THE NOVA SCOTIA MEDICAL BULLETIN

Editor-in-Chief Dr. IAN E. PURKIS

Board

DR. I. D. MAXWELL
DR. D. A. E. SHEPHARD
DR. W. E. POLLETT
DR. A. J. BUHR

Editorial Board

Corresponding Members
Secretaries of Branch Societies

Managing Editor
DR. C. J. W. BECKWITH
Departments
Medico-Legal Column
DR. I. A. MAXWELL
Advertising
DR. D. A. E. SHEPHARD
Thousand Word Series

Cancer In Nova Scotia

The patient with cancer continues to be of great concern to all in the community. After diseases of the circulatory system, cancer is the commonest cause of death in Nova Scotia. It is estimated that twelve hundred people will die of this disease here in 1967, and nineteen hundred new cases of cancer will be diagnosed. With this picture, the medical profession must continue its interest in this problem wherever possible.

These issues of the Bulletin are devoted to presentations on cancer and relate the experience of the authors who are members of the Nova Scotia Tumour Clinic and Victoria General Hospital. Over seventeen thousand patients are recorded in the files of this clinic, with data on the initial findings and treatment as well as the subsequent history of the patient. Over ninety-eight percent of patients have been followed after diagnosis and treatment, a record of which we can be very proud. It shows interest on the part of many to make this program possible, including the Provincial Department of Health, Medical Staff of the Victoria General Hospital, Medical Faculty of Dalhousie University, Canadian Cancer Society. In particular the medical profession of Nova Scotia have cooperated and given their support at all times.

It is important that support of this clinic should continue in order that the experience gained is increasingly made available to the profession and people of this province. It is only by having a group with special interest in cancer that new ideas and treatment will be made available as quickly as possible and research into this dreaded disease stimulated.

J.A.M.

This issue has been contributed by
the staff of
THE NOVA SCOTIA TUMOUR CLINIC
Coordinating Editor: Dr. G. R. Langley

THE MEDICAL SOCIETY OF NOVA SCOTIA

NOVA SCOTIA DIVISION OF

THE CANADIAN MEDICAL ASSOCIATION

MEMBERS OF EXECUTIVE COMMITTEE

OFFIC	LO I	De

BRANCH SOCIETY REPRESENTATIVES

PRESIDENT G. McK. Saunders	Antigonish-Guysborough G. Silv	
PRESIDENT-ELECT A. L. Sutherland	Cape Breton J. B. Tempkins, J. A. MePh Colchester-East Hants H. D. Lav.	
IMMEDIATE PAST PRESIDENT - A. J. M. Griffiths	Cumberland N. G. G.	len
***************************************	DARTMOUTH W. F. Vel	
CHAIRMAN EXECUTIVE COMMITTEE S. C. Robinson	HALIFAX J. K. Purves, H. C. Still, C. H. Grahi	
VICE-CHAIRMAN EXECUTIVE - J. H. Charman	Inverness-Victoria C. L. MacMill	lan
HONORARY TREASURER C. D. Vair	LUNENBURG-QUEENS D. C. Cantele PICTOU COUNTY J. B. MacDom	
HONORARY SECRETARY F. G. Mack	Shelburne F. Mark	cus
Honolani openini	Valley D. J. G. Mor Western Counties M. W. O'Br	
EXECUTIVE SECRETARY - C. J. W. Beckwith	Western Counties M. W. O'Br	en
	OBSERVERS	
REPRESENTATIVE TO C.M.A. EXECU		
CHAIRMAN PUBLIC RELATIONS COMM		
CHAIRMAN MEDICAL ECONOMICS COM		
Editor	I. E. Purkis	
CHAIRMAN OF STANDING COMMITTEES	BRANCH SOCIETIES	
	President Secretary	
	Antigonish-Guysborough - G. R. Greening - S. B. Donigiew	
COMMITTEE CHAIRMAN	Cape Breton D. S. Robb - H. R. Corb	
	Colchester-East Hants - D. R. MacInnis - K. B. Shepha	
Aging P. C. Gordon	Cumberland J. A. Y. McCully - J. F. Donacl	
Annual Meeting President	Dartmouth W. F. Verge - I. M. MacLe	
Archives D. R. MacInnis	EASTERN SHORE D. MacMillan - A. C. Marsh	
By-Laws J. E. Hiltz	Halifax J. K. Purves - P. C. Gord	
CANCER J. A. Myrden	INVERNESS-VICTORIA - N. J. MacLean - C. L. MacMill LUNENBURG-QUEENS - D. C. Langille - W. I. Be	
CHILD HEALTH B. S. Morton	LUNENBURG-QUEENS D. C. Langille - W. I. Be PICTOU COUNTY E. B. Skinner - W. D. MacLe	
CIVIL DISASTER S. B. Bird	Shelburne W. H. Jeffrey - A. S. Robbi	
EDITORIAL BOARD (EDITOR) I. E. Purkis	VALLEY D. McD. Archibald - D. H. Kirkpatri	
FEES J. H. Charman	Western N. S V. K. Rideout - F. S. Ozve	
FINANCE (Hon. Treas.) C. D. Vair	SECTIONS	0.0
Hospitals J. A. Smith Insurance E. B. Grantmyre		
LEGISLATION & ETHICS H. K. Hall	CHAIRMAN SECRETARY	
MATERNAL & PERINATAL HEALTH - D. F. Smith	Section for Anaesthesia - A. A. Drysdale - J. H. Feine	iel
MEDIATION & DISCIPLINE President	Section for General PRACTICE D. C. Brown - M. M. Bru	ice
Medical Economics - K. B. Shephard	Section for Internal	
MEDICAL EDUCATION - R. N. Anderson	Medicine A. H. Shears - S. E. Yo	rk
MEDICAL LEGAL LIAISON I. D. Maxwell	Section for Obstetrics &	
Membership M. G. Tompkins	GYNAECOLOGY - D. F. Smith - D. W. Cudmo	re
Mental Health R. J. Weil	Section for Ophthalmology & J. A. Langille - J. H. Quigl	ev
Nutrition C. F. Brennan	Section for Paediatrics - N. B. Coward - R. S. Gra	-
OCCUPATIONAL MEDICINE J. C. Wickwire	Section for Pathology - A. MacKenzie - A. J. Lev	vis
PHARMACY A. F. Pasquet	Section for Psychiatry - J. F. Nicholson - S. Hir	sh
Physical Education & Recreation J. K. B. Purves	Section for Radiology - E. B. Grantmyre - H. B. Sabe	an
Physicians' Services Insurance - President Public Health V. K. Rideout	Section for Residents in	187
PUBLIC RELATIONS O. H. Millard	Training R. A. Langille - T. J. Murr	ay
REHABILITATION A. A. Macdonald	Section for Salaried Physicians A. W. Titus - J. R. Camer	on
- III III MACCOUNTED	The state of the Chiller	-

AUTHORIZED AS SECOND CLASS MAIL BY THE POST OFFICE DEPARTMENT, OTTAWA, AND FOR PAYMENT OF POSTAGE IN CASH-PUBLISHED BY THE MEDICAL SOCIETY OF NOVA SCOTIA, 5849 UNIVERSITY AVENUE, HALIFAX, N. S.

J. F. Ross Section for Surgery -

- M. E. Delory Section for UROLOGY -

TRAFFIC ACCIDENTS

W. C. B. LIAISON -

C. H. Graham

W. A. Ernst

J. A. Noble -

F. G. Mack -

Introduction To Cancer Symposium

The group of papers which have been selected for this Cancer Symposium provide the physician in this province with a unique opportunity to obtain comprehensive and up-to-date information on cancer in Nova Scotia. The authors, writing from a vast experience in cancer diagnosis and treatment, present their observations for your information. In several of the articles, data obtained from analysis of cases from Nova Scotia are included thus providing the reader with a ready source of information from the same population which he serves.

The opening article by Dickson, although specifically related to cancer of the stomach, illustrates one of the major problems present in achieving better cure rates in any cancer, the delay in diagnosis. He shows that three periods of delay can be recognized, the delay in the onset of symptoms, the patient's delay in seeking medical advice and the physician's delay in diagnosis. In the succeeding article, Millard, in studying genitourinary tract cancer in Nova Scotia, found more than 90% of 107 cases of cancer of the prostate, at the time of diagnosis, had either local or distant spread. With the prostate so easily examined and cancer of this organ such a common tumor, an effort to improve these figures should be important to all of us.

Cancer chemotherapy has proven to be of great value in recent years in choriocarcinoma. Although the drugs show great toxicity, with careful use impressive survival figures are being obtained as Flight indicates in his article, Neoplasms of the Placental Trophoblast. He reviews the therapeutic programs for this and other tumors and in addition gives important information of the recognition of neoplasms of the placental trophoblast.

Ing emphasizes again that radiotherapy remains the treatment of choice for Hodgkin's Disease, but the selection of a treatment program depends on accurate clinical evaluation of the patient, the extent of the tumor and on an understanding of the natural course of the disease. When chemotherapy is required we now have several drugs which will control this disease temporarily, of which he selects Velbe, Nitrogen Mustard and Methylhydrazine as most useful in his group's experience.

An interesting analysis of the causes of death in a matched series of solid tumors with and without radiotherapy and in reticuloendothelial neoplasms by Epstein and Hameed concludes part I of the Symposium. All physicians will be impressed by the findings in this group of patients who died in the Victoria General Hospital and in particular in the frequency of infections as a cause of death.

In Part II of the Symposium to be published in April, Bethune reviews one of the commonest complications of breast cancer, pulmonary metastasis. In 800 cases of breast cancer studied, he found at some time in the course of the disease, pulmonary metastasis in 160. His figures on treatment indicate that even with this complication certain therapeutic programs have been quite beneficial and improve patient comfort and perhaps survival.

Norvell reviews cutaneous moles and melanoma and gives valuable diagnostic points on the early recognition of malignant change in moles and accompanies these with excellent photographs. He makes two important recommendations in handling moles, that they should never be treated by electrodissection and incisional biopsies should be avoided. His experience with intralymphatic cannulation and administration of radioactive materials to lymph node secondaries by this route will provide interesting reading.

Myrden reviews 204 cases of carcinoma of the lip in patients from Nova Scotia, his data showing that individuals even in the second and third decade can develop this lesion. The impressive survival figures in these patients should not let us forget the importance of early diagnosis and treatment.

The use of new chemotherapeutic agents in the treatment of myeloma is outlined in the next article and it appears that Melphalan has proved to be helpful in controlling tumor growth healing bone lesions and effecting a reduction of the myeloma serum protein. Whether long term survival will be improved is not as yet apparent.

These articles are offered with the hope that they will be useful in the diagnosis and treatment of patients with cancer in Nova Scotia.

G.R.L.

The Differential Diagnosis of Peptic Ulcer From Gastric Carcinoma*

Robert C. Dickson, MD, FRCP., FACP.

Halifax, N. S.

The title of this presentation could be interpreted in a very limited sense as referring to the determination of whether an ulcer in the stomach is benign or malignant. The problem, however, is really a bigger one which demands assessment of the problem of the early recognition of gastric cancer and its differentiation not only from gastric ulcer but also from duodenal ulcer and other disorders of the upper gastrointestinal tract giving rise to symptoms.

The prognosis of gastric cancer today is grim indeed. Of 100 patients admitted to hospital with gastric carcinoma, 50 will prove inoperable on the basis of the bedside examination and X-ray of the stomach. Of the remaining 50, 25 will prove inoperable from the viewpoint of attempted cure when laparotomy is performed. Of the 25 left in whom a curative operation is attempted, 4 to 5 will be alive in five years. It is fair to say that all efforts to improve the prognosis have to date been unavailing. Some consideration of the factors which contribute to this failure is indicated.

With the existing methods of treatment, any hope of cure of gastric cancer depends upon the surgical removal of the growth before metastasis has occurred. Unfortunately, a large proportion of patients have been found inoperable by the time their diagnosis is made. Three periods of delay can be recognized which contribute to this situation. The first is the delay in onset of symptoms. Unless the tumour ulcerates early and produces pain or bleeding; or unless it causes early obstruction, the first symptoms the patient may note, even though reported immediately and investigated immediately, usually prove to have developed after the tumour had spread beyond the scope of operability.

