Primary Carcinoma of the Lung*

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Bronchiogenic carcinoma today is one of the most important cancer problems. From being a rare condition 50 years ago it has become so common in recent years that now there is evidence indicating that, at least in males, it is the most common visceral cancer. It has displaced cancer of the stomach to second place in several large hospitals where statistical studies have been made. For example, Ochsner and DeBakey¹ at the Charity Hospital of New Orleans, Wheeler² at the St. Louis City Hospital, and recently Avery³ at the Hines Veterans' Hospital at Hines, Illinois, have all found that primary carcinoma of the lung is more frequent in those institutions than carcinoma of the stomach.

There has been some discussion as to whether such findings indicate an actual increase or whether rather they are the result of better diagnosis and of the general greater longevity of people nowadays. In my own opinion, however, there can be little doubt that there has been an actual increase in primary carcinoma of the lung. After all, there were excellent pathologists 50 years ago who could hardly have failed to find the primary lesion in the lung in most instances.

If one admits that an actual increase has occurred, then one's curiosity becomes aroused about a possible explanation. The increase seems to be not limited to only this country but to involve the civilized world. Could there be some exogenous carcinogenic factor associated with our culture which might be responsible for this amazing change in incidence of this disease during the last half century?

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When we pursue this line of thought we are at once confronted with the realization that, although in many respects our mode of living has been changed, there are two factors which have been added which may have a direct bearing on our problem. One of these is that the period of the last 50 years represents the era of the automobile and the extensive use of petroleum and its products. It is tempting to assign importance to this consideration, but preliminary studies which have been made seem to show that although there may be a somewhat higher percentage of lung cancer in garage men and workers in the oil industry the incidence is not strikingly different from that in the general population. The second factor is cigarette smoking. Figures from the Internal Revenue Department of the United States Government show an enormous increase in the production and sale of cigarettes during the last 50 years (Ochsner and DeBakey).

Several investigators have attempted to discover what relationship, if any, exists between the great increase in cigarette smoking and the remarkable increase in bronchiogenic carcinoma. Most of this work, however, has been based on the assumption that the use of tobacco is synonymous with cigarette smoking, an assumption which at least is open to question. Tylecote, in 1927, was one of many who suggested that smoking is an important etiologic factor. Hoffman in 1931, thought there was strong statistical evidence that tobacco is an important factor in the increase of lung cancer. Roffo in 1937, was able to produce experimental cancer in rabbits' ears by the application of tobacco tars. In 1941 Ochsner and DeBakey called attention to the similarity of the curve of increased sales of cigarettes in this country to the greater prevalence of primary cancer of the lung in the human, and they emphasized the possible etiological relationship of cigarette smoking to the condition. Later, however, they seemed to be more doubtful of this relationship. At the present time Wynder and I, with the cooperation of many other surgical clinics, are making a statistical study of this relationship.

It is too early to give even a preliminary report of this study, but it can be stated that in 500 cases of proved bronchiogenic carcinoma it has been rare to encounter a man with a squamous (epidermoid) bronchiogenic carcinoma who had not been an excessive cigarette smoker for years, or at least who had not formerly smoked cigarettes excessively. By “excessive” smoking is meant more than one pack a day. It should be emphasized that it is not necessary that at the time he should be an excessive smoker, because from the abundant work on the experimental development of cancer in animals it is well known that there is a considerable time lag between the application of the carcinogenic
agent and the development of the cancer, which in the human apparently may be a matter of five years or more. The use of tobacco in other forms, as in pipes and cigars, appears not to bear the same important relationship. It would seem, therefore, that if smoking is an etiological factor, it is either the greater inhalation of cigarette smoke or something in the composition of cigarettes which contains the carcinogenic agent. Various possibilities suggest themselves, perhaps something used in the curing of the tobacco, insecticides employed during its growth, or maybe even something in the paper.

The remarkable etiological relationship between cigarettes and bronchiogenic carcinoma which seems to be developing applies chiefly, if not entirely, to squamous, or epidermoid, carcinoma. This is the carcinoma which is by far the most common lung tumor, and it is the one which has shown the striking increase. It is overwhelmingly a male disorder (in our last 75 cases 18 males to one female). It arises usually in a major bronchus and it represents a transformation of adult epithelium into cancer tissue. In our experience when a woman has such a tumor almost invariably she is or has been a heavy cigarette smoker. It is a common belief that, at least in this country, women are as much or even more addicted to cigarette smoking than men. However, a statistical study of this question, not yet published, indicates that only about 40 per cent of the women of cancer age smoke at all and of these only a small percentage smoke to excess. The younger women who have not yet reached the cancer age are more likely to be heavy smokers.

