection at McGill University. We believe that the case then published was the first in which Dr. Roentgen's discovery was put to any practical use. It was also one of the first cases in which the new process was introduced into a court of law as evidence, the man who fired the revolver in this case being condemned to 14 years in the penitentiary."¹⁸

DISCUSSION AND CONCLUSIONS

It is evident that despite the enthusiasm of the editors of the *Montreal Medical Journal*, the article by Cox and Kirkpatrick was not the first clinical x-ray report. That distinction, for the English-language press at least, probably belongs to the paper by Jones and Lodge.¹⁶ In a paper written in 1945 and recently republished, Underwood supports this claim: "One of the first surgical applications to be reported was that of a bullet in a boy's wrist, treated and written up by Sir Robert Jones and Sir Oliver Lodge."¹⁹

Earlier references are all hearsay, or editorial notes, not actual clinical reports. The work done by Professor Mosetig at Vienna may have been published earlier, but I have been unable to check the German literature for references.

In any case, surely, priority here is unimportant. The basic, epoch-making discovery was Roentgen's; the clinical uses were developed with amazing speed, and often priority was determined by the day of the week on which the various journals were published.

It should, however, be of interest to know that the Canadian medical profession was as quick as that in any other country to utilize "the new photography".

ADDENDA

Professor John Cox was born in 1851 and was educated at Trinity College, Cambridge. He was appointed professor of physics at McGill University in 1890 and retired from the position in 1909. He died at Hayes Court, England, on May 13, 1923.²⁰

Dr. R. C. Kirkpatrick: The year after his paper, written with Cox, appeared, Kirkpatrick died of tuberculous meningitis at the age of 34. He has been described as "... a careful, con-

scientious surgeon, possessed of great judgment, and who never endeavoured to be considered a brilliant operator, but preferred to be ranked amongst those whose first consideration was the welfare of the patient." He was the first in Canada to successfully repair the stomach after perforation because of ulcer.³

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ORIGINAL ARTICLES

THE ABERRANT RIGHT SUBCLAVIAN ARTERY

Its Significance in Anterolateral Operations on the Cervical Spine

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THE INCREASING number of injuries to the cervical spine has led to new methods of investigation and new operative approaches to the cervical vertebrae. Injuries or degeneration of the cervical discs are now commonly explored through an anterolateral approach because fusion of the cervical bodies is readily performed by this route. The anatomical landmarks of the neck are well known, but the common vascular abnormalities are perhaps less well recognized. Of these, the commonest is the aberrant or retrosophageal right subclavian artery.

HISTORICAL REVIEW

The first authenticated case was attributed to Hunauld in 1735 by Holzapfel.¹⁴ Bayford² in 1789 first recorded the association between dysphagia and an aberrant right subclavian artery. He coined the term 'dysphagia lusoria', implying that the dysphagia was due to a *lusus naturae* (a trick or deception of nature).

EMBRYOLOGY

In the embryo at five weeks there are six pairs of vessels connecting the ventral and dorsal paired aortae. Of these, the ventral root of the right fourth arch forms the innominate artery. The arch of the right fourth branch forms the proximal portion of the subclavian artery; the distal part of the subclavian artery is formed from the right dorsal aorta. The left fourth arch and its ventral root form the aortic arch. The right aberrant subclavian artery develops from the distal portion of the right dorsal aortic arch, and from a remnant of the dorsal aortic root which persists as a diverticulum (Fig. 1).

INCIDENCE

The incidence of this anomaly, uncomplicated by congenital pulmonary stenosis, is probably about 1%. Cobey⁴ reported the result of an investigation into the incidence of this lesion made by Arthur Thomson for the Anatomical Society of Great Britain and Ireland as five in 500 dissections, 1%. Quain¹⁷ reported four cases in 1000 dissections, 0.4%; Goldbloom,⁸ four cases in 225 cadavers, 1.3%, and Dolgopol,⁶ seven times in 735 autopsies, 0.96%. McDonald and Anson¹⁶ reported 14 cases in 1453 white, Negro and Japanese cadavers. In 610 patients with congenital pulmonary stenosis, Blalock and Bahnson³ found 26 aberrant right subclavian vessels, an incidence of 4%. In 1955, Gross⁹⁻¹² reported his operative technique and results in 12 cases. He freed, doubly ligated and divided the aberrant artery with complete disappearance of the associated dysphagia. The present author recently had the extraordinary experience of finding two such anomalies in a mere 20 consecutive female autopsies.

Holzapfel¹⁴ gave the incidence as 0.6% and reviewed previously reported cases. In his review he recorded that the artery passed behind the esophagus in 127 cases, between the esophagus and trachea in 20 cases and in front of the trachea in six cases. Geddes⁷ was unable to confirm this latter finding, being unable to find a single published description of the aberrant vessel passing between the esophagus and trachea or anterior to the trachea. It is interesting to note that Bayford's original publication includes a drawing showing the aberrant subclavian artery passing between the trachea and esophagus.² Geddes⁷ comments that this drawing by T. Poole, reproduced in Fig. 2, is a crude postmortem diagram. It appears unfair to challenge the accuracy of Bayford's description or the

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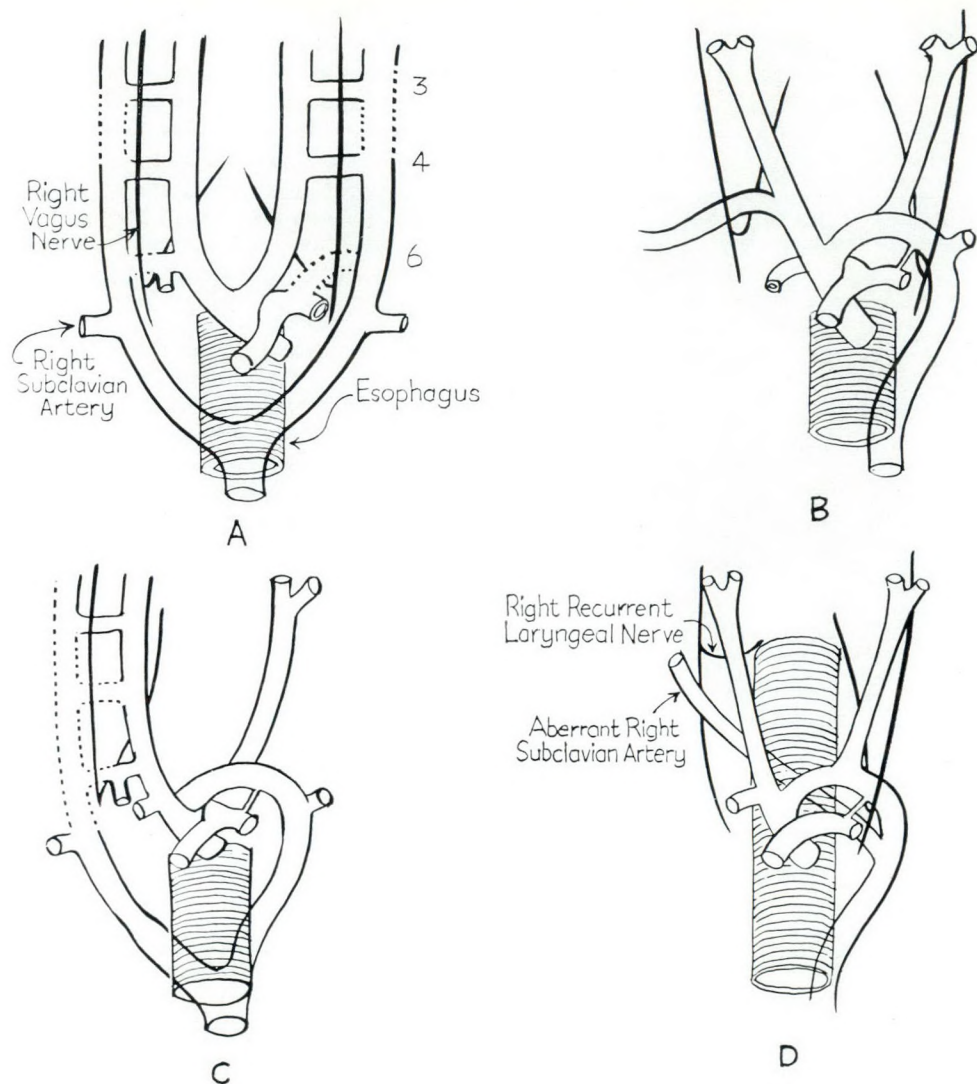


Fig. 1.—Schematic representation of the aortic arches and their transformations, with particular reference to the aberrant right subclavian artery and recurrent laryngeal nerves. The vessels represented as interrupted lines disappear in the course of normal development. A. The right subclavian artery is normally formed from the fourth arch. The aberrant right subclavian artery develops from the distal portion of the right dorsal aortic arch. Both origins are seen in this diagram. B. The normal anatomy of the great vessels and their relations to the recurrent laryngeal nerves is shown. C. The early development of the aberrant right subclavian artery, due to the persistence of the right dorsal aorta, is shown. The proximal portion of the vessel, which is probably formed from the aortic root, is represented as the wider portion of the vessel. The fourth aortic arch has disappeared. D. The right subclavian artery has migrated superiorly and has taken up its adult position. The right recurrent laryngeal nerve fails to recur around the aberrant vessel and passes directly to the larynx.

artist's reproduction of the postmortem specimen.² Such an occurrence, however, must be very uncommon; no other similar case has been reported.

Goldbloom⁸ quotes Oehl and Hyrtl, who postulate an intriguing, but unproved relationship between left-handedness and the presence of an aberrant artery.

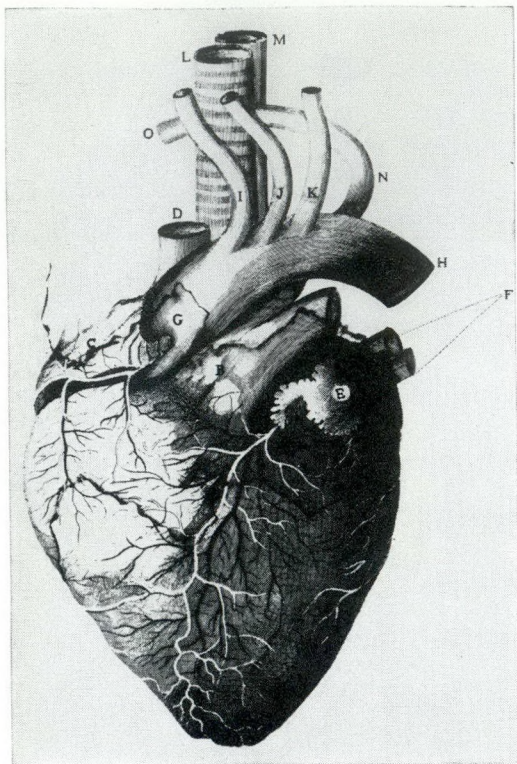


Fig. 2.—Reproduction of original drawing from Bayford's² publication in 1789. The aberrant right subclavian artery (N.O.) is seen passing between the trachea and esophagus. (B, pulmonary trunk; C, right auricle; D, superior vena cava; E, left auricle; F, pulmonary veins; I, right common carotid artery; J, left common carotid artery; K, left subclavian artery; L, trachea; M, esophagus.)

ANATOMY AND PATHOLOGY

Normally three main branches arise from the arch of the aorta. From right to left they are, the innominate, which divides into the right subclavian and right common carotid opposite the right sternoclavicular joint; the left common carotid, and the left subclavian arteries. The aberrant right subclavian artery upsets this arrangement. This artery arises as the fourth branch from the aortic arch, to the left of the left common carotid artery. It ascends to the right, passing posterior to the left common carotid and left subclavian arteries, and posterior to the esophagus and right common carotid artery, before gaining its normal exit from the thoracic cage. It crosses the midline at the level of the second or third dorsal vertebra, but may rise as high as the sixth cervical vertebra. The aberrant

origin of this vessel from the aorta displaces the origins of the other vessels. The right common carotid arises from the transverse portion of the aortic arch as the first branch, from the site normally occupied by the innominate artery. Both the left common carotid and left subclavian arteries occupy positions more to the right than usual (Fig. 3). The branches arising from the aberrant vessel are normal in position and distribution.

The esophageal pathology which results will depend on the degree of obstruction present. In most cases there is only mild indentation of the left lateral and posterior walls of the esophagus, with little or no dilatation or hypertrophy above the artery (Fig. 3c). One of the three specimens in the Anatomical Museum of the University of Toronto shows a definite saccular dilatation of the esophagus present below the aberrant artery.

Holzapfel¹⁴ and other authors have commented upon the dilated portion of the first part of the aberrant vessel proximal to the esophagus. This part probably represents the portion of the vessel formed from the wide dorsal aortic root, while the narrower distal portion is formed from the right dorsal aortic arch (Fig. 1c). This dilatation has been a consistent finding in the five specimens examined by the author, two at autopsy and three in the Anatomy Department of the University of Toronto. It is well illustrated in Fig. 3c.

SYMPTOMATOLOGY

Most cases are asymptomatic. In a few the aberrant vessel stretches across the left lateral and posterior aspects of the esophagus and interferes with the swallowing mechanism. The resultant dysphagia usually arises in infancy or early childhood. The symptom is usually worse when solid or semi-solid foods are being swallowed, but occasionally fluids may be more troublesome. Some unusual modes of presentation have been recorded. In Kirby's¹⁵ patient, a bone which stuck at the constricted site in the esophagus subsequently pierced the aberrant artery and led to a fatal hemorrhage. Kellock's¹⁹ three-year-old patient died in acute respiratory distress when food

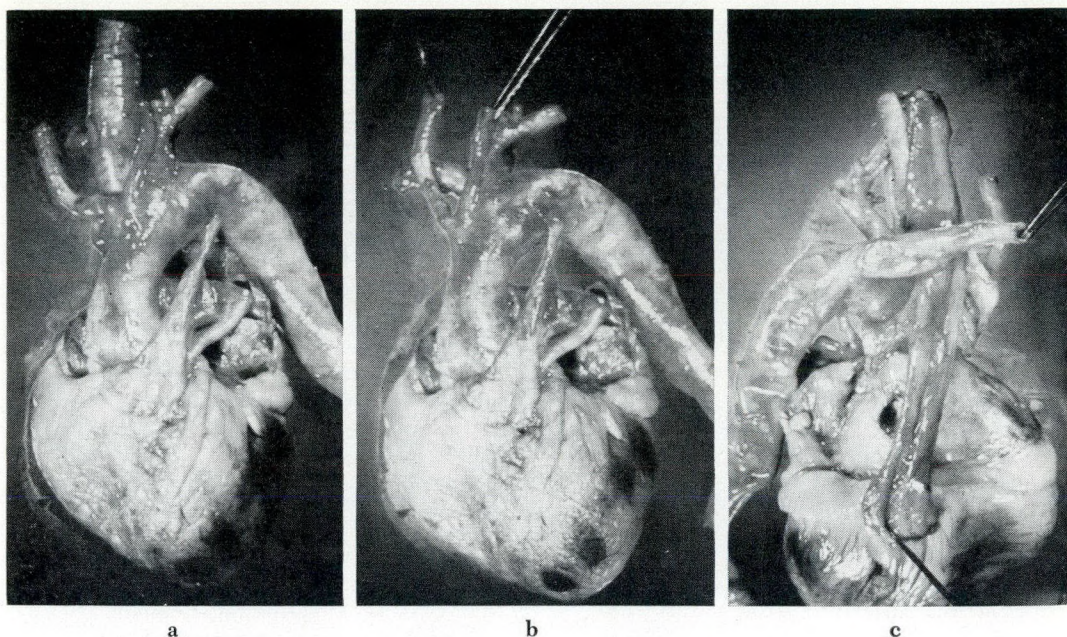


Fig. 3.—Specimen removed at autopsy from an 82-year-old female who died from cerebral thrombosis. The anomaly was asymptomatic. (a) Photograph shows the aberrant right subclavian artery appearing from behind the trachea and esophagus. (b) The trachea and esophagus have been removed and the course of the vessel is clearly demonstrated. (c) Photograph shows the vessel from the posterior aspect. The dilatation of the proximal portion of the vessel and the compression of the esophagus can be seen.

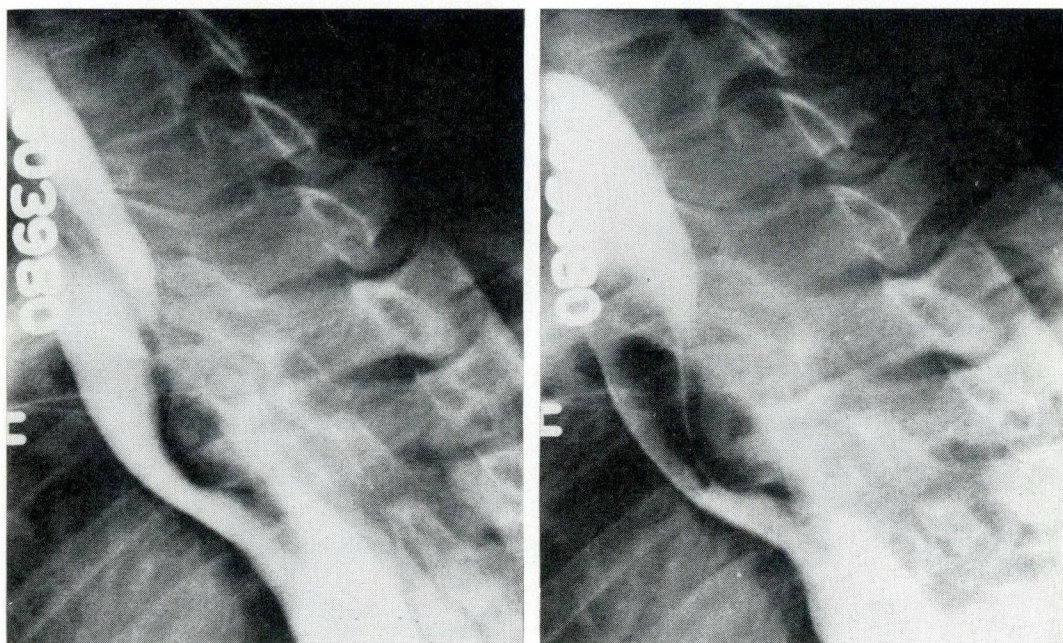


Fig. 4.—Oblique roentgenogram of barium visualization of the esophagus of a 54-year-old man with an aberrant right subclavian artery. The patient had complained of intermittent dysphagia for 10 years. The indentation of the barium column in the esophagus at the level of the second and third dorsal vertebrae is seen.

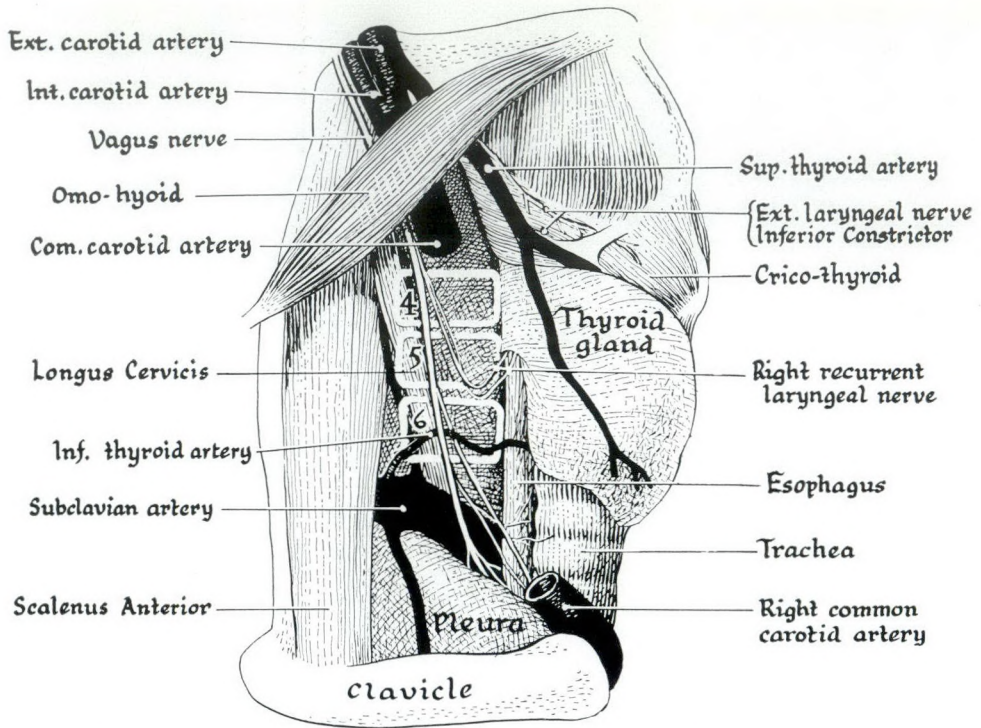


Fig. 5.—Drawing shows an oblique view of the deeper structures of the right side of the neck. The aberrant right subclavian artery is seen emerging from behind the esophagus. The course of the right recurrent laryngeal nerve and its direct relationship to the fifth and sixth cervical vertebrae and intervertebral disc has been emphasized.

became lodged in the esophagus at the constricted site. Symptoms may occasionally arise for the first time in late life. Autenrieth and Pfeleiderer¹ reported a case in which a woman of 60 years of age died of slow starvation because of obstruction of the esophagus by the artery.

DIAGNOSIS

This anomaly should be considered in the differential diagnosis of feeding difficulties in infants. In adults it is a rare cause of dysphagia. Most cases are found by the roentgenologist during routine investigation of the upper gastrointestinal tract. Copleman⁵ has described the radiological features. Plain films, made with suitable penetration, may demonstrate on anteroposterior views narrowing of the esophagus in the region of the third dorsal vertebra. Indentation of the esophagus may be seen on the lateral oblique or lateral projections. The anomaly is well seen during lipiodol or barium visualization (Fig. 4).

PRACTICAL CONSIDERATIONS

The complications of cervical operations carried out through the anterolateral approach can be formidable. Smith and Robinson,¹⁸ in their series of 14 anterolateral cervical fusions, reported the occurrence of two transitory Horner's syndromes, two instances of paralysis of a vocal cord, one vertebral artery perforated and one rupture of the esophagus. They suggest that traction injuries to the recurrent laryngeal nerve are less common when the approach is from the left side.

The aberrant vessel usually crosses the midline at the level of the second or third thoracic vertebra, although it may cross as high as the sixth cervical vertebra and thus it should escape damage in anterolateral operations on the lower cervical vertebrae or intervertebral discs. Unless the operative site has to be extended to include the upper dorsal vertebrae, the aberrant vessel is unlikely to be seen, to interfere, or to be damaged in the usual anterolateral ap-

proach. If this were the only consideration, its importance would be confined to the realms of the anatomist, pediatrician and vascular surgeon, rather than the orthopedic surgeon. Of more serious import, however, is the constant accompanying anomaly of the right recurrent laryngeal nerve (Fig. 5). This nerve arises from the vagus and normally recurs below the right subclavian artery and then, crossing posterior to the right common carotid artery, ascends between the trachea and esophagus to enter the pharynx posterior to the right cricothyroid joint. This joint is opposite the intervertebral disc between the fifth and sixth cervical vertebrae. In the presence of an aberrant right subclavian artery, the right recurrent laryngeal nerve fails to recur, although it may recur in exceptional cases around a persistent right ductus arteriosus. From the vagus it proceeds directly to the larynx, which it enters at its usual site at the lower border of the inferior constrictor opposite the cricothyroid joint. Because the majority of operations on the cervical spine are carried out on the fifth or sixth cervical intervertebral disc or the adjacent vertebrae, this small but important nerve will directly traverse the operative field.

A right thoracic duct, instead of the usual left one, has been described in most cases of aberrant right subclavian artery and is presumably due to interference with the development of the left duct from pressure of this vessel. The associated abnormality is not invariable. Hammer and Meis¹³ found the duct to be normal in origin, course and termination in two of their three cases of aberrant right subclavian artery, but in the third case it lay on the right side of the bodies of the thoracic vertebrae throughout its course.

These anatomical variants, namely, the aberrant right subclavian artery, the abnormal course of the right recurrent laryngeal nerve and the presence of the right thoracic duct, occurring as they do in 1% of the population, should be familiar to the orthopedic surgeon operating on the cervical spine from an anterolateral approach. Knowledge that such abnormalities occur and the use of a careful operative technique will lessen the chance of injury to

these structures. The intimate relationship, however, of the right recurrent laryngeal nerve to the common site for operations on the fifth and sixth cervical vertebrae (Fig. 5) makes a right-sided approach to these structures a hazardous undertaking. Smith and Robinson¹⁸ have suggested that a left-sided approach is safer, because the left recurrent laryngeal nerve appears less susceptible to traction. These factors favour a left-sided approach in routine anterolateral operations on the cervical spine. If special considerations dictate a right-sided approach, the position of the subclavian artery should be confirmed early in the operation. The course of the right recurrent laryngeal nerve may thereby be anticipated; when the nerve has been located it is less likely to be damaged by traction or section.

SUMMARY

The aberrant right subclavian artery is the commonest vascular abnormality in the neck; its incidence is probably about 1%. This anomaly, which is usually asymptomatic, is unlikely to be recognized on clinical examination. Most cases will be discovered by the roentgenologist during barium examination of the upper gastrointestinal tract or during cardiovascular investigation. The literature on this subject has been reviewed; the embryology, anatomy and pathology have been described. Its importance in operations on the cervical spine carried out from an anterolateral approach has been emphasized. Reasons have been advanced for the routine adoption of a left-sided approach in this operation.

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RÉSUMÉ

Récemment, du fait de l'augmentation du nombre des traumatismes de la colonne vertébrale cervicale, des techniques chirurgicales et des voies d'approche nouvelles ont été étudiées et mises au point. Les repères anatomiques de la région du cou sont maintenant bien connus; il n'en est cependant pas de même des anomalies vasculaires dont la plus fréquente est l'existence d'une artère sous-clavière droite aberrante ou rétro-œsophagienne. L'incidence de cette affection, causée par un trouble de développement lors de l'évolution des arcs aortiques chez l'embryon, est probablement de 1%. Les chiffres donnés par d'autres varient entre 0.4 et 4.0%. Anatomiquement, cette artère, lorsqu'elle existe, naît comme une quatrième branche de la crosse de l'aorte, à gauche de l'artère carotide gauche; de là elle monte vers la droite, passant en arrière de la carotide commune et de la sous-clavière gauches et aussi en arrière de l'œsophage avant de sortir de la cage thoracique. Cette disposition entraîne des modifications quant à l'origine des autres branches de la crosse aortique. La symptomatologie de l'affection est très variable. Parfois il n'y a aucun symptôme. Dans d'autres cas, il existe une difficulté à la déglutition, d'importance plus ou moins marquée; certains patients sont morts de faim, étant incapables d'avaler quoi que ce soit. Le diagnostic différentiel doit être fait avec les autres causes de dysphagie, et en général, ce diagnostic est établi par le radiologiste lors d'un examen de routine de la cage thoracique. En ce qui concerne la technique opératoire, il faut savoir que l'existence de l'anomalie s'accompagne d'une variation dans le trajet du nerf récurrent. Les auteurs préconisent l'exploration chirurgicale par une voie latérale gauche.

BACK NUMBERS

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PULMONARY RESECTION FOR TUBERCULOSIS*
Results, Complications, Radiological and Pathological Correlation in 238
Consecutive Operations

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PULMONARY resection has become the accepted method of treatment for residual tuberculosis which has not healed satisfactorily under chemotherapy and sanatorium care. Time may show that with the increasing number of patients who present with drug-resistant tubercle bacilli, this concept may have to be modified. Also, unless more effective drug therapy is developed it is possible that reversion to some of the older ancillary methods of surgical therapy may be necessary. The series now being reported consists of 238 consecutive unselected resections performed on 226 patients in the Aberhart Memorial Sanatorium during the period August 1952 to August 1959. Many of the patients in this series presented with extensive pulmonary tuberculosis and a considerable number of them could be considered as salvage cases. A large proportion of the patients were Metis Indians. In many instances, these people on discharge from the Sanatorium, returned to their homes to live under very poor and very unhygienic circumstances. In such cases it is impossible for patients to follow advice given to them regarding subsequent aftercare.

In spite of this, the results of this series have been quite good. The morbidity and mortality rates compare favourably with modern standards for resection in pulmonary tuberculosis.

PATHOLOGY

Basically, pulmonary tuberculosis begins as a necrotizing pneumonia which is initially segmental in distribution but often extends subsequently to other segments either by direct extension or by endobronchial spread. The subsequent clinical course of the disease may include complete resolution, healing by fibrosis, or caseation necrosis with resultant caseous foci or cavi-

tation. Endobronchial involvement by the disease may produce extensive pulmonary destruction due to bronchostenosis and subsequent infection. A fact not always appreciated but well emphasized by Olson *et al.*¹ is that endobronchial disease in smaller bronchi even in the absence of cavitation or extensive caseation can provide an active focus of the disease.

GENERAL THERAPY

The treatment of pulmonary tuberculosis is primarily medical. The patient presenting for initial care must be carefully assessed with regard to the extent and duration of the disease. An attempt should be made at this time to determine the amount of actual permanent damage to the lungs and the extent of reversible disease which will respond to medical therapy. This is done by history-taking, physical examination and adequate radiological investigation. The evidence from all previous radiographs is taken into consideration. Antituberculous drug therapy is instituted and the patient is placed on a regimen of sanatorium care consistent with the type of disease present. At regular intervals the patient is reviewed and the treatment modified according to the progress made. It must be emphasized that the treatment of pulmonary tuberculosis cannot be standardized but must be adapted to the individual patient. When clinical and roentgenological evidence indicate a cessation of improvement with medical therapy, a decision must be made regarding the need for surgical aid. This is done by carefully assessing the benefits to be derived from and the possible complications of operation.

Indications for Operation

Basically, pulmonary resection in tuberculosis is carried out to eliminate either active disease or a potentially reinfective focus.

*Aberhart Memorial Sanatorium, Edmonton, Alta.

Classification of Lesions Requiring Operation

A. Cavitary Lesions.—(1) Persistent obvious air-filled cavity seen on ordinary roentgenograms. (2) Cavity demonstrable by tomograms. (3) Inspissated cavity.

B. Non-Cavitary Lesions.—(1) Active tuberculous endobronchial disease. (2) Tuberculomas. (3) Large caseous foci.

Preoperative Therapy

In all cases bronchoscopy and bronchograms were done in order to estimate fully the extent of the disease and to determine whether or not endobronchial disease or bronchial stenosis were present. It is our contention that these procedures should be done in all patients. Bronchiectasis may be present in an area larger than the lesion originally considered for resection, as determined by ordinary roentgenography. Respiratory function studies, electrocardiographs and renal function studies were done in all patients, in addition to the usual hematological and urinary investigations. Smears or cultures were made on sputum or bronchial aspiration before operation. All patients scheduled for operation were started on physiotherapy at least one month before the operation. This consisted of postural drainage when necessary; breathing exercises; voluntary coughing practice; arm, shoulder and leg exercises, and education to orientate the patient to postoperative routine. In some instances the results of the respiratory function tests were not strictly followed in selecting patients for operation. Some patients had low values in respiratory function tests but clinically were not in respiratory difficulty. Operations were performed upon these patients because the loss of functionless lung tissue would not decrease pulmonary function. For example, one patient with a vital capacity of 1200 c.c. (35%) had a pneumonectomy; another with a vital capacity of 1100 c.c. (31%) also had a pneumonectomy. One patient, who had a vital capacity of only 850 c.c., had a pneumonectomy performed. All of these patients did well and had a normal postoperative course. In general, although standard pulmonary function tests were of use as a guide, other

factors were more important. The ability of the patient to perform moderate exercise without marked respiratory difficulty, the extent and type of disease and the presence of severe degrees of bronchospasm were of more significance. Each patient must be carefully considered on an individual basis for operation. A patient should not be made to fit a set of predetermined criteria before surgical therapy is carried out; the therapy must be adapted to the patient.

Operative Procedures

All of the resections in this series were performed by two surgeons who employed essentially the same operative technique, with the exception that one utilized the face-down position whereas the other used the lateral decubitus position. This minor variation subsequently proved to have no effect on the postoperative course.

Segmental resections were done when the disease was sufficiently confined and in almost all cases a true segmental or subsegmental resection was performed without crossing the intersegmental planes. Lobectomy was carried out if any doubt arose as to the localization of the disease to a segmental area. In some cases a thoracoplasty was performed either preoperatively or concurrently to enable the residual lung tissue to adequately fill the remaining pleural space. In general, space-reducing thoracoplasties were not used except in the case of pneumonectomy where thoracoplasty was routinely done six to eight weeks after resection. Raw areas left after segmental resection were closed by interrupted and continuous silk sutures provided this method of closure would not result in undue distortion of the remaining lung tissue. We have found that this procedure reduced the incidence of postoperative fistula and air leaks. Closure of bronchial stumps was effected by simple interrupted silk sutures, except in a few cases where pleural or pericardial fat pads were utilized to reinforce the closure. It does not appear that these latter procedures are of value; the main factors in preventing fistula are (1) employing a true segmental resection through healthy lung tissue rather than a modified wedge; (2)

amputating the bronchus proximal to any endobronchial tuberculous disease, and (3) obtaining obliteration of the pleural space as soon as possible postoperatively.

Postoperative Therapy

Intercostal drainage was instituted in all cases using large-bore polyethylene tubing, which because of its rigidity was selected for the maintenance of an adequate lumen. One tube was used for pneumonectomy, and two or more tubes were used for other types of resection. Underwater drainage without suction was used in the earlier cases but suction drainage was instituted with the later lobectomies and segmental resections. A negative pressure of 15 to 25 cm. of water was used in these cases but, in the treatment of persistent fistulae, negative pressures several times this figure were often used with good results. In instances of prolonged air leaks, suction pressure of up to 180 mm. Hg was often employed and proved very effective in dealing with this type of complication. Drainage was maintained until the lung was completely expanded, as shown by radiographs, and until no air leaks or excessive fluid could be demonstrated. The tubes remained in place for four days on the average. In some instances drainage, maintained for two weeks, was necessary to obtain the desired result. Daily radiographs of the chest were used to monitor the condition of the pleural space and if necessary further intercostal tubes were inserted to close a loculated space. The dictum of "no space, no empyema" was rigidly followed to the best of our ability. Inhalations of the aerosols, Alevaire or Tergemist, served to liquify secretions adequately. Sedation was adjusted according to the patient's need to obtain relief of pain with the minimum amount of respiratory depression. The postoperative routine was carried out in a recovery room by special nursing staff for from two to five days. A physiotherapist was considered to be a member of the operative team; each patient was discussed with her preoperatively and postoperatively. Postoperative physiotherapy was commenced as soon as the patient was conscious enough to respond to commands, and continued for the remainder of the

sanatorium stay. Physiotherapy was perhaps the most important factor in the prevention of postoperative atelectasis. Only two cases in this series required postoperative bronchoscopy for this complication.

For the past year the technique of removing dressings from the wound after 48 hours and applying radiant heat for 15 minutes three times a day has been instituted. This procedure results in a dry, clean and comfortable wound, and allows for a better pulmonary ventilation on the operated side. There have been no wound infections in this group of patients.

PRESENT SERIES

A total of 238 resections were performed in 226 patients. The type of operation carried out is shown in Table I.

TABLE I.—TYPE OF OPERATION

Pneumonectomies.....	48
Lobectomies.....	87
Segmental resections.....	64
Wedge resections.....	12
Lobectomies with segmental resections.....	13
Segmental resections with wedge resections....	3
Lobectomies with wedge resections.....	11
	238

Twelve patients in this series had more than one resection; of these, nine patients underwent bilateral resection and in three a second resection was done on the same side because of recurrence of disease after an initial inadequate resection. In many of the patients, long-standing chronic tuberculosis had been diagnosed and treated by older methods before the advent of resection and before admission to this sanatorium. Twenty-seven patients had been in some type of tuberculosis hospital before admittance here. Many of these had more than one type of surgical procedure performed previously. Table II gives some indication of the type of treatment received by these patients.

TABLE II.—TYPE OF TREATMENT IN 27 PATIENTS

Pneumoperitoneum.....	22
Pneumothorax.....	24
Thoracoplasty.....	13
Phrenic crush.....	10
Plombage.....	2
Resection.....	1

TABLE III.—AGE AND SEX DISTRIBUTION

Age	Male	Female
0 - 5 years	1	0
5 - 10 "	0	3
11 - 15 "	1	7
16 - 20 "	8	17
21 - 25 "	14	22
26 - 30 "	17	20
31 - 35 "	22	19
36 - 40 "	16	7
41 - 45 "	11	10
46 - 50 "	9	4
51 - 55 "	6	5
56 - 60 "	3	1
61 - 65 "	1	2
66 plus	0	0
Total	109	117

The age and sex distribution of the patients in this series is shown in Table III.

Complications

During the 238 resections, 31 patients had some complication. Deaths occurring within the first six weeks of the postoperative course were considered to be opera-

TABLE IV.—INCIDENCE OF COMPLICATIONS

Type of complication	Lived	Died
Empyema	20	3*
Atelectasis	2	
Hemothorax	2	
Wound infection	1	
Persistent air space	1	
Pulmonary embolism		1*
Renal failure		1
Superficial wound dehiscence	1	
Respiratory insufficiency		1

* One patient with empyema died of pulmonary embolism

tive deaths, although some later deaths could possibly be attributed to the complications of operation as discussed later. Table IV indicates the incidence of various complications.

A breakdown of the cases of empyema is shown in Table V.

Of the patients with tuberculous empyema, two, one with and one without

TABLE V.—CASES OF EMPYEMA

	Lived	Died postoperatively
Pyogenic empyema	10	0
Tuberculous empyema with bronchopleural fistula	2	2
Tuberculous empyema without bronchopleural fistula	8	1

bronchopleural fistula, are still living; however, the empyema has not yet healed in either case.

The five postoperative deaths were in patients who were considered to be very poor operative risks, except for the one patient who died of pulmonary embolism.

One patient died of renal failure due to an associated extensive bilateral renal tuberculosis following left upper lobectomy. This man had undergone many years of sanatorium treatment. Lobectomy was performed in an attempt to convert his sputum and allow him to live with his family outside the sanatorium for a short while.

Two patients died with extensive spread of disease due to the development of tuberculous empyema with bronchopleural fistula. One of these patients had undergone lobectomy and pleurectomy despite the presence of an established tuberculous empyema and bronchopleural fistula due to rupture of a cavity in the presence of an artificial pneumothorax. In retrospect this man probably should have been treated by pneumonectomy followed by thoracoplasty.

A fourth patient died of pulmonary embolism. This man had developed a tuberculous empyema after resection, but this had been saucerized and was well controlled.

The fifth patient developed a severe respiratory insufficiency postoperatively, probably due to previous prolonged treatment with artificial pneumothorax on the side opposite to that of the operation.

All of the patients with non-tuberculous empyemas healed readily with the provision of adequate drainage. The development of tuberculous empyemas proved to be a serious problem in all the patients in whom it occurred; this complication was responsible for two deaths. The remainder required prolonged treatment. In all instances, the empyemas occurring in the lobectomy cases were in patients who had considerable pulmonary fibrosis. In these people it was necessary to carry the line of resection through fibrotic lung tissue; the raw lung area did not heal properly and the lung never completely re-expanded. Possibly, early thoracoplasty in

these people would have obliterated the air space but generally they were too ill to tolerate such a procedure. It was found that all patients who developed a tuberculous bronchopleural fistula had positive sputum before operation. This conforms with the experience of others^{2, 3} that the incidence of empyema with bronchopleural fistula is much higher in patients who have positive sputum at the time of pulmonary resection. Of our patients who developed empyemas, 14 had far advanced and six had moderately advanced disease. This is evidence that in a patient with minimal and moderately advanced disease of a relatively short duration, surgical procedures should be almost free of major complications. One patient had a tuberculous wound infection, which is a very unusual complication. This low incidence of wound infection is attributed to meticulous wound closure. It was noted that the incisions of thoracoplasties done for empyema were unavoidably and grossly contaminated with pus at the time of operation but healed by first intention.

GENERAL THERAPY

In this series, the mean average hospital stay for surgical patients was 11.3 months, while the mode was six months. All of the patients had a course of treatment with antituberculous drugs during this time. For the most part the drugs used were streptomycin, para-aminosalicylic acid (PAS) and isonicotinic acid hydrazide (Isoniazid) in various combinations. Other drugs were used in certain patients in whom the infection was resistant or in whom an intolerance to the usual drugs had developed. Analysis showed that each patient had received an average of 53 g. streptomycin, 2411 g. PAS and 48 g. Isoniazid. Streptomycin was usually given in doses of 1 g. twice weekly, PAS at the rate of 12 g. per day for adults, while Isoniazid was administered according to the dosage of 5.0 mg./kg. body weight. Postoperative drug therapy was carried on usually for a period of not less than six months and generally for from one to one and a half years. The average amount of drugs administered in the postoperative period while the patient remained in the sanatorium was: streptomycin,

46 g.; PAS, 1805 g.; Isoniazid, 45 g. The average duration of postoperative stay was 6.04 months and the mode was six months. After discharge, many patients continued drug therapy on an outpatient basis.

In 148 cases an attempt was made to predict preoperatively the gross appearance of the resected specimen. This was an attempt to assess the extent and the type of disease on the basis of all available radiological data. In the remaining cases in the series, specimens had been sent for laboratory examination and subsequently destroyed before this study was begun. In 82.3% of patients an accurate estimate of the gross pathological appearance was made before resection. In 1.4% the correlation was only fair. In 16.2% the correlation was poor. In most of the poor results no cavity was found where one was predicted. These results indicate the accuracy with which the extent and type of disease can be assessed if serial radiographs, tomograms and bronchograms are available for examination.

It is generally conceded that a patient should be presented for operation with sputum negative for tubercle bacilli. This minimizes the possibility of postoperative complications, such as tuberculous empyema, bronchopleural fistula and spread of disease. In the present series, 172 patients were producing sputum positive for tubercle bacilli on direct smear at the time of admission to sanatorium. The remainder either had intermittently positive smears or cultures during their sanatorium stay or had other clinical evidence of active disease. After a course of drug therapy adequate to produce a clinical end point in the course of the disease, 93 (54.1%) were still positive either on smear or culture. Of these, 83 patients had sputum which was converted from positive to negative as a result of operation, nine remained positive after operation and the sputum of one patient became positive after his first segmental resection. Of the 133 patients with negative sputum, all remained negative postoperatively. Of the 10 patients with positive sputum postoperatively, two had bilateral cavities, five had bilateral disease and two had empyemas with broncho-

pleural fistula and one patient had only unilateral disease.

Follow-Up Study

A follow-up questionnaire was sent to 218 patients, but it was only completed successfully by 127. Another twelve of the original patients are known to have died. Of the 127 who responded, 12 (9.5%) stated that they did not think they were in good health at the time of the questionnaire. However, re-examination and radiological investigation showed no evidence of recurrent disease in these people.

Fifty-six patients were working full-time, 15 part-time, 48 were engaged in housework and eight were not working. Of the non-workers, two are at present in a sanatorium, one is unable to get employment and the remaining five state they are unable to work because of health reasons. However, three of these people could undoubtedly work if they had the desire and ambition. Based on replies to the questionnaire therefore, the number of people working was 93.8%.

Of the original 226 patients, five died postoperatively and there were two late deaths. Another 12 have since died from causes other than those related to tuberculosis. Of the remaining 207 patients, there have been only two readmissions for further treatment. Of the two readmitted, one has renal tuberculosis and the other has a chronic bronchopleural fistula.

SUMMARY

The results of operation in 226 unselected patients have been presented. Many were poor-risk patients with extensive disease, yet the overall complication rate was only 11.2% which compares favourably with most recorded series. The cure rate in patients surviving operation was exceptionally good. With reference to complications, our experience is similar to that of most other workers in this field in that the patients who have developed drug resistance are extremely bad risks and show a high

rate of complications. Patients with extensive and bilateral disease are a higher risk group but many can be salvaged by surgical therapy. In approximately 80% of patients it is possible to predict adequately the gross pathological picture from radiological investigations.

In conclusion we would like to stress that resection for tuberculosis is perhaps the most difficult type of excisional pulmonary operation. In future, with the possible advent of an increase in resistant bacilli, more meticulous technique will be demanded of the surgeon.

