An Old Concept - A New Method

After reviewing some nine hundred office cards and using numerous patient lists; one is able to conclude that a general practitioner sees approximately 81% of his patients at least once in every year. This research, done to satisfy a personal curiosity has implications that figure strongly in the light of recent medical and political developments. After the arguments put forth are evolved, readers are able to agree or disagree as they see fit.

The great problem today is the concentration of disorders in the middle age group and the elderly. The number of lives saved in this group by antibiotics, sulphas, and surgical advancements has been cancelled out by the great killers. But death cannot be considered the only menace.

Conditions such as chronic bronchitis, diabetes and arthritis take many years to develop and then lead to long illness.

Too often the years during their development are symptomless. These conditions are often insidious and quite persistent, but their social impact is not. The public is not too much aroused.

We also have the diseases of plenty or "too much". The causes are not easily understood but are dependent on living habits—over nutrition, lack of activity, lazy leisure hours, addictions.

These may be survived but one then runs into the disabling diseases of middle life—obesity, hypertension, strokes, rheumatoid arthritis and others. The possibility of curing the "middle-age" disease group seems remote once it is fully developed.

In the chronic conditions and the cancers, causes are unknown and thus not easily dealt with. Even the seeming failure in the problem of smoking is an example of how spectacular campaigns must be if success is to crown any effort.

Renewal of an "old" concept into a "new" effort is an answer to this problem.

Since the doctor sees a good proportion of his practice over and over again, he must practise making the diagnosis even before the symptoms appear. At best disease must be detected early in its onset, before symptoms are experienced. In this way its progress may be halted or retarded. Treatment can be "preventive" if given early enough.

Thus the main preoccupation is with the vulnerable patient. All middle-aged people are vulnerable, but some of this group have characteristics which suggest that for them the risk is even more severe.

One would ask if this business of making a diagnosis before symptoms occur is at all practicable. Yes, and thanks to our more learned confrères it is beginning to be more than at any other time in the past.

Simple tests are becoming available to discover early signs of many diseases before the patient is even aware of the presence of a disorder.

Special chemically treated papers dipped into urine for a few seconds may tell us about the possibility of diabetes as well as possible kidney trouble. Visual field narrowing may lead one to suspect early glaucoma, the common cause of blindness in the middle age or older group.

Cervical cancer can be diagnosed long before symptoms would be recognized or reported.

Elaborate apparatus is not required and the tests depend on hands and eyes only.

Thus the field of "early" detection belongs to the general practitioner and he has become a part of his daily work. It has become his specialty because he is the only doctor who deals constantly with this potential or vulnerable patient.

Of course this must be done in collaboration with the hospital and its facilities and services.
The doctor establishes a base line for his patient; weight, blood pressure, urine tests, hemoglobin, pelvic and rectal examinations etc. These would be checked at regular intervals and rechecked as patients turned up with their ordinary complaints.

To gain the most out of this type of medicine, the doctor has to know his patients, their daily lives, their work, their family situations and environment; various stresses and strains to which they are subjected.

When early abnormality is discovered, on occasion, there may be no definite treatment available.

The doctor may use his knowledge as an adviser or medical educator to show the patient how to alter his environment and to control the disease or the development of disease. The more intimately he knows his patient, the better the chances are for effective results. This is the medicine of health rather than of disease. More emphasis should be put on preventive medicine than ever before, otherwise it is more and more a losing battle. General Practice becomes much more enticing; much more enjoyable; much more challenging when the preventive medicine aspect is practised. This is a personal feeling and one that each individual must feel for himself. As earlier stated it is not an original idea; the firm feeling for it is developed as time goes on and once attained it is "original" in that person.

The doctor must develop a new attitude to need and to what is expected of him - a new approach to his practice - the anticipation of illness which may lead to its prevention or early treatment. We have been told of the numerous unknown diabetics amongst us. Sooner or later each will go to his doctor reporting a sign or symptom or two. But how many of them will have had symptoms for four or five months before it was diagnosed? Some of this delay is the patient's ignorance; but how much because of the doctor's oversight. Delay may increase the severity of disease or favor the development of complications.

Urine tests for sugar every year would make the diagnosis at an early stage and educate the people also. The doctor's anticipation of risk would be alerted by knowing the vulnerable patient - those with strong family history of diabetes particularly if elderly or obese. This would also unearth those women with particular childbirth difficulties.

The Pap smear so widely used is another important presumptomatic field that is so self satisfying. It has now been known for some time that regular yearly use of the smear method could detect cancer at a very early stage even before the woman had symptoms and while the disease is confined locally.

The annual physical examination of an asymptomatic individual is generally believed to be the best means available at this time to improve cancer cure rates. While the specialized cancer detection clinics may help here, every doctor's office is a cancer detection area.

Maybe these haven't flourished as much as they should. Actually it takes two to perform a physical examination; the examiner and the patient. Both have their reasons for not participating freely. Doctors may be too busy to perform annual check ups on apparently healthy persons. This defeats the purpose of finding things before they happen.

Future prospects indicate fewer doctors available to do health check up with more and more doctors being attracted to the specialties.

Internal medicine men, (specialist physicians), surgeons and gynecologists amongst others perform general physical examinations on their patients but they cannot be counted on for annual check up of the asymptomatic. This leaves, general practitioners for the great bulk of this valuable method of finding disease before symptoms appear.

Probably 35 or 40% of future doctors will be available to do these physicals. They are the general practitioners and internal medicine men. Thus it appears that making an appointment for a complete check up is going to be difficult, unless this concept includes the physical examination as done for patients who go to the doctor because of illness of any sort.

A physical exam is required in the proper diagnosis of any condition and if the doctor is alert to the signs of other disease (particularly cancer), then the annual check up concept is practical. Some years ago this writer was engaged in a very stimulating argument with a confrère who felt that when a patient who was obviously healthy wanted a check up, that person was nothing more than a neurotic. It was quite easy to agree with him to a point, but with changing concepts he could not be more wrong. He is now in a specialty where this concept does not apply so forcefully. Cured cancer is a precious accomplishment, whether it is brought about by a clinic or through a complete physical examination for an illness or injury and thus found incidentally.

Now that we can see a new approach to the regular health check up we must ask the question: will the increased workload arising out of further spread of 'Medicare' plan so swamp the practitioner that he has not the time for these examinations. Those with foresight will examine all such plans in that light.

"Is the doctor image due for another tumble?"

W.A.C. □

THE NOVA SCOTIA MEDICAL BULLETIN 288 DECEMBER, 1965
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THE NOVA SCOTIA MEDICAL BULLETIN

DECEMBER, 1965
Lung Cancer In Nova Scotia

C. Edwin Kinley, M.D., M.Sc., F.R.C.S.(C) and E. P. Nonamaker, M.D., F.R.C.S.(C)

Halifax, N. S.

The recent increase in the death rate from lung cancer is well documented.(1) We wish to draw attention to the rapid increase in the number of reported cases of lung cancer in Nova Scotia.

The cases presented in this report were seen at the Nova Scotia Tumor Clinic of the Victoria General Hospital. Some physicians may not be aware of the services available at this Clinic, which was opened in January, 1953. The medical staff members are appointed jointly by the Victoria General Hospital and the Dalhousie Medical School. Dr. J. A. Myrden recently succeeded Dr. N. H. Gosse as Medical Director. Any resident of Nova Scotia is eligible for examination in this Clinic, on referral by their family physician, who may specify that the referral is for consultation only or for diagnosis and treatment. Last year there were about 5,000 clinic visits, including 1,200 new cancer cases. Because of the excellent co-operation of the referring physicians, follow-up on these patients is nearly 100 per cent.

A Provincial Cancer Registry was established a year ago, through the efforts of the Provincial Government and the Medical Society of Nova Scotia. All new cancer cases must be reported to this Registry. There were 1,800 new cases of cancer reported in Nova Scotia last year, and two-thirds of these were seen at the Tumor Clinic.