The second period of delay may be termed "patient delay". It represents the period elapsing between the onset of symptoms and the patient being examined by a doctor. Gray and Ward in the United States in 1952 reported an average patient delay of 7.8 months in 104 cases reviewed. Swynnerton and Truelove in England in 1953 reported that only 16 per cent of their patients sought treat-

ment within six months of the appearance of th first symptoms.

The third period of delay can be termed "physician delay" and represents the period between the time the patient first reports to a doctor and the time diagnosis is established. In the series reported by Gray and Ward in 1952, this was approximately six months. Some estimate that the physician delay has been reduced in the last decade to about three months although this estimate is not well document ed. It is obvious that nothing the physician can do will obviate the first period of delay apart from periodic examination in high risk individuals. It is difficult too for the physician to influence the period of "patient delay". He can, however influence the period of "physician delay".

It is all too common for the patient who report to his physician with indigestion to be treated symptomatically for a period to determine whether or not his symptoms clear. This approach is quite unjustified. Lesions in the region of the pylorus no matter what their cause, will produce symptoms similar to those of duodenal ulcer. The very least examination that can be considered adequate must include careful X-ray examination of the upper gastrointestinal tract immediately the patient reports symptoms. If this X-ray reveals a duo denal ulcer, well and good. The diagnosis has been established the more certainly, the site of the ulcer established and should complications develop later the physician will be in a more knowledgeable position to deal with them. Meanwhile, the patient can be introduced to a regime of treatment which will render such complications less likely.

If on the other hand, the X-ray reveals an ulcein the stomach on the posterior wall near the lesser curvature with all the characteristics of a benignulcer, then one is faced with an entirely different problem which will be considered later. If the ulcer is in the prepyloric region of the stomach on the lesser curvature and appears benign, the problem again is different. This too will be considered later. If the lesion proves to be carcinomated the pyloric end of the stomach, then at least one has brought about its detection at the earliest

*From the Department of Medicine Dalhousie University and The Victoria General Hospital, Halifax, N. S.

possible moment.

The most difficult problem is a patient who presents no evidence of abnormality on X-ray. In this day of great awareness on the part of physicians and patients of the effect of emotion on bodily functions, it is usual to consider the patient presenting these findings as having a functional disorder of the upper gastronintestinal tract, and this may indeed be the case. However, if the symptoms develop first in a middle-aged person previously free from indigestion, then this patient warrants a repeat examination within a month by X-ray and perhaps further examination by other means which will be discussed.

Physical findings in relation to gastric earcinoma may well be present; one may feel a mass; one may find a sentinel gland in the neck or axilla; one may find evidence of metastases in the liver or a rectal shelf but all these findings are indicative of inoperability in so far as cure is concerned.

How then can we hope to improve results of treatment of this dread disorder? I would like to consider with you four main groups: The first, a patient with an ulcer in the pyloric segment of the stomach which appears on first examination to be benign. The second, the patient with an ulcer on the posterior wall near the lesser curvature which appears on X-ray examination to be benign. The third, the patient with the recent onset of indigestion with negative findings on the first examination, and fourth, the high risk group composed of patients with adenomata, gastric mucosal atrophy, achlorhydria or Addisonian pernicious anemia.

Ulcer in the Pre-pyloric Segment of the Stomach

From the statistical point of view, 50 per cent of ulcers in this portion of the stomach will be malignant. However, most of the ones that are malignant are obviously malignant on radiological examination. Of the ones which appear benign, further investigation may be undertaken by gastroscopy or by cytological studies. There is very definite limitation to the value of both these examinations. Only 50 per cent of ulcers in this region can be visualized on gastroscopy usually because of the configuration of the stomach. If the ulcer is seen, it can often be determined whether or not it is malignant but the diagnosis seldom conflicts with that of the radiologist. If it does conflict with the radiologist, then it should not overrule the radiological diagnosis which is more reliable than that of the gastroscope. One very definite contribution the gastroscope can make to lesions in this area is where the radiological examination shows a narrowed and apparently fixed pyloric segment. If this is, in fact, due to spasm and not to infiltration, on gastroscopic examination if the lesion is benign, one can see peristaltic waves progressing through the segment in a normal fashion. This observation is only valid if the pylorus itself is visualized and the waves seen to progress right to it. If all the findings indicate the likelihood that the lesion is benign,

the patient should be treated by bed rest, diet and alkalis for a period of two weeks and then re-X-rayed. Unless the ulcer has decreased in size by 50 per cent the patient should be treated surgically. If the ulcer has decreased by 50 per cent, treatment should be continued for a further two to four weeks and again the patient should be examined by X-ray. If by this time the ulcer has not healed entirely, the patient should be treated surgically.

Ulcer on the Posterior Wall near the Lesser Curvature

Seventy per cent of ulcers of the posterior wall near the lesser curvature are benign. In certain instances, where the X-ray appearance indicates malignancy, operation should be undertaken at once. In all patients with gastric ulcer in whom the augmented histamine test reveals absence of the HCl, operation should be undertaken at once since up to the present no case of benign ulcer has been found in patients who are achlorhydric to this test. In those which appear radiologically benign, further examination by gastroscopy may be undertaken and some gastroscopists feel confident that the gastroscopic appearance enables them to accurately differentiate benign from malignant lesions. My own experience is not so happy and I feel that the gastroscope has little or no place in the differentiation of benign from malignant ulcers on the posterior wall near the lesser curvature. In fact, it is difficult to see how this could be otherwise since the pathologist with a resected stomach in his hands cannot by looking at the gross lesion always be sure whether it is a benign or a malignant ulcer at which he is looking. The management of this lesion in my opinion is similar to that of the lesion in the pyloric segment - two weeks' treatment with 50 per cent healing, complete healing in four to six weeks, otherwise operative treatment.

New Symptoms - Normal X-ray

Consideration of the patient who presents with the recent onset of upper gastrointestinal distress and negative X-ray findings presents an important and difficult problem. Such patients should be placed on treatment by diet and mild sedation and re-examined after an interval of not more than one month. Should the X-ray findings still be normal, then gastroscopy and if available cytological studies and a gastric analysis should be done. Even when greatest care is exerted and a high index of suspicion maintained, cases of early cancer will be missed but, on the other hand, some will be detected at the earliest possible time.

High Risk Group

Finally, a group of conditions in which the incidence of carcinoma is high must be considered. Patients who have adenomata of the stomach discovered should have them removed if they are single or if only one or two are present, unless coexistent disease causes an operative risk which is too great. In different reported series, 7 per cent

to 27 per cent are malignant. In patients with multiple polyps, for example, Peutz-Jeghers syndrome, the problem is more difficult. Some advocate total gastrectomy. Fortunately, the problem is rare.

The patients with gastric mucosal atrophy, patients with achlorhydria, and patients with Addisonian pernicious anemia all have a higher likelihood of developing gastric carcinoma than the average for the population. In pernicious anemia, the incidence of carcinoma is 10 per cent. Some advocate yearly radiological examination of such patients for the earliest possible detection of carcinoma. These examinations of patients with pernicious anemia were carried out on patients attending the Outpatient Haematology Clinic at the Toronto General Hospital. Even this did not result in detection of cancer early enough to improve the five-year survival rate - and the program has been abandoned.

It may be that cytological studies will be useful in this group but this has yet to be proven.

Gastric Cytology

Gastric cytology was first advocated by Lionel Beale, Professor of Medicine at King's College, London in 1858 - he advised examination of the vomitus for malignant cells in patients suspected of having gastric carcinoma. In 1947, Papanicolaou introduced the modern technique and since then considerable effort has gone into the development of cytological studies of material obtained from the stomach by various techniques which include brushes of various types and washing. Percentage accuracy of this method has varied from that of Papanicolaou and Cooper in 1947 who on examining the fasting aspirate had an accuracy of 37 per cent to that reported by Raskin, Kirsner, and Palmer in 1959 using gastric washings with a reported accuracy of 95 per cent. Why then is this technique not used more than it is? The answer seems to lie in the time element. Dennis Gibbs of the Boston City Hospital has an accuracy of 85 per cent by the most meticulous method. He collects the washings himself spending about two hours washing and rewashing the patient's stomach and then takes several quarts of fluid to his laboratory where it is centrifuged and eventually about 20 slides made from the sediment. These are screened by his technician and he himself spends about a half an hour on each of four selected slides. This, then, is obviously a time-consuming and therefore expensive method of examination. The use of tetracycline fluorescent technique has been said to increase the accuracy and the speed of this cytological examination. However, it gives rise to false positives particularly in patients with bronchitis where bronchial epithelium can be swallowed which has picked up the tetracycline and fluoresces in the same manner as does a malignant cell.

One can say that at the present time cytological examination remains in the investigative stage and its exact role and value has yet to be determined. It may have a place in the examination, of any patient suspected of gastric carcinoma but is unlikely to add greatly to the solution of the problem.

The foregoing review of the problem of gastrie cancer and the diagnostic measures available for its study have not included any discussion of enzyme activity in the gastric juice or various biological reactions which have been described by various authors. In brief, these have not contributed seriously to the solution of the problem of gastric carcinoma. Mention should be made of the finding of occult blood in the stools with or without chronic microcytic, hypochromic anemia. The three most likely causes of chronic blood loss into the gastrointestinal tract are peptic ulcer, gastric carcinoma, and carcinoma of the cecum. The finding of anemia of this type in a man or a woman past the child bearing age should immediately demand a search for the source of bleeding and its correction.

In summary, it can be said that new diagnostic methods and increasing awareness of physicians has not seriously altered the prognosis in carcinoma of the stomach. Even were "Phylician delay" and "patient delay" eliminated entirely, the prognosis would remain a grim one, since in so many instances the disease is inoperable from the point of view of cure from the time the patient has his first symptoms. In the natural history of this disease, it would appear obvious that metastasis occurs early, how early this may be, no one can say with certainty. Perhaps it is the second malignant cell which is transported to a distant organ and there starts to multiply. To put forward the hope that early diagnosis is the answer to the conquering of this disease would be ridiculous. To feel that any of our present methods of treatment will be successful in solving the problem would be equally unrealistic. Indeed, further advance in the treatment of this form of malignancy must await the development of new agents capable of dealing with disseminated carcinoma.

References

- Gray, D. B. and Ward, G. E., American Journal of Surgery - 83: 524: 1952.
- SWYNNERTON, B. F. and TRUELOVE, S. C., British Medical Journal - 1: 287: 1953.
- Beale, L. S. The Microscope in Medicine, 2nd. Edition. London J. & A. Churchill Ltd., 1858. (as quoted by Vilardell, F., in Bockus, H. L. Gastroenterology - 2nd. Edition, Vol. 3, p. 329 - W. B. Saunders Company, Philadelphia and London, 1964.)
- PAPANICOLAOU, G. N., and COOPER, W. A., J. Nat-Cancer Inst. - 7: 357: 1947.
- RASKIN, H. F., KIRSNER, J. B., and PALMER, W. R. -J.A.M.A. - 169: 789: 1959.
 re Dr. Dickson's paper on Peptic Ulcer

Carcinoma of the Prostate*

O. H. MILLARD, MD, FRCS(C)

Halifax, N. S.

Introduction

As a cause of death from malignancy, tumors involving the male genitourinary tract rank third in frequency behind those of the digestive and respiratory tracts.

Many of these tumors occur in the elderly, and in view of the increasing proportion of older people in the population, these tumors assume increasing importance as a cause of morbidity and death.

Genitourinary tumors more frequently involve the prostate, the bladder, and the kidney. The incidence of these tumors is shown in Tables I and II, and as can be seen, carcinoma of the prostate is by far the most common.

TABLE I

INCIDENCE OF MALE GENITAL CANCER IN NOVA SCOTIA PER 100,000 MALE POPULATION

Prostate.			 				 	 ٧.			. ,	28.6
Testis				1		-						1.3
Penis and	Scrotum	100							-		٠,	2.4

TABLE II

INCIDENCE OF KIDNEY AND BLADDER TUMORS IN NOVA SCOTIA PER 100,000 POPULATION

	Total	Male	Female
Kidney	4.2	5.9	2.5
Bladder	9.0	15.2	2.5

Incidence

The incidence of carcinoma of the prostate, as seen from Table I, is about 28 cases per 100,000 of the male population per year. These cases are found mainly in men over 50 years of age. The age distribution can be seen from Table III, and it is noteworthy that 95% of cases occur in the 60 - 90 year age group, and that almost 50% of all cases occur in the seventh decade.