By contrast the adenocarcinoma is a tumor which occurs about equally often in the two sexes, but slightly more in the female. It is much less common than the squamous or epidermoid type, and it seems to be influenced slightly, if at all, by cigarette smoking. There is considerable evidence that in at least many cases this tumor begins as a so-called bronchial adenoma. It seems to represent a transformation of embryonic epithelium into cancer tissue, rather than a change of adult epithelium into cancer cells as in the case of the epidermoid type. It is therefore to be regarded as an entirely different condition from the ordinary squamous cell bronchiogenic carcinoma.

Many histological varieties of bronchiogenic carcinoma have been created by the pathologists. Thus some are designated as undifferentiated, as oat cell or round cell, others as alveolar carcinomas. There is some evidence, however, which justifies a conception that these types are only variants of the two main kinds of bronchiogenic carcinoma, namely the squamous or epidermoid and the adenocarcinoma. It will be impossible to discuss
here the evidence for this conception, but the interested reader may find a further discussion of the idea in other publications of ours.9-11

The two principal types of primary carcinoma of the lung which I have been discussing are bronchiogenic in the sense that they arise within or close to a bronchus which is usually a major one. Recently there has been discovered another type which apparently begins in the parenchyma of the lung and perhaps actually in the alveolar epithelium. When first found this tumor is generally confined to one lobe, although multiple nodules or foci of cancer are present throughout the lobe. From the gross appearance it may be difficult to be certain whether the lesion is malignant or inflammatory in nature. In most instances, even if the diseased lobe is removed, the condition becomes evident in the remaining lobes of the same lung after months or years and even in the other lung. In the microscopic appearance and in some of the clinical features (especially the presence and the discharge of a large amount of mucus) there is a striking resemblance to the disease of sheep known as "jagziekte."12 This disease is known to occur sometimes in epidemic forms in sheep, and it is supposed to be due to a virus which as yet has not been found. This disease has also been described sometimes under the name of "multiple adenomatosis."13 Case reports of this most recently discovered type of primary cancer of the lung will be found referred to in a recent article of ours.14 In addition, Stephens and Shipman15 of San Francisco reported a case at the last meeting of the American Association for Thoracic Surgery. More extensive recent articles are those of Swan16 and of Laipply and Fisher.17

Clinical Features

Because of the frequency of primary carcinoma of the lung it is highly important that every doctor should be familiar with its principal features. There is nothing pathognomonic in the clinical history. However, in a typical case there is cough with blood streaked sputum and a shadow in the x-ray which is generally seen as an uncircumscribed abnormal density in the region of the hilus. These features are so commonly found in most cases that it is imperative to proceed with the necessary additional examinations. In fact, the burden of proof is on anyone who doubts the presence of a bronchiogenic carcinoma under such circumstances. Of course, there are many variations from this more or less typical clinical picture. For example, if the tumor arises in a small bronchus there may be but little cough and sputum with perhaps no expectoration of blood. In such a case the x-ray shadow is often spherical and rather sharply circumscribed at a
distance from the hilus. In other cases the tumor arises in the apex of a lung and the first suspicion of its presence may come from the pain experienced by the patient because of the invasion of the brachial plexus or intercostal nerves. In still other cases the complicating infection of the tumor with its attendant fever may be the first symptom of illness noted by the patient; or again, more rarely, the presenting symptom may be from a metastasis in the brain or in a bone.

Whenever suspicious evidence is present it becomes an urgent and compelling matter to pursue the necessary special examinations. Of these there are two which stand out as particularly important; bronchoscopy and examination of the sputum for cancer cells, preferably by the Papanicolaou method.18

Unfortunately, many tumors arise in bronchi too small or too unfavorably situated to be seen with the bronchoscope. In our own experience only about 60 per cent of them can be visualized adequately enough to obtain tissue for a biopsy. The additional examination of the bronchial washings and sputum will give a higher percentage of positive diagnosis, although actually, as in the use of the bronchoscope, in our experience we obtain only about 65 per cent of positive results. The advantage, however, of supplementing a negative bronchoscopic examination with sputum examination is that in some cases a positive diagnosis can be made in that way. Similarly sometimes a positive bronchoscopic diagnosis can be made although the sputum examinations have been negative. It must be realized, however, that the search for cancer cells in the sputum must be made by an expert. There is a very great danger of reports of both false positives and false negatives when the examinations are made by one who is not thoroughly familiar with the cytology of the secretions which he is examining. The use of the bronchoscope should not be neglected even if a positive diagnosis has been made by sputum examination. Very valuable information can often be obtained by the use of this instrument which a study of the sputum alone will not yield. For example, there are the questions of the proximity of the growth to the trachea, the fixation of the carina, etc.