TABLE I. Lung Cancer at Nova Scotia Tumor Clinic

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Cases</th>
<th>Alive After Five Years (5.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1953</td>
<td>35</td>
<td>2</td>
</tr>
<tr>
<td>1954</td>
<td>30</td>
<td>2</td>
</tr>
<tr>
<td>1955</td>
<td>31</td>
<td>3</td>
</tr>
<tr>
<td>1956</td>
<td>37</td>
<td>1</td>
</tr>
<tr>
<td>1957</td>
<td>50</td>
<td>2</td>
</tr>
<tr>
<td>1958</td>
<td>34</td>
<td>2</td>
</tr>
<tr>
<td>1959</td>
<td>48</td>
<td>—</td>
</tr>
<tr>
<td>1960</td>
<td>53</td>
<td>—</td>
</tr>
<tr>
<td>1961</td>
<td>66</td>
<td>—</td>
</tr>
<tr>
<td>1962</td>
<td>66</td>
<td>—</td>
</tr>
<tr>
<td>1963</td>
<td>85</td>
<td>—</td>
</tr>
<tr>
<td>1964</td>
<td>98</td>
<td>—</td>
</tr>
</tbody>
</table>

Lung Tumors

Table I shows the increasing numbers of lung tumors seen at the Clinic since its inception in 1953. At present, we cannot say whether this alarming increase is due more to a rising incidence of lung cancer in Nova Scotia, or to more frequent use of the Tumor Clinic by physicians of the Province. It is hoped that the Provincial Cancer Registry will soon provide the answer. The crude five-year survival rate of 5.5 per cent agrees with experience in other areas.

An analysis of the first 50 cases seen in 1964 has been made. In Table II are given the age and sex of these patients. There are more females (one out of every four) than could be expected in this small group. The average age was only 58 years.

TABLE II. 50 Consecutive Cases in 1964

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Average Ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cases</td>
<td>50</td>
<td>58.4 years</td>
</tr>
<tr>
<td>Males</td>
<td>38</td>
<td>59.7 years</td>
</tr>
<tr>
<td>Females</td>
<td>12</td>
<td>54.3 years</td>
</tr>
</tbody>
</table>

Table III shows the method of diagnosis. Cytology confirmed the diagnosis in nine cases. Thirty-eight cases were diagnosed by tissue examination. This examination was on an operative specimen or biopsy in 25, a bronchoscopic biopsy specimen in 8, a "scalene node" biopsy specimen in 3, and autopsy specimen in 2. In only 3 cases was the clinical diagnosis unconfirmed by cytology or histology.

TABLE III. Method of Diagnosis

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray only</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Cytology and X-ray</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Histology</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>— Thoracotomy Specimen</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>— Bronchoscopic Biopsy</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>— Scalene Node Biopsy</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>— Autopsy Examination</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

*From the Nova Scotia Tumor Clinic and the Department of Surgery, Victoria General Hospital, Halifax.

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Table IV shows the treatment given. Twenty-eight patients were explored, with biopsy alone in 15. Resections were done in 13 patients, including 8 lobectomies, 3 pneumonectomies, and 2 local excisions. Radiation was given to 32 patients, and chemotherapy was used in 3 patients with far advanced disease who died in hospital. Since radiotherapy was sometimes combined with resection, and often used when thoracotomy disclosed an unresectable tumor, some of the 50 patients are included in more than one of the treatment categories of Table IV.

**TABLE IV. Treatment**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation</td>
<td>32</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>2</td>
</tr>
<tr>
<td>None (died in hospital)</td>
<td>3</td>
</tr>
<tr>
<td>Explored</td>
<td>28</td>
</tr>
<tr>
<td>- Biopsy only</td>
<td>15</td>
</tr>
<tr>
<td>- Pneumonectomy</td>
<td>3</td>
</tr>
<tr>
<td>- Lobectomy</td>
<td>8</td>
</tr>
<tr>
<td>- Local Excision</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>65</td>
</tr>
</tbody>
</table>

**Delay in Diagnosis**

Table V indicates, as nearly as possible, the delay in diagnosis. With regard to the patient, this means delay in consulting a physician for the onset of, or change in, lung symptoms. The physician delay extends from the time he first saw the patient for chest complaints to when he proceeded with investigation other than a physical examination. The hospital delay extends from the day of admission of a patient with lung symptoms to the day when lung cancer was first considered a possibility. There is room for improvement at each stage. The patient delay was seven weeks, the physician delay four weeks, and the hospital delay one and one-half weeks, resulting in many instances of a total delay of over three months. In this period of time, many bronchogenic carcinomas may assume an advanced stage.

**TABLE V. Delay in Diagnosis**

<table>
<thead>
<tr>
<th></th>
<th>Average time in weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>7</td>
</tr>
<tr>
<td>Physician</td>
<td>4</td>
</tr>
<tr>
<td>Hospital</td>
<td>1½</td>
</tr>
</tbody>
</table>

What are the reasons for the delays in diagnosis? Among the fifty cases analysed, the following factors came to our attention:

1. **Patient delay.** Usually due to a failure to consult a physician concerning symptoms of recent onset, e.g., dyspnea on exertion, increasing cough, vague chest pain, and weight loss. Hemoptysis was not a common early sign.

2. **Physician delay.** There seems to be a low index of suspicion concerning lung cancer. There is frequently a failure to follow-up cases with respiratory symptoms. Respiratory symp-

toms call for a chest X-ray; any abnormality found should result in (a) hospital admission for further investigation, or (b) a trial of drug therapy, with discharge from medical care only if follow-up X-ray after two or three weeks shows complete resolution of the radiological abnormality. Even then, these patients should have sputum specimens sent for cytological examination after another month. There also appears to be a fair degree of despair concerning the outlook in lung cancer, which is not justified in adequately managed cases.

3. **Finally, delay in hospital is inexcusable.**

**Management**

In the management of cases when the diagnosis of lung cancer is established or reasonably certain, it is fair to say that surgery remains the standard treatment. Having said this, we must point out that the selection of cases suitable for surgery can still be haphazard. Currently (Table IV) we explore about half of the new cases we encounter, and do resections in about half of the explorations.

We are attempting to be more critical in selecting cases for exploration. Sealed fat pad biopsy, if nodes are not palpable, is not usually of help in this regard. But two recent developments may improve the selection for surgery: (1) The use of mediastinoscopy (2) to assess mediastinal and hilar pathology, both for diagnosis and as a guide to operability. (2) The advent of pulmonary arteriography is assessing the extent of hilar involvement.

Another aspect of management which needs further definition is the place of radiotherapy. Customarily, radiotherapy has been used for inoperable cases, or as an added measure where resection has left obvious tumor in the chest. We have recently been using radiotherapy as the primary treatment for certain tumors, e.g., anaplastic carcinomas in younger patients, and sometimes doing a delayed resection several months later. Our experience is limited, but we have been impressed with the results thus far, as have others 3.

Radiotherapy is always worth trying as palliation for locally troublesome tumor deposits, e.g., bone lesions, or superior vena cava obstruction.

Our experience with chemotherapy for lung tumors is limited, but on the whole unsatisfactory.

**Education and Early Diagnosis**

Just as difficult as the management of lung cancer is the problem of early diagnosis. The profession and the public (the latter as a result of education by the profession) must become more aware of the importance of adequate investigation and follow-up of patients with new or changing lung complaints. Cancer is much more often the cause of lung pathology in male or female adults than tuberculosis. The significance of solitary

(Continued on page 309)
Cancer of the Lung

J. J. QUINLAN, M.D., V. D. SCHAFFNER, M.D., F.A.C.S., AND J. E. HULTZ, M.D., D.P.H.1

Kentville, N. S.

Fifty years ago, cancer of the lung was a medical curiosity as evidenced by the fact that in 1912 Adler (1) reviewed the entire literature on the subject, and found that a total of only 375 cases had been reported. Today, primary cancer of the lung accounts for 10% of all malignant tumors. The incidence in the male sex is even more striking, as 20% of primary cancers in men occur in the lungs. It used to be argued that this increase in incidence was for the most part due to better diagnostic facilities and to the fact that more people were living to enter into the so-called cancer age group. These factors undoubtedly account for some of the increase but most students of the problem agree that the disease is occurring far more frequently today than it did 50 years ago. In both Canada and the United States, deaths certified as due to cancer of the lung in 1962 were 10 times the figure of 1932.

The tumour was first described by Laennee in 1805 and again more completely by him in 1819. However, as early as the 16th century, a fatal disease of the lungs was known to occur in a high percentage of men working in the mines of Schneeberg, Germany and of Jaoehinasthal, Czechoslovakia. The nature of this disease was obscure until, in 1879, it was identified as cancer of the lung and was found to be responsible for 75% of the deaths in miners in these areas.

Following Adler's review of the subject, criteria for diagnosis were established by Weller (2) in 1913. Bronchoscopic examination with biopsy popularized by Chevalier Jackson in the early 1920's was responsible for the finding of many cases before death. A most significant step in treatment was the first successful pneumonectomy for carcinoma of the lung carried out by Evarts Graham in 1933. In the years since then, the introduction of newer methods for diagnosis and the refinement of older ones, together with the absolute increase in incidence, has made the discovery of primary cancer of the lung a common occurrence.