TABLE III

Age Distribution in 107 Cases
of Carcinoma of Prostate

Age	Number of Cases	Percent
40-49 50-59 60-69 70-79 80-89 90+ Total	1 5 21 52 27 1	0.9 4.6 19.6 49.0 25.0 0.9 100M

Pathology

Carcinoma of the prostate is typically an adenocarcinoma, which includes over 95% of all prostatic tumors. The tumor arises in the posterior lobe of the prostate in about 70% of cases, and spreads from here to involve the remainder of the gland. It spreads by direct invasion, by lymphatic permeation and via the blood stream, to involve the bones of the spine and pelvis, with the typical dense sclerotic metastatic lesions seen on X-ray.

Diagnosis

In the diagnosis of malignant disease in general it is our aim to diagnose malignant tumors at as early a stage as possible in order that curative steps may be taken.

When the tumor is confined to the prostate, curative surgery can be employed to attempt to remove the tumor, in the hope of preventing death from carcinoma.

If this disease is diagnosed in the later stages, when the tumor has spread beyond the prostate, only palliative treatment is possible.

Carcinoma, when still confined to the prostate, may have no specific symptoms and no radiological or laboratory findings. The tumor is detectable at this stage by rectal examination, although some cases will be discovered following surgery for what was taken to be benign enlargement. It has been said that unrecognized carcinoma of the prostate will be found in from 3 to 5% of all operations for benign prostatic enlargement. Some of these so-called occult carcinomas are candidates for further radical surgery to remove completely any malignant tissue that may remain.

One of the more important aspects of the diagnosis of prostatic carcinoma is the estimation of the clinical stage of the tumor. This depends on rectal examination under anesthesia, combined with cystoscopy and possibly biopsy, determination of the serum acid phosphatase levels and metastatic bone survey. These tumors are staged as A, B, C or D, Stage A being the occult carcinoma discovered, as it were, accidentally, having been unsuspected prior to surgery. Stage B tumors comprise the hard nodule clinically limited to the gland on rectal examination. In both these stages the tumor is potentially curable. In Stage C, the tumor has clinically spread through the capsule, and the prostate is said to be fixed. No radiological or biochemical evidence of distant metastases can be found. In

^{*}From the Department of Urology, Dalhousie University and the Victoria General Hospital.

Stage D, distant metastases are evident, by physical examination, by radiologically demonstrable osteoblastic metastases or by elevated serum acid phosphatase. The last two stages, as mentioned here, are presently considered to be incurable stages of the disease. Table IV shows the distribution by stage of carcinoma of the prostate diagnosed at this hospital.

TABLE IV

CLINICAL STAGE OF PROSTATIC CARCINOMA AT FIRST DIAGNOSIS VICTORIA GENERAL HOSPITAL

Stage D.....

Stage	A																	1%
ounge	D								ļ,									5%
Stage	C		. ,		÷				,	,					,			40%

The diagnosis, then, of potentially curable carcinoma of the prostate rests entirely on periodic rectal examinations in all males over the age of 40. A hard prostate or prostatic nodule should be considered to be carcinoma until proven otherwise by biopsy. We can only hope to reduce the morbidity and mortality from carcinoma of the prostate by means of early diagnosis, and radical surgery, before extension beyond the prostatic capsule has occurred. It is notable that of all men seen with carcinoma of the prostate at the Victoria General Hospital over the past 10 years, only 5% have been considered to be candidates for radical surgery by virtue of the growth being considered clinically to be confined to the prostate. All other cases have had local invasion or distant metastases when first seen. The patient with carcinoma of the prostate clinically confined to the prostate, has a reasonable chance of cure of his disease. All others can expect a variable degree of palliation by means of bilateral orchiectomy and estrogen therapy.

In view of the foregoing, it is obvious that most cases of carcinoma of the prostate are presently not being diagnosed early enough to be curable, and this vast majority are usually discovered because of symptoms of urinary obstruction or symptoms of metastatic disease.

The accuracy of diagnosis of carcinoma of the prostate by means of rectal examination alone, has been estimated to be in the vicinity of 80%, depending on the experience of the examiner. This clinical method of diagnosis, however, should be supplemented by biopsy of any area of hardness in the Experience with transperineal needle biopsy in the Department of Urology at the Victoria General Hospital, has shown that this method will establish the diagnosis in over 95% of cases in which carcinoma exists and is subsequently proven by surgery.2 No false positive biopsies have been found in over 300 cases.

The diagnosis in later stages of carcinoma of the prostate is usually made by discovery of a hard prostate rectally, combined with radiological evidence of osteoblastic skeletal metastases and/or elevation in serum acid phosphatase.

It should be emphasized here that the finding of a normal serum acid phosphatase does not exclude the diagnosis of carcinoma of the prostate. biochemical test has significance only when the level is elevated, in which case carcinoma of the prostate is about 99.9% likely.

Treatment

The treatment of carcinoma of the prostate at the Victoria General Hospital is divided into two categories, depending on the clinical stage of the tumor.

Radical Surgery. Cases of prostatic carcinoma suitable for radical surgery are those tumors clinically estimated to be limited to the prostate, with no evidence of local or distant metastases as determined by cystoscopy, pyelography, bimanual rectal and abdominal examination, metastatic survey and serum acid phosphatase determin-

The surgical procedure is radical retropuble prostatectomy, in which the entire prostate is removed, along with the seminal vesicles and bladder neck, anastomosing the bladder to the membranous urethra. In most of these individuals, bilateral orchiectomy is also performed, and estrogen therapy is administered indefinitely.

Postoperative problems are those of incontinence and impotence. A high proportion of these patients will show a variable degree of stress incontinence on coughing or straining, and about 5% will be totally incontinent and will require some type of urinary drainage apparatus. Impotence is almost always present, due to removal of the nerve supply surrounding the prostate.

Survival statistics indicate that this is a worthwhile procedure, and even if not curative, removal of the prostate frequently prevents local symptoms of dysuria and tenesmus from the malignant growth. Of 22 eases of radical prostatectomy for carcinoma of the prostate performed at the Victoria General Hospital between 1956 and 1961, 13 are still alive without evidence of cancer, one person is living at the present time with evidence of disease, five patients have died of cancer, there were two postoprative deaths - both due to myocardial infaretions - and one patient has been lost to followup.

b. Palliative Treatment. All cases of carcinoma of the prostate belonging in Stages C and D as estimated clinically, and confirmed by evidence of local or distant metastases, are treated by means of bilateral orchiectomy and estrogen therapy in the form of Diethylstilbestrol 5 mg. daily indefinitely. Those with symptoms of urinary obstruction are treated by transurethral resection of the obstructing tissue if the general condition of the patient justifies surgery. Some patients are too ill to withstand surgery and are put on catheter drainage and Stilbestrol. In some of these cases, the dramatic relief from pain and improvement in appetite and wellbeing from Stilbestrol, may make limited resection of the urinary obstruction feasible and justified.

The problem of the localized painful metastatic lesion in the vertebrae, hip, or long bones is not uncommon. This may be a presenting symptom of the tumor. Most of these lesions will respond favorably to orchiectomy and estrogens. Those which do not respond and remain painful, or those which relapse from control, should receive local radiotherapy. Those cases not responding to Stilbestrol and orchiectomy and/or radiotherapy, may respond to chemotherapy, in the form of Velbe (Vincaleucoblastine) intravenously. Caution should be used, due to the likelihood of other complications from chemotherapy.

Prognosis

It is generally agreed that the addition of Stilbestrol and orchiectomy to the armamentarium in the treatment of carcinoma of the prostate has resulted in about one extra year of life as regarding average survival time. Nesbitt and Plumb³ published a report on the survival of untreated carcinoma of the prostate prior to the use of Stilbestrol and castration, and showed an average survival rate in the vicinity of 32 months for all cases.

At present, the average survival of Stage C carcinoma of the prostate is about four years, that of Stage D carcinoma is about three years. Stage A tumors survive ten or more years, and Stage B tumors about ten years, in the absence of radical

surgery.

None of the foregoing prognostic implications should be allowed to detract from the usefulness of orchiectomy and/or estrogen therapy in the treatment of prostatic carcinoma. While the life span may not be markedly lengthened in the average case, the remarkable relief from pain, and improvement in appetite and outlook of the sufferer from metastatic carcinoma of the prostate are the legacy of Dr. Charles Huggins and those workers who preceded him, and constitute a milestone in the neverending fight against cancer.

Acknowledgments

 The author wishes to thank Dr. C. L. Gosse, Head of the Department of Urology, for his advice and suggestions in the preparation of this paper.

The author also wishes to thank Dr. J. A. Myrden and the Staff of the Nova Scotia Tumour Clinic for the provision of statistical data.

References

- BAUER, W. C., McGAVRAN, M. H. and CARLIN, M. R.: Cancer 13: 370, 1960.
 GREENE, L. F. and SIMON, H. B.: J.A.M.A. 158: 1494, 1955.
- 2. Gosse, C. L. and MILLARD, O. H.: Unpublished data.
- 3. Nesbitt, R. M. and Plumb, R. T.: Surgery 20: 263, 1946.

FORTY YEARS AGO

From the Nova Scotia Medical Bulletin March 1927

Those were the days, when the horse was both telephone and automobile. In sickness, someone must drive to the Doctor's office. The Doctor's wife was the office boy. She had an intimate personal acquaintance with all the Doctor's patients, and with their complaints. Mrs. Geddes was wise and discreet, with an abounding sympathy and genuine goodness of heart. She could dispense medicine for a cold or a cough, or a toothache, or fever, to tide along until the Doctor could see the case himself; or, in case of an accident, could meet the emergency to clean and bandage a wound, or splint a broken bone. It was very common then, for people who had driven a distance, say ten to twenty-five miles, to wait for hours. With such occurrences, the Doctor's table had to be a long one, and the Doctor's wife had to be prepared for unexpected visitors. His house was a hospitable place. full of bustle and activity. There was always the proverbial servant maid, a smart, clean, healthy, country girl; and a man, generally a middle-aged married man, to look after the horses, cow and garden. The Doctor generally kept two horses. but as he grew older and became less active, fell back to one. In the two-horse stage, he was a busy man, always on the road, practically day and night, and only at home to change horses, one might say. Dr. Geddes for years rode in the saddle. but after coming to Yarmouth used the carriage. Though constantly in the saddle, he was an awkward looking equestrian, I am told.

Dr. Geddes excelled as a medical man, and from his training, was a skilled dispenser. He was no surgeon. He had his nose always in a book, and was not apt with his hands. There was one accomplishment, however, that he had acquired, that he excelled in. He could shoe his own horse, and I have often seen him put a shoe on it, in the stable. I have never known another medical man with this accomplishment.

It might be interesting before closing the sketch of Dr. Geddes, for you to know what he was earning. The January 1876 earnings as shown by his day-book, with total charges and cash, were \$110.80.

Total	earnings	for	1876, w	ere	 \$1,123.15
**	"	"	1877	**	 1,358.00
,,,	- 11	17	1878	"	 1,210.00

Editors Note: from reminiscences of the 1870's by Dr. C. A. Webster.

Appreciation

Geoffrey Alden Barss

The death occurred suddenly at his home after a short illness of Geoffrey Alden Barass, aged 80 years, on January 27th, 1967. Dr. Barss was born in Dartmouth, Nova Scotia, the son of the late William Lawson Barss and Florence Payzant Barss. He received his education at Acadia and Dalhousie Universities.

His first practice was in Newfoundland where he spent two years until World War I, when he joined the Royal Medical Corps and served as Medical Officer in the front line, first with the 19th Durham Light Infantry, and later with the Second Battalion Scots Guards. He was twice mentioned in Dispatches for bravery. Following his discharge from the army in 1919, he moved to Rose Bay, Lunenburg County, where he remained to the present, living with his son and family. His wife predeceased him in 1948.

Dr. Barss had an active interest in community affairs, being a former President of the Riverport District Board of Trade. He was a member of the Presbyterian Church Choir, a former Sunday School teacher at the Rose Bay United Church and a member of the I.O.O.F. Lodge, the Canadian Legion as well as the Board of Directors of the Lunenburg Sea Cadets.