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RÉSUMÉ

Cet article est une étude d'ensemble sur les résultats de la résection pulmonaire pour tuberculose. Il groupe 238 interventions effectuées sur 226 malades au "Aberhart Memorial Sanatorium" de 1952 à 1959. Une importante proportion de ces patients étaient des métis indiens. En majorité ils étaient atteints de tuberculose pulmonaire extensive; le pourcentage de complications était de 11,2%. Chez ceux qui survécurent à l'opération, les résultats du traitement furent exceptionnellement satisfaisants. En ce qui concerne les complications, l'expérience des auteurs est très semblable à ce qu'ont trouvé d'autres chercheurs dans ce domaine: les malades chez qui une résistance aux antibiotiques s'était installée formaient un très mauvais groupe et présentaient un pourcentage élevé de complications. Les cas de tuberculose bilatérale et extensive ont également un mauvais pronostic, mais beaucoup peuvent être sauvés par la thérapeutique chirurgicale. Dans environ 80% des cas, il est possible de prédire le status anatomo-pathologique d'après les données de l'investigation radiologique. En conclusion, les auteurs insistent sur le fait que la résection pulmonaire pour tuberculose est peut-être la plus délicate des interventions sur le poulmon. Dans l'avenir, il est vraisemblable que le nombre de cas résistants aux antibiotiques augmentera; ceci exigera la création et l'emploi de techniques opératoires encore plus raffinées par le chirurgien.

AN APPRAISAL OF THE EXPOSURE METHOD IN MANAGEMENT OF SEVERELY BURNED PATIENTS*

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THE BURN wound has been treated in several different ways; of these, tanning with tannic acid has been abandoned because of its toxicity. Currently, the method of treatment depends on the surgeon's individual preference; occlusive dressings; artificial crusting with aluminum powder; the "exposure" method, that is, leaving the wound without any dressing, or the "semi-open" method, that is, covering the wound with a thin wet dressing which is changed every four hours.

At the Notre Dame Hospital, Montreal, in our search for an improved method of management of the severely burned patient, since June 1959 we have given up the "closed" method of treatment in favour of the exposure method, whenever possible. This has given us an opportunity to compare in terms of personal experience both methods and their clinical results.

Having found that the exposure method is easy, simple, quick and inexpensive, and that our clinical results have improved since the exposure method was used, we reviewed all cases of severely burned patients under our care from January 1955 up to December 1960.

CLINICAL MATERIAL

This series included 69 severely burned patients, of whom 58 were treated by means of the closed method, January 1955 to June 1959, and 11 were treated by means of the exposure method, June 1959 to December 1960.

CLINICAL RESULTS AND TENTATIVE OBSERVATIONS

Of the 58 patients treated by means of the closed method, 26 died; those who died had an average burn area of 60.9%; 32 survived with an average burn area of

37.5%. Of the 11 patients treated by means of the exposure method, one died; he had a burn area of 78%; 10 survived with an average burn area of 46.5%.

The hospitalization time was reduced from 107.6 days for patients treated with the closed method to 76.1 days for the survivors treated with exposure, even though the average involved burn area was greater for the latter group. Retarded healing with infection at the split-thickness donor sites was less frequent when the donor sites were left to heal without dressing.

Despite the relatively small size of this series, it is nevertheless evident that, in our hands, treatment by the exposure method does lessen the mortality rate and time of hospitalization of our severely burned patients. Exposure does not mean neglect; it is a form of treatment that favours a cool, dry, sterile wound, and thus a cool comfortable patient with little or no fever. It eliminates restrictive bandages, and favours active movements, better muscle tone and less wasting. Because the patient is more active, he has a better appetite and his activity prevents ankylosis at affected joints. This method of management eliminates foul-smelling dressings that could nauseate the patient and lead to unconscious neglect on the part of surgical and nursing staff. Furthermore, it is much less time-consuming for the surgical staff.

On the other hand, care by the exposure method offers little or no protection from direct trauma to the wound. It requires a co-operative patient and is not applicable to infants or mentally disturbed patients. Also, it does retard the sloughing and spontaneous removal of the burn eschar.

It is therefore our definite opinion that exposure should play a major part in the treatment of a severely burned patient, but, nevertheless, as Blocker *et al.*⁵ have said, the closed and exposure methods should be complementary, not antagonistic to one another.

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DESCRIPTION OF THE EXPOSURE METHOD
USED SINCE JUNE 1959 FOR THE
MANAGEMENT OF BURNED PATIENTS
ADMITTED TO NOTRE DAME HOSPITAL

First Stage

On arrival at the emergency ward, the severely burned patient is examined to ensure that he has a clear airway; a tracheostomy is done under local anesthesia if necessary. Pain is relieved with morphine sulphate administered by *intravenous* route only. All of the patient's clothes are stripped off and he is put on clean sheets. The burned area is measured accurately. Intravenous fluids are immediately given in amounts based on an estimate of the extent of the burned area. The bladder is evacuated by means of a Foley catheter, which is left in place. Every hour the urinary output is measured and fluids are given to keep it between 35 and 50 c.c. per hour if at all possible.

The patient is left undisturbed, lying nude on clean sheets, covered by cradles over which clean blankets are spread to keep him warm. No further insult is offered to an already seriously injured patient. No cleansing is done unless the body is very dirty; no blebs are opened, no washing or scrubbing or debridement is carried out. No anesthesia is given. Every attention is given to the well-known means of systemic therapy and the prevention or control of shock.

The patient is kept lying supine or ventrally according to distribution of the burned areas. If the patient has suffered a circumferential burn, he is kept lying supine on special pads covered with nitrofurazone (Furacin). After two or three days, the circumferentially burned patient is turned over every eight to 12 hours and the Furacin pads are changed. Thus with a circular burn, the patient has one-half of his body treated by means of the closed method and the other half treated by means of the exposure method. And the mode of treatment is alternated every eight to 12 hours with the change of position of the patient.

Second Stage: Tubbing

After two weeks, superficial second-degree burns are healed. Deep second or third-degree burns are still covered by crusts of adherent eschar.

If pus forms under loose crusts, both are removed and the wound is cleaned with a bland detergent.

At this stage, *tubbing* is started. An ordinary bath tub is used which is cleaned before and after each use with soap and chlorinated Javel water. The tub is filled with water to which is added a half-cup of salt and a *half-cup of bland powdered detergent or four ounces of bland liquid detergent*. Tubbing will be done twice daily and each bath will last for an hour, or more if possible. After 30 minutes the water will be changed by running in a continuous flow of clean water and adding more salt and detergent accordingly.

Active movements in the water are essential for the restoration of good muscle tone and to prevent stiffness. Furthermore, these movements have a whirlpool effect which helps to remove crusts. Loose crusts are removed with forceps while the patient is in the water, and care is taken not to provoke bleeding. During each bath, the bed sheets are changed and, if the patient has circumferential burns, fresh Furacin pads also are prepared. If these pads are adherent to the wound, the superficial layers are removed leaving the deepest adherent layers to fall off in the water, thus minimizing trauma and pain, and preventing bleeding.

Third Stage: Debridement

After three weeks, second-degree burns are healed; the wounds still covered by crusts and eschars are third-degree burns. Daily debridement is done before, during or immediately after the bath, but it is very important that this should never be done deep enough to provoke pain or bleeding. In this way, general anesthesia is not necessary; the debridement does not provoke bleeding in a patient already in great need of blood, and it does not open up deep avenues to infection.

By the end of the fifth week, tough, deep, adherent eschars have been removed,

and the third-degree burn wounds are covered only by crusts that fall off in the water. After the bath they appear as bright red wounds covered by a flat, non-exuberant, healthy granulating tissue, ready for grafting.

Fourth Stage: Skin Grafting

If during the preparation of the wounds for grafting, some are ready earlier than others, these may be skin-grafted, and the sooner the better. After grafting, the patient is kept out of the bath for seven days, after which time tubing is resumed.

Also, if during the preparation of the wounds, or after autogenous skin-grafting has begun, the general state of health of the patient is too poor to permit further autogenous grafting, homogenous fresh cadaver skin-grafts are used to cover the wounds temporarily.

The donor site is chosen on the same side as the recipient site, if at all possible, because after operation, the patient may rest for a few days on the opposite side and the recipient and donor sites can be left without dressing.

Thin skin-grafts are taken with an electric dermatome, at one 10/1000 to 12/1000 of an inch. This is very important because, by this technique, two or more crops of skin may be taken from the same donor area. To cover more area, each strip of skin removed is cut into small 1 x 1 cm. pieces, called "stamp" grafts. These pieces are then laid on the wound at 0.5 cm. to 1 cm. apart. Eventually, they will be united by scar epithelium. We have even done this over joints. The aim is rapid early covering of large areas. Secondary contractures of scar tissue are easily corrected by clean elective surgery performed later on a healthy patient.

Before the patient is brought to the operating-room for skin-grafting, he is given a one-hour bath to help remove the crusts from the wounds without causing bleeding. Then under general anesthesia, after the skin-grafts have been obtained and set aside in a separate bowl, *the burn wounds are very gently washed with pHisoHex and rinsed with saline, without provoking any great bleeding. The granulating tissue is*

not shaved or scraped, and no blood is lost except from the donor area. The small pieces of skin are laid on the granulating tissue, very gently and without stitching so that no blood collects under the grafts. After a few minutes these "stamp" grafts are naturally glued to the wound by fibrin. They are left exposed, and the patient leaves the operating-room protected by cradles over which blankets are laid. A dressing is applied to the grafted wound only if the patient is uncooperative or if the wound needs to be protected from contact with the mattress. This dressing will be removed after four or five days, leaving the deep adherent layers to fall into the water after an hour of soaking in the bath: this will not traumatize the fresh grafts.

No dressing is applied to the donor site if this can be avoided. However, a dressing will be used if persistent bleeding occurs, if donor and recipient sites are not on the same side of the patient, or if the patient is uncooperative.

After 12 to 14 days, donor sites are healed and more grafting may be done.

Management of Burns to Lower Limbs

Deep second-degree burns will heal spontaneously and third-degree burns will be skin-grafted. But the patient must remain in the recumbent position at all times *without allowing dependency of the limbs until complete healing has occurred.* Only then will dependency be permitted, otherwise bleeding from the wounds will occur, and ecchymoses will appear under the grafts. To prevent swelling or ecchymoses, legs must be bandaged tightly with good resilient *elastic* bandages. For this reason it is essential to wait for complete healing before applying these, otherwise the bandage will stick to the wounds, resulting in trauma, bleeding, infection and much retarded healing. Dependency is undertaken slowly and progressively. Elastic support must be worn for at least six months after full recovery and until no swelling occurs. Varicose veins are a late complication and should have appropriate treatment at a later date. If such treatment is necessary, daytime elastic support should be worn indefinitely after vein surgery.

CONCLUSION

In our hands, and with our limited experience, exposure is the method of choice in treating severely burned patients.

SUMMARY

The results obtained after treating 58 severely burned patients with the closed method and 11 patients with the exposure method at Notre Dame Hospital were compared, and the results of the comparison favour the exposure method.

A complete description of the exposure method of management of severely burned patients has been presented as it has been carried out at Notre Dame Hospital, Montreal, since June 1959.

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RÉSUMÉ

Depuis juin 1959 les auteurs traitent leurs grands brûlés par la méthode ouverte, laissant les plaies à l'air. Auparavant, ils employaient la méthode fermée, recouvrant les brûlures de gros pansements occlusifs. La méthode ouverte s'est avérée être facile, simple, rapide, peu coûteuse, et s'est accompagnée de résultats cliniques de beaucoup améliorés. Les auteurs ont revisé tous leurs cas de malades sévèrement brûlés depuis janvier 1955 jusqu'à décembre 1960. C'est ainsi que 69 cas de malades sévèrement brûlés ont été analysés. Cinquante-huit furent traités par la méthode fermée de janvier 1955 à juin 1959 et 11 furent traités par la méthode ouverte de juin 1959 à décembre 1960. Depuis que, pour les grands brûlés, la méthode ouverte est utilisée à l'hôpital Notre-Dame de Montréal le taux de mortalité et de morbidité de même que le temps d'hospitalisation de ces malades sont nettement diminués.

Le traitement du grand brûlé par la méthode ouverte est divisé en quatre étapes.

Première étape.—Le traitement d'urgence est institué. On traite ou on prévient le choc. Le grand brûlé est déshabillé, étendu sur des draps propres et ses plaies sont laissées à l'air sans aucun pansement. Le malade est recouvert de cerceaux sur lesquels des couvertes tiennent le malade au chaud et protègent ses plaies. On laisse le malade se reposer. Pas de savonnage ni débridement ni de période à la salle d'opération sous anesthésie générale pour un grand nettoyage.

Deuxième étape.—Les bains quotidiens. Après 10 ou 15 jours le malade est plongé dans une eau savonneuse pendant une heure de temps, deux fois par jour. Ceci tient les plaies propres et inodores et prévient l'ankylose.

Troisième étape.—Le débridement des escharres. Il est fait au lit du patient tous les jours avant, pendant ou après le bain et doit être fait très superficiel afin d'éviter la douleur et l'hémorragie.

Quatrième étape.—Les greffes cutanées. Après quatre ou cinq semaines les brûlures du deuxième degré sont guéries et les brûlures du troisième degré sont prêtes à recevoir des greffes cutanées. A cause de la grande étendue des brûlures chez les grands brûlés et le peu de surface pouvant servir de site donneur, les greffes sont prélevées très minces afin de pouvoir retourner plusieurs fois au même site donneur. Les greffes sont fragmentées en plusieurs morceaux de 1 x 1 cm. appelés timbres-poste. Et les greffes de même que les sites donneurs sont très souvent laissés à l'air sans aucun pansement.

Les auteurs concluent que même si leur expérience est limitée c'est la méthode ouverte qui leur a donné les meilleurs résultats dans le traitement des malades gravement brûlés.

IMPERFORATE ANUS: A REVIEW OF 147 CASES*

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PERHAPS the most satisfying aspect of neonatal surgery is the opportunity to give a normal life expectancy to an infant with an otherwise fatal condition. Nowhere is this more true than in the treatment of that complex anomaly known as imperforate anus. Yet, unless the surgical technique and aftercare are adequate, the infant with this lesion may be faced with a lifetime of gastrointestinal or genitourinary disability. Imperforate anus is a relatively significant problem, occurring about once in every 1500 to 5000 births. In approximately one-fifth of patients, the anomaly is mild and easily repaired, while the other four-fifths present themselves with a lesion which demands meticulous surgical correction.

This paper is a review of 147 cases of imperforate anus treated at The Hospital for Sick Children, Toronto, from 1952 to 1959 inclusive. The subject was previously reviewed at this hospital by Palmer¹ for the years 1942 to 1951, and although the incidence of the various types of imperforate anus with their associated fistulae remains the same, the surgical therapy has changed. In 1948 Rhoads *et al.*² described the primary abdominoperineal repair of imperforate anus in infancy. Although often performed as a secondary procedure some time after a preliminary colostomy, there has been a growing tendency to attempt a one-stage primary abdominoperineal correction on certain cases shortly after birth. Such procedures are extensive operations for an infant and the choice between them requires careful planning. In an attempt to assist in making this decision, a long-term follow-up of gastrointestinal and genitourinary function was carried out in children with type III and type IV imperforate anus. (Fig. 1).

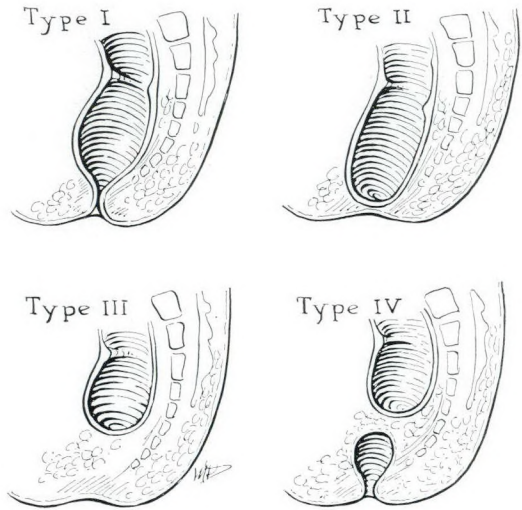


Fig. 1.—Classification of imperforate anus into four types according to the formation of the rectum.

EMBRYOLOGY

Some knowledge of the development of the anus and rectum is necessary if one is to understand and properly treat the many variations which this anomaly may present. The classical theory maintains that the rectum is derived from the primitive cloaca (Fig. 2).³ In the human embryo at the fifth week the cloaca forms a terminal chamber into which open the allantois, hindgut and Wolffian ducts. Beginning in the sixth week the crescentic urorectal fold gradually partitions the cloaca into an anterior chamber, the urogenital sinus, and

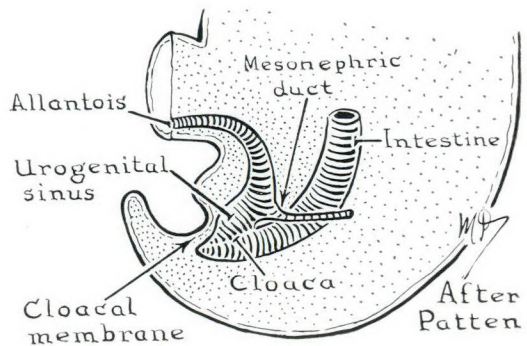


Fig. 2.—At the fifth week of intrauterine life the allantois, mesonephric ducts and hindgut open into a common chamber, the cloaca.

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a posterior chamber, the rectum. This process is completed during the seventh week and the cloacal membrane which separated the cloaca from the perineal ectoderm is thereby divided into the urogenital and the anal membranes. The proctodeum, an invagination at the site of the future anus, then appears and in the eighth week it meets and communicates with the rectum. If the communication fails to occur, the anus will be imperforate. If it is incomplete, the anus is stenosed. Since the external anal sphincter is formed from mesenchyme surrounding the proctodeum, some trace of this muscle is nearly always found and often in association with a small dimpling of the perineal skin. The internal sphincter develops with the rectum and is usually absent.

If the urorectal fold fails to divide the cloaca completely, the opening between the two chambers will persist as a fistula joining the hindgut to the genitourinary system. In the female, some time after the urorectal septum has formed, there is a further subdivision of the urogenital sinus into bladder and vagina. Any persistence of the cloacal duct will connect with the posteriorly placed vagina, thus accounting for the high incidence of rectovaginal fistulae in comparison with rectovesical fistulae in females.

In order to explain more fully certain of the congenital anomalies found in this region, Wood-Jones⁴ proposed what has become known as the "heretical theory". Favoured by many British authors,^{5, 6} this theory suggests that the rectum develops entirely from the hindgut rather than from a cloaca. Wood-Jones stated that with rapid growth of the hindgut and urogenital sinus, the opening between them displays an apparent or relative decrease in size. With the urogenital sinus enlarging superiorly, the communication with the rectum becomes progressively more caudal in position. Finally in the seventh week this opening closes and the hindgut subsequently migrates to the proctodeum.

INCIDENCE

Males predominate slightly and in this series of 147 cases, 90 patients (61%) were of this sex (Table I).

TABLE I.—INCIDENCE OF TYPES OF IMPERFORATE ANUS
147 CASES, H.S.C., 1951-59

Type	Male	Female	Total %
I	12	10	22 (15)
II	8	0	8 (5)
III	67	47	114 (78)
IV	3	0	3 (2)
	90	57	

There are several methods of classifying imperforate anus each with certain advantages. However, the classification first presented by Ladd and Gross⁷ in 1934 has gained wide acceptance and is used here (Fig. 1). The various anomalies are divided into four main types. In type I the anus is patent but stenosed. This type comprised 15% of the patients and approximately half of these lesions were in females. In type II the anus is imperforate but the obstruction is due to a thin membrane separating the anus and the rectum. There were only 8 (5%) cases of this malformation and all were in males. Membranous imperforate anus is rare in females.

By far the most common form of imperforate anus is type III (78%), where the anus is imperforate and the rectal pouch ends blindly at varying distances above it. For purposes of treatment and prognosis, type III is further subdivided into low and high groups according to whether the rectal pouch is more than, or less than, 1.5 cm. from the perineal skin. In this series approximately one half of the type III cases fell into each subgroup.

In type IV the anal canal, anal sphincter and lower rectum are normal but the upper rectum ends blindly some distance above. The two rectal pouches are sometimes joined by a fibrous cord. This is the least common variety of imperforate anus and most authors agree that it occurs more frequently in males. In this series, as in Palmer's, there were no females with this deformity.

Fistulae between the rectum and either the genitourinary system or the perineum occurred in one half of the patients (74 of 147) and only in association with type III imperforate anus (Table II). Of 67 males with type III imperforate anus, 29 (42%) were found to have fistulae and these were

TABLE II.—INCIDENCE OF FISTULAE IN TYPE III IMPERFORATE ANUS

29 <i>Fistulae in 67 Males (42%)</i>	
Rectovesical.....	9
Rectourethral.....	10
Rectoperineal.....	10
45 <i>Fistulae in 47 Females (96%)</i>	
Rectovesical.....	3
Rectovaginal.....	37
Rectoperineal.....	5

fairly equally distributed between rectovesical, rectourethral and rectoperineal types.

By comparison however, of the 47 females with type III imperforate anus, there were only two who did not possess a fistula. It was interesting to note that both of these infants were mongoloid and because of inadequate follow-up a minute fistula could have been missed. Most fistulae (37 of 45) in females were rectovaginal in type. There were only three patients with rectovesical fistulae. In one of these there was a more extensive anomaly with a fistula between the bladder and a large distended sac of colon, the rest of the large bowel being absent.⁸ In the other two the vagina was absent, thus explaining the site of the fistula.

Associated congenital anomalies were very common. Fifty-six patients (38%) were found to have 99 additional congenital anomalies (Table III); not infrequently these were severe and prevented survival.

CLINICAL FEATURES

The clinical diagnosis was usually made very soon after birth. Most of these patients were admitted when they were between 12 and 24 hours of age and the majority were in good condition. If the lesions were diagnosed later, abdominal distension and vomiting had occurred with deterioration of the child's general condition unless a fistula of sufficient size existed to allow intestinal decompression. Inspection of the perineal region quickly differentiated the various types, although in type IV cases the diagnosis may be delayed due to the normal external appearance of the anus. Patients with anal stenosis (type I) presented in a variable manner. In all

TABLE III.—ASSOCIATED CONGENITAL ANOMALIES (present in 56 of 147 patients)

Genitourinary.....	36
Hydronephrosis.....	9
Hypospadias.....	7
Horseshoe kidney.....	4
Urethral obstruction.....	4
Others.....	12
Gastrointestinal.....	23
Tracheoesophageal fistula.....	11
Colon agenesis.....	4
Hirschsprung's.....	2
Others.....	6
Cardiovascular.....	12
Musculoskeletal.....	10
Mongolism.....	7
Central nervous system.....	6
Miscellaneous.....	5

of the female and one-half of the male infants, the stenosis was relatively mild and the diagnosis was not made at birth. These children usually presented at two to five months of age with a history of chronic constipation, pain with defecation and the passage of ribbon-like stools. The other half of the male group presented at birth with a stenotic opening which was sometimes so minute that the patient was considered to have a type II or III anomaly when first seen. Fistulous connections with the genitourinary tract were frequently heralded by the presence of meconium in the urine.

RADIOLOGICAL EXAMINATION

Radiographic studies are of paramount importance in planning the operative program for type III cases of imperforate anus. In 1930, Wangenstein and Rice⁹ described the radiographic views which have become routine in the investigation of these patients. The infant is held upside-down for several minutes to allow the gas in the colon to displace the meconium at the distal limits of the blind rectal pouch. A radio-opaque marker is held on the anal dimple. A lateral film then reveals the distance between the rectal pouch and the skin (Fig. 3). It is important that the radiographic examination is supervised by someone who is familiar with the proper technique. Errors may occur if the radio-opaque marker is misplaced by applying too much or too little pressure. Furthermore, it is important to delay this examin-

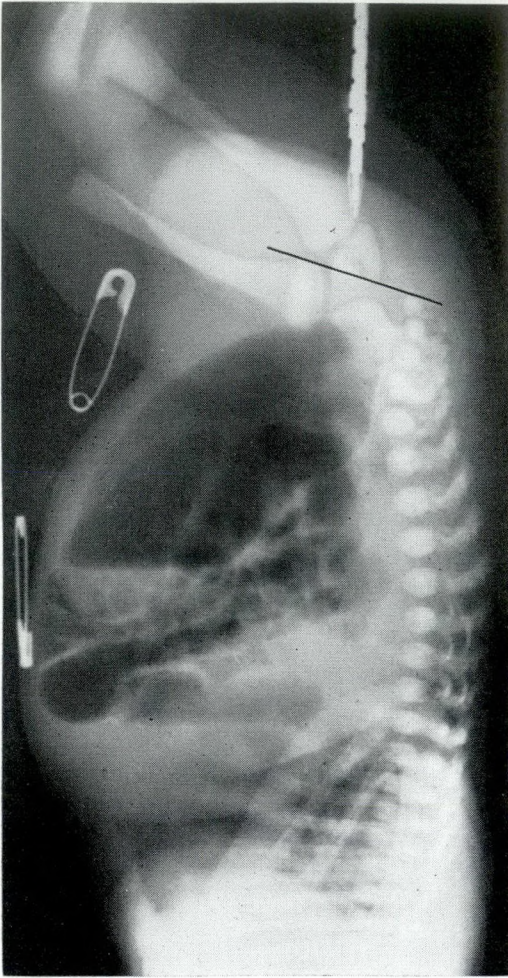


Fig. 3.—Wangensteen-Rice roentgenogram in imperforate anus. Since the rectal pouch is over 1.5 cm. from the radio-opaque skin marker and proximal to the pubococcygeal line, this is a high type III malformation.

ation until 18 to 24 hours after birth in order to allow sufficient gas to reach the distal colon and rectum.

The type III cases are divided into a low group in which the rectal pouch has passed through the pelvic diaphragm, and a high group with the rectal pouch situated above the pelvic diaphragm. This is determined by measuring the distance from the rectal pouch to the skin marker. Those in whom the distance is over 1.5 cm. are considered high and the others low. In other words, the pelvic diaphragm is estimated to be approximately 1.5 cm. from the anal dimple. Not infrequently the

presence of a rectovesical fistula will be diagnosed by finding air in the urinary bladder on the lateral roentgenogram. Partial or complete sacral agenesis is another finding of importance. When present this indicates defective innervation of the pelvic diaphragm, bladder and distal bowel and implies a poor prognosis with respect to bowel and bladder function.

MANAGEMENT

In type I and type II cases, therapy consists essentially of dilatations with Hegar dilators for as long as six months. With membranous imperforate anus, an anoplasty is performed initially. Occasionally in older infants and children with anal stenosis, an anoplasty will decrease the length of time over which dilatations are required. After the anus has been dilated to an adequate size and maintained there for some weeks, the frequency of dilatations can be gradually decreased but still should be continued several times a week for a full six months.

The major problems in the treatment of imperforate anus evolves around the type III malformations. In this group it is most important to determine by radiographic means whether the rectal pouch is high or low, for there is a marked difference in treatment, mortality and the final functional result.

A low rectal pouch can be treated by a perineal anoplasty. The rectum, having passed through the pelvic diaphragm, will be relatively easy to find and mobilize without injury to this muscle, which is so important for subsequent rectal control. In the past, many instances of poor rectal function have probably resulted from injury to the levator ani while attempting to locate and dissect out a high rectal pouch from the perineum. When the level of the pouch is still in doubt at the time of operation, the child can be prepared for an abdominoperineal procedure (if indicated) but the perineal part of the procedure carried out first. If the rectal pouch is not found below the pelvic diaphragm the abdominal portion of the operation is then performed in the usual manner.

In the male, since part of the dissection will be adjacent to the urethra, it is impor-

tant to have a urethral catheter in place. Dissection should be carried well up along the anterior aspect of the rectal pouch in order to identify and treat a rectourethral fistula if it is present. In addition to routine care, starting about 10 to 14 days after operation, anal dilatations are usually of value.

An abdominoperineal anoplasty is the operation of choice in those patients with high type III or type IV imperforate anus. This procedure was frequently performed as a secondary operation after a primary colostomy. Recently, however, there has been an increasing tendency to do the abdominoperineal anoplasty in a single stage. This has been restricted to infants seen soon after birth whose general condition was good and not complicated by serious associated anomalies. When the infants were premature, were handicapped by serious associated anomalies or were in poor general condition, a colostomy was constructed in either the sigmoid or right transverse colon. Later, when the child reached a weight of 20 lb. to 25 lb., the abdominoperineal procedure was undertaken. Occasionally, serious genitourinary infection arising from a rectovesical or rectourethral fistula necessitated completion of the abdominoperineal repair at an earlier age.

Several details must be carefully observed if good rectal function is to be achieved. It is believed that rectal sensation is important for normal continence and defecation. Scott and Swenson¹⁰ have recently re-emphasized that since a short length of terminal bowel in imperforate anus represents the upper segment of definitive rectum, it should possess some sensory appreciation and must be preserved if at all possible.

It seems likely that the motor component of rectal control in children with type III imperforate anus is chiefly due to action of the levator ani or pelvic diaphragm. The striated muscle of the external sphincter is not only poorly developed but is also difficult to preserve accurately at operation. The internal sphincter is completely lacking. It is therefore important that the tunnel through the pelvic diaphragm be made as accurately and as carefully as

possible. Not only should this tunnel be placed in the midline but it should be situated well forward in an attempt to bring the bowel anterior to the fibres of the puborectalis portion of the levator ani. It is unlikely that this is possible to any major extent; however, it would appear that better rectal function results when the rectum is brought through anteriorly.

Cases of type IV imperforate anus are managed in a similar fashion to type III cases. It is necessary to excise the blind rectal pouch which is associated with the anus. The fibrous cord which frequently joins the upper and lower rectal pouches may assist in locating the proper opening in the pelvic diaphragm. Theoretically, since the external sphincter is well formed, good rectal continence should be obtainable.

Two male and two female infants in this series presented with a colon malformation sufficiently severe that corrective surgery was impossible and a permanent colostomy or ileostomy was necessary. The colon was represented by a large sac-like structure with no other evidence of large bowel aside from one of these four cases in which there was a small cecum.⁸

Because of the high incidence of associated genitourinary conditions, all patients should have an intravenous pyelogram during their original hospital admission. Further investigation such as cystoscopy and retrograde pyelography may be indicated.

In type III imperforate anus the above program of treatment is frequently rendered more complex by the presence of various fistulae. Children with rectoperineal fistulae need little or no treatment other than a course of dilatations. A rectal opening at this site is no disability and good continence can be achieved due to normal rectal sensation and levator ani function.

Rectourethral and rectovesical fistulae should be identified and repaired at the time of definitive surgery. Where a fistula remains because it was not encountered during a perineal anoplasty or because a colostomy was constructed for a high rectal pouch, genitourinary infection may ensue. This will necessitate an early abdominoperineal procedure for repair of the fistula.

TABLE IV.—MORTALITY IN UNCOMPLICATED TYPE III AND TYPE IV CASES

<i>Level of pouch</i>	<i>Operative procedure</i>	<i>Number of patients</i>	<i>Deaths</i>	<i>Mortality rate</i>
(a) Low	Perineal anoplasty	37	3	6.2%
	No operation (adequate fistula)	11	0	
		48	3	
(b) High	Primary abdominoperineal	13	4	19%
	Colostomy and later abdomino-perineal	25	3	
	Permanent colostomy or ileostomy	4	1	
		42	8	

Rectovaginal fistulae demand special consideration. When situated very low in the vagina or in the fourchette, as approximately 60% are, the orifice can be dilated if necessary and used as a temporary anus for intestinal evacuation. At an elective age of three to five years, when the anatomy of the region is well formed and more easily identified, the fistulous orifice is transplanted to the normal anal position with the expectation of an excellent functional result. When situated higher in the vagina the fistula is closed during the abdominoperineal anoplasty.

RESULTS

There were 39 deaths in the 147 cases, giving an overall mortality rate of 27%. Severe associated anomalies were considered responsible for death in almost half (18) of these infants, and in a further nine, death appeared to be related in part to prematurity.

The infants with uncomplicated type I or type II malformations all do well with excellent early and late results. The main interest lies in the type III and type IV malformations, for it is in this group that operative therapy and techniques are most important. In Table IV, the type III and type IV cases uncomplicated by serious associated anomalies are analyzed with regard to the level of the rectal pouch, the operative procedure and the mortality. Where the rectal pouch is low, perineal anoplasty is associated with a relatively low mortality. The three deaths were due to coliform septicemia, generalized peritonitis and uremia due to urethral obstruction secondary to operative trauma.

In children with a high rectal pouch the mortality is definitely higher. As previously stated, four children presented with a severe anomaly of the large bowel and were treated with permanent colostomy or ileostomy. There was one death in this group. In the remaining 38 uncomplicated cases an abdominoperineal anoplasty was carried out in either one or two stages. In 13 children subjected to a primary abdominoperineal anoplasty there were four deaths, and in 25 children subjected to a two-stage procedure there were only three deaths. Two of these three deaths were due to complications of the primary colostomy while the children were awaiting the second operation. Cardiac arrest during operation accounted for the third death.

An attempt was made to study the long-term results with regard to bowel and bladder function in patients over the age of three years who had type III or type IV defects. Questionnaires were returned by the parents of 28 children treated from 1951 to 1956. Where practical, these children were interviewed and examined. In addition, the low type III cases in Palmer's series treated from 1942 to 1951 were questioned. There were seven replies in this group, giving a total long-term follow-up of 35 cases. The high type III cases of Palmer's series were not interrogated because the treatment of this group has changed.

Rectal function was graded as follows: good, always continent and not requiring enemas or laxatives; fair, occasional soiling and requiring periodic laxatives and enemas; poor, always incontinent with or without the use of enemas or laxatives. Bladder function was graded similarly: good, al-

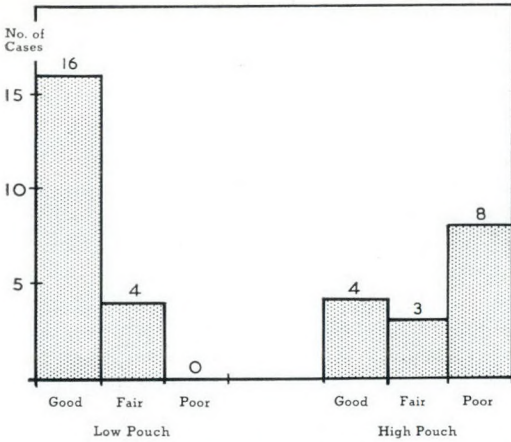


Fig. 4.—Rectal function in 35 patients with type III or type IV imperforate anus followed-up for three to 15 years.

ways continent; fair, occasional wetting either day or night; poor, complete lack of control.

Children with low rectal pouches had good long-term rectal and bladder function (Figs. 4 and 5). The one exception was a girl with a rectoperineal fistula. An attempt had been made elsewhere to transplant this fistula to the normal anal site, and she was seen at this hospital for dilatation of a recurrent fistula. She subsequently developed fair rectal function but owing to urethral injury her bladder function remained poor.

Children with high rectal pouches did not fare as well; approximately one half had poor rectal function. In two children there was sacral agenesis with lack of proper innervation of bowel, bladder and pelvic diaphragm. Two other children were mentally defective. Four had been subjected to multiple operations in this region. In one, the abdominoperineal procedure had been repeated for Hirschsprung's disease. In the others, operation was necessary to treat complications such as infection, stricture and gangrene of the terminal rectal segment. In four children there was poor genitourinary function. Again, sacral agenesis was responsible for this disability in two. In the other two, lack of urinary control was considered to be due to injury to the genitourinary tract from multiple operative procedures; in addition, in one child, associated mental deficiency was present.

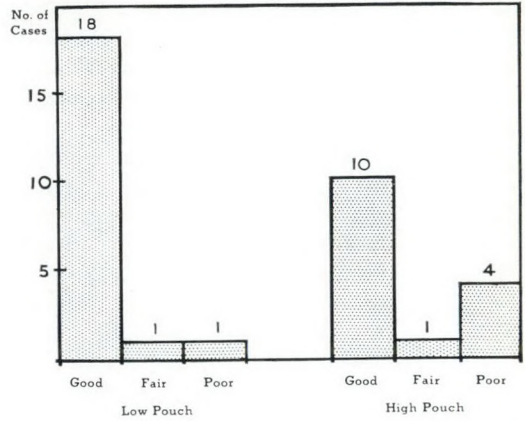


Fig. 5.—Bladder function in 35 patients with type III or type IV imperforate anus followed-up for three to 15 years.

DISCUSSION

It is interesting to note the types of anal malformation usually found in female infants. In this series there were no females with type II or type IV malformations. Since females with anal stenosis were not seen until two to five months of age, it can be said that those presenting with imperforate anus at birth all had a type III malformation. Furthermore, fistulae were found in all but two of these infants and were usually rectovaginal. There were only three cases of rectovesical fistula in the female group. Two were associated with absence of the vagina, and the other with an extensive anomaly of the large bowel.

In all of the females and one-half of the males with anal stenosis, the lesion was not diagnosed until some two to five months after birth when the infant presented with chronic constipation, pain on defecation and the passage of ribbon-like stools. The other male infants displayed a more marked degree of stenosis and their condition was diagnosed at birth.

In type III imperforate anus, the level of the rectal pouch is the most important factor in determining the method of treatment, the prognosis and the functional result. When the rectal pouch is situated below the pelvic diaphragm, it can be treated adequately through a perineal approach with a low mortality rate and a good functional result. However, when the rectal pouch remains above the pelvic dia-

phragm the picture is entirely different. Not only is the treatment necessarily more extensive but the mortality rate is high and the long-term results, particularly with regard to bowel function, are often only fair or poor. Wangenstein-Rice radiographic views are used to determine whether the rectal pouch is above or below the pelvic diaphragm. The dividing line is considered to be 1.5 cm. proximal to the anal dimple. It is most important that this examination be undertaken carefully to avoid errors. Recently Scott and Swenson have categorized their cases with reference to a line drawn from the lower border of the symphysis pubis to the sacrococcygeal joint. Stephens¹¹ also refers to the pubococcygeal line. They consider that this line represents the level of the pelvic diaphragm. On reviewing our radiological material it appears that such a landmark, although not infallible, may prove a more accurate guide than a measurement utilizing the anal dimple. It may be wise to use both methods together to obtain maximum information.

As noted in Table II, associated congenital anomalies are common (39%) and often fatal. Genitourinary anomalies, excluding fistulae, comprise the largest group and are found in approximately one-quarter of children with imperforate anus. It is important that such conditions be detected early so that treatment can be started and complications prevented. Consequently, each child with imperforate anus should undergo genitourinary investigation during the original hospital admission. An intravenous pyelogram in addition to routine urinalyses is usually sufficient, but cystoscopy and retrograde pyelography may be necessary.

By reviewing the long-term results, we had hoped to determine whether a high type III malformation should be treated by a one or a two-stage procedure. Unfortunately, the long-term statistics in children treated by primary abdominoperineal anoplasty are incomplete and it will be some years before an accurate assessment of function can be made in this group. One should note, however, that even though the infants were often in poorer general condition, there was a lower mor-

tality associated with colostomy and secondary abdominoperineal repair than there was with the primary procedure. In the primary abdominoperineal anoplasty it may be difficult to work with the dilated, thin-walled, distal colon in the tiny infant pelvis. Interference with the blood supply of the distal colon may necessitate excision of an important part of this section of the bowel. It is difficult also to position the tunnel through the pelvic diaphragm accurately and atraumatically in a small infant. When one considers the importance of the sensory function of the distal bowel and the motor function of the pelvic diaphragm, it seems reasonable to suggest that these two structures might be preserved more accurately and easily at a secondary elective procedure when the child is older and the pelvis larger. Stephens¹¹ subscribes to this view, but others do not.

On the other hand, with increasing experience, the mortality rate associated with primary abdominoperineal anoplasty has definitely decreased. Furthermore, there are obvious advantages to completing a repair in one stage. In a large series recently reported by Gough,¹² better functional results were obtained with the primary abdominoperineal operation. Therefore it would seem fair to state that, for the present, the choice of procedure in each case must be made cautiously until more studies of long-term bowel and bladder function are reported.

SUMMARY

One hundred and forty-seven cases of imperforate anus treated from 1952 to 1959 are reviewed with particular emphasis on incidence, management and the results obtained. Approximately one-fifth of the group were patients with type I or type II lesions. These lesions were easily treated with excellent results. In the other 80% the lesion was type III or type IV. The importance of accurately determining the relationship of the distal rectal pouch to the pelvic diaphragm is stressed. Where the rectal pouch ends below the pelvic diaphragm, a perineal anoplasty can be accomplished with low mortality and good long-term bowel and bladder function. In

contrast, when the rectal pouch ends above the pelvic floor a combined abdominoperineal procedure in either one or two stages is necessary. The mortality is higher and the long-term functional results are less satisfactory.

The authors wish to thank Drs. S. A. Thomson and C. A. Stephens for their assistance in the preparation of this paper.

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RÉSUMÉ

L'imperforation anale a une incidence variable; il semble que l'on en rencontre environ un cas pour 1500 à 5000 naissances. Dans le cinquième de ces cas, l'anomalie est légère et peut être facilement réparée. Le présent article est une étude portant sur 147 malades atteints d'imperforation anale traités à l'Hôpital des enfants malades de Toronto entre 1952 et 1959 inclusivement. L'affection a pour origine une anomalie lors du développement embryonnaire: selon les degrés il peut y avoir imperforation totale ou simple sténose anale. Les enfants du sexe masculin sont les plus souvent frappés: ils représentent en effet 61% des cas de cette série. Dans ce rapport, on a procédé à une classification en quatre types selon la gravité. Le premier groupe (15%) rassemble les sténoses simples de l'anūs. Dans le deuxième groupe (5%), il y a imperforation, mais l'anūs n'est séparé du rectum que par une mince membrane. Dans le troisième groupe (78%), qui est de beaucoup le plus important, il y a imperforation complète et le rectum se termine en poche à une certaine distance de l'anūs. Le dernier groupe (2%) comprend les cas où il existe un rectum inférieur et un canal anal normaux, mais séparés du rectum supérieur, ce dernier se terminant en cul-de-sac à une distance variable au-dessus. Parmi les complications, les fistules représentent la moitié des cas. Les autres complications ou anomalies associées sont: l'hydronéphrose, l'hypospadias, le rein en fer à cheval, les fistules trachéo-œsophagiennes, l'agénésie colique, etc. Le diagnostic est en général facile et est posé très tôt après la naissance, sauf dans les cas du quatrième groupe où l'aspect extérieur est apparemment normal. Les diverses fistules génito-urinaires peuvent se traduire par le passage de méconium dans l'urine. L'examen radiologique est de toute première importance et doit être pratiqué selon une technique particulière décrite ici en détail. Le traitement varie selon l'importance des anomalies. Les cas du groupe 1 et 2 seront traités par simple dilatation avec des bougies de Hégar. Dans les autres cas, il faudra effectuer une reconstruction du canal anal, ce qui parfois nécessite une mobilisation du rectum par voie abdominale. Il est évident que dans cette dernière éventualité, le pronostic est moins bon et que la mortalité opératoire s'élève.

MANUSCRIPTS IN DUPLICATE

The attention of prospective contributors to the *Canadian Journal of Surgery* is drawn to a recent change in the section "Instructions to Contributors" which requires that, henceforth, all manuscripts should be submitted to the Journal in duplicate.

HISTOLOGICAL STUDY OF WOUND WASHINGS FOR TUMOUR CELLS

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A NUMBER of studies, including those of Smith *et al.*² and Moore *et al.*,¹ have demonstrated an appreciable percentage of wound washings in which tumour cells were found. However, in all of these investigations the pathologists knew that the material had been obtained from proved cancer cases. No attempt was made to provide a control series of "washes" from non-cancer cases.

The present study differs from those of the aforementioned authors in that an attempt was made to detect tumour cells in wound washings obtained during the surgical removal of both malignant and non-malignant tissue. As a further control, the procedures employed were repeated at necropsy on patients who had died either from cancer or from some non-malignant disease.

The pathologist who examined the slides had no knowledge of the origin of the material because a double-blind technique was used to assist in the critical evaluation of the results.

METHODS

All wound surfaces were washed with an isotonic solution of saline and the washings were aspirated into a bottle. About 500 ml. of saline was used in each washing. The saline was introduced into the wound as a gentle flow and it was recovered by gentle suction. Whenever possible, three washes were obtained, one before resection of the tumour, one after removal of the tumour and finally, one after closure of the body cavity, such as the peritoneal cavity

or pleural cavity, but before closure of the skin. In cases of tumours of the breast, two washes only were done, one before and one after removal of the tumour. Sufficient of a 10% solution of formalin was added to yield a final concentration of 5% formalin. The surgical staff was responsible for the collection of the washings and for the completion of a requisition for pathological examination of the specimen. Each wash was then coded by the stenographer in the Department of Laboratory Medicine, and the wash, with its code number, was given to the histology technologist for preparation of cytologic material for microscopic examination. The cells and debris were collected by sedimentation, followed by centrifugation. Paraffin blocks were prepared from the precipitated cells and from these blocks hemotoxylin and eosin-stained slides were prepared for examination by the pathologist.