As with malignant disease in the rest of the body, the cause of cancer of the lung is still obscure. Recently, however, a great deal of evidence has been accumulated regarding the role of various factors in the etiology of the disease. Four hundred years ago, cancer of the lung apparently was quite common in the Schneeberg miners after about 20 years' exposure in an environment where the air contained a high percentage of arsenic, cobalt, and radio-active substances. An increased incidence of lung cancer exists in chromate workers in the United States and Europe, and it is common among workers in the nickel industry in England and Norway. In 1950, Wynder and Graham (3) in the United States, and in 1952, Doll and Hill (4) in England, found that cancer of the lung was far commoner among heavy cigarette smokers than among nonsmokers, and these observations have been well substantiated by numerous surveys during the past 14 years. It is found that there is one case of lung cancer in 800 nonsmokers, compared to one case in 23 heavy cigarette smokers who have smoked for more than 30 years. Cancer of the lung is less common in cigar and pipe smokers than it is in cigarette smokers, but it still occurs more frequently than among abstainers.

It is generally accepted that the condition is much more common in cities than it is in rural areas. This has been commented on by Stocks (5) of England in the following vein: "Either smokiness of the atmosphere is an important factor of itself in producing lung cancer, or sunshine is an important factor in preventing its incidence". He showed that there is a marked fall in death rate in relation to the hours of sunshine recorded and, when 20 large boroughs were divided into three groups by their main annual sunshine hours, the lung cancer mortality ratios were as follows:

<table>
<thead>
<tr>
<th>Hours</th>
<th>Cancer</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sunshine</td>
<td>1,150</td>
<td>152</td>
</tr>
<tr>
<td>1,150 to 1,400</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>over 1,400</td>
<td>58</td>
<td></td>
</tr>
</tbody>
</table>

Summarizing the evidence, therefore, it may be stated that the strongest case can be made for cigarette smoking as a cause of lung cancer but that its etiology, as in other cancers, is a multifactored equation.

The great majority of lung cancers originate within this organ, but the lung is also a common site for metastases from malignant tumors in other parts of the body. Bronchogenic carcinoma accounts for about 98% of the primary malignant

1Presented at the Meeting of the Nova Scotia Institute of Science, Valley Chapter, March 1965.
2From the Nova Scotia Sanatorium, Kentville, Nova Scotia.
tumours, the remaining 2% being made up of Hodgkin's Disease and sarcomas arising from one of the connective tissue elements of the lung. The secondary tumours may originate anywhere in the body, but the commonest sites are the gastrointestinal tract, the breast, the prostate, the kidney, and the adrenal glands. Metastases from melanomas and sarcomas also commonly occur in the lungs.

The most common type of malignant lung tumour, the bronchogenic carcinoma, may be of several cell types which are, at times, very difficult to distinguish histologically one from the other. The classification generally accepted divides them into four groups:

1. The most frequently encountered is the epidermoid or squamous-cell carcinoma which accounts for one-half of them. Most of these tumours originate in the first branches of the main bronchi, grow relatively slowly, and are likely to produce symptoms early. Because of these factors, they are more frequently diagnosed in a treatable state, and the recovery rate is highest in this group. This is also the group in which, etiologically, cigarette smoking is thought to play its most prominent part.

2. The next most common type is the anaplastic or undifferentiated carcinoma which makes up about one-third of the primary bronchogenic tumours. These cancers tend to arise in the main stem bronchi. They grow rapidly and are highly invasive. The adjacent regional and distal lymph nodes are invaded extensively at an early stage. For this reason, surgical treatment or any other treatment of these tumours is most disappointing.

3. Next in frequency is the adenoacarcinoma accounting for about one-sixth of primary carcinomas. These tumours, for the most part, occur in the peripheral regions of the lung and, consequently, the early occurrence of symptoms is uncommon. They grow more rapidly than the epidermoid type, but are less malignant than the undifferentiated. However, unless they are picked up by a routine roentgenogram long before symptoms occur, evidence of inoperability is frequently found when the chest is explored.

4. The least common cell type is shown by the bronchiolar, or “alveolar-cell” carcinoma which comprises about 2% of primary lung cancer. These tumours may be single or there may be numerous nodules scattered throughout the lung.

If single, resectional surgery can be carried out and, because they seem to be confined to the lung without metastases for relatively long periods, the results of surgery are better in these than in other types of pulmonary cancer.

The symptoms of lung cancer will depend on the location of the tumour. There is unquestionably a long, silent period between the inception of the cancer and the appearance of symptoms. It is during this interval, by routine X-ray examination of the chest or cytological examination of sputum, that we must diagnose cancer of the lung if the results of surgical treatment are to be improved.

The most common symptom is cough which occurs in 90% of the patients with any complaints referable to the lungs. It is usually nonproductive at first, but by the time that patients reach hospital more than half of them are raising sputum. The cigarette cough of the heavy smoker usually becomes much worse when a bronchogenic cancer develops. There may be fever associated with the cough due to a localized peripheral pneumonia caused by obstruction of the bronchus by the growth. Many patients complain only of vague discomfort in the chest, localized to the side of the tumour, but a few patients have severe pain which usually indicates involvement of the chest wall. Unfortunately, hemoptyisis, the most frightening of all lung symptoms occurs only in about 6% of cases. Nothing is more apt to arouse both the patient and the physician to action than the expectoration of blood. Wheezing will occur when the bronchus has become partially obstructed by the tumour. In the more advanced cases, there will be loss of weight or hoarseness of the voice due to involvement of the recurrent laryngeal nerve. In a few individuals, the first indication of cancer of the lung will be the appearance of a metastatic deposit in some other organ.

In the diagnosis of lung cancer, physical examination of the chest may be of little value, but in some cases, particularly when there is a complicating destructive process, the findings may be quite marked. X-ray examination of the chest is of extreme importance and will reveal some change from normal in 98% of patients with bronchogenic carcinoma. In 86%, the changes are sufficiently characteristic to suggest the diagnosis. A plain film of the chest may be augmented by carrying out planigraphic studies, bronchography and, in some cases, angiography.

About one-third (6) of all primary lung cancers can be seen during bronchoscopy and a definite diagnosis can be made by obtaining a biopsy specimen. In another one-third, there will be very suggestive evidence of the presence of tumour such as narrowing of the bronchi or the presence of bronchial rigidity. Secretions, if present, can be obtain-
ed for cytological examination or, if the tracheobronchial tree is dry, saline washings will sometime produce positive findings.

Cytological examination of the sputum is very important in the diagnosis of bronchogenic carcinoma and in about one-half (6) of the patients with peripheral tumours where a bronchoscopic biopsy cannot be obtained, cancer cells can be found in either the bronchial washings or the sputum.

Other diagnostic measures include needle biopsy of the pleura and presealene lymph node biopsy. If the nature of the condition is still not obvious, no time should be lost in exploring the chest. At operation, if a definite diagnosis has not been made previously, it can now be established and surgical extirpation undertaken if possible.

In regard to treatment, the only effective measure is surgical removal of the tumour by either pneumonectomy or lobectomy. Pneumonectomy will have to be carried out if the tumour is encroaching on the main bronchus, but for peripheral lesions lobectomy is the procedure of choice and, in a number of large series of surgically-treated cases, (7,8,9,10,11) the results of lobectomy are superior to those of pneumonectomy. At operation, if it is not possible to remove the tumour with any prospect or cure because of extension of the tumour to lymph nodes and adjacent structures such as the great vessels, a palliative resection of the involved lobe may be worthwhile in order to render the remaining days of the patient somewhat more comfortable. Palliation may also be secured by radiation therapy which can be of great benefit in alleviating symptoms in properly selected patients. In some cases, too, the patient will be made more comfortable and his life prolonged by the use of the newer chemotherapeutic agents.

The results of treatment in primary cancer of the lung are only fair. In various series of patients reported in recent years the cancer was excised in 15–40%. About one-fourth of all patients whose tumours were removed survived without evidence of recurrence 5 years or longer (7,8,9,10,11). The prognosis is markedly affected by whether or not the tumour has spread beyond the lung. Only 10% of the patients in whom the cancer had spread beyond the lung were alive at the end of 5 years, whereas when the tumour was confined to the lung, 40% were alive 5 years after surgery. In patients whose cancer was not removed, 90% did not survive 1 year, and less than 1% lived more than 2 years.

In the past 2 decades, there have been several reports of surgical treatment of metastatic lung cancer. This is possible if the secondary tumour of the lung is single and has occurred 2 years or more following the surgical removal of the original cancer.

The following information summarizes briefly the experience with cancer of the lung among patients at the Nova Scotia Sanatorium during the past 25 years.

In this period, there was a total of 100 individuals who were found to have some form of lung malignancy. There were 71 male and 29 female patients (Table 1). The youngest was 8, and the oldest 79, the 8-year old individual having Hodgkin's Disease of the lung. Opinion is divided as to whether or not this is a true cancer or a very malignant infective process. Only 10 were under the age of 40 and 79% of the group were in the 40–60 age range.