Dr. Barss was elected to senior membership in both The Medical Society of Nova Scotia and the Canadian Medical Association. He was an Honorary Member of the Lunenburg - Queens Medical Society and the Medical Staff of the Fishermen's Memorial Hospital, Lunenburg. Dr. Barss was also a member of the staff of the Dawson Memorial Hospital, Bridgewater.

Dr. Barss recollected that in the early years of practice, major operations were carried out in the homes, the nearest hospital being Halifax. It was not unusual to have a neighbour as an anaesthetist with illumination from an oil lamp. Returning from a night call he would have to "bed down and feed his horse and then split firewood for the next day". In those days medical accounts were often paid by "one pork roast, four pounds lobsters, two bags of potatoes, or one load of firewood".

During recent years Dr. Barss was engaged in part-time practice with his son. He devoted most of his time to non medical interests such as gardening, reading, painting and bird study. He was also engaged in writing a history of the Lunenburg-Queens Medical Society.

Dr. Barss is survived by his son, Dr. Allison H. Barss, Rose Bay.

International Symposium Electrical Activity of the Heart

An International Symposium on Electrical Activity of the Heart is being held May 24th, 25th and 26th, 1967, in London, Ontario, Canada.

This Symposium is jointly sponsored by the Ontario Heart Foundation and the University of Western Ontario. It will be of value to those interested in the more recent developments in electrical activity of the heart, electrocardiography, vectorcardiography and computer analysis.

The invited speakers are from Europe, Asia, United States and Canada.

Accommodation has been reserved at the Symposium centre, The University of Western Ontario.

For further information please write to Dr. G. W. Manning, Victoria Hospital, London, Ontario, Canada.

Neoplasms of the Placental Trophoblast*

G. H. Flight, MD, CM, FRCS(C) Halifax, N. S.

Hydatidiform mole, chorioadenoma destruens and choriocarcinoma are neoplasms of trophroblastic origin. The common feature linking them is proliferation of the epithelial cells lining the placental villus. The histological features are highly varied, as are the behavorial characteristics, making exact diagnosis sometimes difficult without detailed clinical and laboratory investigation.

Hydatidiform Mole

This complication occurs in 1 in 2,000 pregnancies in North America and for some unexplained reason is ten times more common in the Asian countries.

The classical clinical picture is the well known situation where, with first trimester bleeding, the uterine size is larger than the period of amenorrhoea would indicate. Not infrequently, however, the diagnosis is made only when the patient who has been bleeding for some weeks passes edematous vesicles. Absence of a fetus by X-ray is an additional aid in confirming a suspected diagnosis. Gonadotrophin levels in the urine or blood are not diagnostic, since high levels may be seen in multiple pregnancy or even in normal pregnancy. Bilateral ovarian enlargement will be found in 50% of cases due to the formation of multiple theca lutein cysts. These spontaneously regress after complete evacuation of the molar tissue and need not cause undue concern.

Complications associated with hydatidiform moles are infection, hemorrhage, preeclampsia and choriocarcinoma. Even though only one or two percent of patients will develop true choriocarcinoma this complication is very serious. Follow-up is therefore exceedingly important to find the earliest indication of the development of this complication.

Two studies show the value of pregnancy tests in follow-up. Brewer1 reports information from the Mathieu Chorionepithelioma Registry in the United States where in 161 patients the pregnancy test was positive in 60% at the end of one month and still positive in 36% (59 patients) at the end of two months. The significance of a positive test 60 days after expulsion of the mole was determined by a further follow-up of these 59 patients. In 30 the test became negative within the next six months, but 29

remained positive. In the 29 cases with positive pregnancy tests 16 developed chorioadenoma destruens and 13 choriocarcinoma. Delfes2 reported a similar study with similar results. It would seem wise therefore to regard with real concern those patients who have positive pregnancy tests longer than two months after expulsion of a mole, since half of them will develop a neoplastic complication. This is especially true since Hertz³ has shown that results are much better when treatment is started promptly.

The routine in the Department of Gynecology, Victoria General Hospital is to do the test once a month for one year and every two months in the second year. Pregnancy should be advised against during this time and any of the oral progestational agents may be used for this purpose. They do not interfere with determination of chorionic gonadotrophins in the urine. Chinical examination is carried out at the same time, noting the involution of the uterus, and shrinkage in size of ovarian cysts if present. The return of normal menstruation is indicative of the absence of, or decreasing levels of chorionic gonadotrophin, whilst abnormal bleeding, and the reappearance of gonadotrophin implies trophoblastic growth. The possibility of a new pregnancy of course must always be borne in mind.

There is reasonably general agreement that hysterectomy is the primary treatment in the woman over 40 years of age, since the incidence of neoplastic change is higher in this group. In other patients evacuation of the molar tissue by oxytocin stimulation, dilatation and curettage or even hysterotomy with follow-up as outlined, is the standard treatment. The suggestion4 has been made recently that all women with hydatidiform mole be given a prophylactic course of a folic acid antagonist, 4-amino-N-methyl-pteroylglutamic acid (Methotrexate), to eliminate the possibility of further complications. The dosage and duration of therapy have yet to be determined as trials are still in progress.

Chorioadenoma Destruens

Also known as Invasive Mole where the trophoblast is invading the myometrium deeply and occasionally producing distant metastases. It complicates about 1 in 50 molar pregnancies. It gener-

^{*}From the Department of Obstetrics and Gynecology, Dalhousie University, the Grace Maternity Hospital and the Victoria General Hospital, Halifax.

ally makes its presence known by continued vaginal bleeding after evacuation of molar tissue. In addition, the pregnancy test remains positive, generally with a high or rising titre. Repeat dilatation and curettage may not yield tissue since the lesion is deep in the uterine muscle. Histologically it is distinguished from choriocarcinoma by preservation of villous structure which is absent in the latter.

Treatment used to be hysterectomy and resection of all accessible extrauterine lesions. Recent experience with folic acid antagonists suggests that medical management may supplant hysterectomy and permit preservation of reproductive function. Results of this approach are very promising.

Choriocarcinoma

This is a rare but very lethal neoplasm. It is seen in about 1 in 60,000 live births.⁵ It represents a malignancy originating in the tissues of one individual which has the ability to invade and destroy the tissues of another individual. Fifty percent of the time it occurs following hydatidiform mole.

The clinical course is one of continued uterine bleeding after moles or abortion from a uterus that has failed to involute properly. Signs and symptoms secondary to metastatic lesions may occur without demonstrable evidence of choriocardinoma in the uterus. In such cases, hemoptysis from pulmonary metastases or neurological manifestation from cerebral metastases may herald the presence of the disease.

The diagnosis should be suspected in every case where abnormal bleeding occurs following a normal or an abnormal pregnancy. The uterus may be larger than expected since proper involution has not taken place. Vaginal metastases may be visualized. Chest X-Ray may reveal pulmonary metastases. The pregnancy test will be positive since the living trophoblast will produce large quantities of gonadotrophin. Pregnancy tests are generally negative a few days after normal delivery or complete abortion since the levels of circulating gonadotrophin are too low to be detected by the test. Bilateral ovarian cysts are sometimes encountered and their presence in a patient with continued bleeding further strengthens the diagnosis. Dilatation and curettage may permit histological confirmation of choriocarcinoma but of course will not unless the tumor is on the surface of the endometrial cavity.

Treatment until relatively recently consisted of total hysterectomy and bilateral salpingo-oophorectomy plus removal of metastatic lesions in accessible sites. Unfortunately many patients have overt or silent metastases at the time of hysterectomy, and in the past, the mortality rate from this malignancy has been approximately 90 per cent. X-ray therapy, endocrine preparations, nitrogen mustard used in conjunction with surgery failed to change the prognosis, which remained grave until the advent of effective chemotherapy.

It is now evident that treatment with 4-amino-N-methylpteroglutamic acid (Methotrexate) provides a 5-year survival in approximately 50 percent of individuals with known metastases from choriocarcinoma, and even better results where metastases have not occurred. It is clear that chemotherapy provides better results than hysterectomy and that hysterectomy performed in conjunction with chemotherapy does not increase the remission rate above that obtained with chemotherapy alone. Hysterectomy may be necessary in the occasional case to control bleeding or to obtain remission where in the absence of metastases the pregnancy test remains positive after drug thereapy.

Methotrexate in the recommended doses (2 mgm per kilogram) is not without hazard, since severe bone marrow depression may occur. Repeated courses of the drug are usually required, based upon the clinical response and variations in titres of chorionic gonadotrophin.

Summary

New hope has dawned for patients with trophoblastic disease. By meticulous attention to detail, by adequate follow-up and early diagnosis of the highly malignant choriocarcinoma it might be possible to virtually eliminate deaths from this source in the field of cancer. It would seem that in very many of these young women that their reproductive function might be safely salvaged.

References

- Brewer, et al: Am. J. Obst. & Gynec. 90: 566-573, 1964.
- Delfs, E.: Ann. New York Acad. Sc. 80: 125, 1959.
- Hertz, R., Lewis, J., and Lipsett, M. B.: Am. J. Obst. & Gynec. 82: 631, 1961.
- Tow, W. S. H.: J. Obstet. Gynaec. Brit. Cwlth. 73: 544, 1966.
- DANFORTH, D. N.: Textbook of Obstetries and Gynecology, ed. I, New York, 1966, Harper and Row, Publishers, Inc., p. 285.

"BEQUEST TO UNIVERSITY MEDICAL ALUMNI ASSOCIATION

A bequest to a university medical alumni association for the purpose of establishing a student loan fund was exempt from estate tax, according to the Supreme Court of Canada which reversed an earlier Exchequer Court judgment in a three-to-two decision. The Court held that the gift was absolute and indefeasible and that the association was a charitable organization that met the requirements of section 7(1) (d) (i) of the Estate Tax Act.

Towle Estate v. M.N.R."

Chemotherapy Of Hodgkin's Disease*

VINCENT W. ING, BSe, MD, FRCP(C)

Halifax, N. S.

Hodgkin's disease is a complex pathological entity of obscure etiology, involving both the lymphoid and non-lymphoid tissues, the management of which requires a good understanding of its natural history, patience, experience with various modalities of therapy. The choice and success of any specific form of treatment for a patient depend upon meticulous clinical assessment, the importance of which cannot be over-emphasized.

Assessment

The commonest presenting feature is lymphadenopathy, the sites of preference include cervical (60-80%), axillary (10-20%), inguinal (5-10%), and mediastinal (5-10%). The enlarged lymph nodes are usually painless, discrete or fused, with or without symptoms such as fever, pruritis, weight loss or malaise. Retroperitoneal, hepatic and splenic involvement is infrequent in the early phase, Generally speaking, the areas of involvement are contiguous, suggesting that the disease is of unifocal origin, starting from one site and spreading to the adjacent nodes. For example, cervical and supraelavicular involvement tend to be associated with disease in the mediastinum, ipsilateral axilla and contralateral side of neck. The appearance of enlarged nodes in two isolated areas, for example, the neck and one inguinal region should call for a search for the missing link.

The final diagnosis of Hodgkin's disease depends on the histological study of a biopsied lymph node. In most cases a single biopsy of a large node, most commonly from the neck, will reveal the pathological process. Occasionally a certain diagnosis cannot be made by the pathologist on the tissue sections, in which case lymph node biopsy should be repeated prior to consideration of any therapy.

Other studies considered to be desirable for the clinical assessment include:

- Careful history and physical examination.
- Complete hemogram including hemoglobin, white blood count, differential count and platelet count as well as a reticulocyte count and an examination of a blood film.
- 3. Radiological investigations including:
 - (a) chest films, PA and lateral views and lung tomography in the presence of hilar involvement.
 - (b) intravenous pyelography
 - (e) skeletal survey.

- 4. Bone marrow aspiration.
- Liver function tests including alkaline phosphatase and Bromsulphthalein exeretion test.

With the information available from the above studies, the patient's disease can be staged in conformation to the system originally proposed by Peters and later modified by Kaplan.

- Stage 1 Disease limited to one anatomical region or to two contiguous regions on the same side of the diaphragm.
- Stage 2 Disease in more than two contiguous regions or in two noncontiguous regions on the same side of the diaphragm.
- Stage 3 Disease on both sides of the diaphragm but limited to involvement of lymph nodes and spleen.
- Stage 4 Involvement of bone marrow, lung parenchyma, pleura, liver, bone, skin, kidney, and gastrointestinal tract or any non-lymphoid tissue.