The surgical staff was not informed of the code number and the pathologist was not informed of the identity of the specimen. Decoding was performed by a medically qualified person with the aid of the hospital records and follow-up reports on patients. Washes from postmortem material were dealt with in the same way. A control series of washes were performed on selected non-tumour cases in the operating room and, at necropsy, on patients who had died of diseases other than cancer.

RESULTS

A total of 361 washes were done on 169 patients. The data presented in Table I show the distribution of cases between patients with and without cancer and when an operation or a necropsy was performed.

The incidence of tumour cells detected in wound washings is given in Table II. There were 10 instances among 77 patients without cancer where slides were read as positive for tumour cells, although no cancer was suspected or subsequently proved. These cases are hereafter referred to as

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TABLE I.—DISTRIBUTION OF CASES STUDIED

<i>Patients</i>	<i>Surgical</i>	<i>Autopsy</i>	<i>Total</i>
With cancer	65 (39%)	27 (16%)	92 (55%)
Without cancer	69 (41%)	8 (4%)	77 (45%)
Total	134 (80%)	35 (20%)	169 (100%)

false positives. It should be emphasized that all slides, in which the identification of tumour cells was questionable, were re-viewed by a second pathologist.

TABLE II.—INCIDENCE OF TUMOUR CELLS* IN WOUND WASHES

<i>Patients</i>	<i>Surgical</i>	<i>Autopsy</i>	<i>Total</i>
With cancer	13 (20%) 65	10 (37%) 27	23 (25%) 92
Without cancer	7 (10%) 69	3 (38%) 8	10 (13%) 77
Total	20 (15%) 134	13 (37%) 35	33 (20%) 169

*This includes positive washes obtained from patients who did not have cancer.

Table III provides the final pathological diagnosis in the 10 cases where false positive washes were obtained. It is important to keep in mind the fact that the pathologist had no knowledge of the source of the material used in the preparation of the slides presented to him for microscopic examination. The effects of re-examination of the false positives on a double-blind basis by a second pathologist resulted in reducing the list of false positives by only one case.

TABLE III.—CASES PROVIDING FALSE POSITIVE WASHES

<i>Final pathological diagnosis</i>	<i>Number of positive washes</i>
<i>Surgical cases</i>	
Reactive hyperplasia of lymph nodes	2
Old scar tissue of duodenum	1
Duodenal ulcer	1
Endometriosis	1
Nodular synovitis	1
Acute penetrating ulcer of stomach	1
Fibroid uterus*	1
<i>Postmortem cases</i>	
Cirrhosis of the liver	1
Jejunal polyp with intussusception	1
Cystic tumoma	3

*A second pathologist called the slide from this case negative.

Nine out of 13 instances where positive wound washes were obtained were in adenocarcinomas of the gastrointestinal tract. Cancer of the lung accounted for three cases, and one positive wash was obtained after resection of a papillary cystadenocarcinoma of the ovary. Twelve radical mastectomies were included in these series and only one positive wash was obtained. This patient is still alive, whereas two deaths have occurred among those who had negative washes.

Table IV shows the final pathological diagnosis and prognosis in those instances where at least one positive wash was obtained. The false positive washes are not included in this table because the final pathological diagnosis and prognosis re-

TABLE IV.—FINAL PATHOLOGICAL DIAGNOSIS WHERE AT LEAST ONE POSITIVE WASH WAS OBTAINED ON SURGICAL CASES

<i>Pathological diagnosis</i>	<i>Premanipulative wash</i>	<i>Postmanipulative wash</i>	<i>Prognosis</i>
Adenocarcinoma of rectum	Positive	Positive	Under observation
Adenocarcinoma of stomach	"	"	" "
Adenocarcinoma of the gastrointestinal tract with metastases	"	"	Dead
Adenocarcinoma of the left lung with metastases	"	"	"
Adenocarcinoma of stomach	"	Negative	Under observation
Anaplastic carcinoma of the stomach	"	"	" "
Lymphosarcoma (carcinoma of the lung?)	"	None	"
Adenocarcinoma of sigmoid	"	"	Dead
Adenocarcinoma of lung	Negative	Positive	Under observation
Carcinoma of the duodenum with metastases	None	"	Dead
Comedocarcinoma of breast	"	"	Under observation
Papillary cystadenocarcinoma of ovary	"	"	" "
Cancer of stomach with metastases	"	"	" "

TABLE V.—DEATHS AMONG SURGICAL PATIENTS

	Positive wash*	Negative wash†
With cancer	$\frac{4}{13}$ (31%)	$\frac{13}{52}$ (25%)
Without cancer	$\frac{0}{7}$ (0%)	$\frac{8}{62}$ (13%)‡

*Positive wash means that tumour cells were found.

†Negative wash means that no tumour cells were found.

‡Follow-up study incomplete.

garding these patients can be obtained from Table III and Table V.

Table V shows the incidence of death among surgical patients from whom a positive or a negative wound wash was obtained. It was not possible to obtain a complete follow-up study on all of the 62 patients who did not have cancer and in whom washes were negative.

DISCUSSION

The detection of free tumour cells in cancer cases using the double-blind technique produced results which are essentially in agreement with the findings of Smith, Thomas and Hilberg.² These authors identified cancer cells in wound washings in 26% of 120 surgical procedures on cancer cases. In our study, 20% of 65 surgical procedures on cancer cases yielded positive washes, although the examining pathologist was completely unaware of the source of the material which he studied. It is noteworthy that in both studies there is a comparable percentage of positive washes.

On a comparable series of autopsy cases, the percentage of positive washes from 27 cases was 37. A pathologist who is unaware of the origin of the material is likely to detect tumour cells in about 25% of wound washes taken from cancer cases.

It is very important to note that in 77 patients who did not have cancer at operation or at postmortem, there was an incidence of 13% of positive washes which we have called "false positives". This is almost a 1:2 ratio of positive washes in non-cancer as compared with cancer patients. To our knowledge, this has not been demonstrated previously and serves to emphasize the value of double-blind studies. The identification of tumour cells is not an easy ac-

complishment. Detached mesothelial cells and other cells occurring singly or in clumps pose a problem of identification. This study certainly emphasizes the need for the development of improved cytological techniques.

In the complete series of 92 malignant cases, 23 had positive washes. Of 13 surgical cancer patients with positive washes, four have died within a brief period of time. The remaining nine are still alive at the completion of this report (a two-year period) and are being followed by the Cancer Clinic. To date, there has been no evidence of recurrence in this group.

An analysis of the source of the false positives indicates that confusion can develop in the interpretation of the cytologic sample because of the nature of the disease. Thus, cells associated with inflammatory reactions, especially mesothelial cells, may be misinterpreted as malignant cells.

It is interesting to note that at least in some cases of surgery, malignant cells remain resident in the wound bed, as indicated by the positive wound washes; in our series the incidence was about one in five. The surgical procedure, at least in these cases, appears to represent the major assault upon the lesion. The destruction of tumour cells which "seed" the wound bed must still be accomplished; for this we require anti-neoplastic agents that may be introduced into the wound bed and/or be administered systemically during the very critical phase which follows the operative treatment. It is probably in the interval between the operation and the application of radiation therapy, where it applies, that these tumour cells become established.

Justification for the category, false positive wash, may be found in the fact that none of these seven patients without cancer subsequently developed this disease during the period of observation. We did not employ a category of "questionable" because in actual practice it is necessary to decide whether a lesion is positive or negative for cancer cells. This eliminated the possibility of compromise, because material which was not definitely positive was designated as negative.

During the course of this study it occurred to us that washes may be used as a substitute for biopsy in some cases; however, experience has not borne this out. This confirms the traditional opinion of pathologists that there is no substitute for an adequate sample of tissue for histological examination.

SUMMARY

The use of a double-blind study demonstrated that tumour-like cells could be identified in wound washes from non-cancer cases. It is apparent that there is a need for improved techniques for the cytological identification of detached tumour cells. This study confirms the observation that tumour cells can be detected in wound washes in about one out of four cancer cases. The need for an adjuvant to be used immediately after operation is becoming increasingly apparent.

This study does not substantiate conclusions regarding local recurrence or metastatic extension of cancer in cases where positive wound washes were obtained. The problem of evaluating the potential malignancy of tumour-like cells remains unsolved.

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the saline washings from surgical and autopsy patients; C. Ower, who decoded the results, and A. E. Rodin, who assisted us by re-examining the false positives on a double-blind basis, is gratefully acknowledged.

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RÉSUMÉ

Des études antérieures ont montré que dans un nombre important de cas, il est possible de trouver des cellules cancéreuses dans des liquides de lavage de blessures. Dans cet article, les auteurs présentent les résultats de leurs expériences en vue d'estimer les possibilités diagnostiques d'un tel examen. Pour ce faire on procéda à des lavages de plaies opératoires pendant des excisions de tissus cancéreux ou non cancéreux. Le liquide obtenu était aspiré dans une bouteille de 500 ml. et fixé à la formaline. Les cellules étaient alors séparées par centrifugation, enrobées en paraffine. Après confection des blocs on effectuait des coupes colorées à l'hématoxyline-éosine: ces coupes furent soumises à l'examen de l'anatomopathologiste qui ignorait tout de la provenance des spécimens. A titre de contrôle, des expériences similaires furent faites pendant les autopsies. Au total on examina ainsi 361 de ces liquides de lavage de plaies, provenant de 169 malades. Cette étude confirme qu'il est parfaitement possible de retrouver dans ces liquides des cellules cancéreuses, mais dans une proportion de un cas sur quatre seulement. Mais il n'est pas possible, par cette méthode, de juger du degré de malignité d'un cancer, ainsi d'ailleurs que de tirer aucune conclusion en rapport avec les possibilités de récurrence locale ou de métastases. De plus il est certain qu'il reste indispensable de mettre au point des techniques histologiques spéciales et améliorées en vue de procéder à l'identification cytologique des cellules carcinomateuses.

MALFORMATIONS OF THE FACE. D.

Greer Walker, with foreword by T. Pomfret Kilner. 202 pp. Illust. E. & S. Livingstone, Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1961. \$6.75.

This scholarly volume presents a "morphological survey of facial malformations". Chondrocranial disorders are not included. Variations in the nomenclature plus the complicated relationship between genetic potential and environment have made the author's task difficult.

Nevertheless, he has presented us with an admirable book, the result of much experience and reading. From the first chapter on hyper-telorism to a discussion on the plasticity of craniofacial structures, followed by a review of the environmental hazard of pregnancy, to the final chapter on the hazards of heredity, the author has successfully achieved his aim. His efforts will be of great value to all those interested in congenital malformations of the face; for example, the plastic surgeon, the orthodontist and the geneticist.

CARCINOMA OF THE FEMALE BREAST

A Review of 238 Cases Treated at the Women's College Hospital, Toronto

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THIS PAPER is based on a review of 238 patients with carcinoma of the breast admitted to the Women's College Hospital, Toronto, during the years 1941 to 1953 inclusive. Ninety-five per cent of the patients in this series were treated by means of radical mastectomy with or without irradiation. This study was undertaken for two reasons; first, to assess the results of treatment of carcinoma of the breast at our hospital, and second, to give the authors a base-line for future comparison with the results of newer methods of treatment.

These patients were all under the care of one or the other of the two senior authors. As far as possible this is a consecutive series, but possibly some of the more advanced cases of cancer of the breast in patients seen during this period, who were not submitted to operation, were not traced and therefore not included.

AGE INCIDENCE

This is shown in Fig. 1. The maximum age incidence is in the range between 40 and 70 years, that is, in the years immediately before and the two decades after the menopause. The average age in this series was 54.7 years. This is a little older than the 51.3 years given by Harrington² as the average age in 6195 women with carcinoma of the breast.

METHODS OF STAGING AND TREATMENT

Before considering the survival rates in this series, the staging of the lesions has to be defined and the methods of treatment used in each stage stated. Our cases have been divided into four stages, which are similar to, but do not absolutely coincide with, those recently proposed for international trial based on the T.N.M. (tumour, node and metastases) classification. The criteria for staging and the general meth-

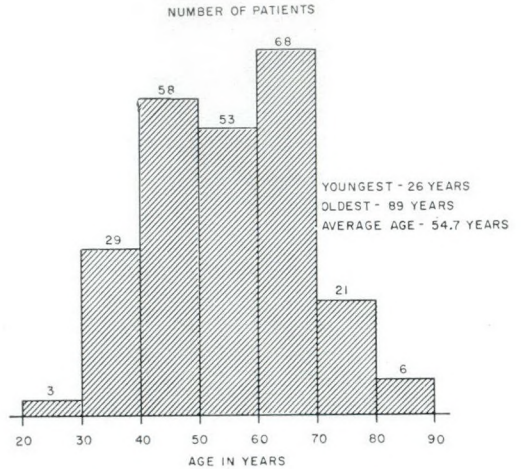


Fig. 1.—Graph of age distribution.

ods of treatment which were employed are shown in Table I. The staging is based largely on the pathological examination of material from a radical mastectomy specimen, especially in differentiating Stage I and Stage II lesions.

Whatever methods were used, the principles of treatment were, as stated by Smith,⁵ "the eradication of all tumour from the largest amount of tissue at the earliest moment with the least risk".

SURVIVAL RATES

In the 238 cases under review, the overall five-year follow-up rate is 92%. It is hoped that this figure can be improved upon in the future through the institution of a tumour registry in this hospital. The crude five-year survival rate is considered to be the most objective measure of results. All patients known to be alive at five years, whether or not they show evidence of recurrent disease, are classed as five-year survivals; whereas all other patients, whether dead of disease, dead of extraneous disease, or lost to follow-up study, are considered to have died of carcinoma of the breast.

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TABLE I.—GENERAL METHODS OF TREATMENT

Stage	Criteria for staging			Treatment	
	Primary tumour	Axillary nodes	Distant metastases	Operation	Irradiation
I	Minimal skin involvement	Negative	None	Radical mastectomy	In selected cases only (no irradiation in 75% of this group)
II	Minimal skin involvement	Positive, mobile, under 2 cm. in diameter	None	Radical mastectomy	Postoperative irradiation (given in over 90% of this group)
III	May have extensive skin involvement, with ulceration or localized <i>peau d'orange</i>	Positive, may be fixed, may be over 2 cm. in diameter	None	Radical mastectomy	Preoperative irradiation more common than postoperative
IV	As any of above. May have <i>peau d'orange</i> extending beyond breast	As any of above	Present, as shown clinically (e.g. liver, supraclavicular nodes), or radiologically (e.g. lungs, bones)	Simple mastectomy, if necessary, for removal of ulcerated lesion	Irradiation main method of treatment, combined with alteration of hormone balance

Table II relates the five-year survival rates in this series to the stage of disease. It is well known that the patients with less extensive lesions have a better prognosis. There are, however, factors which, although related to the clinical staging, may alter the outcome in any given patient. As pointed out by Delarue¹ in his review on the free cancer cell, the fate of the circulating malignant cell depends both upon the nature of the cell and upon the resistance of the host. These influences may favourably affect the prognosis, as in one patient with a Stage III lesion alive and well 12 years after treatment; or, conversely, may favour rapid dissemination of the tumour, as in three patients with Stage I lesions who were dead from carcinoma within two years.

TABLE II.—CRUDE FIVE-YEAR SURVIVAL BY STAGES

Stage	Number of patients	Five-year survival	
		Patients	Per cent
I.....	124	94	76.8
II.....	90	45	50.0
III.....	19	4	
IV.....	3	0	
Not known.....	2	0	
Total.....	238	143	60.0

As shown in Table III, of the 79 patients treated before the end of 1948, 31 or 39.2% are known to have survived for 10 years. It is of interest to note that of the 47 patients in this group who survived the first five years, two-thirds were known to

TABLE III.—CRUDE TEN-YEAR SURVIVAL BY STAGES

Stage	Number of patients	Ten-year survival	
		Patients	Per cent
I.....	36	23	
II.....	29	7	
III.....	11	1	
IV.....	1	0	
Not known.....	2	0	
Total.....	79	31	39.2

be alive after 10 years. Of the eight known to have died of disease after five years, five patients had clinical evidence of recurrence at the five-year follow-up examination. Although metastases may become apparent many years after mastectomy, the longer a patient lives clinically free of her disease, the greater are her chances of surviving to die of extraneous causes.

TABLE IV.—SURVIVAL RELATED TO MENOPAUSE

Status	Number of patients	Five year follow-up		
		Alive	Died of disease	Lost or died of other disease
Premenopausal.....	84	58 (69*)	22 (26.2)	4 (4.8)
Less than five years postmenopausal.....	60	34 (56.7)	20 (33.3)	6 (10)
Over five years postmenopausal.....	94	51 (54.3)	26 (27.6)	17 (18.1)
Total.....	238	143 (60.0)	68 (28.6)	27 (11.4)

* Figures in brackets are %.

SURVIVAL RELATED TO AGE GROUPS

An attempt was made to appraise survival rates in relation to the patients' hormonal status as judged by their menstrual histories. It is thought that this may be one factor influencing the resistance of the host against the tumour. Table IV shows survival in relation to age groups, or more specifically, to the menopause.

This suggests that the younger, premenopausal group has the highest survival rate. However, it should be noted that the percentage of patients classified under "lost or died of other disease" is highest in the late postmenopausal group, and the percentage of patients known to have died of carcinoma of the breast is highest in the early postmenopausal group. It is our impression that it is this latter group which has the worst prognosis. These are the patients whose natural hormone balance is changing, and whose cancers are less likely to be influenced by artificially induced changes in balance.

POSTOPERATIVE MORTALITY AND MORBIDITY

Any discussion of the advantages and disadvantages of radical mastectomy necessitates an analysis of the morbidity and mortality associated with this operation.

The operative mortality rate in this series was 0.4%, i.e. one case. This 70-year-old hypertensive patient died two days after a *simple* mastectomy for an advanced lesion. There was no mortality in the 226 patients treated by radical mastectomy, but undoubtedly the poor-risk patients were treated more conservatively.

In carrying out an objective assessment of the morbidity following radical mastec-

tomy in this series, the added physical deformity resulting from the axillary dissection has not been taken into account. We have found that the patient herself rarely realizes the distinction between a simple and a radical mastectomy. What concerns her is the constant reminder that she has been operated upon for cancer. In addition there is often a minor degree of shoulder stiffness or puffiness of the arm, which is not considered serious enough to be noted in the records.

TABLE V.—MORBIDITY AFTER TREATMENT

Complication	Number of patients	Percentage of series
Edema of arm.....	39	16.4 } 18.5
Edema + recurrent infection	5	
Postirradiation effects.....	7	
Other complications.....	4	
Total complications.....	55	
Total of patients with complications.....	52	21.8

Table V shows that postoperative or postirradiation morbidity was recorded in 52 cases, or 21.8% of the series. Three patients had more than one complication.

The commonest cause of morbidity was lymphedema of the arm, which occurred in 44 patients. In every case the patient had had a radical mastectomy. Of 101 patients who had radical mastectomy alone, 15.8% developed edema of some degree, whereas of 126 patients who had irradiation in addition to a radical mastectomy, 22.4% developed edema. Although the percentage is rather higher when irradiation has been used in treatment, the radical mastectomy is probably the major factor. In six of these patients the swelling of the arm was a real disability, and in one this symptom led to amputation of the arm.

CASE 1.—Mrs. J. H., aged 60, was admitted to the Women's College Hospital in February 1948 with a 10-day history of a lump in the right breast. She was found to have a mass about 2.5 cm. in diameter in the upper outer quadrant, with slight skin dimpling. One small hard axillary node was palpable.

A radical mastectomy was performed for Stage II carcinoma of the scirrhous type; involvement of only one axillary node was present. The operation was followed by three courses of radiation therapy. It was noted that this patient had an unduly marked reaction to her irradiation.

In June 1948, while still under treatment, she developed edema of the right arm. Over the ensuing years, the lymphedema became progressively worse, and responded only temporarily to conservative measures.

Early in 1951, after a trivial injury, the patient sustained fractures of the right clavicle and right upper ribs. These healed without difficulty, and it was thought that the fractures were related to postirradiation osteoporosis. There was no evidence of metastases at this time or subsequently.

In 1958, her right arm was amputated because of increasing, disabling lymphedema. Since this operation, she has had at least one attack of erysipelas in the amputation stump.

As far as the malignant disease is concerned, the patient has remained well for over 12 years.

POSTIRRADIATION MORBIDITY

Seven patients had complications related to radiation therapy. The majority of these patients were treated in the earlier years of this survey. The decrease in morbidity in the later years may be related to the long latent interval before the effects become apparent, but is more probably due to improved methods of irradiation.

One patient suffered fractures after trivial injury, owing to her postirradiation osteoporosis, as noted above. Several patients had marked skin changes, leading to ulceration in three cases. In one patient the ulcer did not develop until 16 years after irradiation. This healed with conservative treatment, but broke down again three years later.

Another patient developed an osteogenic sarcoma in an irradiated area. This case is to be reported elsewhere.

UNEXPECTEDLY LONG SURVIVALS

As noted previously, a patient with a clinically advanced carcinoma may survive apparently free from disease for a surprising number of years.

CASE 2.—Miss E.C., aged 70, was admitted to the Women's College Hospital in November 1947, with a five-to-six-year history of a lump in her left breast. This had been enlarging for two years, and had been ulcerated for three or four weeks. She was found to have a mass the size of an orange in the left breast, with a central area of ulceration. There were small nodes palpable in the axilla.

This patient was considered clinically to have a Stage III carcinoma because of the advanced local disease. The diagnosis was confirmed by biopsy, and the patient referred for preoperative irradiation. It was thought that there was little hope of controlling her disease.

With radiation therapy, this patient developed a generalized dermatitis which slowly responded to treatment. By April 1948, her skin condition had almost cleared up; the left breast was softer and the mass smaller, but

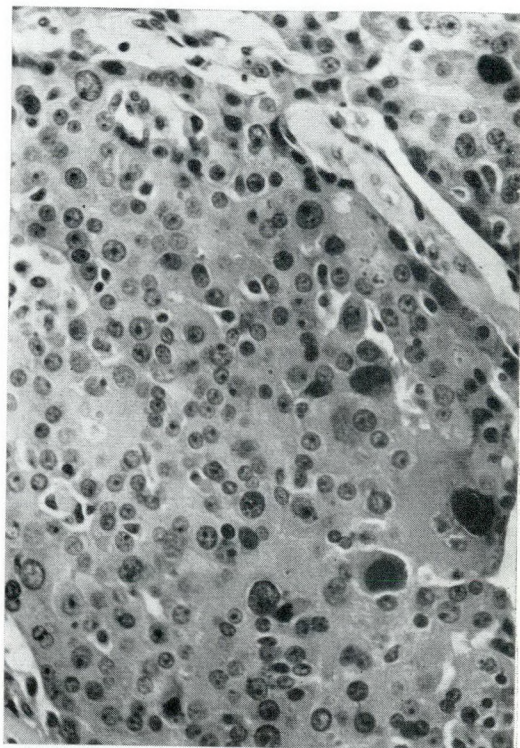


Fig. 2.—Case 2. Photomicrograph of primary carcinoma after irradiation. Tumour viable, with many atypical cells.

there was still a deep ulcer crater. The left axillary nodes were larger, and were thought to contain metastases. There was also an enlarged node in the opposite axilla. This was biopsied and was negative for carcinoma. A radical mastectomy was then carried out in April 1948. Pathological examination showed extensive residual tumour present in the breast (Fig. 2). This was a medullary type lesion, with many atypical cells and plentiful mitotic figures. The lymph nodes were negative.

In spite of her apparently advanced disease, this patient was still alive and well at her last follow-up examination, 11½ years after the beginning of treatment, and there has been no evidence of recurrent carcinoma.

Perhaps the long history, combined with the fact that there was no evidence of distant metastases in the presence of a large primary lesion, should have suggested a more favourable prognosis originally. In addition, it seems that the cellular medullary type of carcinoma of the breast often has a more benign course than its histological picture would suggest.

Another case illustrates some of the possibilities of palliative treatment for a patient with recurrent disease.

CASE 3.—Mrs. B.B., aged 47, was admitted to Women's College Hospital in August 1951 with a four-month history of a lump in her right breast. The lump was the size of a 50-cent piece and was situated in the upper half of the breast, with a suggestion of skin fixation.

Radical mastectomy was carried out for a Stage I carcinoma of the scirrhous type (Fig. 3). Her postoperative course was complicated by skin loss of moderate extent. No irradiation was given at this time.

The patient remained well for 15 months, but in November 1952 she was found to have osteolytic metastases in the ribs and pelvis. These were treated by radiation therapy, with a good response, and conversion to areas of sclerosis was obtained. Over the next seven years, this patient developed multiple metastases, chiefly in the bones, with some local recurrences on her chest wall. These were controlled with repeated courses of irradiation; by surgical castration in June 1955, by testosterone in October 1956, and by prednisone (Metacorten) in October 1957. In each in-

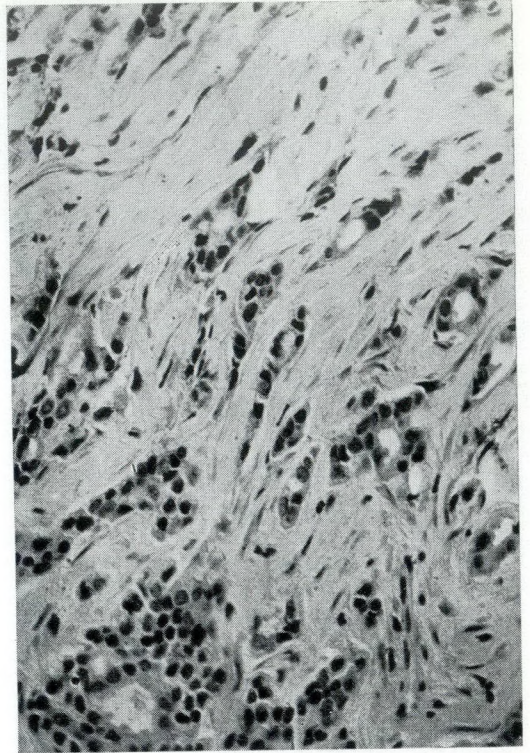


Fig. 3.—Case 3. Photomicrograph of primary carcinoma of scirrhous type.

stance she obtained a good remission and remained remarkably well in spite of gradually progressive disease for over six years from the first sign of recurrent carcinoma.

Finally, in December 1959, she was no longer able to care for herself. In January 1960, she was admitted to a hospital for the chronically ill, where she died the following month. Autopsy showed very extensive metastatic involvement of liver and bones. The lungs were free of tumour.

This case is remarkable chiefly for the long period during which this patient lived in "symbiosis" with her carcinoma, and demonstrates well the potentialities of some of the palliative measures currently available. As pointed out by Janes,³ in many cases life can be prolonged for months or even for years. Another patient is still active and relatively well three and a half years after secondaries in the spine were proved on radiological examination. Her disease is controlled by prednisolone (Metcortelone) and repeated courses of nitrogen mustard.

BILATERAL CARCINOMA OF THE BREAST

Eight patients in this series developed a second primary lesion in the opposite breast 19 months to 11 and a half years after treatment for the first carcinoma. In addition, one patient had bilateral simultaneous carcinomata. The incidence of known bilateral breast cancer in this series therefore is 3.8%, and of non-synchronous cancer, 3.4%. These figures are similar to those of Harrington² and of Moertel and Soule.⁴

No attempt has been made to draw conclusions regarding survival in this group of patients with bilateral cancer, because the number of cases is too small.

SUMMARY

Two hundred and thirty-eight cases of carcinoma of the female breast treated at the Women's College Hospital, Toronto, have been reviewed. Radical mastectomy with or without irradiation was the method of treatment in 95% of the series. In recent years, other methods, either more or less radical, have been developed to challenge this classical form of treatment. The results of the present series give a base-line for comparison in this hospital in the future.

The overall crude survival rates were 60% at five years, and 39% at 10 years. These are comparable with those obtained by this method of treatment at the larger centres, and show, as pointed out by Utzschneider and McCann,⁶ that similar results can be obtained at a smaller community hospital.

Survival rates were also related to the stage of disease and to age groups. It is pointed out that the patient who develops carcinoma of the breast at or just after the menopause probably has a less favourable prognosis.

Some complications of treatment and some potentialities of palliative therapy are illustrated by case histories, and the cases of bilateral breast cancer are briefly presented.

Radical mastectomy will continue to be the basic method of treatment of carcinoma of the breast, until another form of therapy can be found which will eradicate the

tumour from a wider area with less deformity and at no greater risk to the patient. Until such a method is found, radical mastectomy will apparently continue to cure the patients with localized disease and a good host resistance, and remain relatively ineffectual in the face of rapidly advancing autonomous carcinoma.

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RÉSUMÉ

Cet article est une étude d'ensemble portant sur 238 cas de cancer du sein chez la femme, traités au "Women's College Hospital" à Toronto entre 1941 et 1953. Ces cas avaient été traités par mastectomie totale avec ou sans irradiation subséquente dans une proportion de 95%. Récemment de nouvelles méthodes de traitement plus ou moins radicales ont été proposées. Les résultats étudiés ici pourront servir de base de comparaison dans l'avenir quant à la valeur réelle de ces diverses thérapeutiques. Les indices de survie globale furent de 60% après cinq ans et 39% après 10 ans. Ces chiffres sont tout à fait comparables à ceux fournis par d'autres centres de traitement beaucoup plus importants, et montrent que des résultats satisfaisants peuvent être obtenus dans des hôpitaux de moyenne ou de petite capacité. Les indices de guérison sont évidemment liés au degré d'extension de la maladie et à l'âge des malades. Il est certain que les patientes chez qui le mal apparaît au moment ou juste après la ménopause ont un plus mauvais pronostic. Plusieurs histoires de cas sont décrites en détail, illustrant les complications possibles et les variantes de la thérapeutique palliative; les cancers bilatéraux sont également discutés. Dans l'avenir la mastectomie radicale restera le moyen de traitement fondamental du carcinome du sein, jusqu'à ce qu'une forme nouvelle et aussi efficace de thérapeutique puisse la remplacer. Dans l'ensemble le traitement actuel se montre valable dans les cas encore localisés chez des malades ayant une bonne résistance organique.

THE ROLE OF PANCREATIC ENZYMES IN THE PATHOGENESIS OF ACUTE PANCREATITIS*

The Failure of a Trypsin Inhibitor: Benzethonium Chloride to Prevent Experimental Acute Pancreatitis

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KLEBS,¹ in describing acute pancreatitis in 1868, was the first to suggest that autolysis by pancreatic ferments may play a significant role in the pathogenesis of acute pancreatitis. After describing a case of acute pancreatitis with the finding at autopsy of a stone in the common channel of the biliary and pancreatic ducts,² Opie and Meakins³ suggested that autolysis by proteolytic enzymes was the common pathogenetic mechanism of this disease. This problem was subsequently studied by other investigators who have provided circumstantial evidence indicating that the intrapancreatic conversion of inactive precursors of the proteolytic enzymes to their active form plays a decisive role in the development of this disease.⁴⁻⁶

When trypsin inhibitors became available, it was reasonable to try them in the prevention or treatment of hemorrhagic pancreatitis. While Coffey, Brinig and Gillespie⁷ reported in a preliminary study that soybean trypsin inhibitor arrested acute pancreatitis, they did not to our knowledge confirm this in a full publication. Forell, Genewein and Werle⁸ found encouraging results with this inhibitor in rats, but in a well-controlled study using dogs, Hoffman *et al.*⁹ did not endorse this preventive effect. Similar inconclusive effects were obtained with soybean trypsin inhibitor by Rush and Clifton.¹⁰

The authors felt that this failure of trypsin inhibitors to protect against pancreatitis might be explained on the basis that soybean trypsin inhibitor is a large molecule and therefore may not reach the en-

zymes in the necrotic tissue. For this reason a search for a smaller molecule with trypsin inhibitory action was undertaken in our laboratory. Such a compound, benzethonium chloride, was described by us in a previous communication.¹¹ It was shown that this compound inhibits tryptic activity *in vitro* and *in vivo*. The proteolytic activity of rabbit serum was inhibited maximally between six and 12 hours after the subcutaneous injection of benzethonium at a dose of 15 mg./kg.

The present communication deals with experiments performed to test the efficiency of benzethonium in preventing experimentally induced acute pancreatitis in rabbits.

MATERIALS AND METHODS

A total of 39 white rabbits of both sexes, weighing from 3 to 6 lb., were divided into three groups. In Group I, pancreatitis was induced in 18 rabbits and they were treated with benzethonium chloride. In Group II, pancreatitis was induced in 15 rabbits, these were treated with 0.9% sodium chloride (NaCl). This group served as a control. In Group III, six rabbits were operated upon but pancreatitis was not induced. This group was treated with benzethonium chloride as a second control. The rabbits in Groups I and III were given twice daily subcutaneous injections of 25 mg./kg. body weight of benzethonium chloride dissolved in 1.25 ml. of 0.9% NaCl solution. The first injection was given four hours before the operation.

Induction of Pancreatitis

The animals were anesthetized with intravenous pentobarbital (Nembutal) (10 to 20 mg./lb. body weight, given intravenously). Under sterile conditions, the pancreatic duct was identified. A quantity of bile (0.5-1.0 ml.) was injected into the

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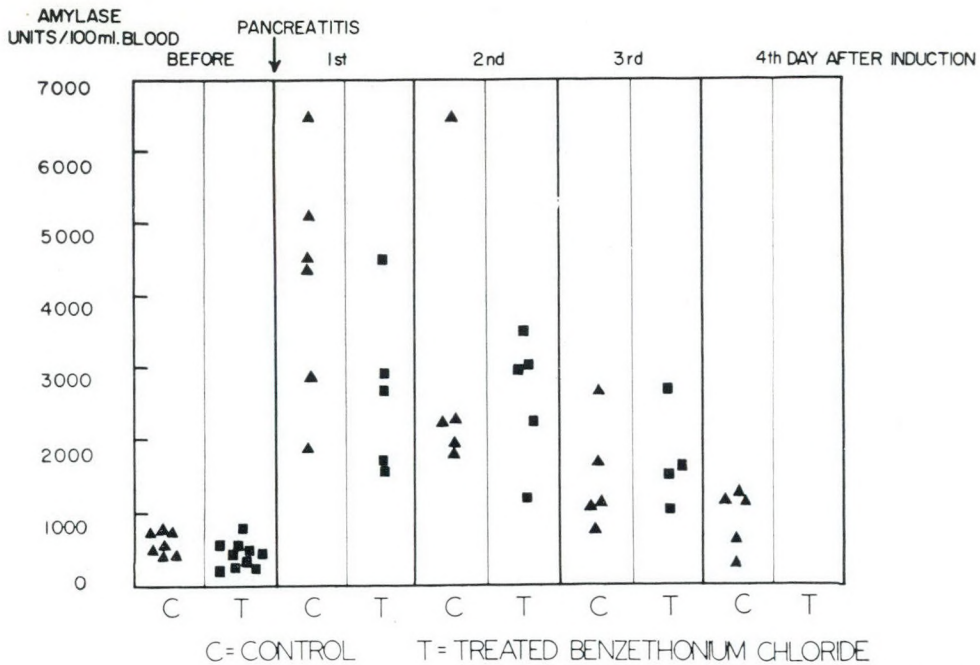


Fig. 1.—Blood amylase values before and after the induction of acute pancreatitis in rabbits.

duct from a syringe under moderate pressure, and the duct was ligated above and below the puncture. In most of the cases, fresh sterile canine bile was used, but in four animals in Group I and in five in Group II, bile was obtained by the puncture of their own gallbladders. The animals were fasted for 24 hours before operation; after operation they were allowed to eat, but feeding was so timed that blood sampling always took place after a period of 18 hours' fasting.

Course of Experiments

Details of the experiments in the three groups, briefly described above, are as follows:

A. The benzethonium-treated group, in which pancreatitis was induced, consisted of rabbits Nos. 1 to 18. In animals 1 to 14, pancreatitis was induced by the injection of 0.5-1.0 ml. canine bile into the pancreatic duct. In rabbits Nos. 15 to 18 pancreatitis was induced using 0.5-1.0 ml. of the animal's own bile. All these rabbits were given 25 mg./kg. body weight of benzethonium chloride twice daily.

B. The first control group consisted of rabbits Nos. 19 to 33. In rabbits 19 to 24 and 30 to 33, pancreatitis was induced using 0.5-1.0 ml. of canine bile, while the animal's own bile was used in rabbits 25 to 29. Starting four hours before the operation, these animals were given 1.25 ml. of 0.9% NaCl solution twice daily by subcutaneous injection.

C. The second control group was created to establish the effect of operative trauma without pancreatitis on the toxicity of benzethonium. This became necessary when we found that survival time in the benzethonium-treated animals of the experimental group was often shorter than that in the first control group. This second control group included rabbits Nos. 34 to 39. In these animals the pancreatic duct was identified but was not ligated and bile was not injected. Treatment with benzethonium was similar to that described for rabbits 1 to 18. In a number of rabbits blood samples for amylase determinations were taken before and after operation (Fig. 1).

The results were evaluated according to the survival data, the blood amylase levels and the records of the autopsies.

Biochemical Determinations

Amylase determinations were performed on fresh venous blood obtained by ear puncture according to a micromethod developed in this laboratory.¹²

Autopsy Studies

Rabbits that died and those that were killed after having survived for four days were autopsied. If they were found soon after death before postmortem changes could take place, their pancreases were examined histologically. Grading of pancreatitis was based on macroscopic and microscopic evaluation. In both the tissue was graded from 0 to 4 according to the degree of edema, fat necrosis and hemorrhage. The microscopic evaluation was done by a consulting pathologist, Dr. D. S. Kahn, who graded the slides without prior knowledge of the experimental conditions.

RESULTS

1. *The effect of benzethonium chloride on survival of rabbits suffering from acute pancreatitis.*—As can be seen in Table I, of the group in which pancreatitis was induced and benzethonium treatment was given, 10 out of the 18 rabbits (55%) died within four days. Four of these died on the first day. In the control group where benzethonium was not given but pancreatitis was induced, only four out of 15 (27%) died within four days. Although it had been previously established that the dose of benzethonium used was not toxic in itself, it was because of this increased mortality that the second control group was created to determine whether the combination of benzethonium and operative trauma produced significant mortality. It may be seen in Table I that all rabbits in this group survived, thus indicating that the increased mortality was not due to any toxic action of benzethonium chloride.

2. *Plasma amylase studies.*—Amylase values are given in Fig. 1.

There was a significant increase in the plasma amylase level in the rabbits in which pancreatitis was induced, both in the group treated with benzethonium and in the untreated group. Although it seems

TABLE I.—CUMULATIVE MORTALITY RATE DUE TO ACUTE EXPERIMENTAL PANCREATITIS

	Days			
	1st	2nd	3rd	4th
A. Control 15 rabbits % died.....	13	20	20	26
B. Benzethonium-treated 18 rabbits % died.....	22	33	50	55
C. Sham-operated, benzethonium-treated 6 rabbits—% died....	0	0	0	0

that the increase in the untreated group was higher, a statistical evaluation is impossible because of the high mortality in the treated group. In the second control group that were given benzethonium but in which pancreatitis was not induced, only one of the six animals showed an increase.

3. *Autopsy studies.*—Review of the pathological specimens suggests that there was no difference in the severity of pancreatitis induced between the benzethonium-treated group and the control groups.

DISCUSSION

A series of experiments has been described indicating that a trypsin inhibitor of small molecular structure, benzethonium chloride, did not prevent or diminish the severity of experimentally induced pancreatitis. The inability of other trypsin inhibitors to prevent or cure experimental pancreatitis in dogs was previously reported by Hoffman, Jacobs and Freedlander.⁹

Popper and Necheles¹³ excised the pancreatic duct in dogs and left it free in the abdominal cavity. This method produced peripancreatic fat necrosis, but not actual pancreatitis. Using this procedure, they tested antitryptic compounds for their actions in preventing fat necrosis. They also concluded that soybean trypsin inhibitor¹⁴ and other antitryptic chemicals of small molecular structure (e.g. acridine) did not prevent peripancreatic fat necrosis.¹⁵ Sodium formaldehyde sulphonylate, a drug which inhibits lipase, was, however, moderately active in inhibiting the lipolytic action of pancreatic juice in the abdominal cavity. These experiments, although they support our findings, cannot be considered altogether similar, because pan-

creatitis was not induced, and only one aspect of pancreatitis, the peripancreatic fat necrosis, was investigated.

Forell, Genewein and Werle⁸ reported on the effect of the addition of soybean trypsin inhibitor to a 2% solution of sodium taurocholate before the intraductal injection of the solution into the pancreas of rats. They found that the tissue reaction was diminished and mortality was prevented in an undefined number of rats. The lack of statistical evidence as well as the delicateness of the method used to produce pancreatitis (injecting the substance into the pancreatic duct of such a small animal) makes it impossible to comment on these results.

The method used in our experiments to induce pancreatitis was chosen not because we believe that it resembles the pathogenesis of acute pancreatitis in man, but because it is a simple and easily reproduced procedure. In our opinion, pancreatitis is a reaction which can be induced by many different causes, but which, whatever the cause, results in similar biochemical and tissue changes. For this reason we felt that whatever the method of producing pancreatitis might be, if trypsin liberation plays an important role in the condition, a potent trypsin inhibitor might arrest the process.

Autopsy studies showed that the pancreatitis as judged morphologically was of equal severity in the treated and control groups. The increased mortality in the benzethonium-treated rabbits with pancreatitis is hard to explain. It is impossible to state that the increased mortality is due to toxicity of benzethonium, since the difference between groups A and B is not statistically significant. An exact solution of the four-fold table

	<i>Dead</i>	<i>Alive</i>
Drug	10	8
Control	4	11

shows that the difference is not significant at the 2.5% level of probability for the appropriate one-tailed test.¹⁶ Of the six rabbits operated upon without inducing pancreatitis and treated with benzethonium, all survived. In straight toxicity

studies with the compound carried out on nine extra rabbits, it was found that except for local subcutaneous necrosis, daily doses of 100 mg./kg. could be given without any ill effect.

The failure of trypsin inhibitors to arrest or prevent acute pancreatitis in these animals may be explained in two ways. Perhaps the inhibitor does not reach a high enough concentration in the pancreas and so cannot inhibit trypsin activity there, or perhaps the tissue reaction of acute pancreatitis is not dependent upon tryptic activity. We endeavoured to clarify this point by trying to determine trypsin content in pancreatic tissue in the rabbit before and after benzethonium injection. This approach, however, proved to be unsuccessful due to anatomical difficulties. The pancreas of the rabbit extends in a web-like fashion in the mesentery, and it is almost impossible to isolate it in a clean manner for trypsin determinations. It is, however, rather unlikely that neither soybean trypsin inhibitor nor this compound would reach the pancreatic enzymes in high enough concentration to be effective. Therefore, it is possible that intrapancreatic liberation of free trypsin is not essential in the pathogenesis of acute pancreatitis.

In a subsequent communication in which the ratio of trypsinogen to free trypsin in pancreatic tissue of normal dogs and of dogs suffering from pancreatitis will be reported, we will present evidence that such an enzymatic conversion cannot be detected.

SUMMARY

The effect of benzethonium chloride, a potent tryptic inhibitor, was studied on experimentally induced pancreatitis in rabbits. Thirty-nine rabbits were used. Pancreatitis was induced by the injection of bile into the pancreatic duct. Benzethonium chloride was given subcutaneously at a dosage of 25 mg./kg. body weight twice daily for four days. At this dosage level no favourable effect of this trypsin inhibitor was found on the treated animals when compared in terms of serum amylase determinations, survival rate and pancreatic

pathology. The increased mortality in the benzethonium-treated group is not statistically significant.

The authors are indebted to Dr. D. S. Kahn, pathologist-in-chief, St. Mary's Memorial Hospital, Montreal, and assistant professor of pathology, McGill University, for reviewing the histological slides; to Dr. H. Griff for her assistance in setting up the amylase method,¹² and to Dr. J. S. L. Browne, professor of investigative medicine, McGill University, for his helpful suggestions.