The malignant lesions were classified as shown in Table 2. The first four groups represent the primary bronchogenic carcinomas and account for 79% of the total. There were two cases of lymphoma or Hodgkin's Disease as it is more commonly called, one bronchial adenoma, and five sarcomas. In 13 individuals, the tumour was metastatic in the lung. The most common primary bronchogenic carcinoma was the epidermoid variety and the most striking thing was that all 32 patients in whom this type of cancer was found were men. There is a great preponderance of males in the next most

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>10-19</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20-29</td>
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<td>0</td>
<td>3</td>
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<tr>
<td>30-39</td>
<td>6</td>
<td>3</td>
<td>3</td>
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<tr>
<td>40-49</td>
<td>22</td>
<td>12</td>
<td>10</td>
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<tr>
<td>50-59</td>
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<td>60-69</td>
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<td>70+</td>
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<tr>
<td>All Ages</td>
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<td>71</td>
<td>29</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of Malignancy</th>
<th>Both Sexes</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermoid</td>
<td>32</td>
<td>32</td>
<td>0</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>16</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Bronchiolar</td>
<td>6</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>25</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2</td>
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<td>2</td>
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<td>1</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Secondary</td>
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<td>5</td>
<td>8</td>
</tr>
<tr>
<td>All Cases</td>
<td>100</td>
<td>71</td>
<td>29</td>
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TABLE III. Location of Primary Cancer which Metastasized to Lungs

<table>
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<th>Site</th>
<th>Both Sexes</th>
<th>Male</th>
<th>Female</th>
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<tr>
<td>Oesophagus</td>
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<td>1</td>
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</tr>
<tr>
<td>Kidney</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corpus Uteri</td>
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<td>1</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Not Known</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>All Cases</td>
<td>13</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>

common variety, the undifferentiated carcinoma, with only 5 of the 25 cases being of the female sex. With the adenocarcinomas, the proportions are more nearly equal, there being 10 men and 6 women. In the case of the 6 bronchiolar carcinomas, there were 4 females and 2 males.

In determining the site of the primary tumour (Table 3) causing lung metastases in this series, it was found that the breast was the most common site, four patients having a primary breast carcinoma. Two metastatic lesions originated in the kidney and one each in the esophagus, pancreas, colon, thyroid, and ovary. In one case, the primary site could not be determined.

TABLE IV. Cigarette Smoking Habits – Males

<table>
<thead>
<tr>
<th>Type of Malignancy</th>
<th>Non-Smoker</th>
<th>Less Than 10 Cigarettes Daily</th>
<th>10–20 Cigarettes Daily</th>
<th>21–40 Cigarettes Daily</th>
<th>More Than 40 Cigarettes Daily</th>
<th>Pipe Only</th>
<th>Not Known</th>
<th>All Degrees of Smoking</th>
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</thead>
<tbody>
<tr>
<td>Epidermoid</td>
<td>1</td>
<td>3</td>
<td>12</td>
<td>3</td>
<td>1</td>
<td>12</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Bronchiolar</td>
<td>1</td>
<td>1</td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>1</td>
<td>5</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>20</td>
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<tr>
<td>Others</td>
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<td></td>
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<td>4</td>
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<tr>
<td>All Cases</td>
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<td>2</td>
<td>11</td>
<td>23</td>
<td>4</td>
<td>2</td>
<td>25</td>
<td>71</td>
</tr>
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</table>

TABLE V. Cigarette Smoking Habits – Females

<table>
<thead>
<tr>
<th>Type of Malignancy</th>
<th>Non-Smoker</th>
<th>Less Than 10 Cigarettes Daily</th>
<th>10–20 Cigarettes Daily</th>
<th>21–40 Cigarettes Daily</th>
<th>More Than 40 Cigarettes Daily</th>
<th>Not Known</th>
<th>All Degrees of Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>6</td>
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<tr>
<td>Bronchiolar</td>
<td>1</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>1</td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Others</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>All Cases</td>
<td>9</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>14</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>

During the past 7 years the smoking habits of 61 patients have been investigated and the results are summarized in Table 4. This is too small a series from which to draw any valid conclusions, but the findings may be of some interest. First of all, let us consider the relationship between smoking and the cancer in the male patient, with particular reference to the primary bronchogenic carcinomas, the first four in the table. Of the 32 patients with epidermoid lesions who, as mentioned, were entirely male, the smoking habits of 12 are not known. Of the remaining 20, there were no nonsmokers. Fifteen out of 20 whose smoking habits were known were heavy smokers, i.e., they smoked more than 20 cigarettes a day. Three were classified as moderate smokers, using from 10 to 20 cigarettes daily, and one smoking less than 10, a light smoker. One of the patients used the pipe exclusively. Almost the same relationship is seen in the undifferentiated group—of the 16 patients whose smoking habits are known, 9 were heavy smokers, 5 were moderate smokers, 1 smoked a pipe, and only 1 was a nonsmoker. In the adenocarcinoma group, there was no relationship between cancer and smoking, as 3 of the 5 studied were nonsmokers.

The smoking habits of the female patients are noted in Table 5 and would appear to bear no relationship to the development of bronchogenic cancer in them. Epidermoid carcinoma, the type most closely linked to tobacco, is not represented here at all in the total of 15 primary cancers. Four were smokers, 4 were nonsmokers, and the smoking habits of 7 were not known.
It is generally accepted that the irritation caused by cigarette smoke has to be exerted over a prolonged period, and this was studied in the case of males with epidermoid carcinoma. Table 6 indicates that of the 19 who were known cigarette smokers, 14 smoked for 30 years or more, and 11 of these were heavy smokers. Though not shown in this Table, it was found that of the 14 males with undifferentiated carcinoma who were known cigarette smokers, all had smoked for more than 10 years, and 9 were heavy smokers for more than 30 years.

As mentioned previously, the results of treatment of cancer of the lung are rather gloomy if one considers the overall picture. Because the only chance for prolonged survival is surgical extirpation of the tumour, it has been our policy to explore the chest in all cases unless there was obvious evidence of extension beyond the lung or the physical condition of the patient contraindicated surgery.

The overall survival of the 100 patients according to the type of cancer present is shown in Table 7. For many years the index of “a cure” of cancer has been the 5-year survival. There were only four patients fulfilling this requirement, three of whom had primary bronchogenic carcinoma. Three additional patients have survived more than 3 years, and they are still alive without evidence of recurrence. For them, the prognosis is quite good.

Details of treatment are shown in Table 8. Forty-nine patients underwent exploration of the chest. In 24, the tumour was found to be inoperable, and nothing could be done either for cure or palliation. In 6, a palliative resection was accomplished, i.e., the main tumour was removed with no prospect of eventual cure because the cancer had extended beyond the lung. In 19, the cancer was confined to the lung and a so-called curative resection was done. Fifty-one patients were not subjected to surgery because the cancer was obviously too extensive to warrant such an undertaking.

Twenty patients were treated by radiation alone, 3 of whom survived for one to two years, and 1 for over 3 years (Table 8). One patient had chemotherapy following a palliative resection and lived for less than 6 months. One patient was given radioactive isotopes after a palliative resection and lived for 19 months. Five had chemotherapy with radiation, and one of these survived over 3 years. Two had chemotherapy alone and did not live 6 months, and the one who received radioactive isotopes only lived 19 months.

Reference to Table 9 reveals that 76 patients died of their malignant disease and 16 are still alive, the longest survival period being 14 years in a patient who had a bronchiolar carcinoma resected. There were six operative deaths in the surgical group, three of which were due to cardiac arrest on the table, evidence of the poor surgical risk many of these individuals present due to their age and cardiovascular status. One patient was killed in an automobile accident 8 years following pneumonectomy for an epidermoid carcinoma; there was no evidence of recurrence of the tumour. One patient died of silicosis, the cancer being an incidental finding at autopsy.