All stages are subclassified as A or B to indicate the presence or absence of significant systemic symptoms which include pruritis, fever, weight loss over 10% of normal weight and night sweats. Other symptoms including malaise, fatigue, anemia, leucocytosis, leucopenia, lymphopenia, cutaneous anergy, while important, are insufficient by themselves to relegate the patient to the B group.

Lymphangiography is a useful diagnostic adjunct, especially when dealing with regionally localized disease. It has been demonstrated that of the patients in presumptive stage 1 and 2, 10% and 30% respectively have actual retroperitoneal involvement. Lymphangiography is not indicated in stage 3 disease since 90% of these patients have retroperitoneal spread. In addition, the risk of oil embolism is considerably higher in patients with generalised disease due to the presence of lymphatic-venous anastomoses which are commonly associated with extensive retroperitoneal obstruction.

Radiation Therapy

The choice of therapy depends on the extent of the disease: The treatment of patients with regionally localised disease (Stages 1 and 2) is intensive megavoltage radiotherapy over a wide field. Although a detailed discussion of radiotherapy is beyond the scope of this presentation, one must

^{*}From the Department of Medicine, Dalhousie University and the Victoria General Hospital, Halifax, N. S.

stress that there is an inverse relationship between recurrence rate per treated field and radiotherapeutic dose. While a recurrence rate of 60-80% may be expected when doses of 1000 rads or less are delivered, the relapse rate can be reduced to 5% or less with doses of 4000 rads delivered over four weeks. Long term survival data on large series of cases treated with relatively high doses over a wide field are summarised in Table I.

TABLE I
HODGKIN'S DISEASE TREATED BY RADIATION
Long Term Survival Rate (percentage)

Author	Stage	5 yr.	10 yr.	15 yr.	20 yr.
Peters	1	73	52	42	39
	2A	90	67	43	39
Easson	Localised	55	43	39	

In patients with stage 1 and 2A disease, almost 50% can expect to achieve a 15 year survival. With the aid of lymphangiography to rule out the presence of occult stage 3 disease with silent intra-abdominal involvement, and with improvement of radiotherapeutic techniques, the 15 year survival rate may statistically be increased to 75% or more of patients with disease localised to one region.

Chemotherapy

The chemotherapeutic agents that are useful in the treatment of Hodgkin's disease include the alkylating agents, vinca alkaloids and corticosteroids. N-Methylhydrazine recently has been found to have demonstrable but less well established therapeutic value.

Alkylating agents

These are highly reactive compounds which readily combine with various organic radicles of amino acids and the nucleic acids, and thus interfere with the synthesis and function of nucleic acid, especially DNA of both neoplastic and normal tissues, by formation of cross-linkages.

Nitrogen mustard (Mustargen, HN2) is the most widely used alkylating agent for the treatment of Hodgkin's disease. Its half life in vivo is 2-5 mins, and reacts rapidly with body tissue. Its oncolytic effect is observable in a few hours and clinically evident within one week. It can only be administered intravenously to a total dose of 0.4mgm/kg. This can be given in a single dose or in two to three divided doses. Due to its extreme emetic effect, it is advisable to administer nitrogen mustard in the evening through the tubing of an intravenous infusion set, with chlorpromazine and a barbiturate being given half to one hour before. Its chief disadvantage is myelosuppression which usually appears on the 10th to 14th day after injection. with recovery occurring at the beginning of the third week. The remission induced by one course of therapy usually lasts for two to four months.

Chlorambucil (Leukeran) is an aromatic alkylating agent which can be given orally with predictable absorption and little gastrointestinal intolerance. The dosage required is 0.1 - 0.2 mgm/kg per day. Its onset of action is slow with a period of latent drug effect (PLD) of two - five weeks and hence is mainly used as maintenance drug. In patients with stage 3 disease the therapeutic effect of nitrogen mustard can be improved using chlorambucil as maintenance therapy and the remission duration has been shown to increase from 11.7 weeks to 35 weeks. Its main disadvantage again is myelosuppression. Hepatotoxicity has been reported in a few cases.

Cyclophosphamide (Cytoxan) can be given intravenously (5-10mgm/kg/day for four to five days or orally (50 to 150 mgm per day). It is less emetic than nitrogen mustard and its onset of action is more rapid than chlorambueil with a PLD of 2-7 days, and there is a platelet-sparing effect. Alopecia occurs in about 30% of patients: hemorrhagic cystitis occurs in about 2% of patients.

Vinca alkaloids

Vinblastine and vincristine are extracted from the periwinkle herb, Vinca rosea (Linn.) They act mainly by arresting cell division at the metaphase. In spite of their close chemical similarity, there has been a singular lack of cross resistance between vinblastine and vincristine.

Vinblastine sulfate (Velban) can be given intravenously only. The initial dose is 0.1 mgm/kg per week with increments of 0.05 mgm/kg per week until the appearance of mild leucopenia. A maintenance dose of 5-10 mgm may be given once every one - four weeks depending on the response of the patient. Its onset of action may be as rapid as that of nitrogen mustard. Its major complication is myelosuppression especially that of granulocytes, but the duration of its leucopenic effect is shorter than that of nitrogen mustard. The platelet count is either unchanged or mildly depressed. Other complications include chemical phlebitis, constipation and peripheral neuropathy.

Vincristine (Oncovin). At the dosage of 0.02 to 0.05 mgm/kg per week intravenously, vincristine is less effective than vinblastine. While its myelosuppressive effect is milder, its neurologic toxicity is much more severe than vinblastine. Hence the major indication for vincristine is in patients who recently have had marrow suppression due to cytotoxic agents.

Hydrazine Compounds

N-Methylhydrazine (Natulan) is one of the latest agents found to be effective against Hodgkin's disease. It is not available on the market at the present time, but its therapeutic value is under investigation in this medical centre. The suggested mode of action of Natulan is fragmentation of nucleic acids by the formation of peroxide. The initial oral dose is 50 mgm. daily with increments of 50 mgm. every one to two days until the maximum tolerated dose is reached (usually less than 300 mgm.). This dosage level is then maintained for two to three weeks or until signs of toxicity appear.

The drug can then either be discontinued or reduced to a maintenance dose of 50 - 100 mgm. per day. In our experience, nausea and vomiting are common during the early phase of therapy, and can be controlled with the use of phenothiazines or by a reduction of the dose until the patient has developed better tolerance. Its myelosuppressive effect is similar to that of nitrogen mustard. Numbness and tingling of the extremities without signs of peripheral neuropathy is another complaint encountered. Other complications including stupor, presumably through its synergistic action with the phenothiazine compound, and sensitivity to alcohol, have been reported. In our experience with two patients who have been refractory to the effects of nitrogen mustard, vinblastine and chlorambucil, Natulan was of definite palliative value, resulting in improvement of anemia, reduction of fever, shrinkage of enlarged lymph nodes and amelioration of intractable pruritis. In one patient the duration of remission was about 10 weeks. The other patient has been under control for about five months. Until more data is available we believe that the use of Natulan should be reserved for patients who are refractory to all these other cytotoxic agents.

Corticosteroids

Prednisone and its analogues are chiefly used when evidence of hemolysis or marrow suppression is present. In advanced cases large doses of corticoids may occasionally produce alleviation of symptoms and brief symptomatic improvement.

Indication for Chemotherapy

Not infrequently, chemotherapy will eliminate all evidence of Hodgkin's disease, but the disease inevitably recurs. There is at present no record of actual cure of this disease by chemotherapy. In spite of its definite palliative value, chemotherapy has not proved to exert any important influence on the underlying process, nor does it prolong the survival time.

There are, generally speaking, three indications for the use of chemotherapy.

- In localised disease, chemotherapy may be used in combination with radiation to produce more rapid regression of the disease and to allow the use of less intensive courses of radiation. While this combination is well tolerated by the patient, there is no convincing evidence that such a combination has any additive value over a well-planned adequate course of megavoltage radiation over a wide field.
- There are situations in acute phases of the disease in which rapid relief of symptoms and signs may be life saving, for example, spinal cord compression, superior vena caval obstruction.

Here a course of nitrogen mustard may produce rapid symptomatic relief and allow the patient to receive a full course of radiation. Williams et al reported that in spinal cord compression due to Hodgkin's disease, the salvage rate in terms of recovery of neurological function was 73% in those treated with nitrogen mustard and radiation, in contrast to 43% in those treated with radiation alone.

TABLE II
SYMPTOMS AND SIGNS OF GENERALISED HODGKIN'S DISEASE

Symptoms	Signs	Blood
pruritis	adenopathy	anemia - aplastic
fever	skin infiltration	hemolytic
anorexia	mediastinal	
	infiltration	hemorrhage
weight loss	pulmonary	
	infiltration	leucopenia
weakness	spleen and liver en- largement	thrombocytopenia
	spinal cord compres- sion	
	bone involvement	
	intestinal	
	involvement	

 In widespread disease with systemic manifestations the response to chemotherapy depends on the rate of progression of the disease and the amount of previous therapy.
 (Table II)

Over 75% of patients can be expected to respond favourably to the first course of treatment. The average duration of remission is two to four months after a single course of therapy. This can be prolonged by continuous or intermittent maintenance therapy. When a patient becomes refractory to one agent, another agent, preferably with a different mode of action, should be considered.

In this centre, the agents commonly used for patients with generalized disease are vinblastine sulfate and nitrogen mustard. The choice depends upon the status of the patient's marrow function and his or her availability at regular intervals. We tend to favour vinblastine in view of its milder and shorter myelosuppressive effect. In acute situations, for example spinal cord compression, nitrogen mustard is preferred. Chlorambucil is only used occasionally as a maintenance agent beginning two - four weeks after a course of nitrogen mustard. When a patient has become refractory to vinblastine and nitrogen mustard, the use of N-Methylhydrazine is then considered. For some patients with massive pleural effusion or ascites which fails to respond to the use of systemic oncolytic agents, intracavitary administration of nitrogen mustard may be effective.

In some medical centres, combination of cytotoxic agents, for example cyclophosphamide, methotrexate, vincristine, and prednisone have been used, based on the rationale that full doses of agents with different modes of action and toxicity can be used with safety, and can thus produce more oncolytic effect. While the initial response in terms of frequency and magnitude of tumour regression appears to be greater than that in association with the use of a single agent, the additive value of this scheme in relation to the length of remission and long term survival is still to be determined.

Patients with advanced disease can remain relatively asymptomatic and active for a number of years, if chemotherapeutic agents are used judiciously. With progression of disease, a resistant stage evolves which fails to respond to any form of therapy: most patients then rapidly succumb due to cachexia, respiratory failure, bone marrow failure or infection.

Bibliography

- 1. Kaplan, H. S. Med, Clin. North American 50: 1591-1609, 1966.
- KARNOFSKY, D. A. Cancer 19: 371-377, 1966.
- BRUNNER, K. W. Ann. Int. Med. 62: 69-86, 1965.
- AISENBERG, A. C. N. E. Med. J. 270: 508-514, 565-570. 617-622, 1964.
- WILLIAMS, H. M., DIAMOND, H. D., CRAVER, L. L. and Parsons, H. Neurological complications of lymphomas and leukaemias American Lecture Series 357: 28, 1959.

EXPECTANT FATHERS

While doctors seldom lose a father, it is a well known fact that some expectant fathers have sympathy pains for their pregnant wives.

A British psychiatrist has noted that some expectant fathers suffer symptoms of morning sickness, loss of appetite, abdominal pains, indigestion and colic without any apparent physical cause.

These symptoms usually start at the third month of their wives' pregnancy, become less severe in the middle months only to reappear again in the ninth month.

The British psychiatrist notes that the symptoms disappear after the birth of the baby but reoccur with subsequent pregnancies.

The reason for these sympathy pains, the doctor speculates, is more jealousy than sympathy.

Some men unconsciously fear that after childbirth their wives' affection may be transferred from them to the baby and feeling guilty about these feelings, they punish themselves.

In other cases it may be because some men identify so intensely with their wives.



The doctor spent a comfortable night

Terpo-Dionin with its "3-way" relief (sedative-anodyneexpectorant), gives coughing patients—and their doctor -an undisturbed night.