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RÉSUMÉ

Il existe de bonnes raisons de penser que la pancréatite est causée par la transformation de précurseurs inactifs de l'enzyme pancréatique en diastase active à l'intérieur même du parenchyme du pancréas. C'est pourquoi de grands espoirs se firent jour lorsqu'apparurent sur le marché les drogues inhibitrices de trypsine. On s'attendait à pouvoir ainsi contrôler facilement et efficacement les cas de pancréatites. Assez étrangement, ces espoirs furent cependant décevants. L'opinion des auteurs de cet article à ce sujet est que l'inactivité de la drogue inhibitrice, qui est dérivée du soja, est probablement due au fait qu'il s'agit d'une très grosse molécule, incapable de pénétrer dans les tissus en nécrose. Récemment on a proposé une nouvelle drogue de ce genre, le chlorure de benzéthonium, qui s'est montré actif *in vivo* et *in vitro*. Cet article rapporte les expériences qui furent faites en vue de tester cette activité. Les animaux utilisés étaient des lapins pesant entre trois et six livres. Chez un premier groupe, on produisit une pancréatite par ligature du canal pancréatique et injection d'un peu de bile stérile au-dessus de la ligature; ce premier groupe fut ensuite soumis à un traitement au benzéthonium. Un deuxième groupe fut opéré de la même façon et traité par des injections de chlorure de sodium. Enfin un troisième groupe servit de témoin. En tout on utilisa 39 animaux. Le dosage de l'amylase sanguine fut effectué. En fin d'expérience, le nombre de morts fut plus élevé dans le groupe traité au benzéthonium que dans les groupes témoins, à tel point que l'on envisagea le problème de la toxicité propre de la drogue. De contre-expériences montrèrent cependant qu'il ne s'agissait nullement de cela.

LEFT COLON ISCHEMIA* FOLLOWING OCCLUSION OR LIGATION OF THE INFERIOR MESENTERIC ARTERY

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OCCLUSION of the inferior mesenteric artery can be as dramatic and as lethal as superior mesenteric artery occlusion, but, because of the usually excellent collateral circulation mediated through the marginal artery, it seldom is. Surgeons are able to ligate this artery during aneurysmectomy and radical resection of the left colon with relative safety. Griffiths,¹ in a postmortem study, found that the origin of the inferior mesenteric artery was often markedly narrowed and not infrequently occluded by atheroma.

The collateral circulation to the left colon is derived principally from the superior mesenteric artery proximally and the internal iliac arteries distally. The superior mesenteric contributes to this collateral circulation through the anastomosis of its middle colic branch with the left upper colic branch of the inferior mesenteric artery at the splenic flexure. Basmajian,² in a study of 70 cadavers, found this anastomosis to be good to excellent in over 70% of the subjects. His results have been confirmed by many others.³⁻⁶

Since 1907, when Sudek published his paper concerning the cause of gangrene of the lower sigmoid colon after perineal resection of the rectum, it has been taught that no anastomosis exists between the last sigmoid branch of the inferior mesenteric artery and the superior rectal artery. However, Basmajian found some anastomosis to be present in up to 34% of his subjects. Griffiths,¹ using unique techniques of aortography in cadavers, demonstrated that an adequate anastomosis *always* exists between the above-mentioned arteries. After ligation of all the terminal branches of the inferior mesenteric artery at the point where they joined the marginal artery, he was able

consistently to fill the rectal vessels adequately by injection of the superior mesenteric artery. Thus, this work disproves the existence of Sudek's "critical point" and it is now obvious that the marginal artery can receive a collateral circulation from the internal iliac vessels through the anastomoses between the superior, middle and inferior rectal arteries. This anastomosis was demonstrated quite well by Griffiths in several aortograms done in patients with atheromatous occlusion in the region of the bifurcation of the aorta. The middle rectal artery played a prominent role in these cases.

It is now obvious that the collateral circulation to the left colon from the superior and/or internal iliac arteries must be deficient because of the effects of atherosclerosis, the presence of a vascular anomaly, or surgical interference, before occlusion of the inferior mesenteric artery will lead to pathological change owing to impaired blood supply in the descending colon and rectum.

During the past few years three such cases, after occlusion of the inferior mesenteric artery, have occurred in patients under our care. It is felt that these cases are worth reporting and discussing.

CASE REPORTS

CASE 1.—W.D., a 70-year-old male with long-standing peripheral vascular disease, was admitted for treatment of a gangrenous foot. A mid-thigh amputation was carried out on April 16, 1959. During the postoperative period he developed unexplained fever, complained periodically of a dull, aching, lower abdominal pain and later developed intractable bloody diarrhea. Investigation of the stool for pathogenic bacteria and parasites was negative. The physical findings were limited to mild abdominal distension and slight left lower quadrant tenderness. Sigmoidoscopic examination on two occasions revealed a red raw rectal mucosa that bled easily on stroking. At 10 to 15 cm. from the anal verge, the bowel mucosa was involved by a hyperplastic, polypoid process. A biopsy from this area showed

*Ischemia, as used here, includes all those pathological changes resulting from impairment of blood supply.

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only chronic inflammatory tissue and a non-specific ulcer. The patient received treatment appropriate for chronic idiopathic ulcerative colitis.

On May 8, 1959, evidence of a generalized peritonitis developed and an emergency laparotomy was done. A large amount of pus was found in the abdominal cavity. The whole pelvic colon and upper rectum was inflamed, swollen and quite indurated. Two small perforations were identified in the sigmoid colon. The holes were patched with appendices epiploicae, suitable drains were left in place and a transverse colostomy was accomplished. The patient died that evening.

At autopsy the aorta was found to be occluded by a recent, firm, laminated thrombus, which blocked the origin of the inferior mesenteric artery. The upper left colic branch of the inferior mesenteric vessel was occluded by an old, organized and partly recanalized thrombus. The left common iliac artery was firmly thrombosed. The colon and rectum from the splenic flexure distally showed extensive, confluent, linear ulceration separated by scattered islands of remaining normal mucosa. In the pelvic colon there was a deep ulcer 12 cm. long which had perforated at several points. Generalized peritonitis had resulted.

Comment.—Occlusion of the inferior mesenteric artery by recent thrombosis of the lumbar aorta, a postoperative complication, caused ischemia and necrosis of the left colon and rectum. Collateral circulation from the superior mesenteric artery through the left upper colic artery was impaired by old organized thrombosis. It is of interest that, clinically, the lesion of the bowel which resulted was indistinguishable from idiopathic ulcerative colitis.

CASE 2.—R.B., a 70-year-old male, was admitted to Sunnybrook Hospital on September 17, 1958, for repair of a left inguinal hernia. He was found to have a hemoglobin of 49% and occult blood in his stools. Further investigation indicated the presence of an active duodenal ulcer; herniorrhaphy was postponed. On this admission, however, numerous physical examinations of the abdomen were negative. A barium enema performed during the course of his investigation was also quite normal. The patient was treated conservatively for his ulcer and discharged to the outpatient department where he was seen at three-week intervals.

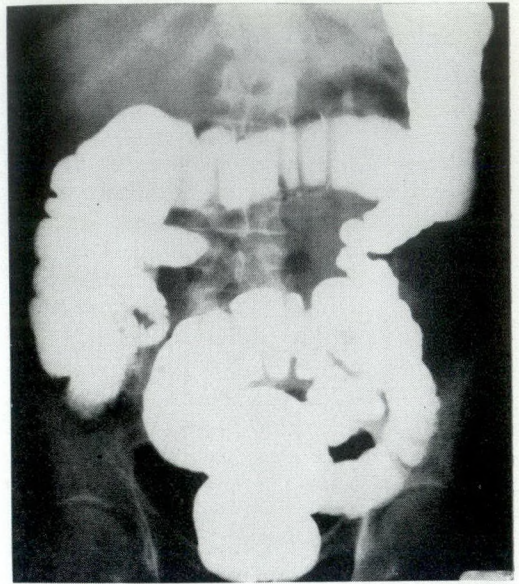


Fig. 1.—Case 2. A normal barium enema performed in October 1958.

On December 4, 1958, he was readmitted to Sunnybrook Hospital because of midabdominal pain radiating through to his back and down into his left groin. A large tender, pulsating abdominal aortic aneurysm was now quite apparent on abdominal examination. An emergency aneurysmectomy with replacement by a Teflon (tetrafluoroethylene) prosthesis was performed that night. The inferior mesenteric artery was noted to be patent before its sacrifice.

This man's postoperative course was complicated by persistent left lower quadrant abdominal tenderness, low-grade fever, and intractable (but never bloody) diarrhea. Stools were always negative on smear and culture for parasites and pathogens. The diarrhea gradually subsided but never completely disappeared. He was discharged on January 10, 1959.

On January 27, 1959, he was readmitted to hospital with a history of intermittent constipation and diarrhea. During the periods of constipation which lasted from four to five days, his abdomen would become distended and tense. Deep tenderness was still present in the left lower quadrant. A barium enema at this time showed a constant narrowing in the upper sigmoid colon which extended more than six inches. Its appearance and the fact that it developed over a four-month period suggested that it was a lesion resulting from impairment of the blood supply to the colon.

On February 20, 1959, a laparotomy was performed and an inflammatory mass was

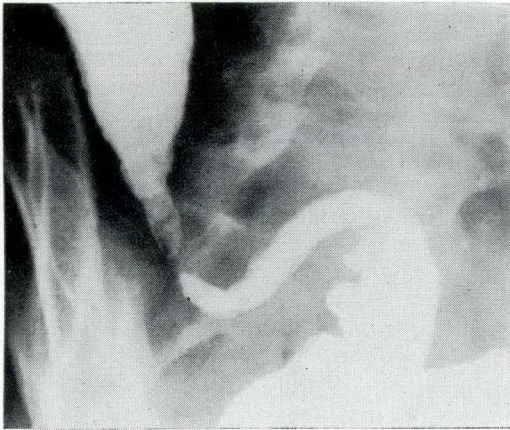


Fig. 2.—Case 2. Barium enema of February 1959 showing a long narrow area in which the mucosal lining is disrupted.

found which involved the lower descending and upper sigmoid colon. The bowel proximal to this mass was greatly distended. A colocolostomy was easily carried out between the transverse colon and a mobile loop of the sigmoid colon distal to the lesion. The postoperative course was uneventful.

On April 27, 1959, the patient was readmitted to hospital in shock. A large tender pulsating mass could easily be felt in the abdomen. He died shortly after admission.

At autopsy the distal anastomosis between the Teflon graft and the aorta, just above the aortic bifurcation, was found to have ruptured, resulting in massive fatal intraperitoneal hemorrhage. In addition, there was marked stenosis of a segment of bowel 7 cm. in length at the junction of the descending and pelvic colon. The bowel wall in this region was thickened and firm. Sections of tissue from this area showed complete replacement of the mucosa and submucosa by fibrous tissue, which was infiltrated by chronic inflammatory cells. The muscularis mucosae and surrounding tissues were markedly scarred and were infiltrated by similar cells.

Comment.—Ligation of the inferior mesenteric artery during replacement of a portion of the lumbar aorta resulted in ischemia of a portion of the left colon. A gradual fibrosis and stenosis occurred in the ischemic segment (Figs. 1-3).

CASE 3.—This 66-year-old male was referred to the surgical service of Sunnybrook Hospital for treatment of a constricting lesion of sigmoid colon demonstrated by a barium



Fig. 3.—Case 2. This is the involved bowel removed at postmortem. Note the long narrow segment, the walls of which are thickened and pearly white.

enema. After suitable preparation of the bowel, the abdomen was opened through a left paramedian incision and, as has been our policy where technically possible, the inferior mesenteric artery and vein were isolated near their origins and ligated. Preliminary inspection indicated a reasonable anastomosis between the superior and inferior mesenteric arteries at the splenic flexure. However, after the lower descending and sigmoid (pelvic) colon had been resected, it became apparent that the blood supply to the remaining colon was deficient as far proximally as the hepatic flexure. Because this patient had undergone a posterior gastroenterostomy some years pre-

viously for treatment of a peptic ulcer, it was considered at first that the branch of the middle colic artery to the splenic flexure had been interfered with during that procedure. However, no vessel, patent or occluded, was seen during transection of the transverse mesocolon. We were forced to conclude that this patient had no middle colic artery. Similarly, no right colic artery was encountered during mobilization of the right colon. The right and transverse colon depended on the ileocolic artery for its blood supply.

Comment.—In retrospect, this patient had two conditions which now and in the future we will recognize as contraindications to high ligation of the inferior mesenteric artery (ligation at its origin from the aorta); namely, an absence of the middle colic artery and a posterior gastroenterostomy. The latter may have compromised the marginal artery.

DISCUSSION

Until recent years little attention has been paid in the literature to the occurrence and consequences of inferior mesenteric artery occlusion. Many recent papers⁴⁻⁷ have shown that such an occlusion can produce a definite clinical picture which varies somewhat, according to the degree of ischemia of the left colon and rectum. The diagnosis can often be confirmed by sigmoidoscopic examination.

Carter and his group⁴ presented 14 cases of inferior mesenteric vascular occlusion proved at operation or at postmortem examination. These cases were all characterized by evidence of an abdominal catastrophe with left lower quadrant pain and tenderness and diarrhea, usually bloody. In all of their patients in whom a sigmoidoscopy was done, ischemic mucosal changes were easily identified in the upper rectum and sigmoid. Two of these patients had an associated abdominal aortic aneurysm; none had embolism of the inferior mesenteric artery. In the series of Carter and his colleagues only one patient survived out of seven on whom laparotomies were performed.

There are several case reports in the literature of left colon infarction occurring as a complication of translumbar

aortography.⁸⁻¹¹ The patients discussed in these reports demonstrated advanced aortoiliac atherosclerosis with varying degrees of vessel obstruction and this most likely accounted for the marked filling of the inferior mesenteric artery and its branches that occurred in each aortogram; in Padhi's patient,¹¹ dye could even be seen outlining the wall of the descending colon. All the patients developed symptoms and signs of acute abdomen upon recovering from anesthesia. The existence of infarction of the left colon was confirmed on postmortem examination. Mortality has been high, partly because of the delay in diagnosis. The opinion of all of these authors was that spasm and thrombosis of the inferior mesenteric artery and its branches, as a result of the injection of an excessive amount of dye directly into the inferior mesenteric artery, accounted for the infarction of the bowel. Unfortunately none of the reports give a description of the pathology present in the arterial tree itself.

Smith and Szilagy¹² and Bernatz¹³ present excellent reviews of ischemia of the left colon as a complication of aortic resection. In a series of 400 patients treated by replacement procedures for lumbar aortic aneurysm reviewed by Bernatz, there were four deaths (1%) from left colon gangrene. Smith was able to demonstrate some degree of ischemia of the left colon and rectum in 10 out of a series of 120 cases in which aneurysmectomies were performed for lumbar aortic aneurysm. The ischemic complications ranged from transient mucosal ulceration (as seen by the sigmoidoscope) to massive gangrene of the left colon. It is worthy of note that Smith found this complication was most common in that group of aneurysmectomies in which one or both internal iliac arteries were sacrificed. This can be readily understood on the basis of the loss of the collateral circulation from the internal iliac vessels, which was discussed at length earlier in this article.

During the past decade many who perform abdominal surgery have advocated high ligation of the inferior mesenteric artery in rectal, sigmoid and left colon resections for carcinoma in order that a more radical removal of the local lymphatic

drainage might be accomplished. Several investigators have studied the anastomoses between the mesenteric vessels at the splenic flexure. All have concluded that in the great majority of cases this anastomosis is excellent and would support nutrition of the left colon in event of ligation of the inferior mesenteric artery. In more than 70% of his clinical cases Goligher³ was able safely to preserve the left colon after high division of the inferior mesenteric artery. Morgan and Griffiths¹⁴ in a series of 214 resections for carcinoma of the distal colon or rectum found that it was often necessary to mobilize the splenic flexure and transverse colon in order to obtain viable intestine after ligation of the inferior mesenteric artery at its origin. They had only one case in which death could actually be attributed to devascularization of the colon. Griffiths recommends a careful examination of the anastomoses at the splenic flexure and of the middle colic artery before proceeding with ligation of the inferior mesenteric artery. In 22 of 100 subjects he found the middle colic artery was absent and significant anastomoses with the left upper colic branch of the inferior mesenteric artery could not be demonstrated. He also recommends caution in those cases in which a transverse colostomy has been or is being done because the marginal artery may be interfered with. This would hold equally true (Case 3) in patients who have had a posterior gastroenterostomy.

SUMMARY

Three cases have been presented in which occlusion or ligation of the inferior mesenteric artery resulted in irreversible ischemia in the left colon. The reasons for the relative rarity of this complication have been discussed.

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RÉSUMÉ

L'occlusion de l'artère mésentérique inférieure peut avoir des conséquences dramatiques et fatales, comme c'est le cas pour l'occlusion mésentérique supérieure, mais en général l'existence d'une circulation collatérale tempère la situation. Les auteurs présentent ici trois cas où la ligature ou l'occlusion de cette artère a provoqué une ischémie irréversible du côlon gauche.

Le premier cas est celui d'un homme de 70 ans souffrant de maladie vasculaire généralisée, hospitalisé pour gangrène du pied. Une amputation avait été pratiquée à mi-cuisse. Un peu plus tard apparut une fièvre difficile à expliquer, accompagnée de douleurs abdominales puis d'une diarrhée sanglante. Une laparotomie d'urgence dut être pratiquée en raison d'un syndrome péritonitique soudain. On trouva une inflammation diffuse du rectum supérieur et du côlon sigmoïde, ce dernier étant porteur de deux perforations que l'on obtura par recouvrement avec des appendices épiploïques. Le malade mourut cependant le même soir. A l'autopsie l'aorte était bouchée par un thrombus récent qui bloquait la circulation mésentérique inférieure.

Deuxième cas.—Un homme de 70 ans, admis à l'hôpital pour une cure herniaire inguinale gauche. Cette intervention fut décommandée, car on trouva que le malade était porteur d'un ulcère duodénal que l'on traita médicalement. Deux mois

plus tard s'installait un syndrome abdominal douloureux et l'examen permettait de diagnostiquer facilement un anévrisme aortique abdominal. On pratiqua d'urgence une anévrissectomie suivie d'une greffe d'une prothèse de téflon; au cours de cette intervention, l'artère mésentérique inférieure dut être sacrifiée. Le patient ne se remit jamais parfaitement; les douleurs abdominales réapparurent et bientôt il fut nécessaire de pratiquer une nouvelle exploration, puis une anastomose entre les côlons transverse et sigmoïde en vue de court-circuiter le côlon descendant engainé dans une tuméfaction inflammatoire. Le patient mourut soudainement quelques semaines plus tard; une désunion de la prothèse de téflon avait provoqué une hémorragie intra-abdominale foudroyante.

Mais en plus, de très importantes modifications pathologiques furent découvertes au niveau du côlon descendant. Dans ce cas, la ligature de l'artère mésentérique inférieure avait provoqué une ischémie lente de cette partie du tube digestif.

Troisième cas.—Un homme de 66 ans avait été hospitalisé pour une sténose sigmoïde radiologiquement démontrée. Une tentative de résection nécessita la ligature de l'artère mésentérique inférieure et là encore des troubles ischémiques apparurent. Il est à signaler que ce malade avait subi une gastro-entéro-anastomose postérieure pour traitement d'un ulcère, de sorte que l'artère colique moyenne fonctionnait imparfaitement.

Une revue de la littérature en rapport avec le sujet est donnée en conclusion.

GALEN ON ANATOMICAL PROCEDURES.

The Later Books. A translation by the late W. L. H. Duckworth. Edited by M. C. Lyons and B. Towers. 279 pp. Cambridge University Press, Cambridge; The Macmillan Company of Canada Limited, Toronto, 1962. \$6.75.

Galen was probably the greatest anatomical writer of antiquity and some would say he was the greatest medical writer. A perusal of this work helps to strengthen these beliefs. Writing in the second century, this Roman physician demonstrated a genius that is matched by only a handful of the world's greatest men. Fortunately, his works were translated into Arabic and so survived the dark ages in Europe. With the Renaissance and well into the sixteenth century, they guided the only scientific medicine practised in the civilized world.

This translated fragment of Galen's scholarship demonstrates a breadth and depth of understanding of structure and function which can only engender awe in the modern reader. Anyone making the slightest claim to an interest in the history of medicine will find this book fascinating to read and essential to own.

The care with which the publishers and the two editors have produced the volume is a fitting tribute to its distinguished translator, W. L. H. Duckworth, who for many years until his death in 1956 was the Master of Jesus College and Reader in Human Anatomy at Cambridge. Furthermore, it is an excellent companion to the late Charles Singer's translation of the earlier book of Galen on anatomical procedures. The Cambridge University Press and the Wellcome Foundation have performed a valuable service to the medical profession in the publication of this delightful book.

MODERN TRENDS IN ANAESTHESIA.

Second Series. Aspects of Hydrogen Ion Regulation and Biochemistry in Anaesthesia. Edited by Frankis T. Evans and T. Cecil Gray. 219 pp. Illust. Butterworth & Co. (Publishers) Ltd., London; Butterworth & Co. (Canada) Ltd., Toronto, 1962. \$12.00.

This volume may be divided into two sections. The first contains six chapters that describe lucidly the confusing nomenclature, the problems of measuring acid-base balance, the physiological effects of hypercapnia and hypocapnia, and the manner in which hypothermia and cardiac bypass procedures may affect acid-base balance. The second section deals particularly with adrenocortical mechanisms and cholinesterases that can be related directly to certain aspects of the anesthetic state.

There is some repetition of the basic concepts related to acid-base balance in the first section, but this is not the usual drawback one expects when several authors are united, for this approach helps to clarify a very difficult subject. However, the contributors might have gone a little further in discussing changes in acid-base balance due to various anesthetic agents, anesthetic circuits and how undesirable alterations might be averted for the benefit of anesthetists who might read this book.

The second section is well done, but it is too brief. Modern trends in the study of protein metabolism that embraces pain mechanisms, hemostasis and female hormones, hypertension, and hypotension, would have been most welcome in this volume.

In spite of the criticisms noted, I would highly recommend this volume to all those who have long suffered from an inadequate understanding of the vital problems of managing acid-base balance during anesthesia and related biochemical alterations.

REVIEW ARTICLE

MEDICAL APPLICATIONS OF X-RAY MICROSCOPY*

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THE USE of x-rays for microscopy is a recent development which is now finding many practical applications in biology, metallurgy and medicine. The reason for using x-rays in microscopy rests on the fact that their wave-lengths are shorter than those of light and consequently offer a higher resolution of detail than is obtainable with the light microscope. Also their penetrating effect, which is likewise due to their short wave-length, permits study of the internal structure of optically opaque objects. In addition, because x-rays are absorbed and emitted in a manner specific to the nature and amount of the elements present, x-ray microscopy offers extensive possibilities for the chemical analysis and localization of particular elements in tissue on the microscale.

The discovery of x-rays by Roentgen in 1895 was immediately followed by attempts to apply them to microscopy. A fundamental difficulty was encountered, which he himself had recognized, namely, that x-rays cannot be readily focused by any sort of lens to form an image. Since no refractive effect could be detected, the idea of making some form of x-ray microscope was early abandoned.

The first and simplest method used to study fine detail with x-rays was contact microradiography, a term introduced by Goby in 1913. Here the specimen is placed almost in contact with a photographic plate at some distance from an x-ray source (Fig. 1). A one-to-one image is obtained, which is then either enlarged photographically or examined with an optical microscope. In definition, the ultimate resolution is about 1 micron at a useful magnification of x300, but it is limited both by the grain

size of the photographic emulsion and the resolving power of the optical microscope.

Subsequently the use of softer x-rays, vacuum chambers to reduce air absorption of such rays, and fine grain (Lippmann type) photographic emulsions has permitted the investigation of tissue on a histological basis (Dauvillier 1930; Lamarque, 1936). Until 1940, microradiography was largely developed in French laboratories, but since that date its biological and medical applications have increased rapidly in various countries, notably Sweden (Engström;¹ Bellman²), Britain (Barclay;³ Ely;⁴ Mitchell⁵) and Canada (Bohatirchuk;⁶ Saunders⁷).

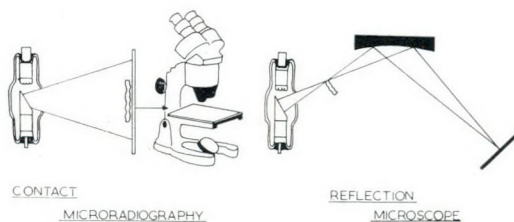


Fig. 1.—Diagram illustrating the principle of contact microradiography and the x-ray mirror or reflection microscope.

THE MIRROR OR REFLECTION MICROSCOPE

Before 1947 there were no x-ray microscopes, but then Ehrenberg⁸ in London and Kirkpatrick⁹ in San Francisco explored the idea of using total reflection from concave surfaces for x-ray imaging, and the first reflection or mirror x-ray microscopes were built.

The essential experimental arrangement of a mirror x-ray microscope (Fig. 1) consists successively of a small source of x-rays, the specimen, and a pair of adjustable crossed mirrors of large radius of curvature, set up before a viewing screen and plate holder. Since soft x-rays (Cu K α : 1.5 A.U.^{*}) are used, a helium atmosphere is employed to minimize absorption

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*One Angström unit (A.U.) = 10^{-7} mm.

in the image throw. In principle, x-rays striking at a small glancing angle of the order of one degree are imaged by the first (horizontal) mirror into a line, while the second (vertical) mirror images the line back into a point, so that an x-ray microscope with point-to-point imaging is achieved, with an initial magnification of $\times 10$ to $\times 50$ and resolution of about 1 micron at the centre of the field. The ultimate prospect of a resolution roughly midway between the limits of the optical (2000 A.U.) and electron (10 A.U.) microscopes stimulates further research with the mirror method.

The mirror microscope unfortunately suffers from marked aberrations, such as spherical aberration and astigmatism, due to the severe optical method of focusing x-rays at glancing angles and also to the surface shape and finish of these mirrors. Also the two mirrors are not at equal distances from the object, unless the catamorphic method of Montel¹⁰ is employed, in which the reflecting surfaces are united. The design of suitably shaped reflecting surfaces and a final finish far superior to that now required in optical working are two outstanding technical difficulties.

THE X-RAY PROJECTION MICROSCOPE

A method of producing magnified x-ray images without the difficulties associated with the use of x-ray lenses or mirrors has consequently been sought. The advent of electron lenses made it possible to focus electrons to a minute point and utilize the x-rays so produced.

X-ray microscopy by point projection, or the idea of using a point source of x-rays to cast a projected and magnified image of an object on to a distant plane, was first suggested in 1939, but was only realized in practice in 1951. For with the advent of electron lenses it became possible to focus a beam of electrons to a minute point, ranging from 1 micron to 1000 A.U. on a target, so forming an x-ray source of great intensity.

In 1951 at the Cavendish Laboratory, Cambridge University, Cosslett and Nixon¹¹ built the first x-ray projection microscope. A second and improved research model

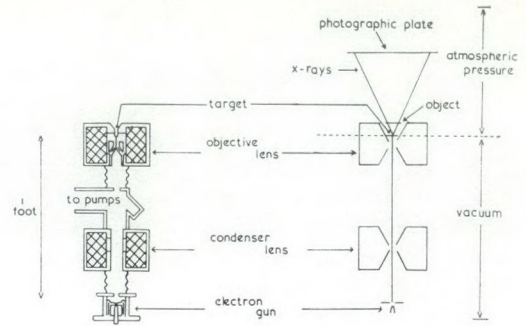


Fig. 2.—Schematic diagram showing the Cosslett-Nixon x-ray projection microscope in cross section.

constructed with their assistance under grants from the National Research Council of Canada was installed in the Anatomy Department, Dalhousie University, in 1957. The principle of the projection method and experimental arrangement will be outlined before describing some of the applications and results obtained with this instrument.

PHYSICAL PRINCIPLES AND APPARATUS

The x-ray projection microscope resembles an inverted electron microscope. Fig. 2 shows, on the left, the physical realization of the instrument and, on the right, a schematic line drawing. A beam of electrons produced by a tungsten filament within the electron gun is accelerated and passed between two magnetic (condenser and objective) lenses, and focused to a minute point smaller than 1 micron on a thin metal foil target, so forming an x-ray point source of great intensity. The electron path is at vacuum, but the x-ray path is at atmospheric pressure since the thin target window allows the x-rays to pass through on to a fluorescent viewing screen or photographic plate.

An object placed close to the target is magnified according to the ratio of the target-object and target-plate distances, both of which are variable. A primary magnification of $\times 100$ is obtainable in a distance of 1 cm., or $\times 1000$ in a distance of 10 cm., that is to say, in a range of $\frac{1}{2}$ to 4 inches.

The x-ray point source casts an enlarged image with a resolution approximately equal to the size of the target spot (1 μ to 1000 A.U.). A piece of silver grid (1500

mesh per inch) consisting of 3μ bars with 17μ spaces is used for focusing the instrument and for purposes of calibration.

Owing to the marked depth of field of the x-ray projection microscope all objects remain in focus, so that microscopic fields can be recorded stereoscopically either by tilting or simple lateral translation of the specimen between successive exposures.

Various metal foils (4 to 10μ thick), such as aluminum, copper, silver or gold, are used as targets, since the wave-lengths of the x-rays produced vary with the metal used. In general soft x-rays are preferred in the interest of contrast, since absorption increases rapidly with wave-length. Vascular studies are best conducted with a copper foil target (5 to 10μ), using an accelerating voltage of 10 to 25 kv.; while tissue sections require the soft radiation obtainable with an aluminum target (4 to 10μ) operated at 5 to 10 kv.

The method of operating the instrument is briefly as follows. After aligning the electron beam with the aid of a fluorescent screen, a target is inserted and further focusing is carried out by judging the image sharpness of coarse and fine metal grids (e.g. 1500 silver mesh grid) while varying the condenser and objective lens currents. The x-ray image of the grid or other test object is viewed on a fluorescent screen with the aid of a $\times 10$ ocular. Once focused, no further adjustments are usually necessary during the course of the experiment. A specimen holder and camera can now be placed over the x-ray beam, at a greater or lesser distance from the point source, an exposure made and the plate developed.

MICROANGIOGRAPHY

Projection x-ray microscopy has many applications in the vascular field, and has been used to study the microscopic blood vessels of a variety of organs and tissues, such as brain, bowel and skin. It is particularly suited to the examination of the small vessels which go to make up the microcirculation, because all the blood vessels remain in focus. This is due to the great depth of field of the x-ray microscope, which also permits the stereographic recording of their volume pattern, by simply

shifting the specimen laterally between successive exposures. The ability to obtain a three-dimensional view of the interior of a specimen is one of the more valuable features of x-ray microscopy, and is very useful for determining the course and connections of vessels within a tissue layer or organ.

Microangiographic studies necessitate the intra-arterial injection of a contrast medium of high radiopacity and small particle size (0.5μ or less), that is readily miscible with the blood, and is capable of traversing the capillary bed. Excellent microangiograms of fresh cadaveric or surgical material are obtainable with a colloidal suspension of barium, such as Micropaque, since it readily penetrates the smallest capillaries. Conventionally fixed material is best avoided because histological fixatives both alter x-ray transmission and produce vascular changes. In the living animal the concentration, volume and toxicity of the contrast medium assume special importance in x-ray microscopy if vascular spasm and shock are to be avoided. The best results have been obtained with Thorotrast, which is a colloidal suspension of thorium dioxide that rapidly enters all parts of the vascular network.

Visualization of the microcirculation in the living animal can be carried out by x-ray microscopy on muscle bridges, trunk flaps, exteriorized organs, or conveniently thin vascular structures such as the rabbit ear. The rabbit ear is easily examined with the x-ray microscope using x-rays generated at 10 to 25 kv. For example, the ear of the anesthetized rabbit can be placed over the point source and studied either by taking a microangiogram immediately after the injection of contrast medium into one of the regional arteries (blood displacement technique), or by taking successive microangiograms following a single intravenous injection of contrast medium to record the vascular pattern during its peripheral transit (circulating slug technique). In the latter case, the dose or slug may be chosen to represent some known fraction of the total plasma volume, with a view to limiting circulatory disturbances.

Microlymphangiography or the visualization of lymphatic capillaries has also been



Fig. 3.—Microangiogram of the margin of a rabbit ear taken with the x-ray microscope. Micro-paque injection. x 22.

performed on the rabbit ear.¹² Contrast medium is injected subcutaneously into the tissues to form a depot area, and thereafter successive exposures are taken until the contrast medium has begun to disappear. Parts of the lymphatic capillary plexus may be seen about the depot area as well as the distribution of the collecting lymph vessels. Non-return flow valves may be observed in the lymph vessels. Both blood and lymphatic vessels have been imaged simultaneously on several occasions by combining the microangiographic and microlymphangiographic techniques described above. Knowledge of the factors regulating lymph flow may be expected to be advanced by such techniques.

Studies have been made of the vascular anatomy of the dead and living rabbit ear to serve as controls for experiments on the

living skin. Such microangiograms¹³ reveal the extraordinary complexity of the peripheral vascular network. The peripheral vessels in a marginal area of the rabbit ear are shown (Fig. 3). The central artery of the ear has divided, and one of its subsidiary branches is seen on the right, dividing into several smaller arteries which anastomose with others to form a series of arterioarterial arcades and thereby a coarse distributor network or macromesh. Within this coarse peripheral network can be clearly seen a more complex and finer nutrient network or micromesh formed by the arterioles, capillary bed and its draining venules. A dense palisade of capillaries can be seen along the ear margin, as well as its draining venules and their termination in the large sinuous marginal vein.

Arteriovenous anastomoses associated with skin vessels can be clearly imaged by x-ray microscopy, and have been recorded in microangiograms of the central area of

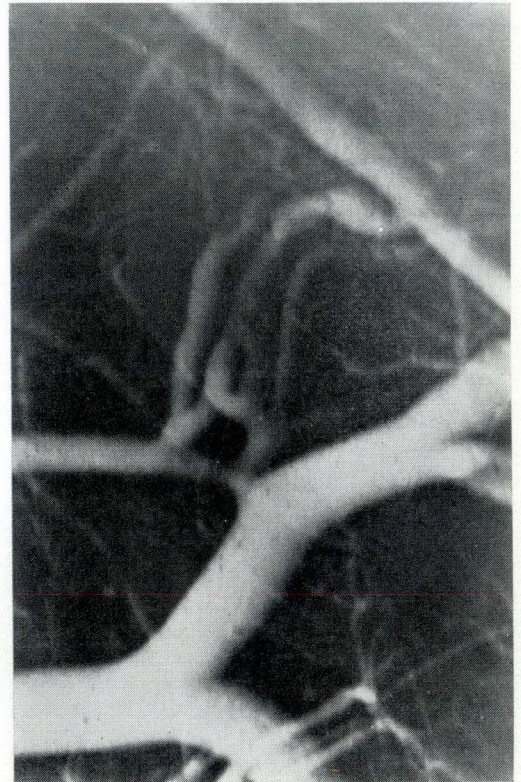


Fig. 4.—X-ray projection micrograph of rabbit ear showing a complex grouped type of arteriovenous anastomosis connecting a small artery to a large vein. x 50.

the rabbit ear in both the dead and living animal. They are frequently of the single S-shaped or coiled type, and are seen to branch laterally from a small artery to empty into an adjacent vein of usually somewhat larger calibre. As a rule there is a marked calibre difference between the narrow arterial and wider venous end of the anastomosis, so that the funnel-shaped venous end usually assists in their identification. The next micrograph (Fig. 4) shows a rarer and more complex grouped type of arteriovenous anastomosis observed in the skin of the rabbit ear. The small artery of origin is seen near the top of the plate, while the larger vein of termination lies at the foot. Note the venular connection with the adjacent capillaries, which has suggested a functional distinction based on Bernoulli's theorem.¹⁴

The living anesthetized rabbit may be used to study vascular reactions in the skin. Heat, cold, trauma and pharmacological agents may be applied. For example, serial x-ray micrographs taken after freezing and thawing a small area have revealed arterial spasm, the trapping of contrast medium within congested capillaries and other features.

X-ray microscopy of human skin injected with contrast medium reveals the smallest vessels beneath the friction or papillary ridges of the skin, and demonstrates that their vascular patterns reproduce the overlying pattern of the sole, toe, palm and fingerprints. Injected skin from human fetuses and freshly amputated limbs, when studied with the x-ray microscope, shows an underlying pattern of longitudinally disposed blood vessels lying parallel to and repeating the longitudinal pattern of the overlying skin ridges. Where a skin ridge forks, the underlying vessel pattern does likewise. Similarly, micrographs of digital pulp skin show that the subpapillary blood vessel pattern repeats the loop and whorl pattern of the skin friction ridges of the finger-tips and toe-tips in a striking manner (Fig. 5).

Higher magnifications demonstrate that the longitudinally disposed vessel pattern beneath the skin ridges consists of double rows of capillary loops (derived from small subpapillary arteries) whose venous ends



Fig. 5.—Microangiogram of skin of human toe showing that the subpapillary blood vessel pattern repeats the loop pattern of the overlying skin friction ridges (i.e. toe-prints), x 38.

terminate in a longitudinally disposed double row of venules that interanastomose and constitute the first subpapillary venous plexus. Projection micrographs of these capillary loops show a narrow arterial limb, a wider tip and a venous limb, which is usually hairpin-like in form but which occasionally appears as a twisted network.

Neither dissection nor traditional histological methods permit the tracing of the cerebral arterial tree in its entirety, but owing to the penetration and depth of field of x-ray microscopy it is possible to determine the course, connections, and volume pattern of the deeply placed microscopic vessels within the human brain and spinal cord.

Injection of the microscopic blood vessels of the brain with contrast medium is difficult, but the subject's eye may be used as a gauge of capillary filling, since the brain vessels are usually well injected when microangiograms show injectant within the iridial capillaries. Using projection x-ray

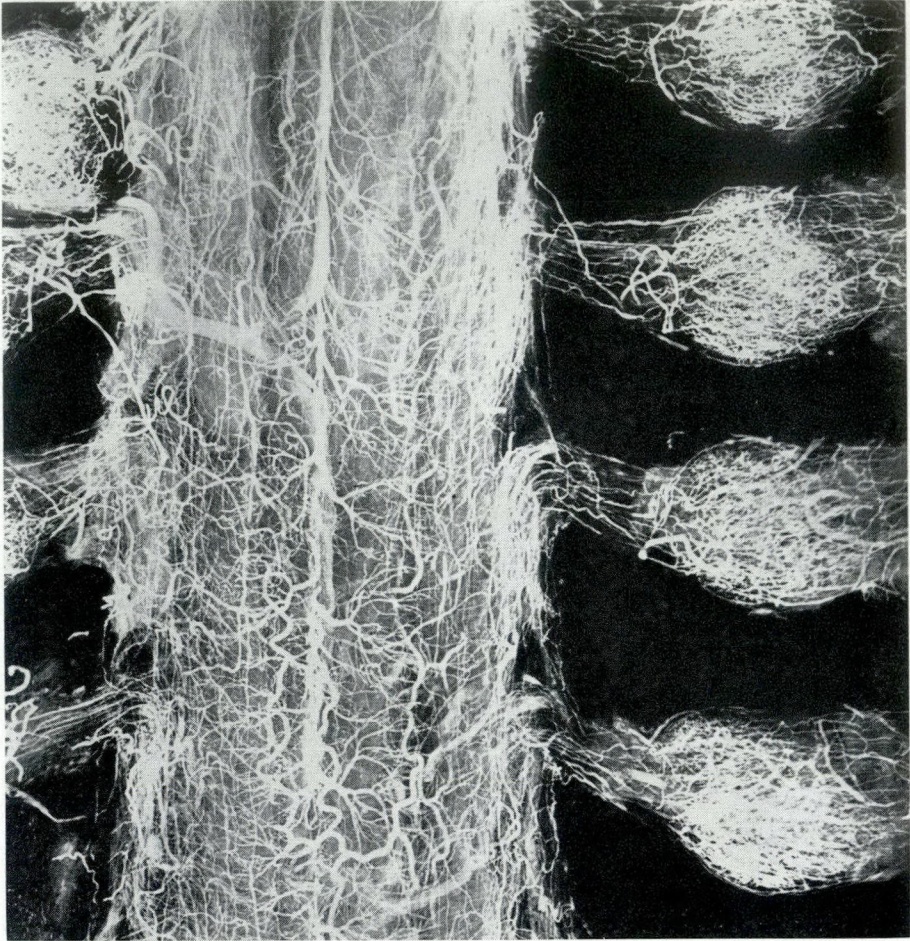


Fig. 6.—Projection microangiogram of human fetal spinal cord showing the peripheral system of blood vessels surrounding the cord, and central arteries in the midline. The nerve root (radicular) vessels and capillary bed in the posterior root ganglia are also shown, x 8.

microscopy it has been possible to record the coarse distributor network and fine capillary bed formed by the pial vessels on the brain surface. Such micrographs reveal almost three-dimensionally the short cortical arteries which supply the grey matter, and also the myriads of long transcerebral arteries which descend into the white matter to terminate in a periventricular capillary bed adjacent to the lateral ventricle. These pial and transcerebral vascular patterns suggest a hemodynamic mechanism concerned with cortical distribution or sub-cortical diversion. The extraordinary vascular density of the brain is well demonstrated.¹⁵

Vessels contributing to the intraspinal circulation, such as the radicular, peripher-

al and central arteries of the spinal cord, have similarly been recorded. For example, a microangiogram of the spinal cord (Fig. 6) shows the peripheral anastomotic network in the pia which surrounds and supplies the white matter. The anterior spinal artery can be seen in the midline, and also the brush-like central arteries which pass both to right and left of the midline to supply the grey matter of the cord. As many as four or five central arteries can be counted between one nerve root and the next. On either side of the spinal cord are seen the spinal nerve roots and their radicular arteries, as well as the rich capillary bed within each of the posterior root ganglia.

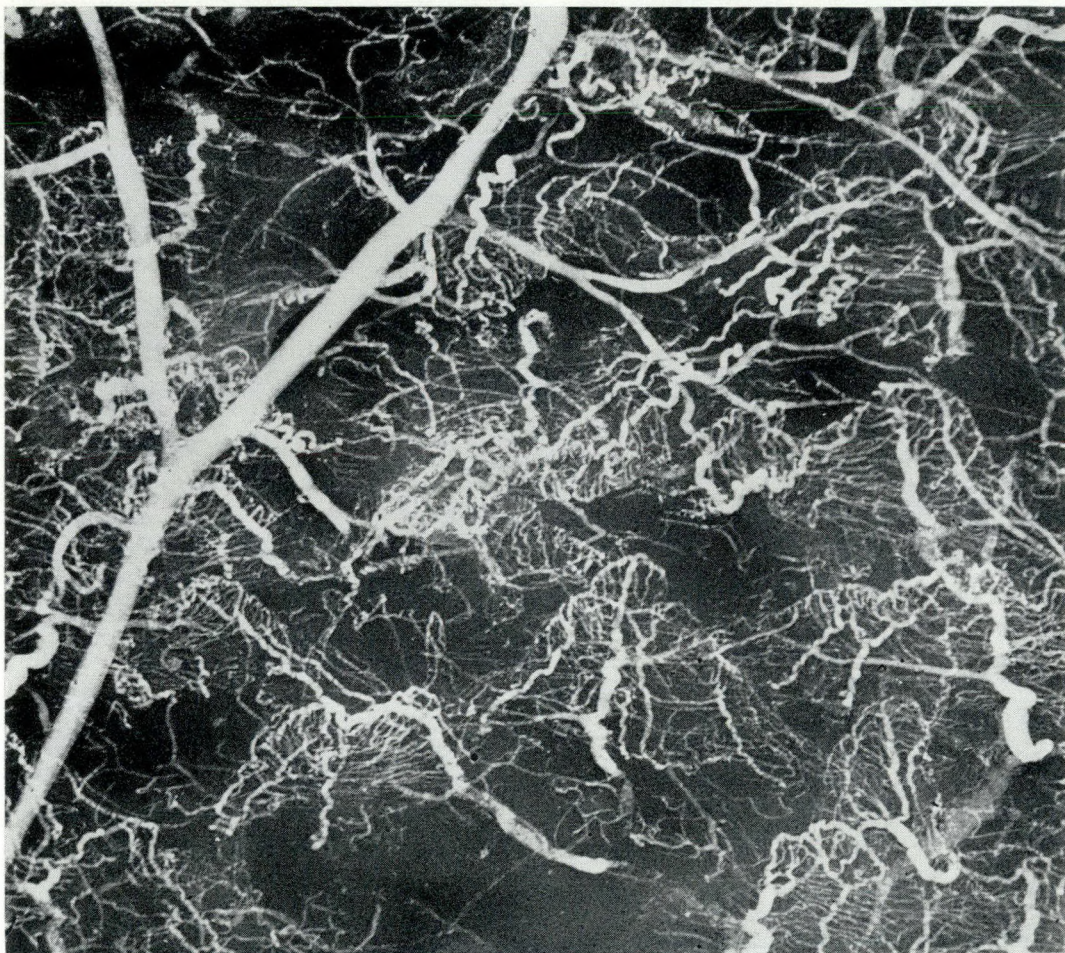


Fig. 7.—Projection micrograph of jejunum showing the villus arteries, capillary bed and draining venules of the intestinal villi. $\times 77$.