### TABLE VI. Length of Time Smoked — Epidermoid Carcinoma — Males

| Number of Cigarettes Daily | Total | Smoked Smoked Smoked Smoked Smoked |
|---------------------------|-------|-----------------|-----------------|-----------------|-----------------|
|                           |       | Under 5 Years 6-10 Years 11-20 Years 21-30 Years 30 Years |
| Less Than 10             | 1     | 1               | 1               | 1               | 1               |
| 10-20                     | 3     | 1               | 1               | 3               | 8               |
| 21-40                     | 12    | 1               | 1               | 3               | 14              |
| More Than 40             | 3     | 1               | 1               | 3               | 14              |
| All Smokers              | 19    | 1               | 1               | 3               | 14              |

### TABLE VII. Survival Times After Diagnosis Related to Type of Cancer Present

<table>
<thead>
<tr>
<th>Type of Malignancy</th>
<th>Total</th>
<th>Lived Less Than 2 Months</th>
<th>Lived 2-6 Months</th>
<th>Lived 7-12 Months</th>
<th>Lived 1-2 Years</th>
<th>Lived 3-5 Years</th>
<th>Lived Over 5 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermoid</td>
<td>32</td>
<td>6</td>
<td>12</td>
<td>8</td>
<td>4</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Adenocarcinoma</td>
<td>16</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td></td>
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<tr>
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<td>6</td>
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<td>1</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>Undifferentiated</td>
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<td>6</td>
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<td></td>
</tr>
<tr>
<td>All Cases</td>
<td>100</td>
<td>29</td>
<td>24</td>
<td>16</td>
<td>22</td>
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<td>16</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>2</td>
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TABLE VIII. Survival Times After Diagnosis Related to Treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>All Cases</th>
<th>Less Than 2 Months</th>
<th>2-6 Months</th>
<th>7-12 Months</th>
<th>1-2 Years</th>
<th>3-5 Years</th>
<th>Over 5 Years</th>
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<tbody>
<tr>
<td>Resection for Cure</td>
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<td>5</td>
<td>2</td>
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</tr>
<tr>
<td>Open Biopsy + Radiation + Chemotherapy</td>
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<td></td>
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<tr>
<td>Open Biopsy + Radioactive Isotopes</td>
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</tr>
<tr>
<td>Radiation + Chemotherapy</td>
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<tr>
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<td>100</td>
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<td>46</td>
<td>16</td>
<td>22</td>
<td>5</td>
<td>4</td>
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<td>Still Alive</td>
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<td>4</td>
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<td>4</td>
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TABLE IX. Causes of Death

<table>
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<th>Cause of Death</th>
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<td>*Cardiac Arrest on Table</td>
<td>3</td>
</tr>
<tr>
<td>*Pulmonary Edema</td>
<td>2</td>
</tr>
<tr>
<td>*Anaphylactoid Purpura</td>
<td>1</td>
</tr>
<tr>
<td>Silicosis</td>
<td>1</td>
</tr>
<tr>
<td>Accidental Death (Automotive)</td>
<td>1</td>
</tr>
<tr>
<td>Still Alive</td>
<td>16</td>
</tr>
</tbody>
</table>

*Operative Deaths

100

Why is it that the results of the treatment are so poor in cancer of the lung? In common with the situation in regard to most other cancers in the body, a late diagnosis plays a very large part in the poor prognosis. It has been stated that if 1,000 patients with cancer of the lung are studied in any given hospital in this day and age, 500 will be found to have evidence of extension of the tumour beyond the lung, making exploratory surgery futile. The remaining 500 will be eligible to undergo an exploratory thoracotomy. When the chest is opened, it will be found that 250 have extrapulmonary extension, and only palliative resection or biopsy can be done. The remaining 250 will have a tumour sufficiently localized so that it can be removed with some prospect of a cure. Unfortunately, in a great many of these, distant metastases will have occurred already, and in only 60-70 will a 5-year survival be obtained. So, out of the original group of 1,000, 6-7% will be cured of their cancer.

This low survival rate represents a very depressing statistic, but a lot can be done to improve it. First, there is the matter of prevention. Ninety per cent of malignant lung tumours are bronchogenic carcinomas, and 75% of bronchogenic carcinomas are made up of either the epidermoid or undifferentiated types in both of which there is an overwhelming statistical link with prolonged cigarette smoking. Undoubtedly, there are other factors at work in the development of these cancers, but here is one about which something can be done and therefore the greatest effort should be directed not so much to adults who are already in the cancer age but to teenagers who are just beginning to take up smoking. As can well be imagined, it is extremely difficult to convince this group that smoking is a dangerous habit, particularly when they hear that it is going to take 20 to 30 years for some of them to develop cancer of the lung.

Secondly, if one is going to get cancer of the lung, the prospects of a cure are greatly enhanced if it is diagnosed in a very early stage in the relatively long silent period before any symptoms appear. Today, we have two very simple but very effective diagnostic tools — the X-ray of the chest and cytological examination of the sputum. Every adult, particularly a male over the age of 40,
should have a chest X-ray examination at least once a year or, better still, every 6 months although the latter may not be too practical. In some centres, a cytological examination of the sputum is being done yearly in asymptomatic individuals and, although this is not practical on a nationwide basis, it may yet be. Malignant cells can be found in secretions from the lung at a very early stage in many cancers, particularly the epidermoid and the undifferentiated types.

Even when symptoms are present or have been for many years, it is remarkable and discouraging to find that a large number of patients ignore them. In some cases, the medical profession may be at fault. Many cancer patients present as cases of pneumonia and when the abnormal X-ray shadows do not clear promptly they are labelled as "unresolved" pneumonias and watched for many months. During this time their cancer is inexorably progressing. In other cases, an abnormality of the chest X-ray film which cannot be diagnosed readily is observed too long to see what will happen instead of having the patient undergo immediate exploration of the chest. Indeed, there are room and opportunity for improvement in the overall grim picture of lung cancer.

Summary

The subject of cancer of the lung has been reviewed briefly and the experience in the management of 100 patients with this disease at the Nova Scotia Sanatorium has been presented. Seventy-nine of these patients had primary bronchogenic carcinoma, the cell types being epidermoid in 32, undifferentiated in 25, adenocarcinoma in 16 and bronchiolar carcinoma in 6.

The usual preponderance of male compared to female cases was noted in the bronchogenic group, there being 64 men and only 15 women. The 32 epidermoid carcinomas occurred exclusively in the male sex.

The smoking habits of 51 of the more recent cases of bronchogenic carcinoma were studied. There was a remarkable relationship between heavy cigarette smoking and those patients with epidermoid and undifferentiated carcinomas. Only one patient in these groups was a nonsmoker.

Surgical exploration of the chest was indicated in but 49 cases. In only 19 was curative resection possible. In the group explored there were six operative deaths. Of those resected for cure, there are to date three 5-year survivors, one of whom is well 14 years after a resection. However, three others are well without evidence of recurrence more than 3 years following the curative resection.

Efforts toward improving survival rates in lung cancer should be directed primarily to prophylaxis, particularly by trying to convince young individuals that there is an undoubted relationship between prolonged cigarette smoking and the development of lung cancer. When the cancer is actually present, diagnosis in the early silent stage by routine regular chest X-ray examinations and cytological examination of the sputum would make it possible to improve greatly the results of treatment.

References


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Genetics and the Physician

P. L. Delva, M.D.

Kingston, Ont.

PART IV

Classification of Cellular Disorders.

In our last instalment, we attempted to describe the mechanism by which DNA could organize the manufacture of a protein, be it an enzyme, or a polypeptide chain such as insulin, or the different chains that make up a hemoglobin molecule. Figure I indicates schematically how an amino-acid becomes incorporated into a protein. There are many cellular disturbances that may lead to deficient or defective protein production: a classification is attempted in Table I.

Mutation - Fitness.

Any inherent change in the sequence or in the composition of the nucleotide pairs that make up nuclear DNA is a mutation; it can occur spontaneously and is usually harmful. Von Recklinghausen's multiple neurofibromatosis occurs once in 3,000 births. It is inherited as a dominant trait. The fertility (fitness) of these patients is decreased, being approximately 66% of normal; to keep the incidence of the disease constant, a mutation at the locus responsible for the disease occurs once in

TABLE I: ATTEMPTED CLASSIFICATION OF CELLULAR DISORDERS

A. NUCLEAR:

(1) Inherited: parents are genotypically abnormal:
   (a) at the chromosomal level parents have a chromosomal anomaly:
      (i) non-disjunction
      (ii) translocation
      (iii) deletion (not yet reported)
   (b) at the gene level parents have an absent or faulty gene, the effect of which may be
      (i) hidden: the fault is recessive and only one parent carries it; it is estimated that everyone carries on average 6 or 7 bad genes in this way.
      (ii) obvious: if the faulty gene is a dominant or a codominant one, or if both parents carry the same bad recessive gene.

   (2) Environmental: normal parents:
      (a) at the chromosomal level
         (i) non-disjunction
         (ii) translocation
         (iii) deletion
      (b) at the gene level
         (i) mutation (spontaneous or induced)
         (ii) neoplasms

B. CYTOPLASMIC:

(1) Inherited: not known to occur in man, but definitely occurs in lower organisms.