Each teaspoonful (5 ml.) contains 5.5 mg. ethylmorphine HCI; 13.9 mg. terpin hydrate; 5.0 mg. guaiacol; 10.2 mg. calcium glycerophosphate; white pine compound base. Dosage: One teaspoonful every three hours, and one at bedtime. Contraindications: May be habit forming. Full information is available upon request.

Scuts down coughing night cal

Cancer Chemotherapy

A Preliminary Survey of Autopsy Cases

Bodo Epstein, MD, and Khalid Hameed, MB, BS.

Halifax, N. S.

In recent years a number of chemotherapeutic agents have become available for the treatment of malignant tumours and although their effectiveness is still being debated, their use has become wide-spread. Medical literature concerning these agents has also increased proportionately. Many studies and reviews 1-7 covering almost every aspect of cancer chemotherapy are now available. Investigations however, of human autopsy material are euriously lacking.

As chemotherapeutic agents are notably toxic, we felt that it would be of interest to investigate the anatomical causes of death in cancer patients who had received these toxic agents and compare the findings with those of an untreated matched control group; thus, a clinco-pathologic survey of the material available in the Nova Scotia Tumour Clinic and the Pathology Institute was undertaken. For this study, a chemotherpeutic agent is defined as a drug which will control and inhibit the growth of or destroy neoplastic cells. Hormones are excluded.

Material and Methods

For this study only those cases in which autopsy was performed and for which matched controls were available could be selected. Solid tumours were chosen since almost all reticulo-endothelial malignancies receive some form of chemotherapy before death and suitable untreated controls are, therefore, not available.

During the period 1953 to 1964, 4041 cases of malignant tumours of lung, breast and gastro-intestinal tract were seen in the N.S. Tumour Clinic. Of these 498 (12%) received some form of cancer chemotherapy before death (Table II).

Tables I and II demonstrate the difference of autopsy rate between the patients dying of cancer with those cancer patients who received chemotherapy. The autopsy rate of 22% of hospital deaths in chemotherapy group (Table II) is considerably lower than the rate of 41.5% for the overall cancer group (Table I).

During 1953-64, 29 cases of solid tumours who had received chemotherapy came to autopsy. These include 24 cases of the lung, breast and gastro-intestinal tract malignancies (Table I), one case of

carcinoma of the ovary, three cases of melanoma and one case of epidermoid carcinoma of skin. Of these 29 cases, two were excluded from this study; these included a skin carcinoma without complete

TABLE I
Autopsies in Carcinoma Patients: 1953-1964

Site	Total Cases	Total Deaths		Number of Autopsies		
Lung Breast Stomach Colon Sigmoid Rectum	643 1503 585 590 247 473	577 818 529 424 151 358	135 141 150 129 50 77	65 47 72 42 22 37		
TOTAL	4041	2857	682	285 (41.5% of hospital deaths)		

TABLE II
Autopsies in Chemotherapy Group 1953-1964

Site	Total Cases	Number Treated with Chemo- therapy	Number Dying in Hospital	Number of Autopsies
Lung	643	161	47	7 3
Breast Gastroin- testinal Tract (Stomach, Colon, Sig- moid,	1503	227	31	3
Rectum)	1895	110	29	14
	4041	498	107	24 (22% of Hospital deaths))

autopsy and a carcinoma of cecum treated initially by surgery and eight months later, by methotrexate for presumed clinical recurrence of tumour; no tumour was seen at autopsy.

^{*}From the Pathology Institute, Province of Nova Scotia and Department of Pathology Dalhousie University, Halifax, N. S.

TABLE III SEX DISTRIBUTION AND MEAN AGE

		GR	OUP I		GR	OUP II	GRO	ישכ	III	
Site	27 M		Tumours Mean Age	27 Sol		mour Controls Mean Age		22 M	R.E.	Neoplasms Mean Age
Lung	5	2	63	6	1	60	Acute Leukemia Chronic MyeLoid	3	4	50
Ovary Breast	=	1 3	81 47	=	1 3	83 58	Leukemia	4	50	50
Skin (Melanoma) Gastrointestinal	1	2	54	1	2	42	Lymphoma	-	4	66
Tract	6	7	56	6	7	58	Myeloma	4	3	60
Total	12	15	61	13	14	60		7	15	56

TABLE IV STAGE OF DISEASE AT AUTOPSY (54 SOLID TUMOURS)

Stage		Lung		Ovary		Breast		Melanoma		G.I. Tract	
	Group	I	II	I	II	I	II	I	П	I	II
I		-	-	-	-	-	-	***		-	-
II		1	1	-		-	-	-	-	1	3
III		6	6	1	1	3	3	3	3	12	10

STAGE I: – Tumour localized to organ of origin STAGE II – Tumour localized to the region of origin STAGE III – Distant metastases

TABLE V CHEMOTHERAPEUTIC AGENTS USED IN 27 SOLID TUMOURS AND 22 R. E. NEOPLASMS

	No. Cases		0.53 (2.50 (11.0.2)	20.7			Methotrexate		5Fu	Vinca Alkaloids
Lung	7	6				1	REPLECT		120	
Ovary	1			1						
Breast	3	2		1	1					
Skin (Melanoma)	3		2				1			
G.I. Tract	13	3		2	2	1	3		2	
Acute Leukemia Chronic Myeloid	7						4	. 7		1
Leukemia	4		1				2	2		
Lymphoma	7	2	2	2	1	1	1	2		1
Myeloma	4		4							

TABLE VI Major "Cause" of Death

			Solid	I ('Treated' Tumours) Cases	Solid	I ('Untreated' Tumours) 'Cases	Neo	p III (R.E plasms, All reated') 2 Cases
1.	(A)	Acute Suppurative Infections Antemortum Positive Blood Cultures	19 0*	(70.4%)	16 6*	(57.1%)	19	(86.4%)
	(B) (C)	Bronchopneumonia Fungal Infections	16	(59.3%)	15	(53.5%)	15	(68.1%)
	1797	(i) Systemic (ii) Body Surfaces	0		0		5 3	
	(D) (E)	Peritoneal Infections Acute Suppurative Pyelonephritis	6	(22.2%)	2	(7.1%)	2	(9.1%)
2.		"Non-Infectious" Deaths	8	(29.6%)	11	(42.9%)	3	(13.6%)
	(A) (B) (C)	Pulmonary Edema (Severe) Pulmonary Thromboemboli (Large) "Sarcoidosis"	4		3		2	
	(D) (E)	Massive Pulmonary Haemorrhage Massive Abdominal Haemorrhage	0		1 2		0	
	(F) (G)	Subdural Hematoma Brain Metastasis "Only"	0		0		1 0	
	(H)	No Anatomical Cause of Death	0		2		0	

^{*}No antemortum cultures obtained.

The remaining 27 cases (Group I) were matched by another 27 cases of untreated solid tumours (Group II) in so far as the age, sex, site and stage of tumour is concerned. Another 22 cases of lymphomas and leukemias were selected as Group III. The latter cases died between 1953-64 and had received chemotherapeutic agents. (Table III)

Hospital records, Tumour Clinic charts, gross autopsy descriptions and microscopic slides were reviewed; special stains were prepared when indi-

cated.

Table III shows age and sex distribution and the type of tumour in different groups. Table IV shows stage of the disease in cases of solid tumours. As seen in these two tables the matching of cases is only approximate. Table V shows the type of chemotherapy used. Nitrogen mustard was the commonest agent employed for solid tumours whereas most leukemias were treated with 6 MP and methotrexate.

Results

Table VI summarizes the major "causes of death" in the three groups and Table VII shows organ weights and major findings in different viscera.

The incidence of "infectious deaths" is highest in group III and lowest in group II. This increase of "infectious deaths" in group III appears significant. 86.4% of cases died of acute suppurative infections with eight cases showing positive antemortum blood cultures. All the systemic fungal infections and three out of four surface fungal infections were also found in group III.

Comparison of groups I and II, however, reveals some interesting features. It is evident that the incidence of infections is a little higher (70.4%) in solid tumours treated with chemotherapy than

the solid tumour control group (57.1%). However, this increase is almost entirely due to the peritoneal infections. Group I had six cases (22.1%) of peritonitis and peritoneal abscesses compared to two cases (7.1%) in group II. Also of some significance is the fact that all the eight cases of peritoneal infection in group I and II belong to gastro-intestinal and ovarian malignancies.

Also in this study three cases of carcinoma of the lung died during chemotherapy and all the seven cases (100%) of pulmonary malignancies died within 23 days of the last dose of chemotherapeutic agent. This is in sharp contrast to the remaining 20 cases in group I where only 10 cases (50%) died within 23 days of the last dose of chemotherapeutic drug while the other 10 cases lived two months or longer. The reason for this is not known but it appears that the cases of pulmonary malignancies do not tolerate chemotherapy well.

Discussion:

The quality and quantity of the material available for this study is limited to the extent that statistical analysis of the results is not possible.

It is worthy of note that the autopsy rate of 22% of hospital deaths in the chemotherapy group is considerably lower than the autopsy rate of 41.5% in the overall cancer cases (Table I, II). The factors producing this discrepancy remain obscure.

The increase of infections, especially, fungal in cases of lymphomas and leukemias (Group III) is not unexpected and only confirms the findings of other investigators. Although no significant increase of "infectious deaths" in group I (chemotherapy group) as compared to group II (untreated controls) was found, it appears that the increased incidence of peritonitis and peritoneal abscesses in the former group is probably significant. The

TABLE VII ORGAN WEIGHTS, AND MAJOR FINDINGS

		Group I	Group II	Group III
Organ Weight	Heart Lungs Liver Kidney Spleen Brain	320 1010 1795 155 150 1265	320 1120 2360 160 180 1250	340 1230 2250 180 480 1336
Cardiovascular System	Tumour Focal Myocarditis	7 3	4 2	5 1
Respiratory System	Tumour Bronchopneumonia Thrombo-emboli	16 16 2	13 15 1	15 15 1
Liver	Tumour Fatty Change Severe Congestion Necrosis Bile Stasis	15 8 5 4 4	21 9 4 6 3	14 10 5 5 1
Kidneys	Tumour	6	5	7
Central Nervous System	Tumour Subdural Hematoma	6	8	3 2

fact that these infections were limited to the primary abdominal malignancies in solid tumours cases, is also interesting. The reasons for this increased incidence of peritoneal infections is however, not entirely known. Chemotherapeutic drugs especially mustards are known to produce extensive intestnal injury (1). It is, therefore, conceivable that in cases of abdominal malignancies especially those of gastro-intestinal tract, the intestinal injury induced by the chemotherapeutic agents promotes the spread of micro-organism to the peritoneal cavity.

This study fails to demonstrate any significant increase of hepatic lesions in relation to chemotherapy (Table VII) even though the chemotherapeutic drugs are notably hepato-toxic. In our material, the hepatic injury correlates better with the presence of metastatic tumour in the liver than with chemotherapy.

Summary

- Clinico-pathologic findings of 27 autopsy cases of solid tumours treated with chemotherapeutic agents were compared with those of 27 untreated control cases and 22 cases of lymphoma and leukemia.
- There was a considerable increase of infections, especially fungal infections in cases of lymphoma and leukemia. This finding confirms previous reports.*
- The incidence of acute suppurative infections in solid tumour cases treated with chemothera-

peutic agents was slightly more than in the untreated control group. This increase was however, entirely due to peritoneal infections which were limited to the cases of gastrointestinal and ovarian malignancies.

 This study seems to indicate that the cases of primary pulmonary carcinoma do not tolerate the toxic chemotherapeutic drug well.

References

- GRAFF, I., KARNOFSKY, D. A., JAGER, V. B., KRICHESKY, B. and SMITH, H. W.
 - The clinical and pathologic effects of nitrogen and sulphur mustards in laboratory animals. *Amer. J. Path.* 24: 1 48, 1948.
- Conference on Experimental Clinical Chemotherapy National Cancer Institute Monograph. No. 3 - 1960.
- Betteridge, T. J.: The pathological aspects of cancer chemotherapy. Proc. Roy. Soc. Med. 55: 925-929, 1962.
- Calabresi, P. and Welch, A. D. Chemotherapy of neoplastic diseases. Annual Rev. Med. 13: 45 - 1962.
- GOLOMB, F. M. Agents used in cancer chemotherapy. Amer. J. Surg. 105: 579-590, 1963.
- REEMTSMA, K. Complications of regional cancer chemotherapy by perfusion and infusion technics. Amer. J. Surg. 105: 645-648, 1963.
- KNOCK, F. E. Newer Anticancer agents. Med. Clin. N. Amer. 48 (2): 501-527, 1964.
- Hutter, A. V. and Collins, H. S. The occurrence of opportunistic fungus infections in a cancer hospital. *Lab. Invest.* 11: 1035-1045, 1962.
- SMETANA, H. F. The histopathology of drug-induced liver disease. Annual N. Y. Acad. Sci. 104: 821-846, 1963.