The microcirculation of the intestinal mucosa and its villi has been studied with the x-ray microscope because of current interest in peroral intestinal biopsy and certain malabsorptive disorders in the human.¹⁶ Also, basic knowledge of the structure and function of the intestinal villus and its vessels has been limited both by the opacity of the gut wall and the short focus of the optical microscope.

Injection of the minute blood vessels of the intestinal villi was achieved by infrarenal retrograde intubation of the rabbit abdominal aorta to effect a 'spill-over' of contrast medium into the superior mesenteric artery and its intestinal branches. Successive irrigation of the small intramural vessels of the intestine with body-warm solutions of a plasma expander

which has an anticoagulant action (Dextran sulfate) and a contrast medium of colloidal dimension (25% Micropaque) was then carried out. X-ray micrographs were then taken of the bowel loop or excised portion thereof while positioned across the target assembly of the x-ray microscope.

Such micrographs show numerous small mucosal arteries arising from both the main and subsidiary anastomosing branches of the submucosal plexus, each of which breaks up into a leash of two, three or more fine villus arteries to supply the adjacent villi. These villus arteries terminate in the capillary bed of the villus. The microangiogram of jejunum (Fig. 7) presented here shows the capillary network within a number of villi, and reveals that the capillary

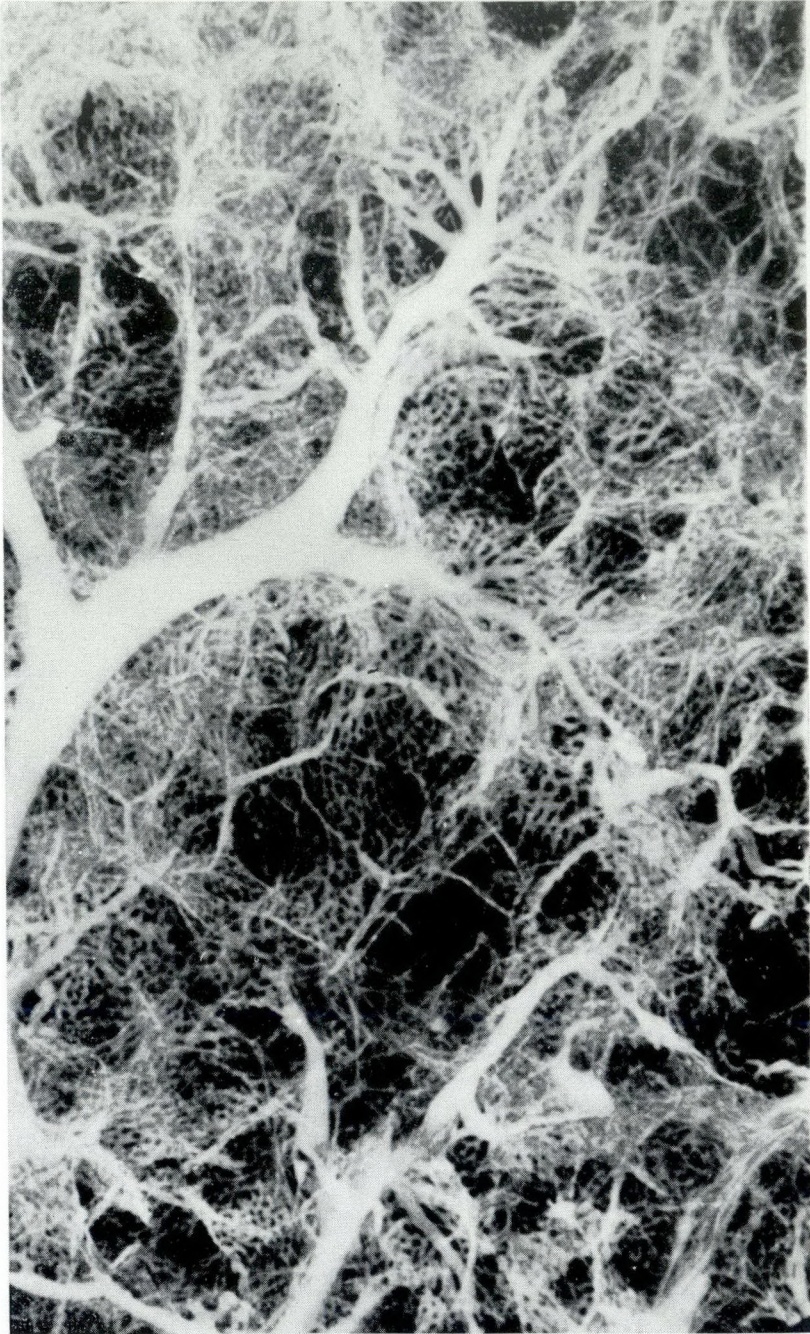


Fig. 8.—Microangiogram of human lung showing the terminal distribution of pulmonary artery branches and the capillary bed of the air sacs or alveoli. Note the honeycomb appearance of alveoli. Projection. $\times 90$.

network is derived from both the villus arteriole and subjacent submucous plexus. The large axial venules which drain the villi are a striking feature, and several are seen to converge upon a mucosal vein.

Micrographs taken at higher magnifications have confirmed the existence of an arteriovenous anastomosis or short circuit at the tip of the villus. Such short circuits apparently bypass the fine capillary net-

work of the villus when digestive processes are less active. Density counts of villi could be readily determined from x-ray projection micrographs.

Projection studies of the small blood vessels of the human lung which constitute the pulmonary microcirculation are currently in progress. Microangiograms taken of human lung after the injection of contrast medium (Fig. 8) demonstrate the terminal branches of the pulmonary artery, and the manner in which they break up into the capillary network within the walls of the air sacs or alveoli. The pulmonary capillaries are seen to arise abruptly from quite large vessels as well as from small ones, and form an almost continuous sheet of capillaries surrounding the alveoli. The fact that the mesh of the alveolar capillary net is frequently smaller than the diameter of the bounding capillaries, and that the network is common to two or more adjacent alveoli, will also be noted. The interalveolar septa seen end-on impart a honeycomb appearance to the air sacs. Veins arising from these capillaries do not immediately join the bronchioles but course in the septa. Other features which have been recorded include details of the vascular anatomy of the bronchi and bronchioles and the abutment of the alveoli upon these structures, and various morphological features connected with the bronchioles, alveolar ducts, interlobular septa and alveolar pores.

HISTORADIOGRAPHY

The study of tissue sections by x-rays has to date been carried out almost exclusively by contact microradiography using conventional histological techniques such as are employed in optical microscopy. Such techniques, however, are not wholly suited to x-ray microscopy, since they are attended by cytological changes and solution losses that produce detectable structural and density differences in comparison x-ray micrographs. Freeze-drying or substitution provides the best tissue fixation for x-ray microscopy, since they produce few or no chemical changes and remove only water, an important consideration when carrying out x-ray analyses at a cellular level.

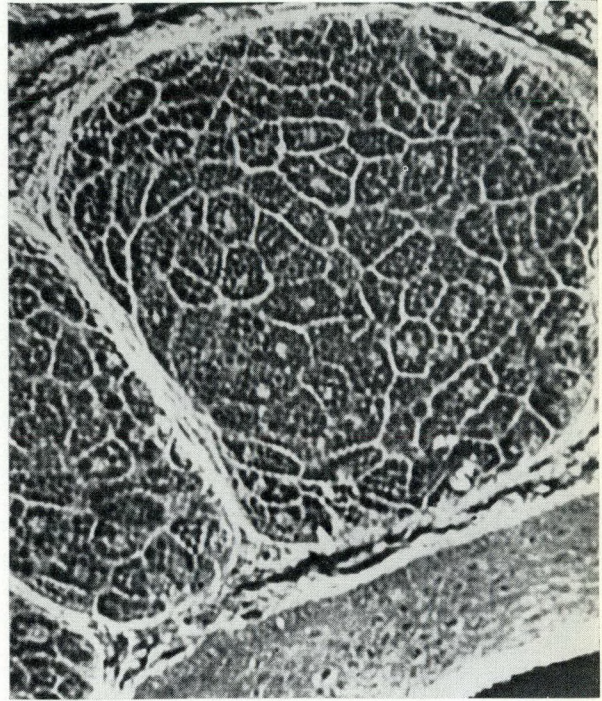


Fig. 9.—X-ray projection micrograph of human sebaceous gland showing dark lipid droplets within the cells and the marked absorption of the cell membranes and nuclei. $\times 500$.

Unstained animal and human tissues and cells can be examined with the x-ray microscope under atmospheric conditions, but preferably by attaching a vacuum camera to the target assembly of the instrument in order to reduce air absorption. Adequate contrast can be obtained with biological specimens of low atomic number provided soft enough x-rays are used, and useful ultimate magnifications of up to $\times 1100$ have been achieved.¹⁷

Tissues that undergo keratinization, mineralization, or which accumulate certain chemical substances (e.g. iodine, lipids) provide contrasty x-ray micrographs. The cells of the unstained human sebaceous glands are strikingly demonstrated by x-ray projection microscopy (Fig. 9). Several lobules encapsulated by connective tissue are shown adjacent to a hair follicle. The accumulation of lipid droplets (sebum) within the cells is strikingly recorded, since these appear as dark radiolucent spherules which contrast markedly with the white x-ray absorbent cell membranes and cell nuclei. Other micrographs have shown how

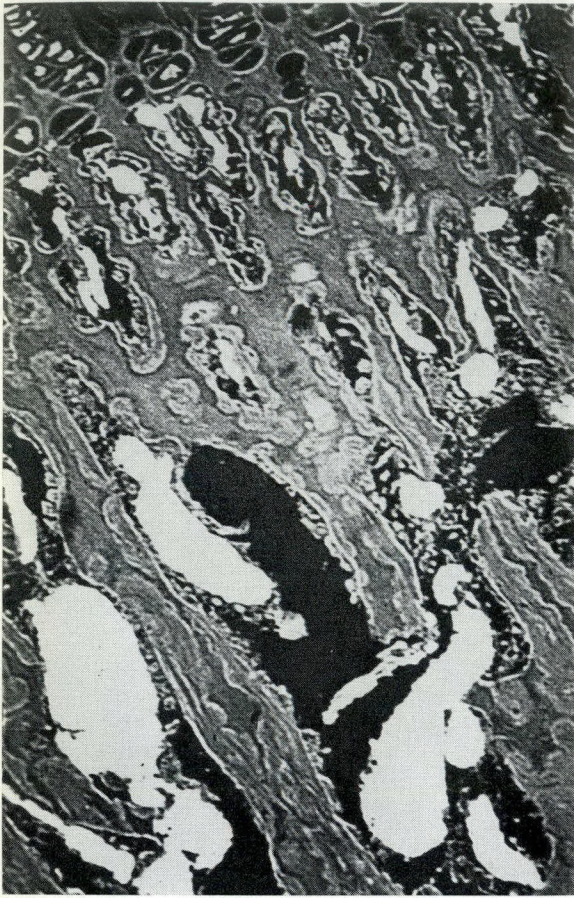


Fig. 10.—X-ray projection micrograph of a section of the epiphyseal growth zone of a rabbit tibia, showing young and calcified cartilage, osteoblasts along the marrow spaces, and blood vessels filled with contrast medium. $\times 450$.

these droplets coalesce to form a uniformly black cytoplasm about the nucleus before the breaking down of the mature cell. Note that the inner root sheath of the hair follicle appears white since its cells have undergone conversion to highly x-ray absorbent soft keratin. The hair itself has been displaced from the centre of the follicle, which consequently records black.

Mineralized tissues, such as developing teeth, cartilage and bone, provide contrasty micrographs even after decalcification. For example, a micrograph (Fig. 10) of a section through the epiphyseal growth zone of a rabbit tibia shows columns of wedge-shaped young cartilage cells, maturing and calcifying cartilage, and new bone being laid down on the cartilage cores in the process of trabecular formation.

Dark marrow spaces lined with osteoblasts can be identified, and also transected blood vessels which appear white since they are filled with contrast medium.

X-RAY MICROANALYSIS

Engström¹ and Lindström were the first to demonstrate how contact microradiographs of histological tissues taken at unit magnification could be studied by densitometry and the absorption measurements applied to elementary analysis and mass determination of cells.

Research in x-ray microscopy is now being directed also toward x-ray microanalysis; that is to say, to the application of the well-established principles of chemical analysis by x-ray methods to the problem of determining the nature and proportion of chemical elements in a specimen within areas of the order of 20 microns diameter. The individual dimension of the average mammalian cell ranges between 10 to 30 μ .

The basic mechanism underlying chemical analysis with x-rays is the fact that when matter is struck by high energy electrons (primary emission) or x-rays (secondary emission of fluorescence), its atoms respond by giving off x-rays whose wavelengths are characteristic of the chemical element at hand. Since these emission effects, and also those of x-ray absorption, have a strong wave-length dependence, the wave-length can be determined with suitable apparatus and the element both identified and estimated.

Microanalysis can be performed by primary emission, by making the specimen the target of the electron beam, and analyzing spectrographically the emitted x-ray beam to determine the elements present. Useful for metallurgical work,¹⁸ it has as yet limited application to biological specimens, although iron has been detected in small areas in both the rat tooth and the human lung by this method.

It will be evident that the magnification provided by the x-ray microscope permits the selection and detailed study of small areas within a specimen by direct absorption analysis with counters, without intermediate photographic recording. The rela-

tive transmission of different points in the specimen is measured directly by placing an aperture, above which is a spectrometer crystal and counter, at the required points in the projected image. Comparison of the transmissions at wave lengths on either side of the absorption edge of the element under investigation, immediately provides information on the mass of the element present. The transmission of any material is given by the equation $I = I_0 \mu/\rho^m$ where μ/ρ is the mass absorption coefficient and m the mass per sq. cm. of the absorber. Microanalysis by differential absorption has been applied to calcium estimation in rock sections and teeth by Long¹⁹ and Röckert.²⁰

The small focal spot and its high intensity per unit area make the projection x-ray microscope particularly suitable for fluorescence studies on the micro-scale. Adaptation of the microscope to fluorescence microanalysis is accomplished by placing a series of apertures (20 to 200 μ diameter) immediately over the target so that a small area of the specimen can be irradiated. The specimen, placed directly above the aperture system, is therefore within 2 to 3 mm. of the target. Fluorescent or secondary x-radiation emitted by and characteristic of the chemical element within the irradiated area is detected by a proportional counter placed to one side of the specimen at an angle of about 45° to avoid recording the primary beam. The fluorescence counter pulses are amplified, passed through a pulse height analyzer and then fed to a scaler. The method of measurement consists of comparing fluorescent intensities obtained from the specimen with those obtained from a reference standard containing a known amount of the element under study. Initial experiments devoted to the study of the amount of iron present in rat blood are encouraging. The minimum detectable mass of calcium in a specimen area defined by a 50 μ aperture was estimated at 7×10^{-11} g.²¹

It will thus be evident that x-ray microscopy lends itself to spatial localization and microchemical analysis of small tissue areas, and possesses as yet unrealized possibilities.

SUMMARY

X-rays are being used in microscopy because their shorter wave-lengths offer higher resolution of detail than light and permit the study of optically opaque objects. Because x-rays are absorbed and emitted in a specific manner they are particularly suited to microanalysis of tissue. Methods of obtaining magnified images with x-rays are reviewed, and the recently developed x-ray projection microscope which utilizes a point source to cast a projected image is described. Owing to its great depth of field, all parts remain in focus and can be recorded stereographically.

Microangiographic techniques and methods of studying microscopic blood vessels by projection x-ray microscopy in various organs and tissues are discussed. New evidence on the microcirculatory patterns of the human skin friction ridges, brain and spinal cord, intestinal villi, and lung is presented and described, as well as detail of the peripheral vascular network and arteriovenous anastomoses associated with skin vessels.

Applications to historadiography or the study of various sectioned tissues by projection x-ray microscopy are outlined. X-ray microanalysis of small tissue areas by the methods of primary emission, direct absorption analysis with counters, and fluorescence, is described.

The author would like to thank Miss Mary Bell, B.Sc., Miss Molly Clayden, Miss Sandra Power and Mr. Victor R. Carvalho for assistance with various aspects of this work.

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RÉSUMÉ

L'utilisation des rayons X en microscopie est une technique nouvelle qui est susceptible de trouver de nombreuses applications en biologie, en métallurgie et en médecine. La longueur d'onde des rayons X est considérablement plus courte que celle des rayons lumineux et par conséquent, le pouvoir de résolution du système peut être très augmenté. De plus les rayons X sont absorbés et réémis par les diverses substances d'une façon qui est spécifique et ceci peut mener à d'intéressants développements au point de vue histo-chimique. Plusieurs méthodes ont été proposées pour l'utilisation de ces rayons en microscopie. La plus ancienne et la plus simple de toutes, consiste à placer l'objet à observer en contact étroit avec une plaque photographique et à soumettre le tout à une irradiation X. Le résultat est une microradiographie de contact qui peut ensuite être examinée au microscope ordinaire. Il est bien évident qu'avec cette technique, le grossissement final se trouve limité par le grain de l'émulsion photographique; on a partiellement pallié à cet inconvénient en employant des émulsions sans grain, type Lippmann. Dans les années 1940, on construisit des microscopes à rayons X à miroirs; des rayons X mous doivent être utilisés et le microscope doit être rempli d'hélium pour éviter les pertes par absorption. Malheureusement ces microscopes à miroirs souffrent d'aberrations de courbure de champ et d'astigmatisme. Une troisième technique consiste à agrandir l'image par projection; dans ce cas, l'objet est traversé par des rayons X provenant d'une source ponctuelle très petite et l'image est recueillie à distance par simple projection. L'université de Dalhousie possède un de ces instruments dans lequel la surface de la source X est de l'ordre de 1 micron; le pouvoir de résolution est sensiblement égal à la taille de cette source. Les grossissements obtenus varient entre 100 et 1000, la variation de grandissement étant obtenue en variant la distance de projection. Les microradiographies en relief peuvent se faire facilement, par simple déplacement latéral de l'objet. Les études de la circulation sanguine peuvent grandement bénéficier de cette nouvelle technique. On peut en effet opacifier le trajet des vaisseaux et des capillaires par des injections spéciales et, grâce à la pénétration du faisceau de rayons X, grâce à la grande profondeur de champ du système et à la facilité d'obtention des clichés stéréoscopiques, de très belles images peuvent être fournies. Des études de ce genre peuvent être faites sur l'animal vivant.

CASE REPORTS

ADENOCARCINOMA OF ANAL DUCT ORIGIN

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WELL-DOCUMENTED reports of carcinomas arising from accessory structures of the anal canal are very rare. The author recently had occasion to study a tumour in which anal duct origin could be established beyond reasonable doubt.

CASE REPORT

History and clinical findings.—The past and family history of this 66-year-old white female patient are non-contributory. The patient had been constipated for several years. Six months before admission she began to experience anal pain and difficulty in passing stool, as though there was a mechanical obstacle in the anal canal. In the last two months, defecation was possible only with laxatives. Stools became watery and loose, with occasional traces of bright red blood.

The patient was admitted to the Ottawa Civic Hospital on June 13, 1961. She was well developed, well nourished and weighed 168 lb. Physical examination revealed no abnormal findings, except for those noted below. In particular, there was no palpable abdominal mass, and the inguinal lymph nodes were not enlarged. On rectal examination, a rigid and tender mass was palpable in the right half of the wall of the anal canal, partially obstructing the latter. Irregular firm projections, impressing themselves as nodular structures, with diameters of between 3 and 4 mm., were felt in and below the overlying anal skin and mucosa. The latter appeared thickened and infiltrated. The provisional clinical diagnosis was carcinoma of anus.

A biopsy was taken, followed by an abdominoperineal resection on June 22, 1961, which was performed by Dr. I. J. Vogelfanger. The patient made an uneventful recovery. However, the tumour recurred locally, and this necessitated a second operation on March 28, 1962.

Pathological findings.—Submitted for examination were the distal portion of the colon, with attached mesentery, and the entire rec-

tum including the anal canal and perianal skin. At the anorectal junction, firm greyish-white tissue was seen to infiltrate and replace the wall of the anal canal in approximately two-thirds of its circumference. While the anal mucosa appeared to be intact on gross examination, there was focal involvement of the perianal skin by tumour, in particular in the area of the previous biopsy. However, the bulk of the lesion presented itself in the deeper portions of the wall of the anal canal. The tumour was fairly well delineated, measuring 2.5 cm. in its long axis and up to 1.5 cm. in width.

Blocks from all areas of the anal wall, including adjacent portions of rectal mucosa and perianal skin, were processed and stained with hematoxylin and eosin. Step sections were prepared from some of the blocks. Sections from the anorectal junction showed orderly non-keratinizing stratified squamous epithelium at one end and normal rectal mucosa at the other, with an intervening narrow zone of stratified transitional epithelium. From the latter, several anal ducts, also lined by transitional epithelium, were seen to extend into the underlying stroma (Fig. 1) and into the muscle of the internal sphincter.

From one of these ducts, the tumour originates (Figs. 1-4). The orderly stratified transitional epithelium of this duct gives way to an irregular, thickened layer of cells with an increased nucleo-cytoplasmatic ratio. Many of the nuclei appear hyperchromatic, others are vesicular. Mitotic figures are rare. The neoplastic cells form gland-like and duct-like structures which extend into the surrounding tissue, infiltrating between the muscle bundles of the sphincter and into the anal skin. Some of the newly formed ducts bear a close resemblance to normal anal ducts (Fig. 5). Only a few mucin-containing cells are seen. Focally, the adenomatous pattern is less evident, and there are features suggestive of a weak attempt at epidermoid differentiation (Fig. 6).

The rectal mucosa was found to be invaded in one area only, and merely in its lower third (Fig. 4). The described changes in the adjacent anal duct, the histological character of the tumour and the direction of its spread,

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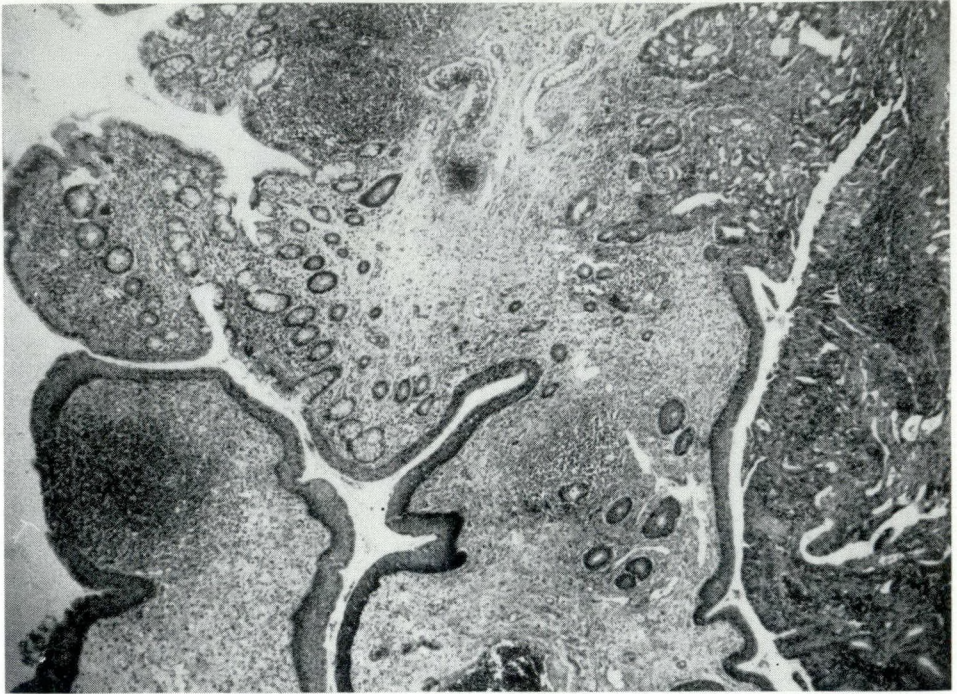


Fig. 1.—Junction of rectal mucosa and transitional zone with a normal anal duct at left, and anal duct giving rise to carcinoma at right.

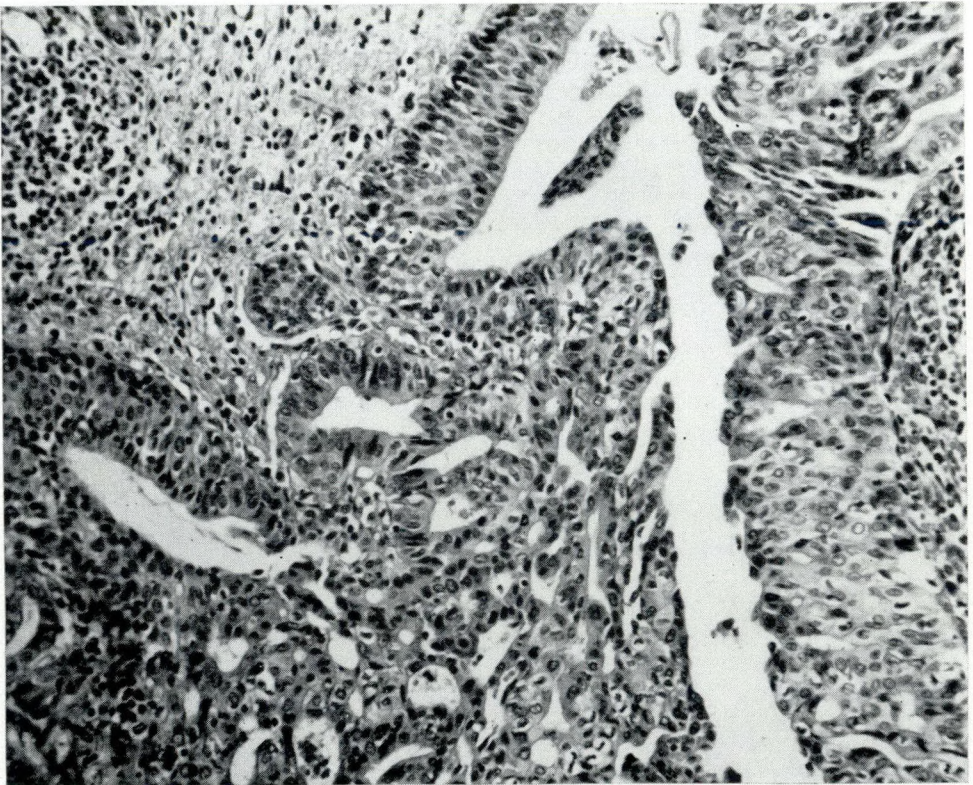


Fig. 2.—Higher magnification of anal duct pictured in Fig. 1. Note normal transitional epithelium in upper left, carcinomatous epithelium with formation of glands in lower left and right half of duct. Notice also duct-like neoplastic structure in centre.

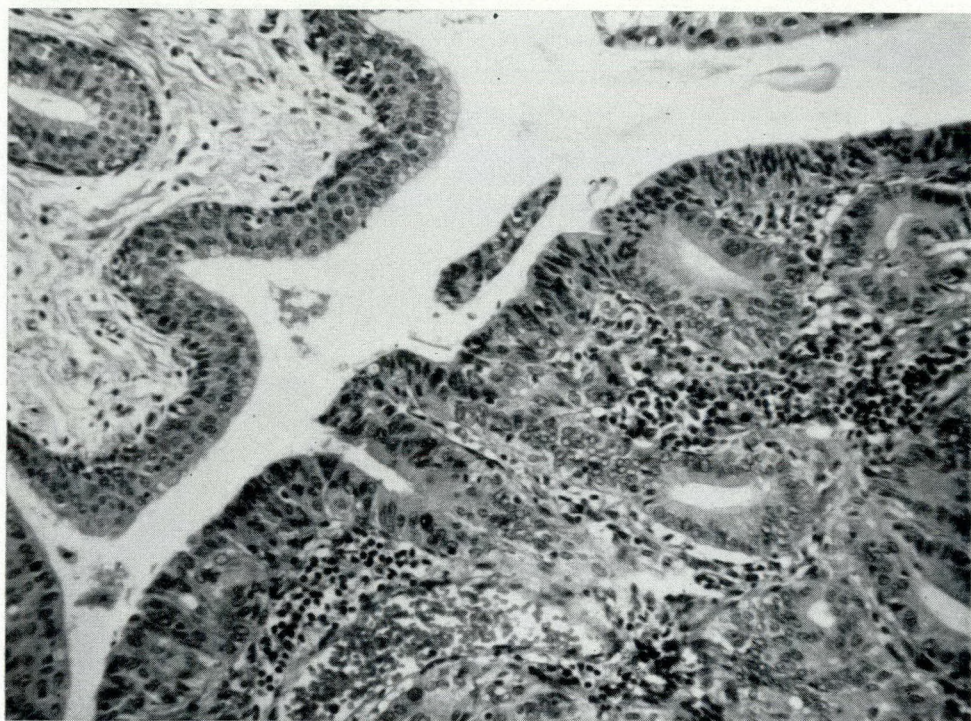


Fig. 3.—Another portion of the same duct. Note luminal layer of cylindrical cells containing mucin vacuoles in normal duct epithelium on left and well-differentiated carcinomatous epithelium with infiltration of the stroma on right.

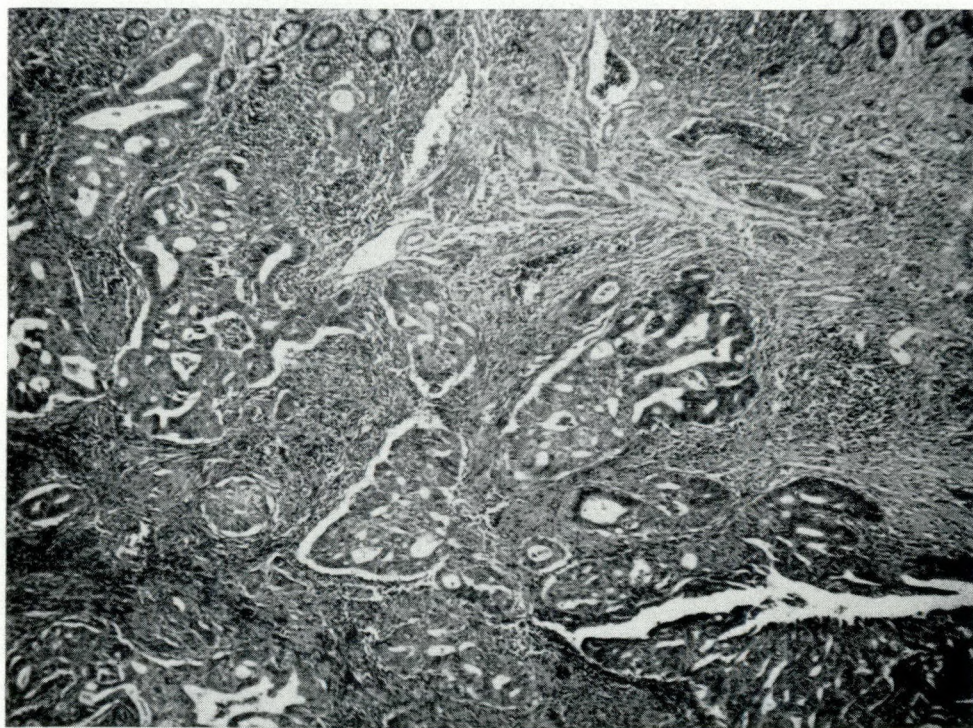


Fig. 4.—Carcinomatous duct at lower right; beginning of invasion of the rectal mucosa at upper left. The bulk of the tumour is below the duct (not in picture).



Fig. 5.—Neoplastic structures, resembling anal ducts, infiltrating between bundles of internal sphincter muscle (compare with Fig. 3 in Close and Schwab's paper⁴).

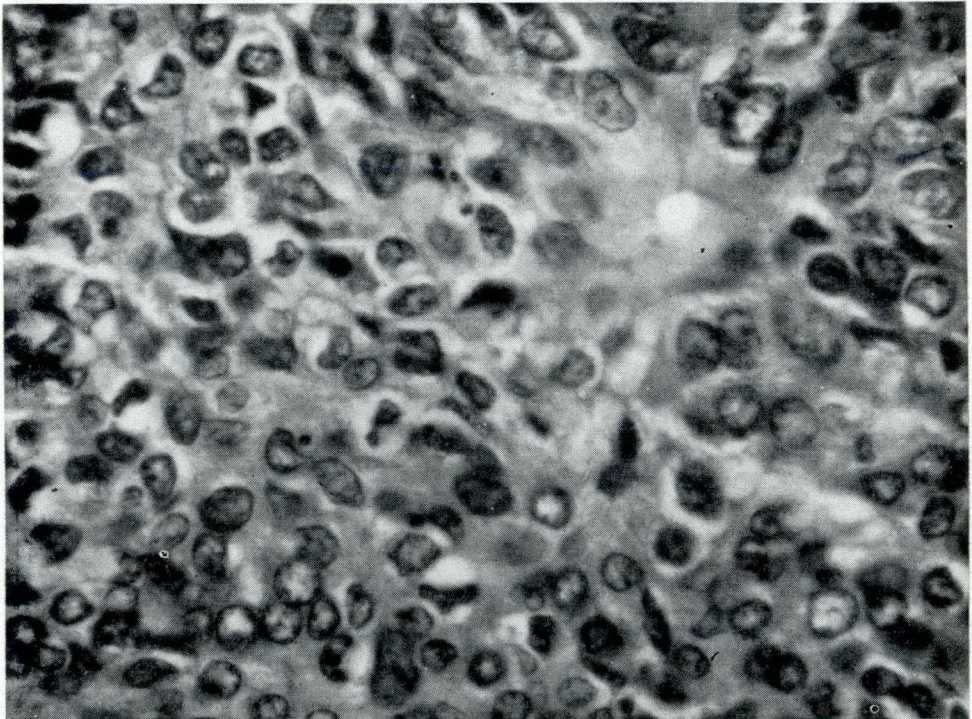


Fig. 6.—One of the few areas in which an epidermoid pattern is weakly suggested. However, note gland-like structure at upper right.

away from the rectal mucosa, exclude with certainty the possibility that this carcinoma originated from rectal mucosa.

DISCUSSION

The anal ducts and glands.—The normal histological structure of the anorectal area, neglected in most textbooks in which such discussion would be pertinent, has been ably described by a number of authors, most recently by Grinvalsky and Helwig,⁸ and others,^{2, 4, 15, 20} with reference to the work of earlier writers.^{3, 5, 10-12, 14} While a detailed review of these papers is outside the scope of this report, knowledge of certain histological features of this region is essential for a proper understanding of the pattern or patterns of anal duct carcinoma.

Between the rectal mucosa, which ends at the dentate line, and the anal mucosa, which begins at the anal valves, there is a narrow zone of transitional and sometimes stratified columnar epithelium which measures between 3 and 12 mm. in length⁸ and is thought to represent a remnant of cloacal entoderm. From the sinuses of Morgagni, which belong to this zone, ductular structures extend through the lamina propria deep into and sometimes even through the internal sphincter. Most of them are found in the posterior portion of the anal canal² and run in a caudad direction; rarely, they course cephalad. Their average number appears to vary with the individual; extremes are given as zero and four,⁸ six and eight,⁴ or one and 13.¹³ These ducts are long and tortuous and may divide into several branches. They are lined by transitional, less frequently by stratified columnar epithelium, with occasional stretches of squamous cells. The epithelial layer is four to six cells thick at the point of origin, gradually diminishing in height toward the ducts' blind ends. Cylindrical, mucus-producing cells are frequently interspersed.

Aberrant glands constitute a second set of accessory structures in the transitional zone between rectal and anal mucosa. They are short and tubular, with some branching; their lining consists of mucus-producing cylindrical cells surrounded by several layers of transitional or undifferentiated epithelial cells. They resemble

Littre's glands of the urethra⁸ and, like the latter, are entirely confined within the lamina propria of the mucosa.

Aberrant glands are less frequently identified than are anal ducts. The latter were found in 63 of 93 human specimens, whereas aberrant glands were present in only 24.² According to Kratzer and Dockerty,¹⁶ 51% of men have perianal glands. A connection between anal ducts and glands and the anal canal is not always demonstrable. Burke, Zavela and Kaump² were able to trace anal ducts to the crypts of Morgagni in only 39 of their 93 cases, while all of the fetal specimens examined by Hill *et al.*¹³ showed connection with the anal canal.

Carcinomas of anal duct origin.—Considering the varied character of the anorectal mucosa and its accessory structures, it is hardly surprising that carcinomas of this area display a bewildering variation in histological pattern. The presence of other histological structures in the immediate vicinity of the anorectal region, such as modified sweat glands, sebaceous glands and hair follicles, all of which may give rise to neoplasms, adds to the confusion. The resulting difficulty in properly classifying many of these tumours is clearly reflected in the great number of names under which tumours of this area have been reported.⁸

Apparently, Rosser,²² in 1934, was the first to draw attention to the anal glands as a possible site of origin of anal carcinomas. In the years since, a number of case reports have appeared in which the anal glands or ducts were implicated as the primary sites of carcinomas, but the total number of acceptable cases reported to date is still low, somewhere in the neighbourhood of 20.

Recently, an extensive review of the subject was presented by Pollice and d'Abbicco.²¹ These authors divide the known cases into three groups, according to localization: (1) anal; (2) perianal, perirectal and ischio-rectal, and (3) those developing in a fistulous tract. Since portions of anal ducts are normally found in any of the locations mentioned under (1) and (2), such classification seems to be of im-

portance mainly in view of the pathways of possible lymphatic spread which differ according to localization of the primary growth (see below).

The relationship of anal carcinoma, anal ducts and fistulae-in-ano is more complex and therefore more difficult to evaluate. A growing number of carcinomas following fistula-in-ano have been reported, but comparatively few have had a history long enough to rule out antecedent malignancy.²⁵ It is possible, and even likely, that some of these carcinomas stem from the anal ducts. Thus, the one or the other of the cases reported by Bru *et al.*,¹ Skir,²⁵ and others, may fall into this category, although, in our opinion, definite proof is lacking. To conclude as Zimberg and Kay³¹ do, that practically all anal carcinomas of extramucosal seat have their "logical common origin" in the anal ducts and glands, would seem to constitute undue simplification of the problem of the pathogenesis of tumours of this region. At present, our knowledge is insufficient to clarify this point.

Many of the larger tumours have destroyed their primary site or altered it beyond recognition, and the presence of inflammatory lesions, as in most carcinomas associated with fistulous tracts and in some others as well, may all but obliterate the last remaining traces of origin. It is therefore hardly surprising to find that a considerable number of authors^{2, 9, 15, 17, 25, 26, 28} are somewhat less than definite in their claim of an anal duct origin of their respective cases. Also, accompanying photomicrographs are often lacking or are inconclusive with respect to histogenesis.^{17, 18, 24, 27, 29, 31}

Our attempted tabulation of previously reported cases (Table I) deviates somewhat from those of other authors.^{4, 21, 30} For reasons mentioned above, we did not include two of Whimster's²⁸ cases (Nos. 2 and 3) or the cases reported by Skir²⁵ and by Bru and his associates.¹ Close and Schwab⁴ attribute two cases, "the first acceptable cases", to Tucker and Hellwig,²⁷ but we were unable to find more than one pertinent case (Case 4) in Tucker and Hellwig's original communication; further-

more, this report is not accompanied by photomicrographs and the description is very short.

Important clinical features of 19 confirmed or probable cases of anal duct carcinoma are listed in Table I. There is a significant preponderance of males (14:5), and only one patient was younger than 45 years. Most tumours measured between 1 and 5 cm. at the time of intervention, but some were allowed to assume larger proportions. In the majority of cases, clinical symptoms, chiefly rectal pain, bleeding, discharge, or difficulties at defecation, were present for from 6 to 18 months before operation.

Metastasis to the inguinal nodes was found in three or four cases at the time that the primary growth was discovered. The rate of recurrence is high, particularly if the tumour is treated by local removal only, and the carcinoma may spread to the regional lymph nodes and beyond. It should be remembered that the lymphatic spread from the rectum is mainly to the preaortic nodes and from the anal canal to the hypogastric glands, while the anus and perineum drain to the superficial inguinal nodes predominantly.⁶ A conventional abdominoperineal resection therefore will not result in a cure in all cases.^{15, 31} Some authors^{21, 23, 31} therefore suggest more extensive abdominoperineal resection which includes the pelvic fascia and the pelvic (inferior mesenteric, hypogastric and external iliac) lymph nodes. Inguinal node dissection may be warranted if the primary tumour is located in the anoperineal region. Patients who have undergone a less radical procedure should be followed up at regular intervals for at least five years after operation in order to detect recurrences.

The clinical diagnosis of anal duct carcinomas is difficult. In their initial stages, they do not involve the mucous membrane. Because of their comparatively slow growth, they may be mistaken for inflammatory lesions which are so frequent in this region. An adequate biopsy is the only procedure that will confirm or exclude a diagnosis of suspected malignancy. Repeated biopsies may be necessary.

TABLE I.—CONFIRMED OR PROBABLE CASES OF ANAL DUCT CARCINOMA

Authors	A* M†	Sex	Age	Presence of metastases when first seen	Treatment	Recurrence			Reported results
						Time interval between operation and recurrence	Local	Distant	
Manning ¹⁷	A	F	68	—	local	3 mo.	+	ing.§	Died 10 months after operation.
Tucker and Hellwig ²⁷ Case 4	A	F	45	—	local	—	?	?	Not stated.
Scarborough ²⁴	A	M	48	Brain, liver	local	—	—	—	Died after brain operation.
Willis ²⁹	A	M	80	—	—	—	—	—	Autopsy case. Death unrelated to tumour.
Burke <i>et al.</i> ²	A	M	64	—	local	—	—	—	Well after 2 years.
Martin and Dargent ¹⁸ Case 1	A	F	73	—	local	—	—	—	Well after 3½ years.
Case 2	A	M	65	—	local	—	—	—	Death after 4½ years, unrelated to tumour.
Gupta ⁹	A	M	50	—	APRϕ	—	—	—	Well after 6 months.
Whimster ²⁸ Case 1	A	M	53	—	local, then APR	3 yr.	+	ing.	Well 4 years after APR.
Kay ¹⁵ Case 1	M	M	67	—	APR	1 yr.	+	—	Lives, with recurrent tumour.
Case 2	M	M	35	—	APR	—	—	—	Well after 22 months.
Close and Schwab ⁴	M	M	54	—	local	—	—	—	Death after 15 months, unrelated to tumour.
Pollice ²⁰	A	M	64	—	local	4 yr.	+	ing.	Lives, with recurrent tumour.
Zimberg and Kay ³¹ Case 1	A	M	57	—	APR	—	—	—	Well at discharge; no follow-up.
Case 2	A	M	80	Inguinal nodes?	local	1 yr.	+	—	Persisting tumour after 13 months (incomplete removal).
Case 3	A	M	55	Inguinal nodes	APR	5 mo.	+	ing., liver	Died with metastases, 6 months after operation.
Pollice and d'Abbieco ²¹ .	M	F	48	Inguinal nodes	local	6 mo.	+	—	Lives, with recurrent inoperable tumour.
Xavier ³⁰	A	M	58	Inguinal nodes	local, then APR	1 yr.	+	—	Died after 5 years from unrelated disease.
Author's case	A	F	66	—	APR	9 mo.	+	—	Well after second operation.

*A = adenocarcinoma.
§ing. = inguinal nodes.

†M = mucoepidermoid carcinoma.

ϕAPR = abdominoperineal resection.

Histologically, 15 of the 19 tumours in Table I constituted adenocarcinomas, while only four were of mucoepidermoid character. However, three of the latter^{4, 15} showed adenomatous features as well, albeit only after prolonged search, as in Kay's second case.

The tumour reported in this paper is an adenocarcinoma. In a very few fields there were weak attempts at epidermoid differentiation (Fig. 6). The formation of duct-like structures was apparent in several areas (Fig. 5). The internal sphincter

muscle was extensively involved and contained the bulk of the neoplasm.

As in other cases,^{4, 29} the tumour had spread in an annular extraluminal manner around the anal canal; mucous membrane invasion had just started (Fig. 4).

SUMMARY

A case of an adenocarcinoma of anal duct origin is reported. The normal histological structure of the anorectal region and previously recorded cases of anal duct carcinoma are reviewed with regard to clinical and morphological features.