(2) Environmental:

   (i) nutritional deficiencies
      minerals
      vitamins
      essential amino-acids
   (ii) cytoplasmic poisons
      chemical
      physical
      inflammatory
   (iii) old age

C. MIXED: probably most common, but difficult to define.

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conversion of excessive amounts of phenylalanine to tyrosine, is either absent or present in a very defective form and not detectable. The main features of the disease (mental deficiency, seizures, decreased pigmentation) can not be explained by a deficiency of tyrosine, since this common aminoacid is present in more than adequate amounts in the diet. Instead one must invoke secondary effects following accumulation of large amounts of phenylalanine in the body: this theory is almost certainly correct as affected infants improve on a low phenylalanine diet: their pigmentation increases, their mental status improves.

10,000 births. This is possibly the most commonly occurring spontaneous mutation at a given locus in man. Mutations can also be induced by radiation or by chemical means.

**Enzyme Production Defect - Phenylketonuria.**

The effects of a block in the production of an enzyme can be primary or secondary (cf. figure II). The primary effect is due entirely to absence of the end-product. The secondary effect is related to the accumulation of metabolites following absence of the enzyme. Phenylketonuria is a genetic disease inherited in a recessive fashion in which the enzyme phenylalanine hydroxylase—found normally in the liver and responsible for the

1 of 20 amino-acids (essential or synthesised)

Soluble transfer RNA - amino-acid complex

Ribosomal transfer RNA - amino-acid complex

Transfer or Soluble RNA (specific to each amino-acid)

DNA w/ RNA template

Nucleus

Cytoplasm

Polypeptide chain (enzyme or other protein)

**Figure I: Intracellular Protein Synthesis.**

Other Defects in Protein Synthesis - Sickle-cell Disease - Heterozygote Advantage.

The four polypeptide chains that make up the normal hemoglobin molecule are of two types, referred to as α and β chains. In sickle-cell disease, the sixth amino-acid (glutamic acid) of the 141 that make up the β-polypeptide chain is replaced by valine. In the homozygous form, affected persons suffer from severe anemia due to increased susceptibility of red cells to low oxygen tension, and seldom survive. In the heterozygous form, there are no abnormal clinical findings, but such individuals can be detected by exposing their red cells to low oxygen tension in vivo, when sickling occurs: we can thus detect normal carriers in the laboratory. The incidence of sickle-cell disease is high in areas of the world where malaria is endemic: it is now realized that carriers of the sickle-cell trait show an increased resistance to malignant malaria. This concept that a carrier of a really bad gene is protected in some way by this bad gene is known as heterozygote advantage.

Mutation and heterozygote advantage are largely responsible for evolution, and for maintaining the gene pool in a state of balanced polymorphism. It would be interesting to know what will happen in future generations to carriers of the sickle-cell trait: with the eradication of malaria, one would expect their incidence to drop.

**Figure II: enzyme block.**

**Substrate** — enzyme block.

accumulates

excreted

| enzyme block |

changed to one or more other products

| Product |

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Which tablet is film coated?*

You probably can't see the difference... But your patient will know! New film-coated P.G.A. tablets are tasteless and easily swallowed.

P.G.A. TABLETS
(Penicillin G Ammonium B.D.H.)

The new micro-thin film coating on P.G.A. 0.25 and 0.5 tablets does not alter disintegration time, rapid absorption or the effective therapeutic tissue levels which P.G.A. reliably provides at no extra cost to your patient.

For Therapeutic Security with Economy
Prescribe
"P.G.A.—A gram a day"
P.G.A. 0.25 Gm. (250 mg.) P.G.A. 0.5 Gm. (500 mg.)
3-4 tablets daily 2 tablets daily

BCH BRITISH DRUG HOUSES TORONTO, CANADA

*It's the tablet on the right.
On October 28, 1965, the medical profession of Nova Scotia lost a noble member in the death of A. B. Campbell of Halifax, at the age of seventy-two.

"A.B." as he was known to many of us was a big man. He was large in stature, he was tall and he was broad. He towered over most of us in body, and also in spirit. Medicine was his love and he brought to its practice a transcendent idealism. He was ethical beyond reproach but his ethics sprang from a fair and generous nature rather than from a set of rules. It was a source of joy to him and humble gratitude that during the twenty-four years of his country practice he had never refused a call in sunshine or in storm to the influential and affluent or to the humble and poor. That they were in trouble and needed him called for his total effort.

Lofty in ways that count, he was also broad. Above his broad shoulders there was a broad mind. This writer knew him for many years and saw him consider and deal with problems of the sick and injured as well as those of his professional brethren. For him each question had two sides and he weighed both with care and fairness. He could detect sophistry and insincerity unerringly, as well as honesty. His judgments were made on what he considered to be right regardless of consequences tempered, however, by great sympathy and understanding.

As a person he had his own beliefs and his own standards. He would readily agree that others might be equally good. He forced his beliefs on no man and expected the same in return, but when his opinion was sought he gave it freely and many found it good.

The details of his life are known to all but the present generation:

He was born in Westville, Pictou County, Nova Scotia, the son of Alexander and Janet (Roy) Campbell. His father was an engineer at the Drummond Colliery. When he was about eight years old the family moved to Mabou Mines, Inverness County, and later to the town of Inverness. There he grew up. As he often said, "After two or three summers of running the beaches, I started to work in the coal mine during the holidays." He went to the local schools and then to Pictou Academy from which he matriculated into Dalhousie in 1911, his mind set on the study of medicine.

Almost from the first his large frame and great strength marked him for the football team, Rugby of course, and he was centre lock from the first day he played to the last.

In 1911 Dalhousie lengthened its medical course to five years, and World War I intervened before "A.B." finished. He joined up, went overseas, was in France and returned to resume his studies and graduate in 1921.

The next year he spent on the Staff of the Nova Scotia Sanitorium at Kentville, but seeing an opportunity to begin general practice in Bear River, Digby County, he seized it and remained there for twenty-four years. To us it may seem commonplace but it is worthy of remark that all obstetrics and a great deal of surgery was then done in the home. The country doctor had to be resourceful to a degree and "A.B." was not found wanting. The years of World War II were extremely busy ones for him. He welcomed the opportunity to come to Halifax in 1946 as Chief Medical Officer of the Workmen's Compensation Board, a position demanding all his skill and experience but capable of regulation in terms of daily effort.

The success of a general practitioner in the country largely depends upon his wife and in this "A.B." was singularly blessed in Mabel ("Daisy") Morrison Campbell. She answered his calls, looked after the office and the household, kept his books, sent out bills, brought up Jim, their son, and in spare moments wrote poetry of genuine merit which was published anonymously.

Following retirement in 1958 "A.B." was busier than ever. Many activities in which he had only been able to take a casual interest, now occupied a great deal of his time. The Canadian Club, the North British Society, the Dalhousie Alumni Association, Dalhousie's Board of Governors, Pine Hill Divinity Hall, were a few which come to mind. He was an elder and an energetic member of Fort Massey Church. His college days' avocation as a resident at the Blind School made him an active member of the Canadian National Institute for the Blind. To keep his medical "hand in" he was consultant to the Provincial Department of Welfare.

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Appreciation

Dr. A. B. Campbell
BOOK REVIEW

Advice to Authors - American Medical Association 1954, pages 24.


These two slim volumes were found to be a veritable gold mine of advice and help to one overworked Editor. As practical work books and help to preparing material for publication in any scientific Journal. They can be highly recommended. Who, for instance, is quite certain that quotation marks should go outside commas and periods, but inside colons and semi-colons or that numbers from one to ten should be spelled out but from 11 up are better in figures?

A modest expenditure of 50 cents for Advice to Authors will bring much help in this and in other matters such as preparation of illustrations, tables, etc.

J.F.F.

Phenylketonuria
Screening Tests for Aminoacidopathies in Newborn Infants

C. P. Handforth, M.B.1

Truro, N. S.

The Guthrie test for phenylketonemia in newborn infants has now reached the stage at which it can be performed in any regional laboratory in Nova Scotia. Some laboratories are not performing this test at present, and this is partly because it has not been requested.

The Guthrie test is a microbiological assay of the quantity of phenylalanine in infants blood. It has replaced the previous test which depended on the reaction between ferric chloride and abnormal amino acids in the urine. The urine was difficult to collect, and the ferric chloride test was insensitive so that false negative results were obtained. By contrast, the Guthrie test is too sensitive so there may be a few false positive results. For this reason, positive results with the Guthrie test indicate the need for immediate further investigation.

At present it is suggested that every newborn infant in Nova Scotia should be tested for phenylketonemia by the Guthrie test. As most infants are born in hospital, this test is most conveniently performed on the day before the infant leaves for home. In this way it is theoretically possible to prevent the tragic and costly mental and physical manifestations of this biochemical disorder.

For the future, it is apparent that better tests will be available. These depend on chromatographic techniques, and will detect multiple abnormalities of amino acid metabolism. An account of the use of such a test was published in a recent issue of the Canadian Medical Association Journal (June 26, 1965, Vol. 92, page 1331).