A DOCTOR A DAY KEEPS THE APPLES AWAY

What on earth does this mean? Well, it doesn't mean anything but it rather amused us and we liked the look of it. That's how a lot of insurance is bought; it doesn't make much sense but there it is.

Did you know we operate an insurance "clinie"? It exists for the sole purpose of putting insurance in its proper perspective.

ALFRED J. BELL & GRANT, LIMITED

Insurance Specialists
One Sackville Place, Halifax, N. S.
Telephone 429-4150



Dalhousie Notes

I. HOW MANY MEDICAL SCHOOLS ARE NEEDED IN THE ATLANTIC PROVINCES? (PART II)

C. B. Stewart, MD., Dean Halifax, Nova Scotia

Supply of Physicians in the Atlantic Region

It has been indicated that Dalhousie Medical School was able until recently to take care of all qualified candidates from the Atlantic Provinces. On the other hand, it must be emphasized that Dalhousie Medical School did not supply an adequate number of physicians for this region. If this is to be used as the criterion for success, it would have to be concluded that one medical school was insufficient. The shortage of physicians in this region is a more serious problem than in any other part of The Canadian ratio of population to physicians in 1960 was 879 to 1, in the Atlantic Provinces 1,251 to 1. Both ratios have improved somewhat in the last five years, but the Atlantic Region is still lagging behind the other provinces, and the greatest shortages are in Newfoundland and New Brunswick, in that order. Correction of this shortage by all practical means is urgently required.

It is rather doubtful, however, whether the need for physicians should be the primary criterion in deciding whether or not a medical school should be built or where it should be located. Obviously, this decision must be based upon the availability of students rather than the need for graduates. There would have been little gain in the past in having had several medical schools, or a larger one at Dalhousie, if most of the non-resident students had left the area after receiving their medical education.

It has been stated that the location of a medical school in a province would result in a larger proportion of graduates remaining to practise there. A study, now in progress but not yet published, shows the following preliminary data on a follow-up of the Dalhousie medical graduates of 1949 to 1963. It indicates clearly that students from this region tend to stay here after graduation and non-residents

tend to leave. It also shows that Nova Scotia has gained a few more practitioners, or has lost fewer, than New Brunswick and Newfoundland, but the gain is small and there is no evidence that Dalhousie's location was primarily responsible.

This preliminary study of Dalhousie graduates for the fifteen year period 1949-1963, inclusive, shows that 54 per cent are in general practice. Eighty per cent of these are now in the Atlantic Provinces. We consider this to be a very good record. Perhaps too much has been said about the so-called "brain drain" from this area. It is not as serious as some have suggested. The proportion of specialists remaining in the area after postgraduate training is somewhat smaller than for general practitioners, but still not so critical as some would suggest. On the other hand, less than 10 per cent of the students who came to Dalhousie from other provinces of Canada or other countries have remained to practise in this area after graduation. It is therefore clear that Dalhousie graduates who were residents of this Atlantic Region provided the main source of graduate physicians starting practice here.

Of the Nova Scotia students who went into general practice on graduation, 80 per cent are in the Atlantic Provinces, with 73.3 per cent in their home province and 6.7 per cent in the neighbouring provinces, chiefly New Brunswick. Newfoundland has an even more favourable picture with 93.3 per cent of the general practitioner graduates in the Atlantic Provinces, 76.6 per cent being in their home province. On the other hand, while 71.6 per cent of New Brunswick students are in the Atlantic Region, only 56.7 per cent are in their home province.

New Brunswick has been less successful than Nova Scotia in attracting and retaining its graduates, but both have been exceeded by Newfoundland. The location of Dalhousie in Nova Scotia can hardly be considered as the chief factor explaining the difference between New Brunswick and Nova Scotia. At least other factors must have been effective in Newfoundland.

Expressed in another way, New Brunswick lost 15 per cent of its general practitioner graduates to Nova Scotia, almost 20 per cent to other provinces of Canada outside the Atlantic Region and 9 per cent to the U.S.A. Newfoundland lost 13 per cent to Nova Scotia, 3 per cent to New Brunswick, 3 per cent to other provinces and 3 per cent to the U.S.A. Its total loss to the rest of the Atlantic Provinces was about the same as New Brunswick's, but the latter lost many more to other parts of Canada and the U.S.A. In comparison, Nova Scotia lost only 5.5 per cent to New Brunswick, 1 per cent to Newfoundland, 14 per cent to the rest of Canada, and 5 per cent to the U.S.A. Its loss to the other Atlantic Provinces was only half that of New Brunswick or Newfoundland, and the loss outside the region was less than New Brunswick's but greater than Newfoundland's. It is emphasized that these figures relate only to general practitioners. The loss of trained specialists from each province was greater than of general practitioners. New Brunswick lost 8 per cent to Nova Scotia, but Nova Scotia in turn lost 6 per cent to New Brunswick. foundland lost 5 per cent to each of these provinces. The major loss of all provinces was to the rest of Canada or the U.S.A. Nova Scotia lost 25 per cent to the rest of Canada and 18 per cent to U.S.A., New Brunswick 26 per cent and 23 per cent respectively and Newfoundland 14 per cent and 10 per cent. One might have expected the Medical School to exercise a greater drawing power for specialists than for general practitioners but these figures show little or no evidence of this.

If Dalhousie had much influence on the choice of location, it is difficult to document from these figures. If there was an effect, it was hardly large enough to influence New Brunswick to set up a medical school. It would seem wise to seek other incentives to encourage the retention of both specialists and general practitioners.

The shortage of physicians might have been mitigated by Government financial aid for premedical and medical students. If such support had been available, there might have been a larger number of local students at Dalhousie, and an earlier enlargement of its facilities, or a second school might have been required. The Province of Newfoundland is the only one to have instituted effective measures to achieve these ends, but student aid has been available only in recent years and the result of the support program for premedical students may not yet be fully achieved. We strongly support the introduction of student support of a similar

nature in New Brunswick, Nova Scotia and Prince Edward Island. It seems unfair that all final year science students can obtain support of \$2,000 to \$3,000 if they elect to go into the Faculty of Graduate Studies for an M.Sc. or Ph.D. degree, but those who enter medicine have to pay tuition and support themselves, with only a small amount of aid from loans.

It must be noted, however, that the Newfoundland program of student aid has not produced any magic solution to the supply of doctors. Table III shows that the number of applicants to Dalhousie from New Brunswick and Nova Scotia has increased as rapidly as those from Newfoundland.

We would suggest that the size of the Medical School was not the major factor in the poor supply of physicians. Inadequate government aid to students and to doctors in poorer communities may have been. We have no clear evidence of how much such assistance would achieve, but the low loss from Newfoundland to other regions may be attributed to both of these plans.

TABLE III
TRENDS IN APPLICATIONS TO DALHOUSIE
MEDICAL SCHOOL BY PROVINCE, 1962 to 1966

I. Total
81
89
101
138
141

Estimates of Future Enrolment

As already noted there was an excess of applications for admission to Dalhousie Medical School after World War II. The numbers then decreased sharply as in most other North American schools. In 1954, there were only 89 applicants of whom only 44 were accepted into a class then numbering 57. A larger proportion of non-resident students was then enrolled when the supply of regional students dwindled. There were many in this group of 89 local applicants who had been rejected in previous years and an unusually low percentage was therefore acceptable.

The supply of applicants continued to fall and in 1959 reached the level of only 43 applicants from the four provinces. Of these, 39 were admitted, although some were of dubious academic standing, and the failure rate in that class was substantially higher than usual.

The following table shows the trends in applications from 1959 when an upturn occurred. It is upon these that future planning must be based.

TABLE IV
NUMBER OF ATLANTIC PROVINCE
APPLICANTS AND STUDENTS ENROLLED IN
FIRST YEAR MEDICINE AT DALHOUSIE
UNIVERSITY 1959-1966 INCLUSIVE

	Atlantic Province Applicants	Number Admitted	Total Enroment
1959	43	39	62
1960	55	44	65
1961	74	53 53	65
1962	81	53	71
1963	89	58	72
1964	101	58 64	72
1965	138	67	72
1966	141	75	78

Until 1964, the increase in the number of applicants from the four Atlantic Provinces was steady and almost in a straight line. In 1965, there was a sharp upturn. Instead of the expected 117 there were 138 applicants, about the level the trend line had predicted for two years later. However, 1966 saw only a slight further rise to 141. It is very difficult therefore to estimate what the future trend will be. Based on the 1959 to 1964 straight-line projection, one would expect about 175 applicants by 1970. A more generous estimate, based on the higher numbers in 1965 and 1966, would place the 1970 applicants at about 190.

It must be emphasized that these figures are the total number of applicants who submit documents in January for admission to the class the following September. In the interval this number is sharply reduced by:

(a) Those who fail to complete their premedical course in the spring or fail to reach a grade acceptable to the Admission Committee, usually about 25 per cent of the applicants.

(b) Those who are accepted by another medical school and elect to register there, usually 5 per cent.

(c) Those who decide in favour of another field of study, also about 5 per cent.

This leaves 65 per cent of the applicants as fully qualified candidates for enrolment in September. This proportion has been relatively stable for the last four years. When 70 to 90 per cent of candidates were accepted in 1959 to 1961, during which time the number of local applicants had fallen to a very low level, the failure rate in the medical school was excessively high. One can hardly expect a larger proportion than 70 per cent to be admitted.

It is therefore concluded that by 1967 about 150 Atlantic Province students may apply for admission to Dalhousie, of whom 70 per cent, or 105, will be qualified, and of these 90 to 95 will be available for enrolment in the 1967 class. The Sir Charles Tupper Medical Building will have space for a class of 96. By 1970, according to present trends, the applications may reach 175 to 190 and of these 114 to 124 should be acceptable. If the Dalhousie class of 96 then included about 10 per

cent of non-residents, there would be sufficient students for another school of 30 to 35 students. Assuming a steady rate of growth to 1975, there should be students for a school of approximately 60.

By 1955, the birth rate of the four Atlantic Provinces had begin to decline from its post-war peak. There has been a further sharp drop since 1963. The 20 year age group in 1975 will therefore begin to level off. It would therefore seem a reasonable assumption that medical student enrolment from the four Atlantic Provinces will not exceed the capacity of two schools, one of 96 and one of 64. Incidentally, the latter is usually the minimum figure now quoted in planning new medical schools and is believed by some to be the minimum economic unit.

In considering the number of schools and total enrolment of medical students in this area, two other approaches have been made. If the enrolment of medical students, as shown in Table II is calculated in relation to the population of each province, it will be seen that Prince Edward Island has had the highest rate. It has provided approximately 6 new medical students per 100,000 per year over the 12 year period, Nova Scotia 3.5 per year, New Brunswick 3.0 and Newfoundland 2.2. However, the figures for the last four years are more revealing than a 12 year average, since enrolment has climbed during that time. Prince Edward Island now has a rate of 5 new students per 100,000 per year, Nova Scotia 4.2, New Brunswick 3.3 and Newfoundland 2.6. These rates are based on first year students in all Canadian universities, not the Dalhousie figures only. (Table II)

For many years, Prince Edward Island has had the highest proportion of its 18 to 24 year age group enrolled in universities, slightly higher than the Canadian average and well above the other three Atlantic Provinces. The enrolment of medical students from Prince Edward Island has also been the most stable in spite of the small population, which often results in wild fluctuations of specific rates. In fact, it would seem that the Medical School enrolment from Prince Edward Island has stabilized at 5 or 6 per year, or may even be falling slightly.