ADDENDUM

After completion of the manuscript, another case of an adenocarcinoma of anal duct origin came to our attention.³² It concerns a 52-year-old man who died 3½ months after an extensive abdominoperineal resection; metastatic tumour was found in the inguinal and hemorhoidal lymph nodes as well as in the lungs and liver.

I am indebted to Drs. I. J. Vogelfanger for permission to use the clinical findings, and to Max O. Klotz, Director of Laboratories, Ottawa Civic Hospital, for advice and criticism during the preparation of this paper. I am also grateful for assistance from Mrs. E. Kidd, Hospital Library, and Miss E. Dahlschen, Department of Photography.

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RÉSUMÉ

Histoire d'un cas. Une femme de 66 ans est admise pour un syndrome de constipation accompagné de douleurs anales à la défécation. L'examen physique ne montrait rien de bien particulier: la malade était en état de nutrition satisfaisant, aucune tumeur abdominale n'était palpable. Par contre le toucher rectal permit de sentir une masse indurée dans la moitié droite de la paroi anale; cette masse était d'une taille suffisante pour obstruer le canal en partie. Une biopsie, suivie d'une amputation abdomino-périnéale fut pratiquée. Les suites opératoires furent sans histoire, néanmoins il y eut une récurrence locale neuf mois plus tard. Au point de vue anatomopathologique il s'agissait d'une tumeur située à la jonction recto-anale; la peau de la région péri-anale faisait partie de la néoplasie. L'examen microscopique révéla une origine anale. L'intérêt de ce cas réside dans la rareté de telles tumeurs. A cette occasion, la littérature qui s'y rapporte est passée en revue.

EPIDERMOID CARCINOMA ARISING WITHIN THE BONE IN CHRONIC OSTEOMYELITIS: REPORT OF A CASE*

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It is often not appreciated that epidermoid carcinoma complicating chronic osteomyelitis may arise deep within a sinus tract and grow as an intraosseous neoplasm. Yet in 11 of the 50 previously reported cases of epidermoid carcinoma complicating chronic

until four years later after two major operations, the nature of which he could no longer recall. Sinuses in the right thigh discharged intermittently upon the skin for the ensuing 39 years. In August 1960 a dull aching pain of a few weeks' duration preceded the devel-

TABLE I.—REPORTED CASES OF MALIGNANT CHANGE OCCURRING AT DIFFERENT LEVELS WITHIN FOCI OF CHRONIC OSTEOMYELITIS

	Number of cases	Deep within bone	Superficial on skin surface	Deep within bone and on skin surface
Hitzrot ¹⁰	1		1	
Benedict ¹	12		6	4
Blanco ³	2	1		1
Henderson and Swart ⁹	5	1	4	
Stewart <i>et al.</i> ¹⁷	1	1		
Bereston and Ney ²	2			2
Neibauer ¹⁵	2	2		
McAnally and Dockerty ¹³	9	2	6	1
Marks and Turner ¹²	3		1	2
Lovell <i>et al.</i> ¹¹	8	1	5	2
Devas ⁶	1			1
Rowlands ¹⁶	1			1
Bowers and Young ⁴	3	1		2
Total.....	50	11	23	16

osteomyelitis,^{1-4, 6, 9-13, 15-17} no evidence of cancer appeared upon the skin surface (Table I). In the eight cases of Lovell, King and Alldredge,¹¹ the three cancers that involved bone were discovered only by histological examination after amputation of affected limbs; and one of these "deep" cancers was discovered only four months after amputation, when a sinus tract in the amputation stump was biopsied. Because metastasis may occur it is important that cancer arising in a chronically inflamed bone should be recognized early, as in the case that follows.

CASE REPORT

The patient, a 57-year-old male wood-yard worker, suffered an injury to his right knee at the age of 14 years. He was unable to walk

opment of an abscess in the deep tissues of the right thigh. When the abscess ruptured spontaneously, four new discharging sinuses appeared. During November 1960, two episodes of bleeding occurred from these sinuses. Because the pain in his thigh became increasingly severe and the discharge from the sinuses increasingly foul and copious, the patient sought medical attention on March 21, 1961, and was admitted to the Ottawa General Hospital on the following day.

Physical examination revealed a well-nourished white male with a temperature of 100° F., pulse 90/min. and a blood pressure of 150/80 mm. Hg. Other abnormal findings were limited to the right lower limb which was fixed at the knee in approximately 15° of flexion. On the skin of the tender and swollen right thigh, six sinuses exuded a seropurulent discharge.

Laboratory procedures revealed mild anemia; the hematocrit was 34% and the erythrocyte sedimentation rate was elevated. The serum alkaline phosphatase level was 5.9 Bodansky units.

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Fig. 1.—Radiograph of femur. There is thickening with irregular sclerosis of the shaft and a large oval defect at the junction of the lower and middle thirds. This represents the area of intraosseous epidermoid carcinoma.

The report of the radiological examination (Fig. 1) was as follows: "There is considerable thickening of the whole length of the femoral shaft with irregular sclerosis. The normal architecture of the bone is completely replaced by an irregular trabecular structure without any differentiation between cortex and medulla. The neck and head of the femur are not involved in this process. There is in addition complete bony fusion of the knee joint. At approximately the junction of the lower and middle thirds of the femur there is an irregular roughly oval defect in the bone about 8.0 cm. x 5.0 cm. which is accompanied by

slight expansion of the shaft at this level. The margins of this defect are in places well defined and slightly sclerotic; in other places the margins of this defect are ill defined and irregular. There are some irregular fragments of dense bone in the soft tissues of the femur lateral to this bony defect. No periosteal reaction is visible in the femoral shaft. The appearance suggests extensive remodelling of the femoral shaft associated with chronic osteomyelitis. The large defect in the shaft has many of the features of a large cloaca associated with separation and extrusion of a previous large sequestrum, but in places the irregular osteolysis of the edge has some features of malignant invasion."

A biopsy of the femur, at the junction of middle and lower thirds, was done. The bone was replaced on its anterolateral aspect by soft reddish-white friable tissue. After the pathological report of squamous cell carcinoma, a guillotine amputation a few inches below the greater trochanter was carried out in the usual manner.

Although the advisability of performing a disarticulation at the hip had been considered, pathological study of the amputated limb showed the level of amputation to be well above the carcinoma. Consequently, no further operation was performed and the patient was discharged from the hospital on May 31, 1961, in good condition and wearing a prosthesis.

Pathological Findings

When the amputated limb was frozen and split longitudinally with a band-saw, six sinuses were traced from the skin of the thigh through the deep connective tissues into a firm grey-white, partly cavitated, intraosseous mass, measuring 9 x 4 cm. and centring in the lower third of the femoral shaft (Fig. 2). Anterolaterally this lesion replaced cortical bone for a distance of 3.5 cm. and extended into the adjacent soft tissues for a distance of 0.5 cm.

Microscopical examination showed intraosseous epidermoid carcinoma (Figs. 3 and 4) with strands and islands of tumour cells growing amidst a dense collagenous stroma. Keratinization was marked and many clumps of tumour cells contained keratin "pearls". The adjacent bone was sclerotic. The sinus tracts were lined by stratified squamous epithelium, showing pseudoepitheliomatous overgrowth contiguous at deep levels with the cancer.



Fig. 2.—Photograph of longitudinally sectioned femur. The intraosseous tumour mass is partially cavitated.

DISCUSSION

In 1847 Rokitansky recognized epidermoid carcinoma within a chronically inflamed bone.⁷ He attributed this neoplasm to malignant transformation in down-growths of squamous epithelium which had penetrated from the skin into the bone by way of sinus tracts. This explanation of intraosseus epidermoid carcinoma was upheld in 1931 by Brunschwig⁵ and by Milgram,¹⁴ who described the process of epithelialization of sinuses and bone cavities in chronic osteomyelitis. Brunschwig ascribed malignant transformation in epithelialized sinus tracts and bone cavities to the irritative effects of chronic infection, but McAnally and Dockerty¹³ questioned the "chronic irritative" postulate, because cancer occurred only in 0.23% of 4000 cases of chronic osteomyelitis reviewed at the Mayo Clinic. Henderson and Swart⁹ re-

ported cancer in only 0.208% of 2396 cases of chronic osteomyelitis. Because of such figures, Marks and Turner¹² suggested that etiological factors other than chronic infection should be considered. Such factors are probably to be sought in the as yet incompletely defined relationships of pseudoepitheliomatous hyperplasia to cancer.

White and Weidman,¹⁸ describing pseudoepitheliomatous hyperplasia at the margins of cutaneous ulcers, noted that lesions diagnosed microscopically as malignant do not necessarily exhibit malignant behaviour. These authors contend that it may be impossible, by histological examination, to distinguish some examples of well-differentiated squamous cell carcinoma from pseudoepitheliomatous hyperplasia, and suggest that such events as recurrence, tissue invasion and destruction, metastasis and development of anemia and cachexia

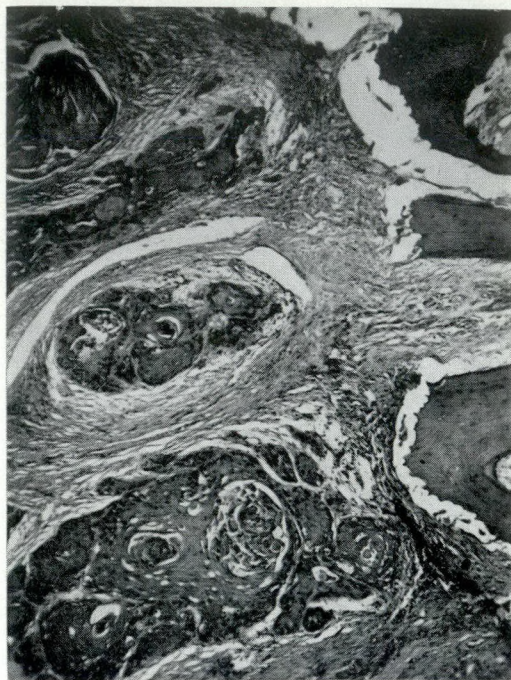


Fig. 3.—Microphotograph of intraosseous tumour. Masses of epidermoid carcinoma are growing in a dense collagenous stroma. Bone trabeculae are seen at the right.

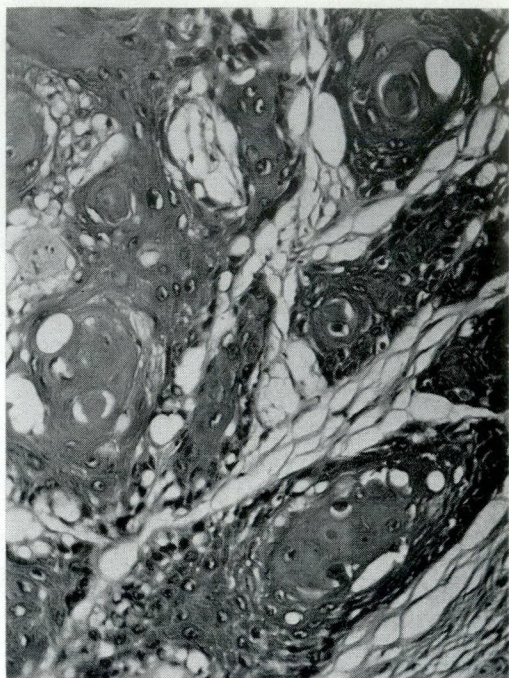


Fig. 4.—Microphotograph of intraosseous tumour. A high power view showing islands of epidermoid carcinoma with central keratin "pearls".

may be required to establish a diagnosis of malignancy. It is clearly impractical to apply criteria of this sort to patients whom one hopes to treat successfully. In our case, erosion of bone and the extraperiosteal extension of tissue, which was histologically consistent with epidermoid carcinoma, seemed to provide sufficient objective grounds for the diagnosis of epidermoid carcinoma.

Bereston and Ney² noted that cancerous complications usually occurred in males of 40 to 60 years of age who had suffered from chronic osteomyelitis for a period of two to three decades. The onset of malignancy in the present case may have dated only from August 1960. Cancer was suspected because pain had recently developed in the thigh, together with bleeding from newly formed sinuses and an increase in the foulness and amount of discharge. When such findings, long established as suspicious,⁸ occur and the danger of metastasis is appreciated, the rationale for a radical approach to this condition, that is to say amputation well above the site of the

cancer, becomes obvious. For patients, such as the present one, who have been so treated and in whom no metastases have occurred, the prognosis is probably excellent.

SUMMARY

A patient is described in whom epidermoid carcinoma arose within the femur in an epithelialized chronic osteomyelitic sinus. The medical literature on this subject is reviewed.

We are indebted to Dr. Conway Don for the radiological report.

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RÉSUMÉ

Histoire d'un cas. Un homme de 57 ans avait été blessé au genou droit à l'âge de 14 ans; cet accident avait entraîné une impossibilité de marcher pendant quatre ans et il avait subi deux interventions chirurgicales dont il est impossible de préciser la nature. De nombreux sinus continuèrent à drainer d'une façon intermittente pour une période de 39 ans. Pour ce qui est de l'histoire actuelle, un abcès s'est formé depuis une année, abcès qui suppure interminablement et se complique. A la suite d'une hémorragie provenant de cette plaie, le malade est admis à l'hôpital. L'examen général ne montre rien de particulier sauf une température de 100° F. et une ankylose du genou droit bloquant celui-ci à 15° en flexion: dans cette dernière région, la peau est tuméfiée et il se fait un écoulement séro-purulent par six orifices anfractueux. La radiographie montre une soudure osseuse totale de l'articulation du genou et, dans le tiers moyen du fémur, une perte de substance osseuse ovale de 8 x 5 cm.; le radiologiste n'exclut pas la possibilité de lésions malignes. On effectue une biopsie qui conclut à l'existence d'un carcinome; le membre est amputé quelques pouces en dessous du trochanter. Les suites opératoires furent sans histoire et le malade put être renvoyé à domicile. L'anatomie pathologique permit de préciser le diagnostic. Il s'agissait d'une ostéomyélite chronique avec présence au niveau du tiers moyen du fémur d'un carcinome épidermoïde kératinisé. Ce genre d'association morbide est connu. Les auteurs procèdent à une revue de la littérature se rapportant à ces cas.

HOME TREATMENT IN INJURY AND OSTEOARTHRITIS. W. E. Tucker. Foreword by Sir Harry Platt. 80 pp. Illust. E. & S. Livingstone, Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1961. \$1.90.

HOME TREATMENT IN INJURY AND OSTEOARTHRITIS. Instructions to Patients. W. E. Tucker. 42 pp. Illust. E. & S. Livingstone, Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, 1961. 65c.

This book and booklet combination is designed for the doctor in practice and his patient. The author has compiled a series of leaflets into a 40-page booklet for patients and these are well illustrated with line drawings. A concentrated two-page instruction regarding diet is also included.

Instructions are detailed and simple. Undoubtedly they represent a concise construction form which relieves the practitioner from the time-consuming responsibility which many of us find a burden and a bore in private practice. However, it is doubtful if the diagram on page six in reference to active alert posture would pass as coming from London rather than California! The descriptive captions include "navel press-buttoned to spine" and "buttocks pinch-proof". It would be unfortunate if a slumped posture were to be internationally interpreted as an invitation in the latter regard!

This is another interesting booklet in the realm of patient instruction forms and is particularly helpful to the person engaged in the treatment of osteoarthritic patients.

ACUTE DUODENAL OBSTRUCTION SECONDARY TO HEMATOMA

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ACUTE intestinal obstruction secondary to traumatic hematoma is a rare occurrence. Periodically, however, cases of intestinal obstruction are reported which are due to hematoma, usually in the region of the duodenum.¹⁻²³

The hematoma is usually traumatic in origin, although some may originate spontaneously in tumour or pancreatitis.^{26, 27} The source of bleeding may be retroperitoneal, intramural, subserosal or submucosal. The majority of cases occur in childhood, although it can occur in adult life.

This is a report of three new cases, two children and one adult, and a discussion of the etiology, diagnosis and treatment of acute duodenal obstruction due to hematoma.

CASE REPORTS

CASE 1.—L.C., a 6-year-old white boy, fell from his tricycle and received a minor blow in the right upper quadrant of the abdomen from the handle-bar. This injury was not sufficient to stop him from playing, nor from eating a normal meal a few hours later. Soon after the meal, however, he complained of upper abdominal pain and vomited. Subsequently he felt weak and nauseated, and vomited everything that he took by mouth. There had been no previous history of gastrointestinal disturbances and he had normal bowel function up to the time of injury. There was no evidence of cranial, cerebral, or other serious associated injury.

On admission to hospital 12 hours after his injury, the patient appeared to be acutely ill, although clinically he was not in a state of shock. The abdomen was not distended. The abdominal wall showed no evidence of external injury. There was some muscle guarding and tenderness in the right upper quadrant, but no masses were palpable in the abdomen. Rectal examination was normal and there was no evidence of rectal bleeding. The hemoglobin was 13.5 g.

During the next three days the boy became irritable and restless. He vomited everything

he took by mouth and the vomitus occasionally contained bile. He had no further bowel movements, but his abdomen did not become distended. The abdominal tenderness noted in the initial examination persisted in the right upper quadrant and bowel sounds were present although reduced.

The cardiac rate increased to 120 per minute and the patient's hemoglobin dropped to 9.2 g. Throughout this period of his hospital stay, he had a low grade fever.

An upper gastrointestinal series performed at this time showed an obstruction to the second portion of his duodenum, and the diagnosis of duodenal obstruction due to extrinsic pressure from a localized retroperitoneal hematoma was made (Fig. 1).

Conservative treatment was administered for eight days after his admission. This consisted of intravenous fluids, continuous gastric suction and sedation. On the eighth day, because complete obstruction persisted, a laparotomy was performed. Under anesthesia, a firm, fixed, smooth, rounded mass became palpable in the right upper quadrant of the abdomen. On opening the peritoneal cavity a retroperitoneal hematoma was seen which was localized to the region of the duodenum; some blood-staining extended down the right side to the region of the hepatorenal pouch of Morison. The entire bowel distal to the obstruction had collapsed. The overlying peritoneum was incised, over 75 c.c. of thick fluid blood was aspirated and a latex rubber drain was sutured into the cavity.

Postoperatively the patient was treated by means of intravenous therapy for 72 hours and gastric suction for 48 hours. Gastrointestinal function returned to normal on the third postoperative day. The latex drain produced a further 50 c.c. of thick dark blood. A minor degree of atelectasis of the right lower lobe occurred on the second postoperative day, but rapid re-expansion was obtained. Soon after, the patient made an uneventful recovery.

CASE 2.—J.Mc., an 8-year-old boy, received a minor blow to the epigastrium while playing hockey. This injury was not sufficiently painful to interfere with his game, and he seemed to be well until several hours later when he developed right upper quadrant pain. On the following day this pain increased in severity

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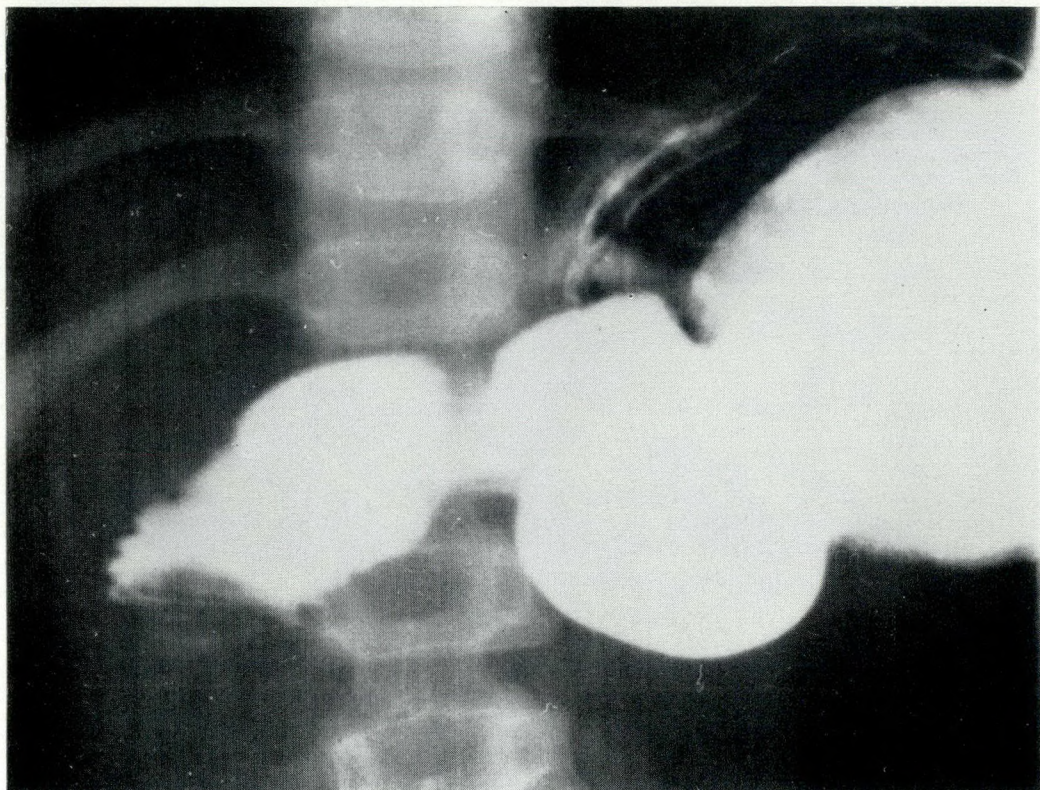


Fig. 1.—Case 1. L.C. A film taken during a gastrointestinal series shows obstruction at the second portion of the duodenum.

and was aggravated by movement. Vomiting began soon after and he was brought to hospital.

On admission, 24 hours after his injury, he appeared to be moderately ill and was in pain. The boy was not in circulatory collapse and there was no evidence of abdominal wall injury. There was some tenderness about the umbilicus and in the right upper quadrant of the abdomen, associated with some degree of muscle guarding and rigidity. Bowel sounds were decreased. There were no palpable masses. His oral temperature was 99° F. and the leukocyte count was 11,500/c.mm. He continued to vomit all oral intake and was placed on continuous intravenous fluids and gastric suction. He developed an intermittent fever with peaks of up to 103° F. and his pulse rate continued at the rate of 110 per minute. The leukocytosis increased to 25,000/c.mm.

After 15 days he was still unable to retain oral feedings and the results of a gastrointestinal series revealed evidence of obstruction at the junction of the second and third parts of the duodenum, presumably owing to extrinsic pressure (Fig. 2).

The child was given a transfusion of 750 c.c. of blood during this period. By the seventeenth day of his illness it was felt that the obstruction would not respond to conservative management and a laparotomy was performed. A fluctuant hematoma was localized behind the third part of the duodenum and was most prominent on the left side of the vertebral bodies. The mass was approached from below the transverse mesocolon lateral to the first part of the small bowel mesentery. A large amount of necrotic dark fluid blood was drained and the obstruction relieved.

Postoperatively, treatment by means of intravenous fluids and gastric suction was continued intermittently for several days. His general condition improved steadily, and he made an uneventful recovery.

CASE 3.—J.V., a 22-year-old mechanic, sustained a minor injury to his midabdominal region when he was squeezed between a garage door and an automobile. At the time, his only symptoms were transient dizziness and pain localized to the area of injury.

He was admitted to St. Joseph's Hospital shortly after the accident with a minor skin

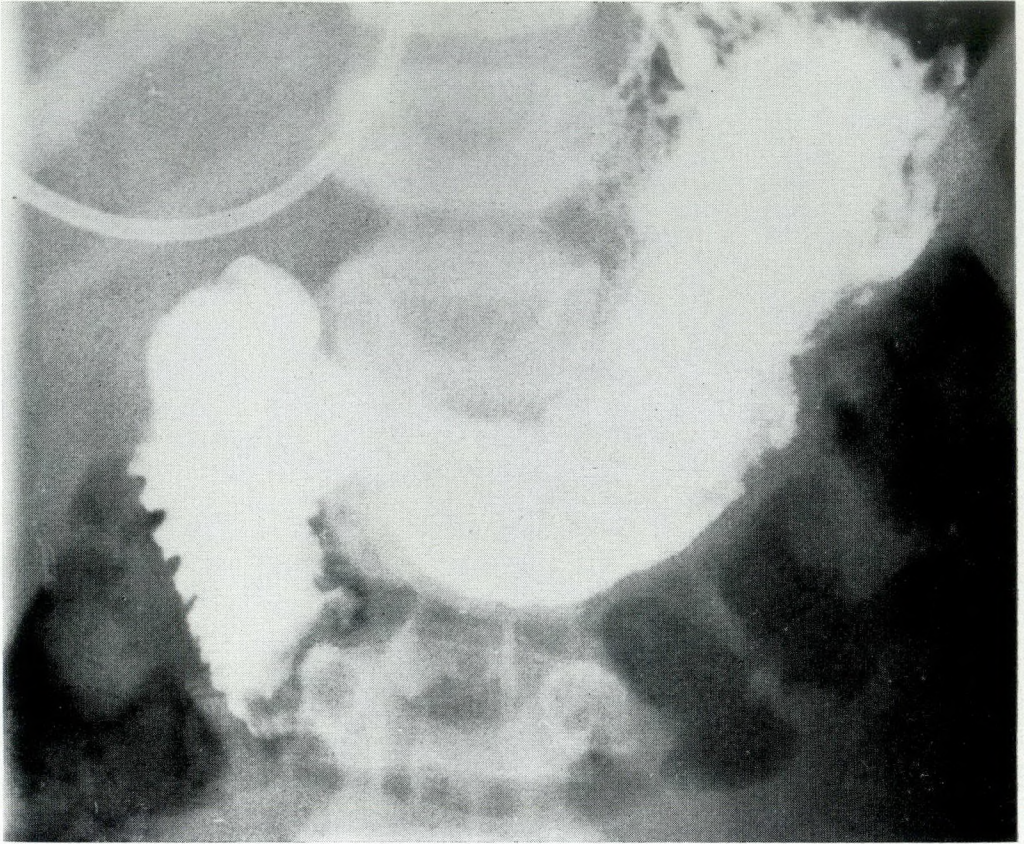


Fig. 2.—Case 2. J.Mc. A gastrointestinal series shows obstruction below the second portion of the duodenum.

abrasion in the umbilical region, and some tenderness of the anterior abdominal wall. The physical examination was otherwise normal and he was allowed to return to work. Over the next three days the man experienced some midabdominal discomfort of gradually diminishing severity.

On the fourth day after the accident, while sleeping, he had a sudden exacerbation of midabdominal pain which progressively increased in severity and was soon accompanied by vomiting of clear gastric content. The pain radiated to the right lower quadrant and into both testes. Muscle guarding and tenderness were present in both the epigastrium and right upper quadrant of the abdomen. There were no palpable masses and the bowel sounds were normal. His temperature was 98.4° F.; the cardiac rate, 84 per minute and regular, and the leukocyte count, 10,800/c.mm. Urinalysis was normal and the serum amylase was 32 Somogyi units.

In spite of the history of injury, a preoperative diagnosis of appendicitis was made.

As in the previous two cases, laparotomy revealed a large, tense retroperitoneal hematoma which was confined to the region of the duodenum with obstruction of the third part. The intestine distal to the obstruction was completely collapsed and a simple gastroenterostomy was performed to bypass the obstruction.

Postoperatively the anastomosis was functioning by the third day, and the patient made an uneventful recovery.

DISCUSSION

Etiology.—These three cases illustrate the usual problems related to the etiology, diagnosis and treatment of acute duodenal obstruction secondary to hematoma. In most instances the trauma is mild and symptoms are delayed. It is probable that perforation of the duodenum occurs with more severe trauma, and more commonly in adults.

The nature of the injury would appear to be a shearing or crushing of the relatively fixed duodenal tissues between the external object and the vertebral bodies.

The exact origin of the bleeding was not apparent in any of our cases. It is likely that the bleeding site will be inconstant, depending upon the exact angle and force applied by the crushing object. Certainly the origin is seldom obvious.

The delayed onset of symptoms may be related to slow, continued bleeding with associated edema, or to the late enlargement of the hematoma by the osmotic imbibition of water. Whether the obstruction is purely mechanical, or is related to local interference with the nerve supply, is not established.

Most of the cases are in active children, but Glass⁵ reports hemorrhage in a newly born infant, causing intestinal and biliary obstruction, and Bergman and Crowson²⁷ report a case in a patient 76 years of age. The hematoma is usually traumatic in origin, often with an asymptomatic period of a few hours to a few days. The bleeding may originate from tumour or pancreatitis, or its origin may be obscure.^{26, 27}

Diagnosis.—This diagnosis must be considered if there is a history of injury associated with the presence of upper intestinal obstruction with or without evidence of hidden blood loss. Pain is usually present in the midabdominal or epigastric regions. The vomiting which occurs in the presence of high intestinal obstruction is present and persistent. Discomfort and tenderness are usually mild and only rarely can the obstructing mass be palpated. Gastric distension may be present, but the intestine distal to the point of obstruction is collapsed; as a result the abdomen remains relatively scaphoid. Bowel sounds are usually present, but may be markedly reduced. The usual evidences of hidden blood loss such as mild shock, tachycardia and anemia may be present.

The diagnosis can be confirmed by radiological studies and the typical radiological findings have been clearly described by Felson and Levin¹ and confirmed by others.^{3, 4, 6, 8, 11, 12, 20, 24, 25} A flat abdominal plate reveals distension of the stomach

and of a portion of the duodenum, while the remainder of the intestine is relatively normal. A thin barium or lipiodol swallow shows the characteristic picture.^{1, 24, 25} The lesion usually involves the descending and transverse portions of the duodenum. The proximal portion of the involved segment shows thickening of the mucosal folds and more distally the barium flows over the surface of a smooth, sharply demarcated intramural mass which widens the lumen of the duodenum. In this segment the valvulae conniventes are often crowded together, producing a coiled-spring appearance similar to that seen in intussusception. Often conditions are such that no barium will pass the obstruction. There may be evidence of extrinsic pressure on the surrounding organs. If an obstruction is demonstrated, the barium should be aspirated and gastric lavage carried out.

Treatment.—Some patients respond to conservative management with intravenous fluids and continuous suction. The obstruction, however, tends to be complete and prolonged, and therefore electrolyte imbalances and other complications frequently occur.

In general it would appear that surgical intervention is the procedure of choice. If the injury and hematoma are recent, as in Case 3, a simple bypass anastomosis in continuity would seem preferable in adults because uncontrollable bleeding that might occur during direct interference is a distinct possibility in this extremely vascular area. The bleeding point is extremely difficult to locate and a search for it is fraught with danger to adjacent vital structures.

When the laparotomy has been delayed until such a time as bleeding is not likely to be a problem, then the simplest effective procedure is incision and evacuation of the hematoma, usually with drainage. This is particularly appropriate in the management of this lesion in children where a gastroenterostomy, although not absolutely contraindicated, is still not desirable.

SUMMARY

The somewhat infrequent but always puzzling problem of acute duodenal obstruction secondary to hematoma has been

discussed briefly. Three new cases of this entity have been presented. Duodenal obstruction due to hematoma usually follows trauma; it is always a problem in diagnosis, and not infrequently this obstruction poses problems in treatment.

We are grateful to Dr. W. M. Roy, Radiologist, St. Joseph's Hospital, Toronto, for assistance in preparing the radiographs, and to Mrs. M. L. Smith, Librarian, Academy of Medicine, Toronto, for secretarial help. We also express our appreciation to Dr. J. V. Ord of St. Joseph's Hospital for permission to include his case.

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RÉSUMÉ

Les cas d'obstruction intestinale secondaire à un hématome sont rares. L'hématome est généralement d'origine traumatique, ou bien se forme spontanément dans une tumeur ou encore à la suite d'une pancréatite. Il peut être situé rétro-péritonéalement, intra-mural, sous-séreux ou sous-muqueux. Trois cas de ce genre sont rapportés ici.

Premier cas.—Un garçon de six ans, souffre de douleurs abdominales vagues et de vomissements à la suite d'une chute de bicyclette. On l'admet à l'hôpital et on le garde en observation pendant quelques jours, au cours desquels les radiographies permettent de trouver un état d'obstruction au niveau du duodénum, deuxième portion. On procède à une exploration; le diagnostic devient évident: il s'agit d'un hématome rétro-péritonéal qui provoque une constriction duodénale. Cet hématome est ouvert et drainé. Le malade guérit parfaitement.

Deuxième cas.—Une histoire très semblable chez un enfant de huit ans qui avait subi un traumatisme abdominal léger en jouant au hockey. La laparotomie permet de découvrir et de drainer un hématome rétro-péritonéal comprimant la troisième portion du duodénum. Les suites opératoires furent sans histoire.

Troisième cas.—Un jeune homme de 22 ans se trouve coincé entre une automobile et une porte de garage. Admis à l'hôpital, il est gardé en observation pendant quatre jours. Une aggravation subite étant survenue, on pratique une exploration abdominale, qui là encore permet de découvrir un hématome rétro-péritonéal localisé à la hauteur de la troisième portion du duodénum. A nouveau, le drainage permet une rapide guérison.

EXPERIMENTAL SURGERY

A STUDY OF THE POWERS OF REANASTOMOSIS OF THE LIMB LYMPHATIC VESSELS AND NODES IN THE DOG

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IN 1960, Dr. C. Danese of Hahnemann Hospital, Philadelphia, demonstrated a very effective new method of visualizing the lymphatic vessels of the limbs of the dog by means of the subcutaneous injection of a radio-opaque material into the paw pad.¹ In this procedure, 9.5 c.mm. of 50% Hypaque (Winthrop) with 0.5 c.mm. of hyaluronidase is injected into the paw pad of the dog. A pressure of 250 mm. Hg or more is then applied to the pad for two minutes after the injection by the application to the limb of a pediatric blood pressure cuff. A radiograph is then taken of the limb, and the outlines of the lymphatic vessels, as well as of the popliteal or axillary lymph nodes, are clearly seen.

It was appreciated, as indicated by Danese in a personal communication, that this would be a useful means of demonstrating the powers of regeneration and reanastomosis of lymphatic vessels. Extensive study has been carried out on normal and abnormal lymphatics by Yoffey and Courtice,² and Kinmonth³⁻⁵ in the human. In 1926, Reichert⁶ demonstrated the regen-



Fig. 2.—Normal lymphangiogram of foreleg of dog showing axillary lymph node.

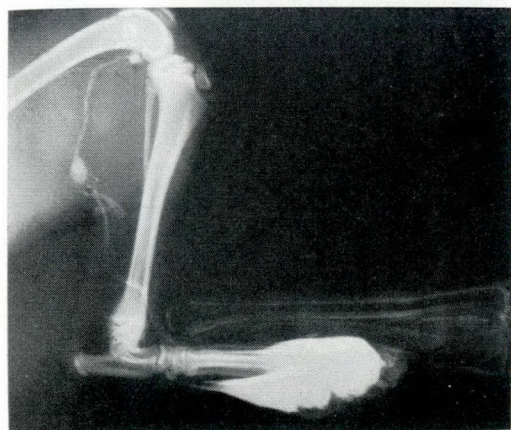


Fig. 1.—Normal lymphangiogram of hind leg of dog showing popliteal lymph node.

eration of lymphatic channels after complete transection of the hind leg of a dog, except for the main artery, vein, nerve and bone which remained intact. Bower *et al.*⁷ have published a variety of lymphangiographic studies on pathological conditions of the lymphatic system in the human. Howard points out that up to the present, surgery of the lymphatic system has been largely extirpative. He suggests that reconstructive surgery may be possible in the future, but before reconstruction can be contemplated, the behaviour of normal lymphatic channels and lymph nodes in response to trauma must be known. This study was therefore undertaken to restudy the regeneration of lymph channels and lymph nodes, using Danese's simple method of radiographic visualization.

This is a method of studying not only the anatomical arrangement of the limb lymphatics of the dog, but also the powers of restitution of lymphatic channels and lymph nodes after extensive trauma, from the anatomical, functional and dynamic aspects. The study was carried out in six steps.

1. Dogs of 12 to 20 lb. in weight were anesthetized with intravenous pentobarbital

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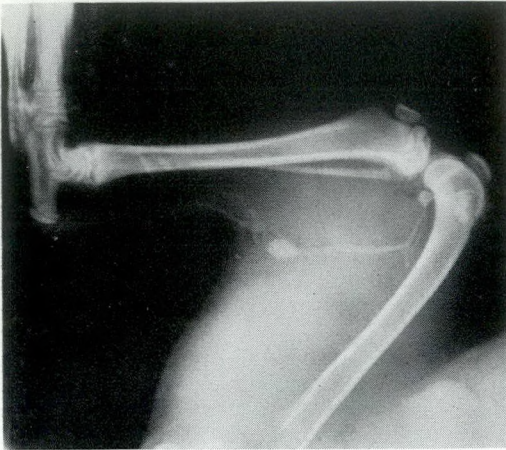


Fig. 3

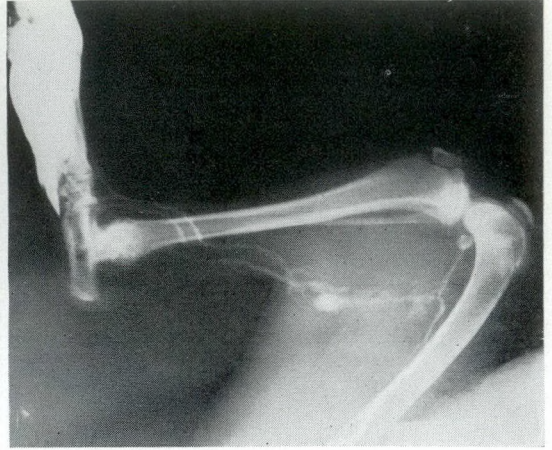


Fig. 4

Fig. 3.—Normal lymphangiogram of hind leg of dog. Fig. 4.—Lymphangiogram 16 days after popliteal lymph node was divided into two, rotated through 180° and resutured.

sodium (Nembutal). The normal lymph channel patterns of the hind and forelimbs were then studied by Danese's method (Figs. 1 and 2).

2. Later one of the dogs was reanesthetized and 2 c.mm. of patent blue dye plus 0.5 c.mm. hyaluronidase was injected into the hind paw pad of the dog. The popliteal lymph node was then explored surgically. The lymph channels were clearly outlined with blue dye. These channels entered and left the popliteal lymph node which was heavily stained with blue. The lymph node was then divided into two across its middle at right angles to the axis of the flow of the lymph. The distal half was turned through 180° and sutured back to the proximal half by four fine silk sutures. Sixteen days later the lymph pattern was studied by Danese's method, which demonstrated an essentially normal flow of lymph through the resutured lymph node. Fig. 3 shows the lymph pattern before division of the node and Fig. 4 shows the pattern 16 days after the division and 180° rotation. This would indicate that lymph nodes can heal and function after being sectioned.

3. The next procedure was to determine what happened when the popliteal lymph node was completely excised, turned end over end, i.e. through 180° in its long axis and replaced in its bed, so that the distal vessels would be adjacent to the proximal

end of the lymph node, and the proximal vessels be adjacent to the distal end of the lymph node.

The same procedure, as in the previous experiment, was used to outline the popliteal lymph node, *viz.*, patent blue dye plus hyaluronidase was injected into the paw pad. The node was found and dissected free, and the proximal and distal vessels were cleanly divided with scissors adjacent to the node. The node was carefully marked with a fine silk stitch on its proximal pole. It was then lifted clear of its limb, turned end over end through 180° and replaced in its bed, so that the proximal pole was distal, and the distal pole proximal.

Fig. 5 shows the normal lymph pattern before operation. Fig. 6 shows the appearance of the limb 24 hours after the reversal of the lymph node. It will be seen that the lymph has flowed from the distal vessels to form a lymph lake around the reimplanted lymph node, but none has flowed on into the proximal vessels. In other words, new anastomoses have not been re-established so far. Fig. 7 is a radiograph taken 14 days later. It will be seen that anastomoses have been established, and flow through the up-ended lymph node has begun again.

4. The next experiment was to see what would happen when all lymphatics passing up a limb were divided; for this pur-

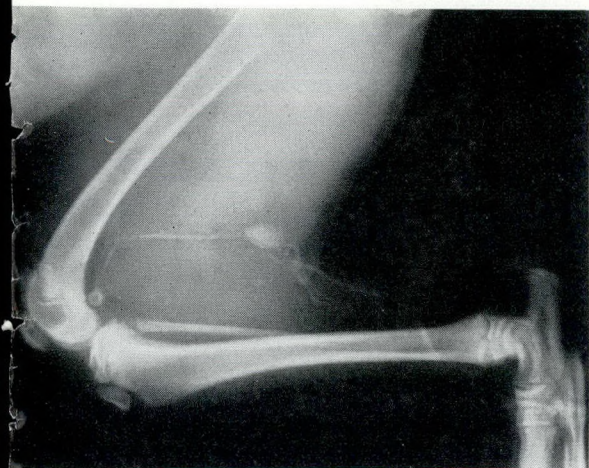


Fig. 5.—Normal lymphangiogram of hind leg of dog.

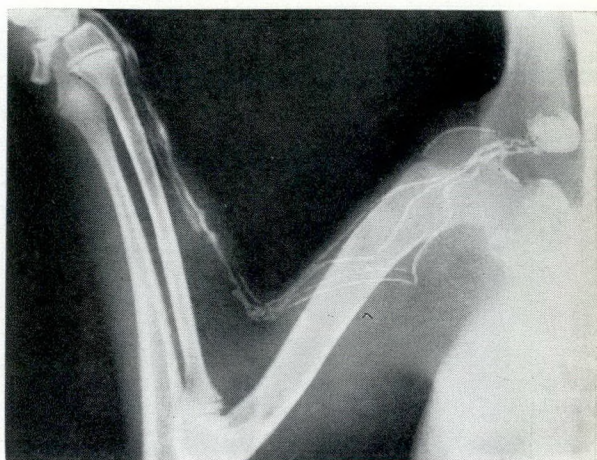


Fig. 8.—Normal lymphangiogram of foreleg of dog.

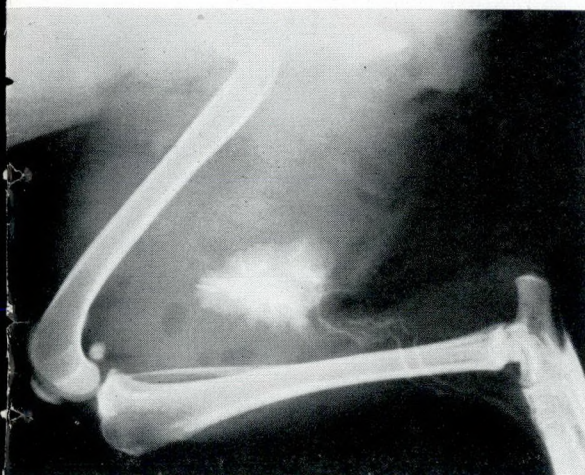


Fig. 6.—Lymphangiogram one day after popliteal lymph node was turned end over end.

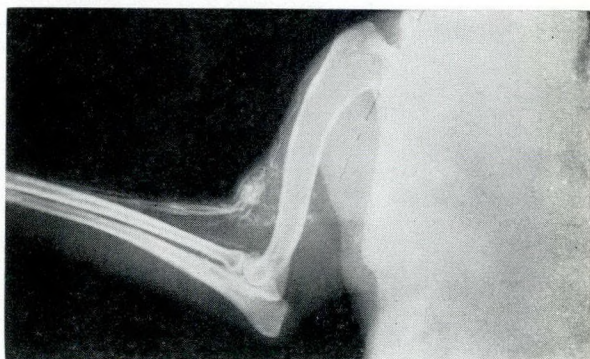


Fig. 9.—Lymphangiogram of foreleg 21 days after transection of limb.

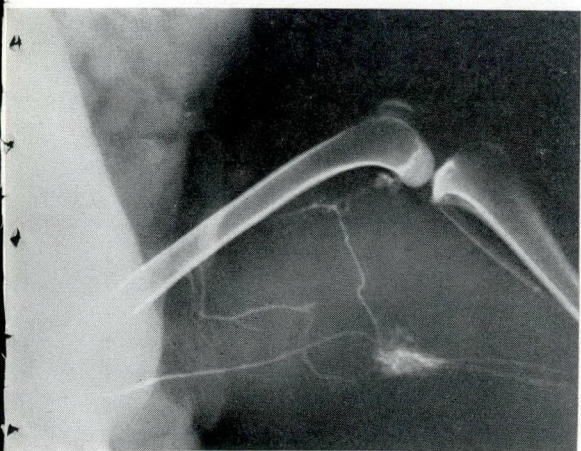


Fig. 7.—Lymphangiogram 14 days after popliteal lymph node was turned end over end.



Fig. 10.—Lymphangiogram of foreleg eight weeks after transection of limb.