1Chairman Section for Pathology.
Antibiotic Prophylaxis In Acute Viral Respiratory Diseases

Carefully controlled trials have not shown that antibiotics are effective in preventing bacterial complications in the common cold. Any unnecessary use of antibiotics should be avoided.

The common cold is everyone's disease and has caused a profusion of all kinds of nostrums. The great losses from morbidity and great cost of remedies, home and prescribed, necessitate critical evaluation of optimum therapy. Since recovery almost always occurs, evaluation of therapy is difficult.

Prophylactic antibiotics have often been recommended and used in these diseases to prevent bacterial complications. The word prophylaxis literally means prevention of or protection from disease. Prophylactic drugs may be given to prevent disease in a normal person or to prevent complications in a person who is ill. Antibiotic prophylaxis cannot be evaluated when bacterial complications already are present.

Antibiotic prophylaxis of acute respiratory disease is generally based on the hypothesis that viral infections lower the resistance of the host and allow the normal bacterial flora to cause infections.

Experience has shown that the risk of superinfection or the acquisition of a new organism is high with broad-spectrum antibiotics and not insignificant with penicillin. The concept that antibiotic prophylaxis will regularly suppress the normal flora has not been substantiated.

Since the effect of placebo on symptoms in acute respiratory diseases has been established by controlled studies, it is essential that therapy trials be double blind. Results with the drug under study should be compared with those of a placebo or with symptomatic treatment, and neither the patient nor the physician should know which patient receives which treatment.

Since even experienced clinicians may miss streptococcal disease and since streptococcal infections will respond to antibiotics, it is essential in these trials to exclude streptococcal disease.

Trials Reviewed

In a review of a number of controlled trials among children, adult volunteers, and military personnel, both in the United States and Great Britain, it was found that the use of antibiotics was not effective in preventing complications of measles, influenza, or the common cold when streptococcal disease was excluded.

In fact, neither continuous nor intermittent antibiotic prophylaxis has been shown to alter the clinical course or reduce the complication rate of these diseases.

It must be recognized that the type of population studied may have an effect on the outcome of the trial. For example, the results of trials on military personnel may have only limited application. Military populations are composed of essentially healthy young adults. Many military bases have no place other than the hospital to care for mild illnesses. Consequently, military hospital hospital patients may represent milder disease than that seen at a civilian hospital.

Civilian study populations may differ also. Only the more severe cases may be admitted to a hospital. Furthermore, many civilian hospital patients may have rheumatic heart disease, emphysema, bronchietasis, or some other chronic disease.

Some British groups have reported beneficial results from antibiotic prophylaxis in groups of miners with pneumoconiosis, children with recurrent infections, and others.

These findings cannot be reconciled with those of well-controlled trials in which antibiotics were not found effective. Possibly a factor in the British trials is the prevalence of chronic bronchitis, in which prophylactic antibiotics have proved effective.

Defining Complications

Even in the face of certain reservations about some of these trials, it is apparent that prophylactic antibiotics will not alter the primary course of acute respiratory disease and will not prevent bacterial complications in healthy persons. Additional trials are needed in special groups such as children with congenital heart disease, pregnant women, and patients with chronic pulmonary diseases, since prophylactic antibiotics have not been thoroughly evaluated in these conditions.

A problem central to all these trials is the definition of a bacterial complication. The ap-
appearance of a new sign or symptom does not necessarily represent a complication and is not always an indication for antibiotics.

Pneumonia may be taken as an example of the problems of defining a complication. Influenza viruses can cause pulmonary infiltrates. Pneumococci are often cultured from sputum or pharyngeal swabs of normal persons. Thus, a sputum culture positive for pneumococci from a patient with influenza and a pulmonary infiltrate is not necessarily proof of a bacterial pneumonia. Perhaps the problem of proving bacterial pneumonia in patients with viral respiratory disease could be approached with frequent, quantitative bacterial counts of the sputum or by lung puncture.

The appearance of new signs or symptoms is not adequate proof of a bacterial complication of acute respiratory disease but is an indication for further examinations or tests.

Sometimes it is said that antibiotics may not help the patient but at least they will not hurt him. The use of antibiotics without reasonable indication is no more rational than the administration of digitalis to a patient without heart disease or morphine to a patient without pain. Antibiotics often cause harm. They are potent agents and should not be given frivolously.

As a guide to therapy, the following statements are now well substantiated:

1. The great majority of acute respiratory illnesses are not bacterial.
2. Antibiotics have no effect on the primary course of viral respiratory diseases and thus have no place in their primary treatment.
3. Prophylactic antibiotics have not been shown to prevent bacterial complications of acute respiratory disease and are not generally indicated.

The patient with measles or influenza with a pulmonary infiltrate is not a problem of prophylaxis but of differential diagnosis. Patients with a cough but without pulmonary infiltrate can usually be managed without antibiotics. The more seriously ill patients require careful evaluation and appropriate cultures. There is little disagreement about the use of antibiotics in the severely ill patient when bacterial pneumonia cannot be excluded.

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DOSAGE: One to four tablets every four hours.

Each “Polymer 37”-coated tablet contains 5 gr. of acetylsalicylic acid.

Bottles of 100 and 500 tablets.

*Patented 1959
**Personal Interest Notes**

A Doctor's Schedule (From the Atlanta, Ga. Journal).

"Nostalgia enhances memory of the country doctor bravely risking the dark and rutted road on a midnight call. Today's physician doesn't hitch up the buggy in the driving rain in the dead of night. What does he do?"

According to the report of a major pharmaceutical firm to its stockholders, he does as follows:

The average physician in the U.S. works 60 to 70 hours a week, sees 20 to 30 patients a day, takes 14 telephone calls from patients daily, and makes hospital rounds and house calls. He treats without charge 400 needy patients a year, donates 100 hours to civic affairs annually and devotes 200 hours to professional meetings and research.

That's enough to make any doctor today a little envious of those who hitched up the buggy in a driving rain in the dead of night." What do you say in Nova Scotia?

**Cape Breton Medical Society**

A total of 64 persons attended the Well Baby Clinics held at Sydney Mines and North Sydney recently under the auspices of the North Sydney Rotary Club. The two sessions were conducted by Dr. Thomas Acker of Halifax. These are a continuation of the clinics which the Rotary Club and Dr. Acker have held for many years.

Dr. and Mrs. A. L. Cunningham and son Peter of New Germany have taken up residence at Sydney Forks (Last month's Bulletin announced the association of Dr. Cunningham with the Workmen's Compensation Board.)

Residents of Isle Madame paid tribute, recently, to 46 years of faithful service by a doctor and his wife at a ceremonial dinner held at Arichat.

Dr. C. F. Herbin was toastmaster and Dr. Thomas Gorman, president of the Nova Scotia Medical Society of Nova Scotia was the special speaker.

The dinner was held in the Royal Canadian Legion Hall, Arichat, where representatives from every corner of the "isle" were present to honour Dr. and Mrs. G. R. Deveau. Dr. Deveau is retiring, due to ill health after nearly fifty years of practice in the Isle Madame area. He was also a member of the Legislative Assembly from 1933 to 1957. Tribute was paid to him by many. A gift was presented from the residents of Isle Madame, and a bouquet of carnations to Mrs. Deveau. They are now resident in a house trailer near the home of their son-in-law and daughter, Mr. and Mrs. David Carlin in Halifax.

Pensioners in the Glace Bay area will continue to receive Medical care from local physicians after November 1st on the same basis as now prevails. (The pensioners received medical care on the payment of a stated amount periodically.)

Dr. Charles Brennan is reported as having delivered "a most challenging, impressive and stimulating address" when he spoke to a capacity audience at an open-to-the-public meeting at St. Joseph's church hall, sponsored by the local council of the Knights of Columbus on the question of early marriage and proper home training and the rising divorce rate.

For the first time in its near-14 year history, the local 562 Cabot Squadron bestowed an honorary office at a special ceremony recently, when Mayor J. S. Munro, M.D. was made an Honorary Flight Lieutenant of the Squadron in recognition of his long time interest and help to the Air Cadet Movement in North Sydney.

Dr. D. S. Nathanson, well known physician and surgeon has decided definitely to offer as a candidate for Mayor in the December civic elections. He is a graduate of Mount Allison and Dalhousie, and has practised in New Waterford for 11 years, having been also the first secretary of the New Waterford Consolidated Hospital Board, and active in many community groups.

At the Investiture of the Venerable Order of The Hospital of St. John of Jerusalem held on Nov. 10 at Government House, Halifax, Dr. Donald Stirling Robb was awarded Priory vote of thanks.