An American medical educator recently quoted a figure of 5 as the expected number of qualified medical students to be drawn annually from a population of 100,000 people. In 1964-65, 8891 medical students were accepted into U.S. schools, a rate of 4.6 per 100,000. Only 10 states exceeded a rate of 5.5, 6 exceeded a rate of 6, and two, New York and North Dakota, reached 7.7 and 7.1 respectively. This would suggest that 100 to 140 medical students might be expected from the Atlantic Province population of just under two million, or 5 to 7 per 100,000.

^{*}Table II was published in Part I of this article N. S. Medical Bulletin, Vol. XLVI Number 2 (February) 1967.

Another approach is based on the physician supply, if it were fully adequate now and the medical schools had to take care only of the replacement of doctors lost from death and retirement and the increase in medical demands from population growth. Let us assume for simplicity that the regional population is two million. Let us further assume that an ideal ratio is a population of 800 per doctor, somewhat better than the present Canadian average and vastly better than the figure for the Atlantic Region. To reach such a ratio would require 2,500 doctors in the four provinces. If each physician has a professional life averaging 40 years, the replacement rate is 2½ per cent per year. This would require 63 new graduates per year. Growth of population of this region is less than 30,000 per year, requiring an additional 37 doctors. The total requirement would then be 100 per year. This will require the graduation (and postgraduate training of specialists) of 125, if 80 per cent stay in the region, or 143 if 70 per cent stay. The latter is the present proportion. To graduate 143 per year would require admission to first year of about 160, allowing for 10 per cent "wash-out" rate.

These estimates, based on present experience, would seem to suggest that the needs of the region could be met by two schools of combined enrolment of 160 per year once the present shortage is overcome. But to achieve this level the recruitment of medical students would have to reach 8 per 100,000 per year, an increase of 60 per cent even in Prince Edward Island, almost 100 per cent or double the

present rate in Nova Scotia, a two and a half fold increase in New Brunswick, and almost 3 fold in Newfoundland.

Unless there are some almost magic means used to raise recruitment to these levels, the two schools will not be fully utilized and the output will not meet the needs of the region. Certainly, the demand for a third school would be hard to justify under such circumstances.

It is not to be forgotten that the above calculation was based on an assumption that we started off with 2,500 doctors. Instead, we have about 1,600. To make up this deficit would require a generation or more, in fact 40 years at the rate shown in these calculations. Some must surely be recruited already trained, leaving the new school and Dalhousie the job largely of maintaining this supply.

On a more optimistic note, if 90 per cent of graduates could be kept here, the recruitment goal need be set at only slightly more than 6 students per 100,000 per year, already reached by Prince Edward Island. This would suffice to fill all the needs. It would provide 120 to 125 first year students, a number easily enrolled in two schools with room for a number of non-residents to "leaven the loaf". Of the 125, there would be 112 graduate and if 90 per cent remained in the region, the estimated maintenance requirement of 100 doctors per year would be met. There would still be room in two medical schools to train more than this number for some years in order to fill the present shortage.

F. GORDON ROBERTSON, C.L.U.

NORTH AMERICAN LIFE ASSURANCE COMPANY

TAX DEDUCTIBLE SAVINGS PLANS AND IMMEDIATE ANNUITIES

Representative for Medical Society Group Plans

MORE THAN THIRTY-FIVE YEARS EXPERIENCE IN ESTATE PLANNING

Bank of Canada Bldg. Phone: O

1583 Hollis St., Halifax

one: Office 423-7144

Home 423-2198

ADVERTISERS INDEX

Bell, Alfred J. & Grant, Limited	64
British Drug Houses	IV
Connaught Laboratories	
Frosst, Charles E. & Company	Ш
North American Life	68
Poulene Limited	II
Searle, G. D. & Company (Canada) Limited	1
Winthrop Laboratories	60



How To Talk With Your Psychiatrist
NANCY LAMPLUGH

Thousands of words have been written about how psychiatrists should talk with their patients: procedures of approach, establishing a correct diagnosis, gaining the patient's confidence, filling him with drugs and eventually sending him on his merry way provided he can fulfill some functional use to society. That's his job. But what about the patient? This is a big business for him to go through and is, to say the least, upsetting to his emotions. His job is just as hard as that of his psychiatrist. If he has sensitivity - and probably he has or he would not be sick - he must work hard to keep his psychiatrist from eventual boredom with his case. Once the patient has made good and lasting contact with his psychiatrist, and assuming there is no personality clash, it is really up to him to keep the ball rolling.

Let us suppose you are the victim. You were led - more likely pushed - into Dr. Zebrowsky's office some months ago. After a lot of preliminaries, and several visits later, it is established that your chief complaint is your wife, and the fact that she is the kind of person who must always have soft butter on the table. Now this is all very well, and it's nice not to have hard butter, but it's the principle of the thing, and this soft butter act smears itself into all aspects of your married life. You become aware that Dr. Zebrowsky, though sympathetic to your complaint (this is what he calls it, though not by actual name) is in some odd way also in sympathy with your wife, and is attempting to show you where you have gone wrong in your relationship with her. She evidently has a compulsion about soft butter, like never being seen without lipstick, or going through swing doors twice to make it even. You realize eventually, by the impression his subtle methods have upon you, that the soft butter business is as much your doing as hers.

Now the trick is not to let your psychiatrist know that he has gotten through to you: that you understand soft butter and doors and accept them. For that would be the end of your relationship with him, giving up a really very interesting episode in your life. A stimulating situation, it has become a game with words, a test of ability, of wits. You realize how much influence you can exert with just an expression on your face, an introduction of a new idea seemingly unrelated to anything im-

mediate: your psychiatrist must endeavour with all his ability to relate that expression or idea to "your problem."

However, he must be in control, master of you and your emotions. Perhaps now is the time to start crying about the butter again. At this point his relief will be so great, he will be in real sympathy with you. Push your advantage while you can and he'll attack the subject again with renewed vigour, in all probability in a more humane manner. After all, you can't just treat an isolated sick emotion, blown, bent and battered by the winds of time you have to look back in order to look forward. He will start probing and questioning, suggesting. Throw them all back to him. Know your man and the purpose behind his questions. Through him you will know yourself.

He may be Freudian in his methods. By now this is old hat to you. Of course everything's basically sex. It was, the instant you were conceived. Point this out to him and watch his reaction. He will read much more into this, and with mounting excitement wonder how long this has been bothering you. It doesn't matter what you say, it's the conviction of your words. If you have enough confidence in your ideas, putting them across with quiet emphasis, he'll lap them up. He may get embarrassed and want to drop the subject, but keep it going, it's always interesting. You will learn a lot, and as a result gain some insight as to the differences between the middle European countries and Canada. This will further your knowledge of him as well. He may have some difficulty in settling into Canadian ways, and accepting the differences in the cultural aspects of life as compared with his homeland. For a time you will epitomize a way of life he has tried to understand for years. But watch it - be careful of your influence upon him. Don't forget the butter - get him back on the job.

Stop for a moment and stare beyond him, look unhappy. Now he's back in his role of helper and healer. But don't allow him to feel all his work is for nothing. Show him you have gained insight. Suggest to him that emotionally ill people are those basically who are not fully alive. This may startle him as he might never have thought of it in quite this light. Dr. Zebrowsky looks troubled: it's evident he has his problems too. You feel this with some uneasiness. Possibly he and his wife have the same arguments about butter because he seems hesitant to discuss his married life. You probe a little. With all your experience you should be able to help. You must'nt let him down now. Show him your continuing interest, assure him of your friendship and willingness to lend an ear to any topic of conversation. You become aware that he is indeed just another rather complex human being. If that is the case, he is somewhat limited in his ability to help you further. But then, you've been slowly realizing this for some time. It's becoming a little tedious anyway. In general, include him in your life, not only your problems. You will find him a tough nut to crack, but no doubt he found the same with you.

FIBRINOGEN

(DRIED, HUMAN)

Fibrinogen (Dried, Human) is prepared from normal human plasma. The material is produced by the cold ethanol plasma fractionation process of the late Professor E. J. Cohn and associates. It is dried in vacuo from the frozen state in quantities which should be reconstituted for use by the addition of sterile, pyrogen-free distilled water.

Fibrinogen (Dried, Human) may be indicated in hypofibrinogenaemia whether this be congenital or associated with other conditions. The product has been found useful in instances of abruptio placentae or in cases involving a dead fetus.

CONNAUGHT MEDICAL RESEARCH LABORATORIES

University of Toronto
1755 Steeles Avenue West, Willowdale, Ontario

Established in 1914 for Public Service through Medical Research and the development of Products for Prevention or Treatment of disease.

A booklet entitled "Products in the Service of Medicine" describing products and their use is available on request from the Laboratories.

MEDICAL-LEGAL INOUIRIES

Permission For Autopsy

- Q. Why does Nova Scotia not have Legislation governing the legal meaning of "next of kin" with respect to autopsy permissions?
- A. In Nova Scotia the hierarchy regarding the definition of next of kin is fairly clearly delineated in the Human Tissue Act.¹

"Where a person has not made a request to be a donor and dies either in or outside a hospital, his spouse or, if none, any of his children of full age or, if none, either of his parents or, if none, any of his brothers or sisters or, if none, a person lawfully in possession of the body of the deceased person may authorize:

a. the use of the body,

 the removal of a part or parts of the body and the use thereof.

for therapeutic purposes or for the purposes of Medical Education or Research"

Under this section it would appear that, in Nova Scotia, if permission for autopsy is granted, say by a "child of full age", and opposed by a parent, the physician is covered under the law if he carries out the autopsy despite the opposition. In such a case, though not a legal requirement, it would be prudent to notify the Medical Examiner or Local Magistrate of his intent.

As Chayet² points out: "obtaining proper consent for an autopsy poses many problems... it has been held almost unanimously throughout the United States that...(the) next of kin can sue the physician who performs an unauthorized autopsy....The theory is that an unauthorized...section of the body prevents burial in a proper manner".

Not all autopsies require consent. Under the Statutes of Nova Scotia the Medical Examiner or the Superintendent of "any Municipal Home, Prison, Morgue, Hospital or other Public Institution having charge or control of dead bodies of persons who previous to death were being maintained at the public expense, ...shall, without fee or reward deliver the body to the Inspector of Anatomy. .for the purpose of being used. .for the advancement of anatomical pathological science" if "such dead body. .. (is) required for the purpose of this act". 4 (our italies)

Under English Common Law there is no property right in a dead body. This is popularly misconstrued as meaning that an individual has no rights over his own corpse and that he may not legally donate it against the wishes of his close relatives. This is not so. During his life a person may direct how he wishes his body to be disposed of and, providing the direction is not overly bizarre or offending to public morals or health regulations, his wishes may be carried out even over the objection of the next of kin. There is no question that this does not apply to a request that an autopsy be performed on his body.

Certain other autopsies may also be performed in the face of opposition by the next of kin; namely those performed by or at the direction of the Medical Examiner under the Fatality Inquiries Act⁵. Were this not the case it would be all too easy for persons to hasten their next of kin into the Next World.

I.M.

References

- 1. Rev. Stat., N.S. (1964) Chap. 5, Sec. 4.
- Chayet, Neil L., New Eng. J. Med., 274:268, 1966.
- 3. Rev. Stat. N.S. (1964) Chap. 16, Sec. 1.
- Stat. N.S., Chap. 8, Sec. 3 (3).
- Stat. N.S. (1960) Chap. 6, Sec. 5.

NOVA SCOTIA MEDICAL BULLETIN Editorial Office

Editorial Office	
THE BULLETIN is planning a regular Medical-Legal section devoted to Medical Legal Enquiries. You are invited to contribute questions.	
5	

Please send completed form to: -

Ian Maxwell, M.D.
Medical-Legal Liaison Committee
Department of Pathology
Halifax Infirmary
Queen Street
HALIFAX, Nova Scotia

Announcement

THE CENTENNIAL FILM

"A CENTURY OF CANADIAN MEDICINE"

Sponsored by the Canadian Medical Association
Produced by Chetwyn Films

will be available to all branch societies for their individual showings from March 15th, 1967

This film, showing the life of a Canadian doctor one hundred years ago and contrasting it with shots taken in all types of practice all across Canada, is a 16 mm. Sound and Colour film, running for 28 minutes.

to book this film for your branch society

write to: - Dr. C. J. Beckwith

Executive Secretary

Medical Society of Nova Scotia

Dalhousie Public Health Clinic

University Avenue

Halifax, N. S.