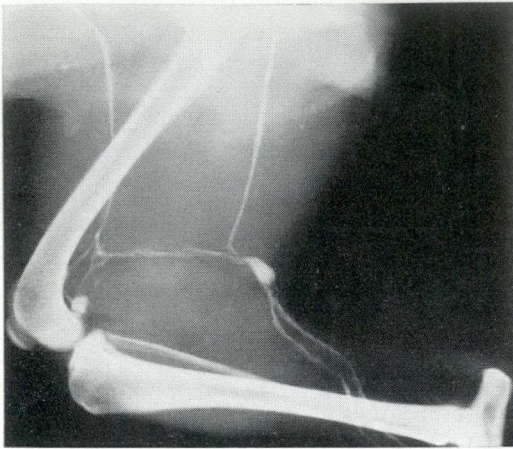


Fig. 11

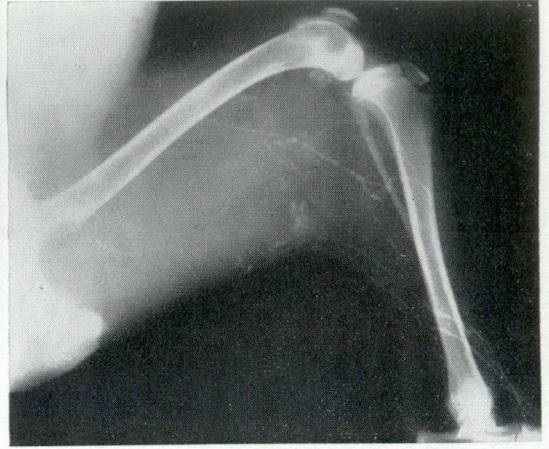


Fig. 12

Fig. 11.—Normal lymphangiogram of hind leg of dog. Fig. 12.—Lymphangiogram of hind leg 22 days after excision of popliteal lymph node.

pose the foreleg was used. Again the lymphatics were outlined with patent blue dye. Then all structures from the skin down to and including the periosteum were divided, except for the main nerve, artery and vein. The division was made at the midpoint of what would correspond to the humerus in the human, i.e., the middle of the proximal bone of the forelimb. All lymphatics duly outlined with blue dye were carefully divided. All divided structures were then resutured except for the periosteum. Gross swelling of the limb beyond the site of division occurred, but regressed completely after two weeks.

Twenty-one days after the division, a study of the lymphatics was carried out. This showed that lymph channels had reformed across the suture line (Fig. 9). A further radiograph eight weeks after the division showed complete re-establishment of lymph flow through new anastomatic channels (Fig. 10). This experiment is essentially a repetition of that carried out by Reichert in 1926, except that lymphangiography is used instead of lamp-black to demonstrate the restoration of continuity of the lymph channels.

5. The next procedure was to excise the popliteal lymph node. Fig. 11 shows the

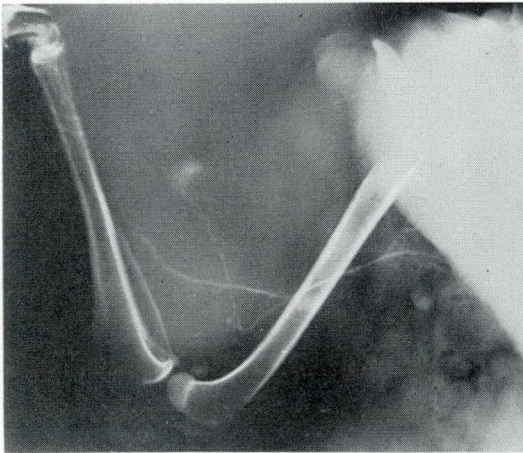


Fig. 13

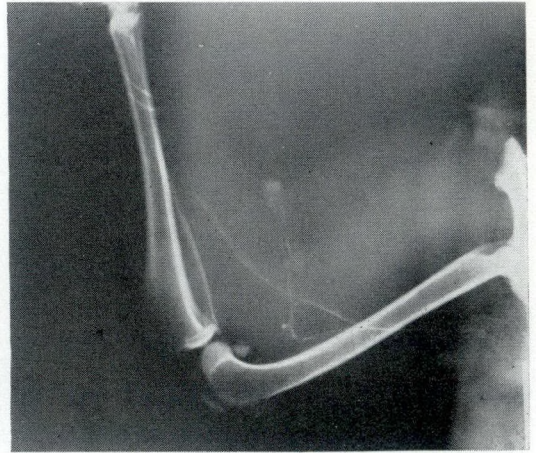


Fig. 14

Fig. 13.—Normal lymphangiogram of hind leg of dog. Fig. 14.—Lymphangiogram of hind leg six days after induction of aseptic inflammation of hind paw.

lymph channel pattern before the operation. Fig. 12 shows a quite different lymph pattern with new bypassing anastomoses around the site of the excised popliteal lymph node. This latter radiograph was taken 22 days after the node was excised.

6. This method of delineating lymphatics seemed to be a useful means of studying the effect of inflammation on the lymph drainage. Therefore a radiograph was taken of a normal hind limb of a dog (Fig. 13). Then an aseptic inflammatory reaction was induced in the paw of this limb by injecting 2 c.mm. of 2.5% formalin. This produced swelling, induration and ulceration in the paw. Six days later a further radiograph was taken (Fig. 14). It will be noted that the lymphatic pattern is the same; the only difference is to be seen in the popliteal lymph node which has increased in size by about three times.

SUMMARY

The preceding series of experiments demonstrates the remarkable propensity of lymphatic channels to re-establish continuity after division, within a relatively short period of time.

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RÉSUMÉ

Cet article rapporte les résultats d'un travail expérimental visant à étudier les capacités de régénération et de ré-anastomose du système lymphatique des membres soumis à divers traumatismes. Cette étude fut faite par la méthode radiographique en utilisant une technique d'injection radio-opaque mise au point par Danese de l'Hôpital Hahnemann à Philadelphie (décrite en détail dans le texte).

On employa des chiens. Dans un premier temps on pratiqua, selon la technique de Danese, l'enregistrement radiographique du système lymphatique des pattes à l'état normal. Dans un deuxième temps, des traumatismes chirurgicaux variés furent provoqués: transection d'un ganglion lymphatique du creux poplité, excision d'un de ces nodules, section de tous les lymphatiques d'un membre en respectant les vaisseaux sanguins et les nerfs, ablation de tous les ganglions du creux poplité. Dans tous les cas des sutures partielles furent faites et le résultat fut étudié après un certain temps par de nouvelles radiographies. Les possibilités de régénération et de ré-anastomose semblent considérables et sont démontrées par les figures qui accompagnent l'article.

CLINICAL HEMATOLOGY. 5th ed. Maxwell M. Wintrobe. 1186 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada, Toronto, 1961. \$19.50.

This excellent text of hematology is probably to be found in every hospital library of North America and in many an internist's office; its Spanish and Italian editions imply that its fame extends well beyond the Anglo-Saxon world. It therefore calls for very little introduction on the occasion of its fifth English edition. Many sections of the book have been rewritten and a number of new topics have been added in keeping with the rapidly advancing progress in hematology. Some of the

sections which have undergone major changes include those on the biosynthesis of hemoglobin, on coagulation, on hemolytic anemias, and on chemotherapy. The bibliography (of international scope) has been revised so as to include mostly references to recent papers (up to 1961), preserving only among the older ones those which are especially pertinent to the subject or those of historical interest.

The text is clearly written and is printed in a two-column make-up in very readable type. Several schematic outlines are incorporated, which are of proved value in teaching. As in the previous editions, the colour plates are accurately reproduced and the sheen of the paper selected is comfortable to the eye.

ASSESSMENT OF SPLEEN SHIELDING AND HOMOLOGOUS SPLENIC HOMOTRANSPLANTS IN THE PROTECTION AGAINST LETHAL TOTAL BODY IRRADIATION*

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PREVIOUS experimental work in this field has demonstrated the value of various procedures in protecting small laboratory animals from the harmful effects of lethal doses of total body irradiation. Jacobson¹ working with spleen shielding, Lorenz and his colleagues² with bone marrow infusions, and Cole *et al.*³ with infusions of spleen cell homogenates, all succeeded in achieving this protection in small animals. At the present time, however, lasting protection can be achieved in larger animals, such as dogs, only by the use of autologous infusions of bone marrow⁴ or spleen pulp.⁵ Experimental evidence has demonstrated that homografts,⁶ autologous whole organ transplants and spleen shielding⁵ are ineffective in affording protection against total body irradiation (T.B.R.).

It was shown by Irvine and Kling⁷ in our laboratory that the use of a homotransplant of bone marrow plus homogenized spleen pulp prolonged the survival time of animals exposed to a lethal dose of total body irradiation as compared with similarly irradiated animals treated with a homotransplant of bone marrow alone, or bone marrow given in addition to a whole organ splenic transplant.

As a further development to this work, it was decided (1) to study the effects of shielding the spleen of dogs subjected to lethal doses of total body irradiation, and (2) to give lethally irradiated animals an infusion of shielded spleen taken from the survivors of the foregoing procedure to determine if these spleens have any special properties which would make them of more value than the ordinary spleen used in homotransplants.

METHODS AND PROCEDURES

The dogs used in this study were unrelaxed mongrel dogs weighing from 10 to 15 kg. The dogs were isolated for 10 days during which time they were immunized against canine distemper and hepatitis.

Before irradiation, a peripheral blood sample was taken in order to determine control values for hematocrit, hemoglobin, red blood cell count, leukocyte count, differential count and platelet count. These studies were repeated periodically after irradiation to evaluate the effect of T.B.R. on the elements of the peripheral blood. All dogs that died were autopsied and one dog was sacrificed at six months for autopsy.

Irradiation was given from a Cs¹³⁷ teletherapy unit; source-skin distance, 70 cm.; the field, 100 cm. in diameter. The irradiation was delivered at a rate of 8.33 r per minute, given laterally to anesthetized dogs, with one-half of the total exposure being given to each side, and the doses were calculated at the midsagittal plane.

PART I

Group 1 (Control group).—Eight dogs were anesthetized with pentobarbital sodium (Nembutal) and given 600 r T.B.R. After irradiation, the dogs were carefully observed and parenteral feedings administered when indicated. Vitamins and daily prophylactic antibiotics were given parenterally. Penicillin and streptomycin were used routinely and terramycin or chloramphenicol added if evidence of infection was detected or if the leukocyte count fell below 100 cells/c.mm.

Group 2 (Spleen shielding group).—Before irradiation, 27 female dogs were anesthetized and the abdominal cavity was opened. The spleen was mobilized, preferably without dividing any of the gastrosplenic omentum, so that it could be easily lifted out of the abdominal cavity with the

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splenic vessels forming a pedicle. The abdominal incision was then closed around the pedicle with four interrupted sutures. Each dog was placed on its side and the spleen enclosed in a lead box. The dogs were then given T.B.R. Three dogs received 1225 r, six dogs received 1000 r and 18 dogs received 600 r. Immediately after exposure the abdominal incision was reopened, the spleen replaced and the incision again temporarily closed. The dog was returned to the operating room where a definitive closure of the incision was done, using four layers of continuous suture.

These dogs were carefully observed until their death or until their clinical picture improved and the peripheral blood picture returned to nearly normal values; this occurred from two to four weeks later.

When completely recovered, that is, in two to four weeks, the dogs were returned to the operating room where a splenectomy was performed. The spleen was made to contract by the intravenous administration of epinephrine before removal, and the abdomen was closed in the usual manner. Then the spleen was homogenized by a method similar to that described by Longerbeam *et al.*⁸ The splenic artery was cannulated and the spleen perfused with Tis-U-Sol (Baxter), a solution with heparin added, which prevented clotting and promoted the separation of splenic cells from stroma.⁸ The spleen was then cut into thin strips and mashed through a fine tea-strainer with a glass pestle, and the stroma discarded. The product was diluted to approximately 200 c.c., with a suspending solution which varied from saline or plasma to whole blood, and was given intravenously to a recipient male dog from Group 3 on the day after its total body irradiation. The solution was given slowly over one to two hours.

PART II

Group 3 (Homotransplant of shielded spleen).—Nine male dogs were used in this group. Six of the dogs were given 1000 r and three dogs were given 600 r total body irradiation. Male dogs were used exclusively as recipient animals and female dogs as donors, so that in the case of a long-term

surviving recipient dog, female leukocytes could be traced in its peripheral blood stream.^{9, 10} On the day after irradiation these dogs received the intravenous homograft of splenic pulp from Group 2 survivors.

RESULTS

Group 1 (Control group).—The dogs receiving 600 r usually became lethargic and refused food by the third or fourth day after irradiation; however, several dogs remained active and well until the day before death. Vomiting or diarrhea was not seen in this group. Examination of the peripheral blood revealed that the leukocyte count declined steadily from the second day

TABLE I.—RESULTS

	No. of dogs	T.B.R.	Survivors
<i>Group 1:</i>			
Control dogs	8	600 r	0
<i>Group 2:</i>			
Dogs with shielded spleens	3	1225 r	0
	6	1000 r	2 (33.3%)
	14	600 r	8 (57.1%)
<i>Group 3:</i>			
Dogs receiving splenic homotransplant	6	1000 r	0
	3	600 r	0

after irradiation and fell below 100 cells/c.mm. on the day before death. The platelets showed evidence of marked stimulation on the first day before falling, usually with a slight recovery on the third to fifth days, then a rapid decline to the 75,000/c.mm. range. The hemoglobin did not fall below 10 g. %. The findings at autopsy were typical of an acute irradiation death with hemorrhagic pneumonia and occasional gastrointestinal mucosal hemorrhage. The spleen was found to be small and pale. All the animals in this group died between nine and 11 days after irradiation (Table I).

Group 2 (Spleen shielding group).—Results are recorded according to the dose of T.B.R. received by these dogs with shielded spleens.

(i) Three dogs received 1225 r and died uniformly on the fourth day. These dogs

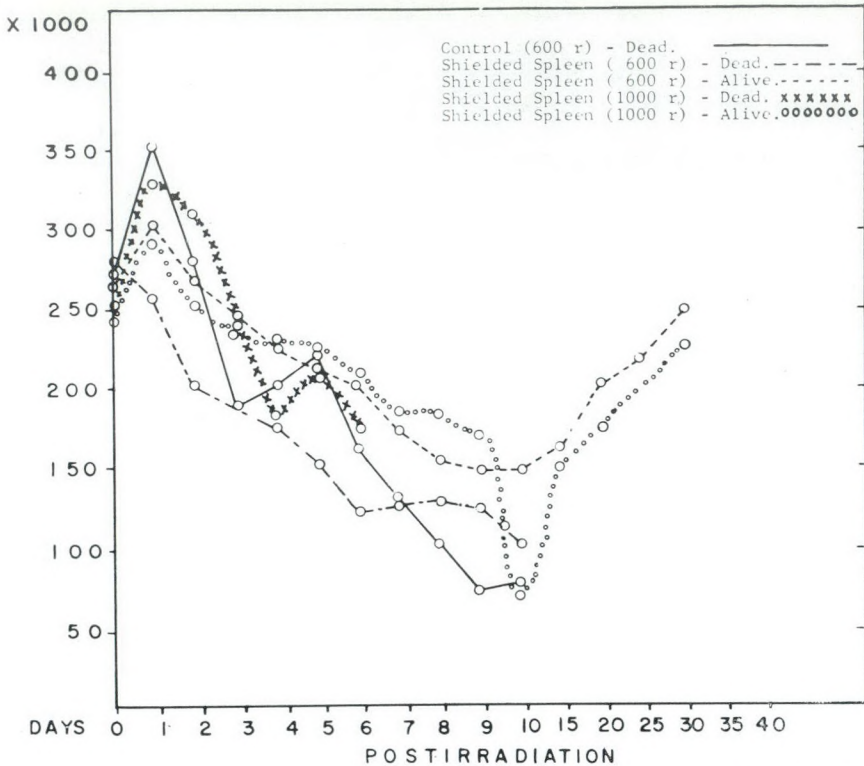


Fig. 1.—Pattern of response of platelets in peripheral blood to 600 and 1000 r total body irradiation.

were listless and anorectic. Bloody diarrhea and vomiting was common. The peripheral blood showed dramatic changes with a leukocyte count of less than 50 cells/c.mm. and platelets in the 50,000/c.mm. range by the fourth day. The hemoglobin remained fairly constant over this short period and one dog showed a rise of 5 g. % just before death.

(ii) Of the six dogs receiving 1000 r, there were two survivors. They remained well and active and required no parenteral therapy after nine or 10 days, but were maintained on antibiotics. The leukocyte count dropped steadily after the second day to reach a nadir of about 200 cells/c.mm. at the seventh day, then rose gradually to normal levels. The platelets reached a low of 75,000/c.mm on the tenth day, then returned to normal. The hemoglobin fell to 10 g. % by the fifth day but returned to normal by the eighth day.

The four other dogs died within six or seven days; however, the clinical course of these dogs was similar to that of the sur-

vivors although some degree of diarrhea and vomiting was seen by the fifth day. The leukocyte count fell rapidly to less than 100 cells/c.mm. by the fifth or sixth day. The platelet count rose on the first day, then fell to around 175,000/c.mm. The hemoglobin fell to its lowest value by the fourth day, but in two dogs it rose until just before death.

(iii) Of the 18 dogs receiving 600 r, there were eight survivors. Of the 10 fatalities, three were due to the effects of anesthesia and one was due to an error in surgical technique. These four deaths, therefore, were not included in assessing the results.

The surviving dogs had an easy post-irradiation course. They remained alert and active, usually not requiring parenteral therapy. There was no vomiting or diarrhea in this group. The leukocyte count of these dogs reached its nadir of about 300 cells/c.mm. on the seventh day, then rose steadily to preirradiation values. Platelets fell to 150,000/c.mm. around the ninth day.

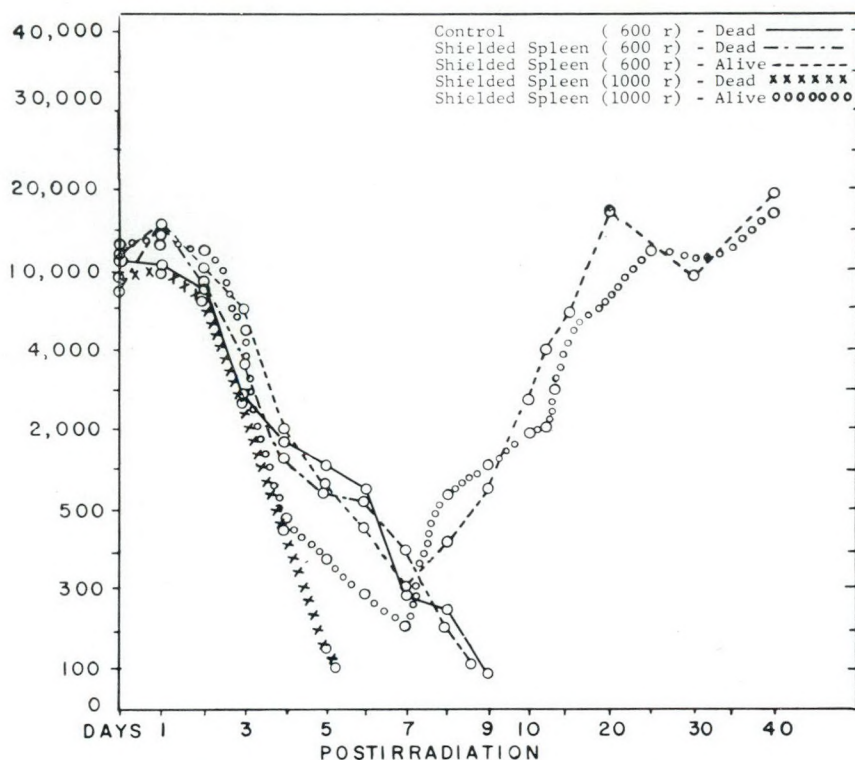


Fig. 2.—Pattern of response of leukocytes in peripheral blood to 600 and 1000 r total body irradiation.

Hemoglobin values fluctuated irregularly during this period (Figs. 1 and 2).

The dogs that died from 600 r usually had a postirradiation course similar to that of the surviving dogs until the sixth to ninth day when they weakened and died two to three days later. On several occasions there was evidence of slow continuous blood loss from the gastrointestinal tract during this period. One dog from Group 2 that had survived the effects of 1000 r was sacrificed at six months. There were no unusual findings (Table I).

Group 3 (Homotransplant of shielded spleen).—The six dogs receiving 1000 r irradiation plus an intravenous homograft of homogenized shielded spleen failed to survive. They became lethargic and weak from vomiting and diarrhea. The usual blood picture showed the leukocyte count dropping steadily in about four days to the 600/c.mm. range; the platelets dropping to around 150,000 and the hemoglobin fluctuating daily. Autopsy revealed the typical findings of acute irradiation sickness.

Of the three dogs which received 600 r, two died during the transfusion of the shielded spleen. The dogs hyperventilated, developed tachycardia and died shortly after, even though the transfusion had been discontinued. The one dog surviving the transfusion remained active and well until his death 13 days after irradiation. Autopsy showed hemorrhagic pneumonia in the left lung, with a serosanguinous pleural effusion. There was no indication of hematopoietic recovery in this dog (Table I).

DISCUSSION

Group 2.—The results from this group show that mechanical shielding of the spleen had a definite influence on the clinical appearance and the survival rate of the irradiated dogs. It did, however, seem to lose its effectiveness in the higher irradiation dose levels.

The histological picture in sections taken from the spleen at the time of transplant showed large numbers of megakaryocytes which are not present in normal spleen

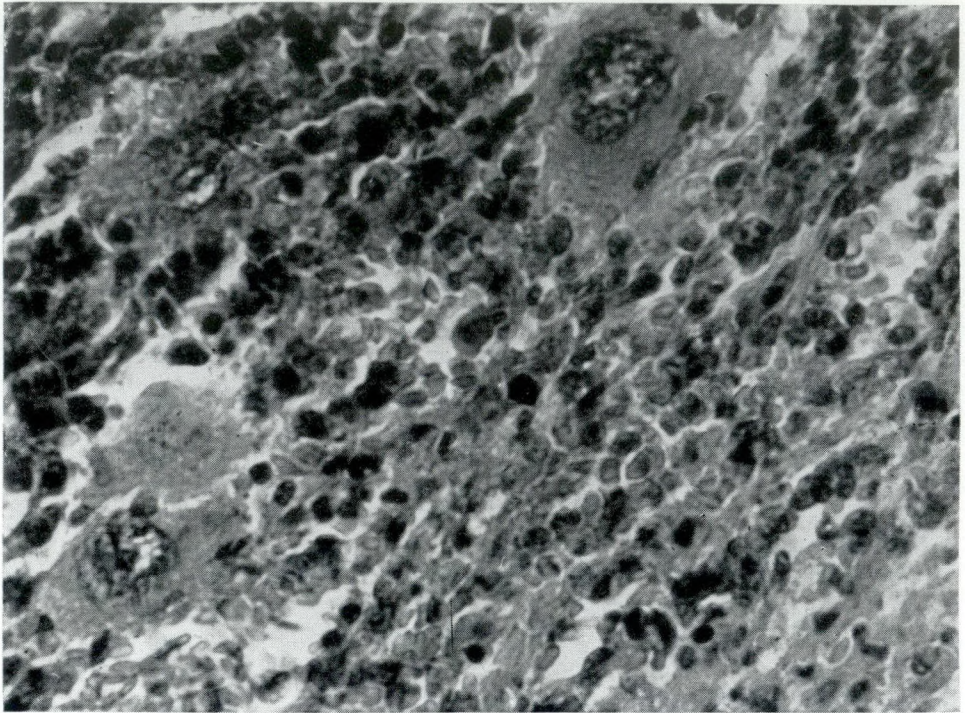


Fig. 3.—Sections of spleen at time of transplantation showing megakaryocytes.

tissue (Fig. 3). This could be interpreted as evidence of extramedullary hematopoiesis in the spleen of the irradiated animal.

Group 3.—The results of this small series would indicate that the emulsion from a specially shielded spleen, as described above, has no appreciable advantage as a donor material. The failure of these homologous spleen homografts to prolong survival time of the recipient dogs in this group could be a result of inadequate irradiation of these animals, which failed to destroy their immune response completely. This was especially evident in the 600 r dogs. Ferrebee *et al.*¹¹ found it necessary to give 1200 r to dogs in order to enable homografted bone marrow to survive.

Also, Longerbeam and his colleagues,⁸ working with autologous spleen cell infusions, showed that the protection provided by the infusion is proportional to the number of viable cells given. With more than a 3×10^9 nucleated cell count in the infusion, they had a 79% survival, but with less than this number, there was only a 50% survival. We obtained counts in the range of 1.5 to 5.8×10^9 cells, but most

were less than the standard of Longerbeam *et al.*

The increased survival rate of irradiated animals which have had their spleen shielded, suggests that in the event of thermonuclear warfare or in industry where shelters may not be practical, a device to shield the spleen of a vulnerable person might be beneficial in preventing a fatality. Also by shielding the spleen one might increase the amount of radiation which could be given to persons with widely disseminated malignancy.

SUMMARY

Spleen shielding was shown to be effective in protecting 57% of dogs after exposure to 600 r T.B.R.

Spleens removed from survivors of presumably lethal T.B.R. appeared to have no special value when given as a homograft infusion in protecting lethally irradiated dogs.

This project was supported by National Research Council of Canada Grant No. 713. Dr. S. R. Usiskin, physicist, Cancer Clinic, The University of Alberta Hospital, Edmonton, is thanked for his assistance in irradiation.

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RÉSUMÉ

Des travaux expérimentaux antérieurs ont démontré la nécessité de protéger les petits animaux de laboratoire contre les effets dangereux des radiations lors d'irradiation totale du corps. Différentes méthodes ont été utilisées à cette fin, à savoir: les injections de moelle osseuse, les injections de cellules de la rate après homogénéisation, et enfin le "spleen shielding" (expression difficile à traduire en français qui désigne la protection de la rate par un écran opaque aux radiations; ci-après nous utiliserons l'expression "blindage de la rate").

Cette dernière méthode fut étudiée dans le laboratoire des auteurs de deux façons: 1) Etude des effets du blindage de la rate devant une irradiation corporelle totale et léthale; et 2) Etude des effets d'injections d'homogénats provenant de rates blindées et irradiées. Dans tous les cas, on utilisa des chiens pesant de 10 à 15 kg. soumis à l'irradiation sous une unité de téléthérapie au Cs¹³⁷. Ces animaux furent répartis en trois groupes: un premier groupe soumis à l'irradiation sans protection et servant de témoins; un deuxième groupe soumis à l'irradiation après blindage de la rate (ce qui se fait par inclusion de la rate dans une boîte de plomb après laparotomie); le troisième groupe fut soumis à l'irradiation et reçut ensuite des injections d'homogénats de rate provenant des chiens du groupe précédent.

Cette étude montre que le blindage de la rate assure une protection efficace des animaux dans une proportion de 57%. Il ne semble pas que les homogénats de rate irradiée donnent une protection quelconque pour des chiens ayant reçu une dose léthale.

PYE'S SURGICAL HANDICRAFT. 18th ed. Vol. I (General). Edited by Hamilton Bailey. 487 pp. Illust. John Wright & Sons Ltd., Bristol; The Macmillan Company of Canada Limited, Toronto, 1962. \$7.20.

Pye's Surgical Handicraft has always been a popular book with recently graduated house staff. The new edition just published, under the general editorship of Hamilton Bailey, should be no exception to this previous popularity.

It has been thoroughly revised and modernized. Thus, in the chapter dealing with shock, the question of shock due to adrenal insufficiency is well discussed. It is interesting that in conjunction with the trends in modern practice the section on bandaging has been considerably curtailed, whereas there has been a new section put in on the use of adhesive strapping, which is indeed valuable.

There is an interesting new chapter on the handling of the patient with portal hypertension and hemorrhage.

This book indeed, in its new edition, has kept up well with the times. There are several distinguished authors who have contributed to this number in their own particular field. It is pleasant to see such men as Sir Denis Browne, John Bruce, R. H. Franklin, W. B. Gabriel, Avery Jones and many other well-known people contributing extensively.

This book is highly practical and full of many useful hints for the newly graduated student as well as for the more mature practitioner. It should be in the library of every emergency department. The idea of bringing it out in two editions, one dealing with general matters and the other dealing with the specialties, is to be commended. It has reduced the volumes to books of reasonable size.

OBSERVATIONS ON THE TEMPERATURE OF THE BRAIN DURING INDUCED HYPOTHERMIA IN DOGS*

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SINCE direct measurement is not possible under clinical conditions, the brain temperature has been estimated by assuming that it is identical with the temperature recorded in accessible locations, such as the pharynx or the temporal muscle. Whereas this method appears to be adequate during slow cooling, the possibility of temperature gradients between various areas of the body occurring during rapid cooling needed to be studied.

The presence of such temperature gradients during induced hypothermia has been described by several authors.¹⁻³ While direct determinations of the brain temperature have been reported in many experimental papers, to our knowledge the possibility that temperature gradients are present between different parts of the brain itself has not been investigated. It was considered likely that such gradients would be present during rapid temperature changes, since it is known that the brain is a poor heat conductor.⁴

In the course of experiments using differential hypothermia with selective cooling of the head of dogs, it became evident that these experiments could include a study of brain temperatures. In addition, the temperatures measured inside the brain were correlated with those in the pharynx and/or the temporal muscle. Similar measurements were taken in a group of dogs subjected to deep generalized hypothermia.

MATERIAL AND METHODS

The experiments were done on 18 adult mongrel dogs weighing 6 to 18 kg. Under pentobarbital anesthesia and with an endotracheal tube in place the following procedures were carried out:

A polyethylene catheter was introduced into the right femoral artery and connected to a mercury manometer.

A Teflon catheter was introduced into the left femoral artery and connected with an open plastic well by means of Tygon tubing.

One carotid artery was ligated and a Teflon catheter was introduced distal to the ligature. This catheter was connected with Tygon tubing attached to the cooling coil.

The right external jugular vein was ligated and a thermistor probe No. 401* was introduced proximal to the ligature and placed in the right atrium.

A thermistor probe of the same type was placed in the esophagus behind the heart and, under direct vision, in the pharynx.

A burr-hole was drilled in the convexity of the skull, and the dura was exposed. Two thermistor needle probes (No. 507) were introduced through the hole, one being placed 5 mm. underneath the dura (superficial brain temperature) and the other 5 mm. from the base of the skull (deep brain temperature).

In six animals, a needle probe was inserted through a small skin incision into the right temporal muscle or into the right retro-orbital space.

In four animals both vertebral arteries were exposed low in the neck and encircled by thick cotton ligatures for temporary occlusion of these vessels.

The temperatures were measured on a five-range, six-channel telethermometer and recorded at two-minute intervals. The accuracy of the temperature recordings of all probes was checked against a mercury thermometer and the calibration curves of the non-interchangeable probes were determined using the same thermometer. The body temperature was maintained at a near normal level by means of a plastic mattress through which water at 45° C. was circulated.

*From the Research Laboratory, Department of Surgery, University of Manitoba, Winnipeg. Supported by a grant from the Manitoba Heart Foundation.

*Yellow Springs Instrument Co. Inc., Yellow Springs, Ohio, U.S.A.

A diagram of the extracorporeal cooling circuit is shown in Fig. 1. The circuit was primed with normal saline solution. Generalized hypothermia was induced in eight additional dogs by the method first described by Kenyon *et al.*,⁵ using a bubble oxygenator,* a roller pump and a stainless steel coil surrounded by iced water.

RESULTS

Even when the procedure was identical for a group of experimental animals, the data obtained in individual dogs were different and it is impossible to report mean values. It is not necessary, however, to report each experiment in detail and so only representative figures are given.

The experiment summarized in Fig. 2 was carried out early in the series when temperatures below 20° C. could not be recorded owing to the limitation of the recording apparatus. The temperature recorded in the retro-orbital space dropped

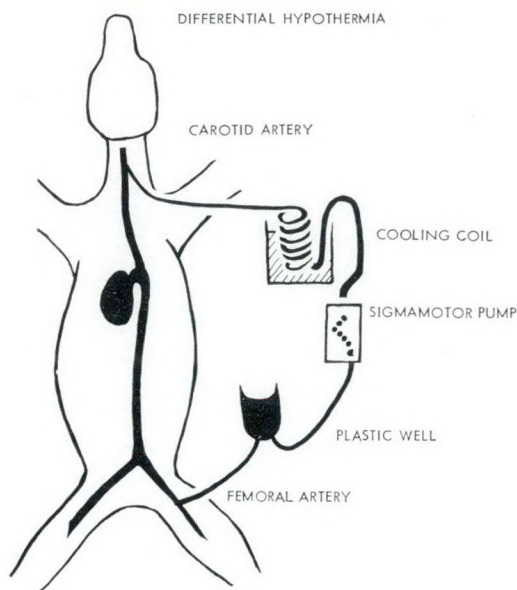


Fig. 1.—The extracorporeal circuit used to induce differential hypothermia.

rapidly, presumably owing to the proximity of the orbital artery which was perfused with cold blood. The same finding was ob-

*Pulmopak (Abbott Laboratories).

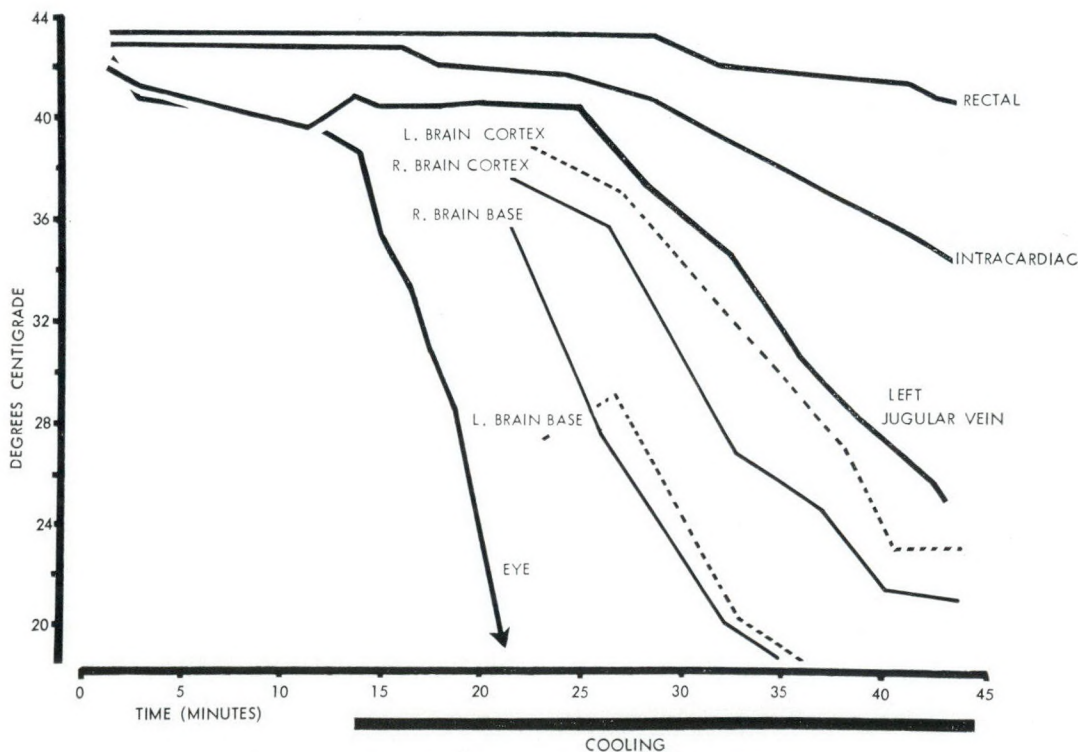


Fig. 2.—Selective cooling of the head.

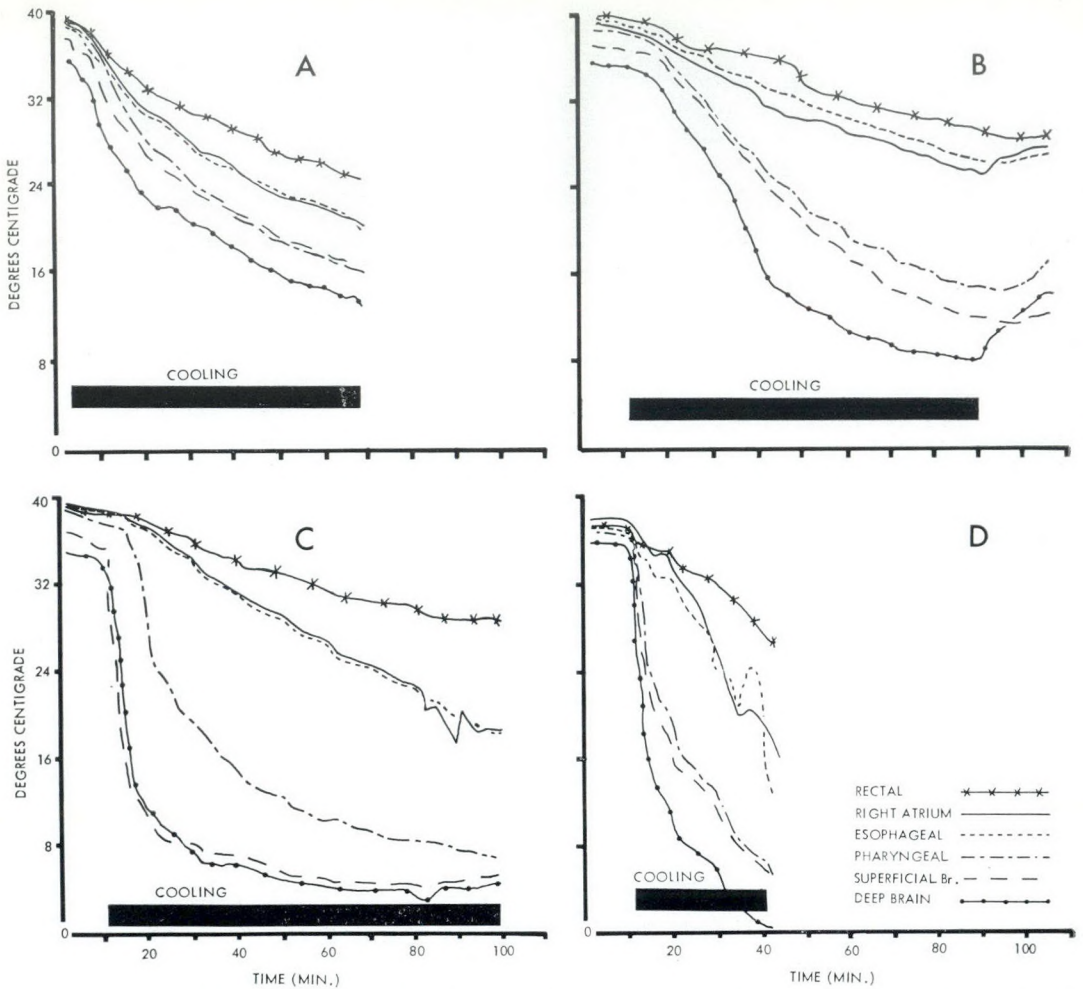


Fig. 3.—Selective cooling of the head. A. No blanket. C. Body on warming-blanket, contralateral No warming of the body, cooling coil surrounded by and both vertebral arteries clamped. The temperature into the ipsilateral temporal muscle.

warming of the body. B. Body on warming-carotid and both vertebral arteries clamped. D. saline-ice mixture at -5° C. Contralateral carotid probe designated "superficial brain" was inserted

served in three other experiments and then the retro-orbital temperature readings were abandoned. In this experiment (Fig. 2), the right carotid artery was perfused and the temperature was recorded in the cortex and at the base of both hemispheres. The levels reached on the right were 3 to 5° C. lower than on the left side of the brain. A similar differential in the temperatures between the perfused and the contralateral side was present in three other experimental animals.

In the experiment shown in Fig. 3a, the body of the experimental animal was not warmed, thus allowing for a certain degree of generalized hypothermia. A considerable

drop in rectal temperature was observed, but throughout the whole cooling period the lowest temperature was recorded in the base of the brain. The superficial brain and the pharyngeal temperatures showed courses similar to the right atrial and esophageal temperature curves, although the former pair of temperature recordings dropped at a faster rate initially.

The results depicted in Fig. 3b were obtained from an experimental animal whose body was kept warm by plastic warming-blankets, while the head was cooled. The drop in rectal, right atrial and esophageal temperatures was less than in the previous experiment. The pharyngeal

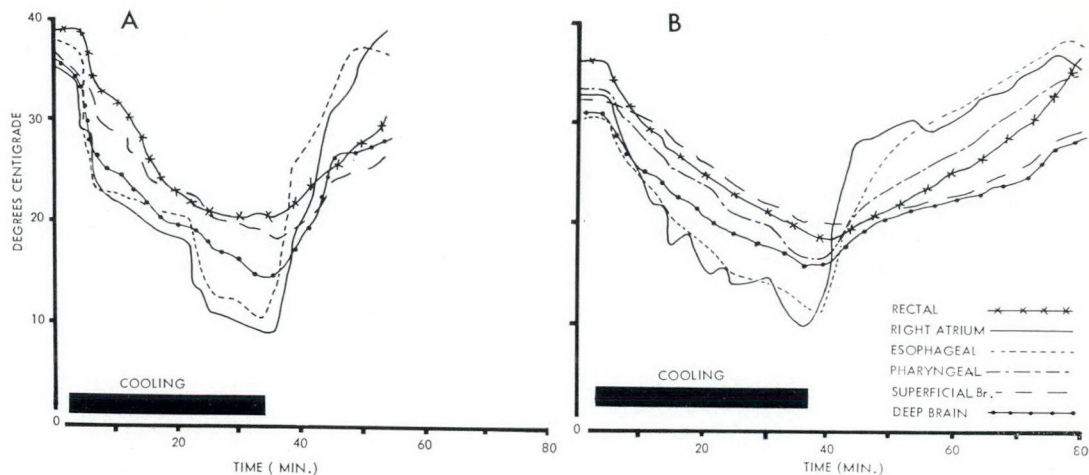


Fig. 4.—Generalized hypothermia.

temperature was slightly higher than the superficial brain temperature. The differential between deep and superficial brain temperatures was again observed. In 16 out of 18 experiments the deep brain temperature was lower than the superficial.

In Fig. 3c, the rate of cooling of the brain was increased by clamping the contralateral carotid artery and the vertebral arteries at the beginning of the cooling periods, thus decreasing the amount of warm blood reaching the brain. The deep and superficial brain temperature remained close to one another and levelled off towards the end of the experiment. Despite the plastic warming-blanket on the body, the rectal, atrial and esophageal temperatures showed a steady fall. The drop in pharyngeal temperature lagged behind the recordings obtained in the brain (the maximum difference being 10° C.) but occurred at a faster rate than those recorded in the warmed parts of the body.

In the experiment presented in Fig. 3d an attempt was made to obtain a lower brain temperature than in the previous experiments by surrounding the cooling coil with a saline-ice mixture at -5° C., by omitting the warming blankets and by clamping the contralateral carotid and the vertebral arteries. The needle, usually placed into the cerebral cortex (corresponding to the line marked superficial brain in the graph), was inserted into the ipsilateral temporal muscle. All tempera-

tures dropped rapidly, the temperature of the temporal muscle being closely related to the pharyngeal temperature.

Fig. 4 summarizes the findings obtained with total body hypothermia. In Fig. 4a the right atrial and the esophageal temperatures were again closely related and responded faster than the brain temperatures both to cooling and to warming. The gradient between the cerebral cortex and the base was again observed, the temperature recorded at the base being lower in seven out of eight experiments.

In Fig. 4b, in addition to the previous measurements, the pharyngeal temperature was recorded. During the cooling period, the pharyngeal temperature was at a level between the two brain temperatures but during the warming period the brain temperatures lagged behind the pharyngeal. In several experiments, for no apparent reason, the temperature recorded in the right atrium showed neither a steady fall during cooling, nor a steady rise during warming. Such fluctuations are well illustrated in Fig. 4b.

DISCUSSION

The temperatures recorded within the right atrium were found to be close to the temperatures recorded in the esophagus at heart level. Although in some animals there was a close correspondence between an extracranial temperature recording and the measurement in one area of the brain, this

situation was not found in the majority of experiments. The temperature recorded in the retro-orbital space was not related to the intracranial temperature. Whereas no significant difference was observed between the temperatures recorded in the pharynx and in the temporal muscle, in some animals there was a difference between these two and the brain temperatures.