**Colchester-East Hants**

The $3 Million Colchester Hospital of 200 beds was officially opened on October 13 with Premier Stanfield cutting the ribbon and the Minister of Health, the Hon. R. A. Donahoe as guest speaker. When the Hospital Commission was formed in 1959, there were 3297 hospital beds in the province. There are now 4561, and the medical facilities cost $33.51 per person in the province which is almost 6 dollars lower than the national average. Dr. L. R. Hirtle, medical officer with the Department of Health and Welfare, Halifax, and Dr. David Moore, chairman of the Medical Staff of the hospital also spoke.

Dr. J. C. Vibert, Truro, has been honoured with appointment as Fellow of the American College
of Surgeons at their recent convocation at Atlantic City, New Jersey.

The East Hants branch of the Canadian Cancer Society met recently at Hants North Rural High School for the annual meeting. Dr. Margaret Gosse, Halifax, past president of the Nova Scotia Division of the Canadian Cancer Society spoke on the basic need for research and how it was carried on.

CUMBERLAND

The Board of Directors of the Cumberland Mental Health Centre met recently in Amherst. Dr. Edmond Ryan is the executive director of the centre.

Dr. Kenneth Gass spoke to the Board on the new approach to mental health care in the province and the effect on the operation of the Cumberland County Hospital in Pugwash.

HALIFAX

Dr. W. A. Cochrane, physician-in-chief at the Children's Hospital, reported on November 8th on the recent Inter-American Conference on Mental Retardation in Puerto Rico to the Rockingham Branch of the Canadian Association for Retarded Children. He was a Canadian delegate to the conference.

Dr. C. E. van Rooyen, professor and head of the Department of Bacteriology at Dalhousie University has been appointed consultant in Bacteriology to the Canadian Forces Medical Council of the Department of National Defence.

The team of Orthopaedic Surgeons Physicians and an Easter Seals field worker finished on November 10th their fall tour to 16 Nova Scotia centres where mobile Diagnostic clinics are held twice yearly sponsored by the N. S. Society for the Care of Crippled Children aided by a Department of Health grant. This year's spring clinics discovered 286 new cases of crippled children throughout the province, most of them in the three to five age group.

Personnel in the clinics include: Mrs. Sigrid Day, associate executive director of the society, Dr. J. C. Acker, Dr. A. M. Sinclair and Dr. Antoni Tria, Orthopaedic surgeons, and Dr. N. E. Coward and Dr. Ronald Ritchie paediatricians. Clinics were held in Neil's Harbour, Baddeck, St. Peter's, Port Hawkesbury, Guysborough, New Glasgow, Pictou, Springhill, Truro, Digby, Shelburne, Liverpool, Bridgewater, Lunenburg, Windsor and New Waterford.

LUNENBURG-QUEENS

The new facilities, recently completed at the Fishermen's Memorial Hospital, Lunenburg were

The doctor spent a comfortable night

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

Each teaspoonful (5 ml.) contains 5.5 mg. ethylmorphine HCl; 13.3 mg. terpin hydrate; 5.0 mg. guaifenesin; 10.2 mg. calcium glycerophosphate; white pine compound base. Dosage: One teaspoonful every three hours, and one at bedtime.

*TERPO-DIONIN
cuts down coughing night calls

THE NOVA SCOTIA MEDICAL BULLETIN 307 DECEMBER, 1965
formally opened on October 24, 1965, by Dr. G. Graham Simms, Executive Director, Nova Scotia Hospital Commission as guest speaker. Dr. R. G. A. Wood, Mayor of Lunenburg, and chairman of the hospital medical staff welcomed those present and paid high tribute to the Ladies’ Auxiliary of the Hospital.

Dr. George Daglish, formerly general practitioner in Mahone Bay and latterly also on the staff of the Anatomy Department of Dalhousie Medical School has been appointed to the University of Manitoba in the Department of Anatomy.

The Mahone District Unit of the Canadian Cancer Society at its annual meeting held at Martin’s River recently was addressed by Dr. S. C. Robinson, Halifax, on “Early Detection of Cancer of the Uterus. Nearly 200 people were present.

VALLEY

The Soldiers Memorial Hospital, Middleton has recently received word from the Canadian Council of Hospital Accreditation that it has been awarded accreditation status.

WESTERN COUNTIES

The Yarmouth Rotary Club’s Crippled Children’s Clinic was held in the Yarmouth Regional Hospital with Dr. Thomas Ack- er, orthopaedic specialist from Halifax in charge for the 78th time. Since 1926 when the Rotar-y Club sponsored the first clinic, Dr. Acker has been in attendance. The clinic lasted four days with 79 children in attendance including 28 new ones.

A series of postgraduate lectures under the auspices of the Dalhousie Postgraduate Committee began in Yarmouth on October 7th. Dr. J. H. Charman, of the staff of the Victoria General Hospital was the special speaker on Inflammatory Disease of the Gastrointestinal tract. Speakers following in the series, held weekly, were Dr. A. J. MacLeod, Dr. M. G. Tompkins, Dr. Leon Cudkowicz, and Dr. C. E. Kinley.

CONGRATULATIONS

The Halifax Chronicle of November 8 has an appreciation of Dr. R. M. Saunders who has been practising in Lunenburg for 53 years. He, a doctor’s son was born in LaHave and went to school in Bridgewater. After high school he went to Normal College in Truro and later taught in Annapolis Co. After graduating from Dalhousie Medical School, he first practised in Bridgewater for a year (1912) but has been in Lunenburg ever since. He was coroner for over 30 years, was member and chairman of the school commission and until recently was jail physician for the county. Curling is his favorite relaxation. He is still busy with office consultations, drives his car and answers calls in the district. He has a son, Reginald, himself an M.D. in Black’s Harbour, N. B. So into the third generation is being carried on the tradition of faithful service to a community.

BIRTHS

To Dr. and Mrs. H. E. (Pete) Hawk, (née Judith McClearn), a son, Gregor McClearn, at the Grace Maternity Hospital, Halifax, on October 11, 1965.

To Dr. and Mrs. John Mc- Kiggan, (née Carol MacLean), a son, at the Halifax Infirmary, Halifax, on October 26, 1965.

To Dr. and Mrs. William Nicholas, (née Sheila Bonnell), a daughter, at the Halifax Infirmary, Halifax, on November 9, 1965.

To Dr. and Mrs. John Tibbles a son, Russell John, at the Grace Maternity Hospital, Halifax, on October 17, 1965.

OBITUARIES

Dr. Alexander Brown Campbell died in hospital in Halifax on October 28, 1965, at the age of 72 after an illness of a few months. An appreciation on page 000 by his long-time friend, Dr. Scammell expresses the regret of his confrères and their sympathy with his family.

The Medical Society of Nova Scotia
extends
sincere wishes for a
Merry Christmas
and a
Happy and Prosperous New Year

THE NOVA SCOTIA MEDICAL BULLETIN 308 DECEMBER, 1965
FORTY YEARS AGO

From the Nova Scotia Medical Bulletin, December, 1925

St. Martha’s Hospital, Antigonish, during the year ending Sept. 30th, 1925, admitted 1425 patients. 1220 were discharged as cured and 146 improved. Eliminating deaths from chronic diseases, and those occurring within 24 hours of admission, the death rate was one and one fourteenth percent. 760 surgical operations were performed with a death rate of one and onehalf percent. Average stay of patients in hospital was 15 days, giving a total of 22,223 hospital days’ treatment.

As soon as there is enough snow for skiing, many summer cottages become winter ski lodges. Since many of these buildings must be heated by coal or wood burning stoves, it should be remembered that there is danger from carbon monoxide fumes. Whatever the fuel, it should be allowed to burn through before the stove is checked. There should also be adequate ventilation until the top of the fuel is quite red and the gases burned through.

1000 WORD SERIES - Continued from page 290

lump nodules on X-ray is the same as that of lumps in the breast; they require excisional biopsy.

Most hospitals have, or should have cancer committees; these committees should: (1) determine the local situation as regards lung cancer, (2) keep the physicians of the area in touch with services available, including X-ray and cytology facilities, (3) inform the public of the early symptoms of cancer, if necessary using local television, press and radio, (4) instruct school populations of the dangers of smoking. The Provincial Cancer Society, 1485 South Park Street, Halifax, has pamphlets and films available to aid in this work.

There is a need for more carefully organized screening of susceptible groups in the population. Such screening is usually done by radiography, but increasing use will probably be made of cytology. The largest susceptible group is the heavy smoking adult population.

This has been a brief, general review of the lung cancer problem in Nova Scotia as seen at the Nova Scotia Tumor Clinic. The problem is growing each year, and the results of handling it can only be improved by the combined efforts of every physician in the Province.

References

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