The observation of temperature gradients within the brain substance merits special emphasis. The maximum difference between cortex and base recorded simultaneously was 7° C. In the majority of the animals the colder temperature was recorded at the base. This phenomenon may be due to the proximity of larger arteries, perfused with cold blood, at the base of the brain. In three animals the cortical temperature appeared to be lower; possibly in these cases the thermistor needle was not placed in the brain substance but in a sulcus close to the sulcal loop. The temperature on the perfused side was found to be 3 to 5° C. lower than the one recorded in a symmetrical area in the other cerebral hemisphere.

The temperature gradients were greater during rapid cooling than during slow cooling. In the lower temperature range the gradients became less as the cooling rate in the coldest areas was slower. Although our experiments were not prolonged sufficiently to demonstrate it, the gradients eventually might disappear altogether in animals subjected to generalized hypothermia.

During operations upon humans, with an efficient heat exchanger in the circuit, temperature gradients between different parts of the body and parts of the brain similar to those found in experimental animals are likely to be present. Gradients between esophageal, rectal, myocardial and skeletal muscle temperatures have already been observed during cooling of patients. Although no direct measurements of human brain temperatures are possible, our observations in experimental animals suggest that the brain temperature, especially of the vulnerable cortex, in patients undergoing hypothermia may be deceptively warmer than the temperatures recorded extracranially.

SUMMARY

During differential and total body hypothermia in dogs, the temperatures were measured in two areas of the brain, in the pharynx, esophagus, retro-orbital space, jugular vein, temporal muscle and rectum. During the cooling procedure a temperature gradient of several degrees was found between the cortex and the base of the brain, the base being cooler in the majority of the animals. None of the temperatures measured extracranially were found to reflect reliably the intracerebral temperature.

It is concluded that during rapid cooling, the temperature of any area of the brain can be estimated only by direct measurement. Since this is not possible clinically, only an approximation can be obtained and it must be realized that the temperature of the brain and especially of the cortex lags behind temperatures in other parts of the body. During the cooling period, the cortex may be several degrees warmer (and during the warming period, colder) than the temperatures obtained in clinically accessible areas.

The authors gratefully acknowledge the interest and help of Dr. C. C. Ferguson. The disposable bubble oxygenators were provided by Abbott Laboratories Limited. The illustrations were prepared by Mr. D. A. Gibson.

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RÉSUMÉ

Dans les conditions habituelles de la clinique, la mesure directe de la température cérébrale est impossible et on admet que cette température est identique à celle trouvée dans des localisations normalement accessibles. Si cette méthode est correcte lors des refroidissements lents, elle est peut-être inexacte dans les refroidissements rapides

et ceci constitue le but des recherches exposées dans le présent article. A cette fin on utilisa 18 chiens adultes pesant entre 6 à 18 kg. Sous anesthésie générale au pentothal, on mit en place des sondes calorimétriques en divers points de l'organisme. On put ainsi procéder à l'enregistrement des variations de température lors d'un refroidissement dans deux régions du cerveau, dans le pharynx, l'œsophage, l'espace rétro-orbitaire, la veine jugulaire, le muscle temporal et le rectum. Lors de l'abaissement de température, on nota des variations et des différences de plusieurs degrés entre le cortex et la base du cerveau, cette dernière étant le plus souvent plus froide. Jamais, les

températures mesurées hors de la boîte crânienne ne donnèrent une correspondance exacte de ce qui se passait intra-cérébralement.

Les auteurs concluent que durant un refroidissement rapide, la température d'une zone cérébrale donnée ne peut être connue que par sa mensuration directe. Puisque ceci est impossible en clinique, il convient de savoir que la température du cerveau et spécialement du cortex reste en arrière par rapport aux températures des autres parties du corps. Lors de la période de refroidissement, le cortex est plus chaud de plusieurs degrés que le corps. Lors du réchauffement, on assiste à un phénomène inverse.

TUMOURS OF THE OESOPHAGUS. Edited by Norman C. Tanner and D. W. Smithers. Vol. IV of *Neoplastic Disease at Various Sites*. General Editor: D. W. Smithers. 352 pp. Illust. E. & S. Livingstone, Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1961. \$11.35.

(especially from lye burns), diverticulum and irradiation.

An analysis of age-specific death rates per 1000 living per year in 18 different countries in the years 1951 to 1955 shows the following incidence: highest, 0.073, in Finnish males; 0.032, in Israeli males; 0.032, in Canadian males; and the lowest, 0.011, in Italian females.

This book is recommended to all who have to do with cancer, and especially those who treat the very malignant esophageal lesion.

HANDBUCH DER ORTHOPAEDIE. In vier Bänden. Band IV. Teil 2. *Untere Extremität (Handbook of Orthopedics. In four volumes. Vol. IV. Part 2. Lower Extremities)*. Edited by G. Hohmann, M. Hackenbroch and K. Lindemann. 1390 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1961. \$32.25.

This is the second part of the fourth volume of a textbook of orthopedic surgery, which is being compiled by 14 distinguished German orthopedic surgeons. It is mainly concerned with orthopedic disorders of the foot. Club foot, congenital (spastic) flat foot, paralytic foot, and arthritic, infective and degenerative foot disorders are described.

The chapter on flat foot by Hackenbroch describing the etiology, mechanics and treatment of this condition is particularly informative and interesting. In an 80-page chapter on vascular disorders of the lower extremity, A. Witt and H. Mittel Meyer provide an accurate and up-to-date discussion of this subject. Sections on tumours and amputations of the lower extremities by Marquardt conclude this work.

This publication is an outstanding addition to the library of the orthopedic surgeon. Its influence will spread beyond the boundaries of Germany and it may become a standard orthopedic textbook in many countries.

The medical world has need of objective surveys of the present knowledge of cancer which this book certainly supplies. Most of the contributors are radiotherapists and surgeons in London cancer hospitals, but Nakayama of Japan, Jacobsson of Sweden, a pathologist and two cancer statisticians are also included.

Being relatively uncommon, diagnosed late, and so rarely successfully treated, esophageal cancer is worth a good hard look. The condition is far advanced before symptoms bring the patient to the doctor or before clinical examination makes its presence suspected. It can be resected and is susceptible to irradiation but the surgical and irradiation techniques are difficult and dangerous. Some ingenious suggestions for earlier diagnosis include intramuscular injection of radioactive phosphorus followed by the use of a Geiger-Müller counter; and a radioactive trigger method for barium swallow films of the hypopharynx and cervical esophagus. At present, the treatment advocated is preoperative irradiation of up to 3000 r followed by surgical excision within a week of the last treatment.

New to this reviewer is the method of cohort analysis to study the statistics of cancer. The death rate from esophageal cancer is very low under the age of 40; it is higher in males and is lower in married women than in single. Increased external irradiation is thought to have something to do with the incidence of this carcinoma for it occurs more frequently in persons living in igneous rock areas. Some predisposing factors are recognized: the Patterson-Kelly syndrome, the presence of achalasia, hiatus hernia, strictures

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A reasonable number of black-and-white illustrations will be reproduced free with the articles. Colour work can be published only at the author's expense. Photographs should be glossy prints, unmounted and untrimmed, preferably not larger than 10" x 8". Prints of radiographs are required and *not the originals*. The magnification of photomicrographs must always be given. Photographs must not be written on or typed on. An identifying legend may be attached to the back. Patients must not be recognizable in illustrations, unless the written consent of the subject for publication has been obtained. Graphs and diagrams should be drawn in India ink on suitable white paper. Lettering should be sufficiently large that after reduction to fit the size of the Journal page it can still be read. Legends to all illustrations should be typed separately from the text and submitted on a separate sheet of paper. Illustrations should not be rolled or folded.

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NOTICE

**CANADIAN JOURNAL OF SURGERY:
NEW SUBSCRIPTION RATE FOR
TRAINEES IN SURGERY**

As a result of a decision taken at the recent annual meeting of the Editorial Board, subscription to the *Canadian Journal of Surgery* is being offered to postgraduate trainees in surgery at the rate of \$5.00 per year. Applications for subscriptions at the reduced rate can only be accepted from those identified by a member of the Editorial Board as trainees in surgery. Because the reduced rate will apply only to bona-fide trainees in surgery, applicants are requested to have their application approved by the head of the department of surgery in the medical school nearest to them.

**48TH ANNUAL CLINICAL CONGRESS:
THE AMERICAN COLLEGE OF
SURGEONS**

The 48th Annual Clinical Congress of the American College of Surgeons will be held in Atlantic City, N.J., from October 15 to 19, 1962.

For information, write to Dr. William E. Adams, Secretary, American College of Surgeons, 40 East Erie Street, Chicago 11, Ill.

**THE CANADIAN SOCIETY FOR THE
STUDY OF FERTILITY**

The ninth Annual Meeting of the Canadian Society for the Study of Fertility will be held at the Château Laurier Hotel, Ottawa, Ont., on October 26 and 27, 1962.

For further information, write to the Secretary, Dr. George H. Arronet, Infertility Centre, Royal Victoria Hospital, Montreal, P.Q.

**INTERNATIONAL FEDERATION OF
SURGICAL COLLEGES**

The Executive Committee of the International Federation of Surgical Colleges met recently in Copenhagen and made arrangements for the next Annual Meeting of the Federation. This is to be held at Atlantic City, N.J., on October 13 and 14, 1962. Thanks to the courtesy of the American College of Surgeons, the meeting will be held in conjunction with the Clinical Congress of that College.

On the afternoon of October 14, there is to be an Open Discussion on "The Interchange of Young Surgeons for Purposes of Training and Research"; the speakers will include Sir Harry Platt (U.K.), President of the International Federation; Professor I. S. Ravdin (U.S.A.), Vice-President; Professor J. F. Nuboer (Holland); Professor Digby Chamberlain (U.K.); Professor F. Linder (Germany); and Professor R. M. Zollinger (U.S.A.).

A further meeting with representatives of the World Health Organization and the League of Red Cross Societies was planned in order to collaborate with these bodies with respect to the objectives of the Federation, particularly in the field of surgical missions, surgical research and the interchange of young surgeons. The Federation seeks opportunities of helping countries in need by sending surgical missions to them. It is also anxious to encourage the interchange of young surgeons between countries of more or less equal surgical status.

The status of the International Federation as an organization in official relationship with W.H.O. has recently been confirmed.

A new member of the International Federation is the Icelandic Surgical Association.

FORTHCOMING MEETINGS

**JOINT MEETING OF
THE CANADIAN CARDIOVASCULAR
SOCIETY AND THE CANADIAN
HEART FOUNDATION**

The Canadian Cardiovascular Society (formerly the Canadian Heart Association) and the Canadian Heart Foundation will hold joint Annual and Scientific Meetings in Quebec City from November 28 to December 1, 1962.

For further information, write to Dr. John B. Armstrong, Canadian Heart Foundation, 501 Yonge Street, Toronto 5, Ont.

**FIRST BRITISH ACADEMIC
CONFERENCE IN
OTOLARYNGOLOGY 1963**

The First British Academic Conference in Otolaryngology will be held at the Royal College of Surgeons of England, London, W.C.1., from June 16 to 21, 1963.

The Conference will consist of formal sessions at which invited speakers will read papers in English, and informal instructional sessions at which known authorities will speak to small groups.

In addition there will be film showings and scientific exhibits.

Membership will be open to anyone medically qualified who engages in the practice of otolaryngology.

Correspondence should be directed to Mr. Ronald Macbeth, Honorary General Secretary, Department of Otolaryngology, Radcliffe Infirmary, Oxford, England.

BOOK REVIEWS

(See also pages 281, 298, 323, 333, 339 and 345)

THE ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA 1920-1960. D. Sclater Lewis. 241 pp. Illust. McGill University Press, Montreal, 1962. \$9.00.

This account of the Royal College of Canada deals with an important area in Canadian medical history, and we are fortunate in the authorship. Dr. Lewis knows that contemporary history has its own difficulties, and he feels that "strict adherence to documentary evidence is desirable" rather than attempting a definitive history, but it is doubtful if there will be another history more definitive than his own; certainly it would be unlikely to combine more happily so intimate a knowledge of the very roots and structure of the College in every phase of its growth with such orderly and lucid arrangement of the material.

Many of the key figures were not only his teachers and colleagues but his close friends, and he manages with his customary incisiveness to give impressions all the more illuminating because they are so carefully tailored; one man moved "without undue haste": the Executive Committee of the Canadian Medical Association gave (as it thought) "a decent burial" to the original resolution presented for investigating the formation of the College "by referring it to a study committee whose members were so widely scattered across the country that it could never meet". It was probably the same Executive, we are told, which spoke of the three Regina members who originated the idea of the College as "the Regina broncos". To the many who remember Dr. A. H. Gordon and his love of fun, there will be additional amusement in his letter regretfully returning a cheque sent him by mistake by the College.

These are enlivening touches which are not too often found in official histories. As Dr. Roméo Pepin pleasantly says in his *avant-propos*: "Une pointe d'humeur qu'il lance ici et là ajoute du charme à son ouvrage . . ."

The story of the genesis of the College is lively enough. "The tree of Man was never quiet"—a restlessness which has been in constant evidence amongst the branches of medical education. It was the compelling solicitude for the teaching of medicine in Canada which brought into being all our medical schools. But even the best undergraduate training needs the complement of postgraduate education and hospital instruction if the highest standards of medical practice are to be maintained. It is the establishment and maintenance of those standards which are the *raison d'être* of the College.

One may quite rightly regard its growth as one of the several manifestations of vigour in Canadian medical life, especially during the period in question, but it provided a severe test of that vigour. Conflicting aims and desires became evident in the initial stages, and these are clearly outlined by Dr. Lewis. He has also communicated something of the attendant atmosphere of tension in the early days of doubts and fears; in the parliamentary debates on the Act of Incorporation; in the actual organization; and in the choice of charter members (*there* was a thorny problem!). There was the gradual evolution of examination methods; the lag of interest until the resolute efforts to improve the form of the annual meetings had their reward; the formidable task of approving hospitals for postgraduate education, a duty whose assumption by the College is one of its distinctive features, as Dr. Robert Janes says in his foreword; and the certification of specialists, a stage in which similar past experiences in selection were re-enacted. The eventual building of the College headquarters in Ottawa was a triumph of capable and self-reliant management.

It is natural to expect that there will be yet other problems for the College of the future, but in dealing with them there should be much to learn from the patience and determination with which the College has faced "past straits and perils long steered through". The difficulties have only been overcome and the achievements made possible through what Dr. Lewis rightly calls "quiet and devoted service". Not only has his own contribution been one of distinction, but in giving us this History he has greatly enriched our medical historical literature. H.E.M.

OPHTHALMIC OPERATIONS. Seymour Philips. 2nd ed. by John Foster. 360 pp. Illust. Baillière, Tindall & Cox, London; The Macmillan Company of Canada Limited, Toronto, 1961. \$12.60.

This book, for its relatively small size, is surprisingly complete. It deals succinctly with minor as well as major surgical procedures. Brief historical summaries of most procedures are included. The profuse and beautifully illustrated sketches and photographs combined with the lucidly written text make it difficult to put the book aside once started.

The book is a "must" for those training in the specialty and for the less experienced ophthalmic surgeon. Also, even the most experienced ophthalmic surgeons will probably want to try one or more of the suggested modifications of a technique.

TRANSTENTORIAL HERNIATION. Louis A. Finney and A. Earl Walker. 162 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1962. \$9.50.

Many patients with expanding intracranial lesions die not from direct involvement of vital structures, but from secondary changes in the brain stem. Brain tissue, displaced from above or below, is compressed against the brain stem by the rigid tentorial ring. This often is followed by midbrain and pontine hemorrhages. The herniated tissue also acts by distorting other structures in the region of the midbrain, such as the oculomotor nerves and the posterior cerebral arteries. Once the herniation has occurred, it aggravates itself by altering blood and cerebrospinal fluid circulation.

The authors of this monograph have reviewed the extensive clinical and experimental literature on the subject and have analyzed a series of 130 cases of brain tumour verified by autopsy at the Johns Hopkins Hospital. They found that 55.4% of these autopsied brain tumour cases had transtentorial herniation. After discussing the anatomy of the tentorium cerebelli and adjacent structures, they describe in detail the many pathological changes secondary to transtentorial herniation. The clinical histories of those patients with and without herniation are contrasted and the investigative procedures needed to reach the diagnosis are described. Surgical management is discussed. Emphasis is laid on the precarious position in which these patients may be placed by unwise or delayed investigation or treatment.

The monograph is clearly written and well illustrated. It will be useful to those concerned with the diagnosis and care of patients with expanding intracranial lesions. The neuropathologist will appreciate the thorough review of the many aspects of the pathogenesis of the process.

CLINICAL NEUROSURGERY. Proceedings of the Congress of Neurological Surgeons, Chicago, Illinois, 1960. Vol. 8. Editor-in-Chief: William M. Mosberg, Jr. 341 pp. Illust. The Williams & Wilkins Company Baltimore 2, Md., 1962. \$12.00.

The latest addition (Volume 8) to this excellent series should be read, in part at least, by every practising physician. It contains the edited proceedings of the Congress of Neurological Surgeons in Chicago in 1960, when Dr. Paul Bucy was the honoured guest. Dr. Bucy's address, A Philosophy of Neurosurgery, published as Chapter 3, sets forth his views on the management of incurable neurosurgical lesions. His realistic approach to such problems, unusual in this day of uncontrolled and sometimes hysterical enthusiasm for treatment

and rehabilitation of essentially incurable conditions, is applicable to the whole field of medicine and should be made available to every medical graduate.

The form of presentation follows previous volumes in that each chapter is a formal paper by a different author, followed by a well-edited summary of questions and answers from the floor. For the recently trained neurosurgeon there is no better way to obtain the personal viewpoint of the authorities in the field, who may have quite different opinions from those pertaining to any one training centre. Since this meeting was concerned with the physiology and surgery of the spinal cord, one finds excellent discussions of the treatment of spinal cord injury. Particularly stimulating is the last chapter, Regeneration in the Spinal Cord, by L. W. Freeman, whose presentation of experimental and clinical observations of functional recovery after spinal cord transections will not fail to bring a breath of hope to any one who is still trying to treat the lesion of paraplegics, rather than "rehabilitate" them without treatment.

Other chapters deal with vascular lesions of the cord, congenital defects and intramedullary tumours. There are separate chapters on pain pathways and mechanisms by a psychiatrist, a neurologist and an experimental neurosurgeon, as well as on the method and results of high cervical cordotomy in the treatment of intractable pain.

With an annual contribution to knowledge of this calibre made available to all in a reasonably short time, one sincerely hopes that this society will continue to prosper.

OUTLINE OF ORTHOPAEDICS. 4th ed. John Crawford Adams. 448 pp. Illust. E. & S. Livingstone, Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1961. \$6.30.

This text is to be recommended to a medical student or practitioner who is interested in a broad but brief coverage of the field of orthopedic surgery. Very naturally, there are gaps in the discussion of certain subjects, and the author could by no means be considered radical in the recommended treatment of the various conditions discussed. There is no mention of the role of synovectomy in tuberculous arthritis. His indications for surgical excision in the area of osteochondritis dissecans when it is demarcated are given in detail, when perhaps the preservation of articular cartilage might better be stressed.

This book, as is customary with those of most English authors, is very clearly written in an easy flowing style. It should be a valuable addition to the book shelf of the student or physician.

TUMORS OF THE BREAST. Their Pathology, Symptoms, Diagnosis and Treatment. Max Cutler. 482 pp. Illust. J. B. Lippincott Company, Montreal, 1962. \$24.00.

The author of this book adds his vast personal experience and an extensive review of the literature to the studies of Cheatle, with whom he collaborated in 1931. The chapters on the benign breast diseases, Paget's disease and the male breast are particularly detailed and informative. Benign diseases are divided into physiological hyperplasia or mazoplasia (the commonest), cystic disease and benign epithelial hyperplasia (both of which the author considers to be pre-malignant). Morphological detail is provided that should interest the pathologist. The value of transillumination, whole microscopic sections of the breast and life-long follow-up are emphasized. In cancer therapy, simple mastectomy and extended radical mastectomy are rejected, though surely the former deserves at least the space in the text that the latter receives. The rarer breast disorders are discussed in depth, but the chapter on radiotherapy is disappointing and there is no mention of cancer chemotherapy.

Generally, pathological and clinical aspects are equally treated. Case history summaries are very liberally and usefully used as examples. But the text at times is irritatingly repetitive, and many of the illustrations do not provide sufficient information to justify the space they occupy. The bibliography is copious and up-to-date, and will serve as an excellent reference source. The European literature, so frequently ignored, is given the place it deserves. The book is desirable for the institutional library and for those particularly interested in breast disease, because of the bibliography and the experience that the text represents. However, its expense, the limited outlook and information in the chapters on therapy, and the overemphasis of the author's personal interests will make it unattractive to most Canadian surgeons.

FRACTURES TRASCOTYLOIDIENNES DU BASSIN. Jean Creyssel et J. Schnepf. 122 pp. Illust. Masson & Cie, Paris, 1961. 20 NF (\$4.00 approx.)

L'étude de ces fractures, dont la conséquence est l'arthrose, dans une proportion de 50% des cas, a été faite par des expériences en laboratoire et par des observations cliniques.

Il s'agit des fractures du bassin où la lésion principale est représentée par une solution de continuité au niveau de la cavité cotyloïde, s'accompagnant ou non d'un déplacement de la tête du fémoral, vers le pelvis.

Cette définition établit une distinction entre les fractures trans-condyliennes et les fractures luxations de la hanche où la principale lésion est la luxation postérieure.

Les observations cliniques ont été faites au Centre de Traumatologie de Lyon. Quarante traumatismes du bassin ont été observés, dont quarante sont des fractures trans-condyliennes.

Le chapitre II est particulièrement intéressant pour un rappel anatomique, dont la partie principale est la définition des zones de fragilité du cotyle et de l'aile iliaque. Ces zones sont, pour une part, verticales, situées dans le tiers moyen de l'aile iliaque, et pour une autre part, horizontales, au niveau de l'isthme de l'os iliaque. Cette dernière zone est le siège du trait de fracture dit "fondamental", alors que les traits situés dans la zone verticale de l'aile iliaque correspondent à la composante dans les fractures dites à "deux composantes".

Dans le troisième chapitre, les données expérimentales de l'étude actuelle sont clairement établies, et les observations cliniques qui ont été à l'origine de cette étude sont rapportées avec exactitude.

L'étude expérimentale, à partir des faits cliniques, est orientée dans trois directions, à savoir: 1. Préciser l'interprétation radiologique des traits de fracture; 2. Analyser le retentissement de la dislocation du cotyle sur la mécanique articulaire, et 3. Etudier les conditions anatomiques offertes par la région cotyloïdienne aux chirurgiens qui envisageraient un traitement sanglant des fractures du cotyle.

Cette expérimentation a permis d'insister sur des faits qui, déjà connus par les observations cliniques et radiographiques habituelles, méritaient d'être précisés davantage.

On insiste sur le fait qu'au niveau de l'isthme de l'os iliaque, cette zone faible située entre la grande échancrure sciatique et le rebord du cotyle, se situe le trait fondamental des fractures trans-condyliennes et que ce trait de fracture se prête bien à l'ostéo-synthèse.

Au quatrième chapitre, il s'agit d'une analyse des cas cliniques, en regard de l'expérimentation.

Il s'agit là d'une répétition de ce qui a été dit au chapitre de l'expérimentation, en particulier au sujet de ce trait fondamental unique qui est en quelque sorte le dénominateur commun de toutes les fractures trans-condyliennes.

Les auteurs en arrivent ainsi à proposer une classification de ces lésions particulières du bassin en quatre grands types anatomiques.

Le chapitre consacré au pronostic des fractures du cotyle n'apporte rien de nouveau aux notions déjà connues.

L'exposé des méthodes thérapeutiques constitue une discussion serrée du problème; elle débute par une critique des méthodes usuelles et insiste surtout sur la nécessité d'une réduction anatomique, d'une stabilisation sûre et de la nécessité d'une mobilisation et réhabilitation aussi précoces que possible.

Pour ce qui est de la contention qui doit suivre une réduction fermée, les auteurs rapportent que, pour 19 cas traités par contention

orthopédique pure, 17 ont montré des déplacements secondaires avec arthrose. Ainsi favorisent-ils l'ostéo-synthèse.

Cette ostéo-synthèse est discutée en détail, en particulier pour ce qui concerne la partie du cotyle à fixer, et la voie d'approche à utiliser. Les différentes voies d'approche sont discutées en détail, pour arriver finalement à suggérer une incision dite trans-fessière.

En résumé, il s'agit "d'une méthode chirurgicale de fixation d'une fracture réduite préalablement par voie orthopédique". La grande indication opératoire est le maintien de la réduction et d'une réduction anatomique. Réduction anatomique qui s'applique surtout aux fractures où le trait fondamental intéresse les surfaces portantes, telles que le toit et l'auvent postérieur.

Le dernier chapitre est consacré à la récupération fonctionnelle.

Dans l'ensemble, il s'agit d'une synthèse claire et précise de notions souvent connues, mais appuyées sur une expérimentation qui a permis une objectivité précieuse.

CLINICAL RADIOLOGY OF THE OESOPHAGUS. Marcel Brombart, Brussels. Translated by Sheila Kenny. 383 pp. Illust. John Wright & Sons Ltd., Bristol; The Macmillan Company of Canada Limited, Toronto, 1961. \$15.10.

"La Radiologie Clinique de l'Esophage" was published in 1956 and is now available for the first time in the English language. It is an excellent book, well set out and printed on good quality paper. There is a profuse bibliography at the end of each chapter but as the book has not been revised, recent work has not been included. The translation is at times too literal and somewhat pedantic, resulting in unnecessarily long and complex sentences, such as the first on page 353. Although the standard of the illustrations in the main is good, the reviewer can find no justification for the continued use of positive prints in a radiological treatise.

The first four chapters are devoted to a consideration of the normal anatomy and physiology as well as to radiological techniques. The author then goes on to discuss the functional disorders of the esophagus such as achalasia, esophageal reflux and tiered (diffuse) spasm.

The effect of extrinsic conditions on the esophagus is considered and in particular there is an excellent account of the embryology of the aortic arch and the great vessels. An unexpected omission is any reference to atresia of the esophagus or tracheoesophageal fistula.

There is a thoughtful discussion on the etiology of diverticula of the esophagus and esophagitis. The Plummer-Vinson syndrome finds place in this chapter, but the statement that the latter is found only in women after the menopause no longer holds true. It has since

been described in males following gastrectomy.

Ulcer and carcinoma of the esophagus are then considered and the author makes the interesting point that contrary to established teaching carcinoma is not confined to the sites of anatomical narrowing but may occur at any point. The examination of the hypopharynx is detailed and this is truly one of the most difficult in radiology. Here, as in many other sections of the book, the author is at his best when giving practical details.

The last two chapters are devoted to examination for varices and hiatus hernia and there is an excellent account of the differential diagnosis between phrenic ampulla and hiatus hernia well worth study by all thoracic surgeons. The particular merit of this book lies in the completeness of the practical details as well as the occasional injection of clinical findings and accounts of personal cases. It is quite obvious in every chapter that the author is well versed in world literature yet quite clear in his own mind what his beliefs on any particular subject are.

The book will be read with pleasure as well as profit. It is recommended without hesitation to the radiologist as well as to surgeons and physicians interested in diseases of the esophagus.

THE MONTEGGIA LESION. José Luis Bado. Translated by Ignacio V. Ponseti. 78 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1962. \$7.50.

The author has written a monograph about the Monteggia lesion.

Conservative treatment is emphasized, particularly in children and younger adults with the type 1 lesion with forward dislocation of the head of the radius and anterior angulation of the ulna. The use of the supinated position to maintain reduction of the head after correction of the angulation of the ulna by traction is emphasized. The author gives due credit to the work of others in the field, especially E. M. Evans who has written the most complete recent treatises in English.

Most readers will appreciate the fine printing effort of the Charles C Thomas company in presenting this excellent monograph on a most interesting and difficult subject.

The author recounts his experiences with the type 2 posterior angulation of the ulna and posterior displacement of the head, as well as the type 3 lateral dislocation of the head of the radius with lateral angulation of the ulna. Fortunately, the type 4 lesion, with the dislocation of the head of the radius and the high fracture of the shaft of the radius in addition to the injury to the ulna is rare. This is one of the most difficult injuries that confronts the accident surgeon. This brief volume should be in the reference library of every doctor who is tempted to drive with his arm extending from the automobile window!

ANTICOAGULANTS AND FIBRINOLYTICS. Edited by R. L. MacMillan and J. F. Mustard. International Symposium held in Toronto, February 2-4, 1961, under the auspices of The Ontario Heart Foundation and the Faculty of Medicine, University of Toronto. 449 pp. Illust. The Macmillan Company of Canada Limited, Toronto, 1961. \$7.00.

This is a collection of papers presented at a symposium organized and sponsored by the Ontario Heart Foundation in February 1961. Contributing to the proceedings were experts drawn from several countries in Europe, from the United States and Canada, and the list of authors resembles the bibliography of any article in the general field of thrombosis. All aspects of the problem of thrombus formation and dissolution are touched upon, but emphasis is placed upon the more controversial, important clinical problems along with some of the newer advances in the basic sciences. On the clinical side, great attention is paid to the role of anticoagulant therapy in occlusive disease of the myocardial and cerebral arteries, nine lengthy articles being devoted to this subject alone.

The clinical value of fibrinolytics is examined in much less detail and, it is felt, with much less intensity in two articles.

The basic mechanism of coagulation and anticoagulation are covered in the first 80 pages in, of necessity, a fragmentary way and likewise papers on thrombogenesis occupy the next section of the book.

In two chapters on the control of and criteria for adequate anticoagulant therapy and the choice of anticoagulants, the reader will gain a great deal of information as well as the impression that even those who have devoted their full time to the study of coagulation are still, to a considerable degree, just scratching the surface.

This book must be read by all those interested in the field, for it is a remarkable assembly of information from key sources. Those seeking assistance in their pressing clinical problems will, as often as not, be disappointed in the book for, by design, it raises and discusses questions rather than attempting to answer them.

SPEECH DISORDERS. Aphasia, Apraxia and Agnosia. Sir Russell Brian. 181 pp. Illust. Butterworth & Co. (Canada) Ltd., Toronto, 1961. \$8.50.

This monograph is a scholarly review and comparison of various types of speech disorders. It is introduced by chapters on the nature of language and the development of speech in the human, as well as a thorough summary of the history of thought about aphasia. While the book is as well written and organized as one would expect, and adequately supplied with up-to-date references, the sub-

ject remains a confusing one—as the author says, “Partly because of its great complexity, and partly, perhaps as the result of this, because of the conflicting interpretations which have been placed upon the facts.” The historical review emphasizes that it is really the lack of facts regarding the normal anatomy and physiology of speech which has impeded our understanding of its disorders. Although the author has no new facts to present, he reviews the old ones in the light of pertinent observations from the fields of psychology, phonetics and communication theory.

This book will make a useful addition to the library where it will serve chiefly as a source of reference to the older publications and provide a comprehensive and up-to-date review for the postgraduate student.

THE SURGERY OF TRAUMA IN THE TROPICS. R. L. Batten, with chapter on anaesthetics by J. V. Farman. 234 pp. Illust. Edward Arnold (Publishers) Ltd., London; The Macmillan Company of Canada Limited, Toronto, 1961. \$6.30.

This book is worth recommending to any doctor going out to tropical Africa for the first time. It is short enough to digest during the plane journey out, and easy to read. If the newcomer is heading for the independence and isolation of the small peripheral hospital, he will find in this book a companion with answers to many questions which his work will soon be raising in his mind. If he lacks training in trauma, he will find a brief guide to the management of many common problems in that field.

The pattern of advice, together with passing references to blood volume estimations and sensitivities on bacteriological cultures, suggests that the author himself has not had to depend on the attractive rules of thumb he offers in various places. In keeping with this, the section on organizing a blood bank for a 500-bed hospital is excellent, but advice for the doctor without a blood bank is inadequate. Similarly, fracture advice is generally orthodox, but no guide is given to the doctor without x-ray facilities as to how much or how little he can do. A greater emphasis on substitutions and improvisations which the author has found dependable would have been useful because the medical officer of the smaller hospital often finds himself contending in a new way with the harsh facts of medical economics.

Of particular interest and value are the chapters dealing with the modifications encountered in the tropics in physiology, anatomy and pathology, the chapter on anesthesia and the chapter on complicating illnesses in the tropics. These tell a newcomer in a few pages many things that he might take months to find out on his own.

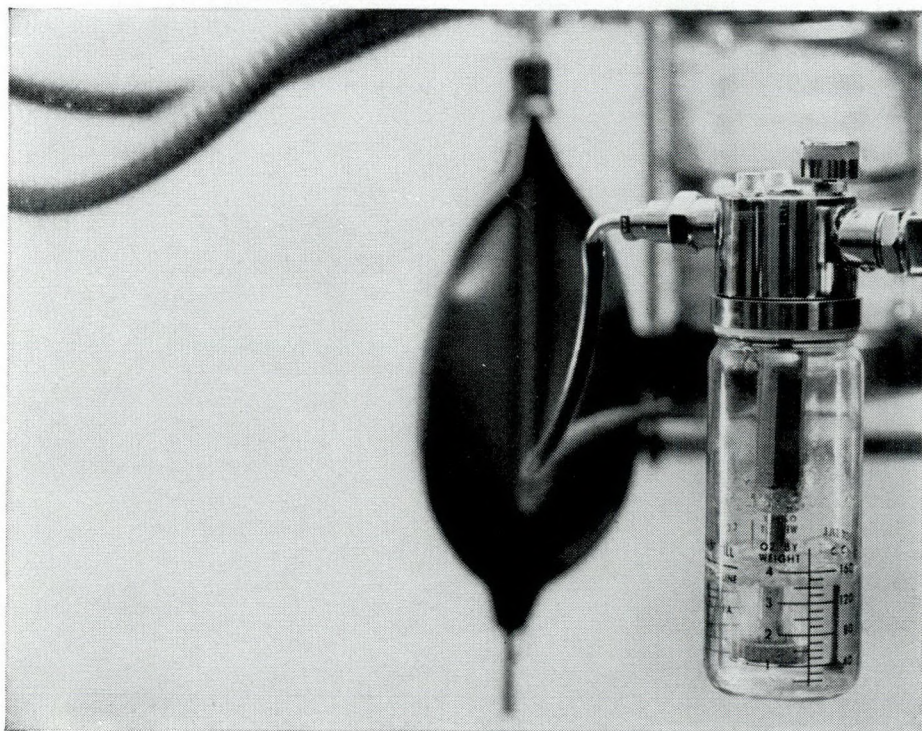
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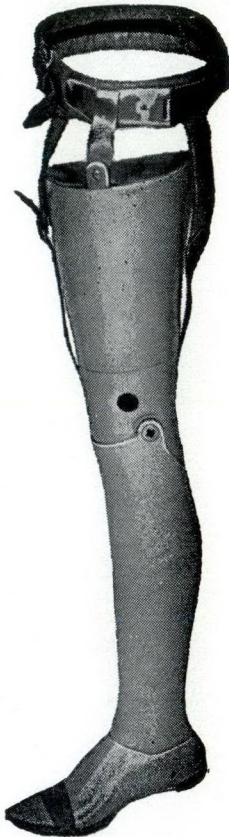
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Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Acquired Surgical Lesions of the Esophagus. Clifford F. Storey, with a chapter on Carcinoma of the Esophagus by E. G. Laforet, J. W. Strieder and J. P. Lynch. Foreword by Alton Ochsner. 365 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1962. \$21.00.

Arteriography. David Sutton. 322 pp. Illust. E. & S. Livingstone, Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1962. \$12.60.

Biological Effects of Freezing and Supercooling. Audrey U. Smith. No. 9. Monographs of the Physiological Society. Edited by H. Barcroft, H. Davson and W. D. M. Paton. 462 pp. Illust. Edward Arnold (Publishers) Ltd., London; The Macmillan Company of Canada Limited, Toronto, 1961. \$9.90.

The Biology of the Trachoma Agent. Annals of the New York Academy of Sciences. Vol. 98, Art. 1, pages 1-382. Conference Chairman: Francis B. Gordon. Illust. New York Academy of Sciences, New York, March 5, 1962.

Blood Groups in Infrahuman Species. Annals of the New York Academy of Sciences. Vol. 97, Art. 1, pages 1-328. Conference Editor: Carl Cohen. Illust. New York Academy of Sciences, New York, May 3, 1962.

π -Complex Mechanism of Catalysis: the Aryl-Coupling Reaction. Minoru Tsutsui. Annals of the New York Academy of Sciences. Vol. 93, Art. 4, pages 133-146. Illust. New York Academy of Sciences, New York, December 22, 1961.

Drugs in Anaesthetic Practice. F. G. Wood-Smith and H. C. Stewart. 464 pp. Butterworth & Co. (Canada) Ltd., Toronto, 1962. \$12.75.

Handbuch der Orthopädie. In vier Bänden. Registerband (Handbook of Orthopedics. In four volumes. Index). Edited by G. Hohmann, M. Hackenbroch and K. Lindemann. Index by Walter M. Dörr. 162 pp. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1962. \$9.00.

Hémophile: Transfusions Massives: Détection des Anticorps: Problèmes Médico-sociaux du Don du Sang. IIIe Congrès National de Transfusion Sanguine, Lyon, 7-10 Juin, 1960. 568 pp. Illust. Masson & Cie, Paris, 1961. 50 NF. \$10.00 (approx.).

The Human Adrenal Cortex. Proceedings of a Conference held at the University of Glasgow, 11th-14th July, 1960. Edited by Alastair R. Currie, T. Symington and J. K. Grant. E. & S. Livingstone, Ltd., Edinburgh & London; The Macmillan Company of Canada Limited, Toronto, 1962. \$9.90.

Hypertension: Recent Advances. The Second Hahnemann Symposium on Hypertensive Disease. Edited by Albert N. Brest and John H. Moyer. 660 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1961. \$12.50.

(Continued on page 356)

(Continued from page 352)

FUNDAMENTAL APPROACH TO SURGICAL PROBLEMS. Lester F. Williams, Jr. and Garnet F. Wynne, Jr., with introductory chapter by Warner F. Bowers. 216 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1962. \$8.50.

In this book, the authors have described the fundamental principles underlying the surgical management of patients. This has been done for the most part in a general way, without reference to specific problems. The aim has been to provide the reasons behind the adoption of certain methods of treatment, so that these then may be applied by the "thinking" surgeon in the day-to-day care of his patients.

Included are discussions covering the physiological responses of the body to injury and the principles of the management of wounds, infections, hemorrhage, fluid and electrolyte imbalance. Preoperative assessment, preparation, operative technique and postoperative care are fully discussed. The reasons for the development of several operative and postoperative complications—including cardiac arrest, paralytic ileus, wound disruption, bleeding, thromboembolic disease and adrenal, hepatic and renal failure are considered in detail. Methods of prevention are particularly stressed.

This book is easily read and contains much practical information. It should appeal especially to the busy surgeon who may have established a "routine" approach to surgical problems and who may want to reassess his care of patients in the light of recent advances in surgical physiology.

DISSEMINATION OF CANCER. Prevention and Therapy. Warren H. Cole, Gerald O. McDonald, Stuart S. Roberts and Harry W. Southwick. 462 pp. Illust. Appleton-Century-Crofts, Inc., New York, 1961.

Four surgeons and a pathologist have set down in some detail the interactions between neoplastic cells and the animal host, primarily man. They have examined the literature extensively but also made use of their own clinical and experimental observations. They have confined themselves to the title of the monograph, discussing etiology, diagnosis, pathology and therapy only in so far as it relates to the spread of an established neoplasm and to its prevention. Liberal use of diagrams, experimental data and photomicrographs is made. Both author and subject indices are complete.

The general physician will benefit from reading the first two and the last chapters dealing generally with the growth, spread, natural history and preventive aspects of cancer. The chapter dealing with the natural history of cancer is perhaps the most important one for clinicians in that it points up the paucity of knowledge in this area, but also sets the base on which reliable observation

must be made, particularly that relating to the value of a specific form of therapy.

The surgeon who deals with the operative management of neoplastic disease will undoubtedly derive benefit from considering, in addition, the chapters describing the spread of cancer by contiguity, by the lymphatics, by the vascular system and by implantation.

Three chapters deal with the relationship of stress, hormones, and immunity to the spread of cancer, and another deals with experimental chemotherapy. These four chapters record many observations and provide a detailed review for persons interested in the experimental aspects of cancer. However, they do not go on to integrate sufficiently these observations nor to relate them to general cellular biology. Thus, reading becomes laborious and the persistent reader is left with many facts but few provocative hypotheses.

In summary, this book reflects the persistent, forward-looking, experimental approach which Dr. Cole and his colleagues have applied to the problem of cancer both at a clinical and laboratory level. It is a useful addition to the library of anyone interested in oncology.

ILLUSTRATED GUIDE FOR THEATRE NURSES. A. M. Matthias, M. J. Penfold and S. Fry. 87 pp. Illust. Butterworth & Co. (Canada) Ltd., Toronto, 1961. \$3.50.

Those who are responsible for the administration of and are familiar with the clinical teaching in the operating room recognize the value and importance of good visual aids as a means of instruction and also for on-the-spot reference.

The right way is the only way. This statement exemplifies the only basic principle whereby safe surgical technique in the operating room may be maintained. All operating room personnel are constantly aware of this. The principle is well demonstrated by means of the clear-cut illustrations. The precise explanations accompanying them are very impressive. This reviewer is in complete agreement with the authors when they state in their introductory remarks ". . . meticulous descriptions tend to defeat their objects . . . and one often loses sight of the principle involved".

The "Illustrated Guide for Theatre Nurses" will serve its most useful purpose in the operating room proper, not only for the nursing personnel but also for the operating-room technician and the medical student. One should not lose sight of the fact that theory has and will continue to have a most important place in teaching student nurses basic operating-room technique. This text with its illustrations will be of definite assistance to all instructors.

The book will be invaluable in small hospitals where there are no clinical instructors and nursing service is often dependent on inexperienced personnel. The text contains an excellent index for quick reference.

(Continued from 354)

Klinische Chirurgie fuer die Praxis. In vier Bänden. Band III, Lieferung 4 (Clinical Practice of Surgery. In 4 volumes, Vol. III, Part 4). Edited by O. Diebold, H. Junghans and L. Zukschwerdt. 250 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1962. \$12.00.

Lectures on the Methodology of Clinical Research. Max Hamilton. 139 pp. Illust. E. & S. Livingstone, Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1961. \$3.80.

Lehrbuch der Chirurgie (Textbook of Surgery). 3rd ed. Edited by H. Hellner, R. Nissen and K. Vosschulte. 1120 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1962. DM 87.00. \$23.00 (approx.).

Malformation Luxantes de la Hanche. Pierre Bertrand, avec la collaboration de H. Guias et H.-M. Bénard. 295 pp. Illust. G. Doin & Cie, Paris, 1962. 76 NF. \$15.20 (approx.).

Mathematical Theories of Biological Phenomena. Annals of the New York Academy of Sciences. Vol. 96, Art. 4, pages 895-1116. Conference Editor: N. Rashevsky. Illust. New York Academy of Sciences, New York, March 2, 1962.

Miscellaneous Mycological Notes. Aldo Castellani. Annals of the New York Academy of Sciences. Vol. 93, Art. 5, pages 147-206. Illust. New York Academy of Sciences, New York, February 12, 1962.

The Postthrombophlebitic Syndrome. Roy J. Popkin. 221 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1962. \$9.25.

Progress in Medical Laboratory Technique—1. Edited by F. J. Baker. 189 pp. Butterworth & Co. (Canada) Ltd., Toronto, 1962. \$7.00.

The Senile Brain. A Clinical Study. R. S. Allison. 288 pp. Illust. Edward Arnold (Publishers) Ltd., London; The Macmillan Company of Canada Limited, Toronto, 1962. \$9.00.

The Spine. A Radiological Text and Atlas. 2nd ed. Bernard S. Epstein. 616 pp. Illust. Lea & Febiger, Philadelphia, 1962. \$17.25.

Surgery of the Stomach and Duodenum. Edited by Henry N. Harkins and Lloyd M. Nyhus, with 43 contributors. Foreword by Sir Charles Illingworth. 736 pp. Illust. Little, Brown and Company, Boston; J. B. Lippincott Company, Montreal, 1962. \$29.50.

Die Traumatologie des Kniegelenks. Diagnostik und Therapie (The Traumatology of the Knee Joints. Diagnosis and Therapy). S. Weller and E. Köhnlein with a foreword by H. Krauss. 221 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1962. DM. 49.50. \$12.40 (approx.).

Vesico-Vaginal Fistulas and Related Matters. C. Scott Russell, with foreword by Norman F. Miller. 97 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1962. \$6.00.

ILLUSTRATED OBSTETRICS

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