After using all the standard methods of examination there will remain about 30 or 35 per cent of cases in which, in spite of a suspicious clinical history and suggestive x-ray films, it has been impossible to establish a positive diagnosis. What shall be the disposition of those cases? Unquestionably, in my opinion, the best thing to do under such circumstances is to perform an exploratory operation. In most instances at operation the diagnosis can be readily established by direct inspection and palpation. If there is still doubt it is nearly always possible to remove some tissue
for an immediate frozen section. Experience shows that when the clinical history and x-ray examination are suspicious the exploratory operation will nearly always reveal the presence of a carcinoma even when no positive evidence has been obtained by bronchoscopy and cytological examination of the sputum.

Until 1933 the question of establishing the diagnosis of bronchiogenic carcinoma was largely a matter of only academic interest because there was no successful treatment. In April of that year, however, the writer was fortunate in having presented to him a patient with a squamous carcinoma of the left upper lobe bronchus which was not too far advanced for radical treatment. At operation the left lung was completely removed in one stage, and the patient made a completely satisfactory recovery. He has had no recurrence. He is a physician who is carrying on an active practice more than 16 years after his operation. This happened to be not only the first successful total pneumonectomy for cancer but also the first successful one-stage pneumonectomy performed for any reason.

The operation of one-stage total pneumonectomy has now become by common consent the preferred treatment for primary carcinoma of the lung. By this operation it is easier to remove possibly invaded lymph glands; and, by analogy with well-established surgical principles in treating cancer of other organs, the disease is more likely to be eradicated by the removal of the whole organ than by the removal of only a part, as by a lobectomy. The high operative mortality in the early days of nearly 50 per cent has been reduced to one now of 10 per cent or less. In 139 consecutive operations of total pneumonectomy for carcinoma in a period comprising the last four years and seven months from January 1, 1945, to August 1, 1949, at the Barnes Hospital we have had 12 hospital deaths, an operative mortality therefore of 8.4 per cent. Since the first successful one-stage total pneumonectomy on April 5, 1933, we have performed the operation on 367 patients. Of more importance than the operative mortality in cancer of the lung is the question of five year freedom from recurrence. In our own experience our results indicate that 28 per cent of our patients are free from recurrence after five years. Of those with glands involved there have been 15 per cent of five year survivors. In another five years there will probably be a higher percentage of survivors, because the operative mortality is considerably lower now than it was 10 years ago.

Ochsner, DeBakey and Dixon, in 1947, stated that in an experience of 11 years from January 1, 1936, to December 1, 1946, they had performed 129 pneumonectomies for cancer with a hospital mortality of 24.8 per cent and with a survival rate of 22 per
cent for five years or more. Rienhoff,21 also in 1947, stated that he had performed 112 pneumonectomies for cancer with a hospital mortality of 22 per cent and a survival rate of 10.7 per cent for a period of five years or more. Too much importance should not be placed on mortality rates, because some surgeons are probably more conservative than others in the selection of their cases for operation. Probably we have been more conservative than the authors just mentioned. The important fact is that the results of many surgeons show that the condition is curable if the operation is done early.

One of the most distressing features of the whole problem is the large percentage of patients who present themselves with the cancer too far advanced for a successful operation. Although we have made an exploratory operation in about 40 per cent of the cases, we have been able to perform a pneumonectomy in only 25 per cent of the patients who present themselves with proved primary carcinoma of the lung. In almost all cases the reason has been that the cancer was too far advanced. In a few cases the operation has not been performed because the patients were considered to be too bad risks for reasons of being too old, bad heart disease, etc. My oldest successful pneumonectomy was in a patient 75 years of age. Very old people do not tolerate the operation well.

The features which in general lead us to decline to operate are (1) cachexia from advanced cancer; (2) evidence of nerve involvement, such as severe pain, paralysis of a vocal cord (usually the left), and paralysis of the corresponding half of the diaphragm; (3) the presence of demonstrable metastases in other organs, notably the brain, liver, bones, etc.; (4) the presence of pleural fluid which is found to contain cancer cells; (5) extension of the growth into the wall of the trachea. At exploratory operation very often the cancer is found to have invaded the large vessels or to involve the mediastinal glands to such an extent that obviously all the tumor cannot be removed. Again, sometimes the cancer is disseminated over the parietal pleura in small nodules. If, however, only a localized invasion of the chest wall is found, we prefer to remove that portion of the wall with the lung.

The question of palliative pneumonectomy frequently arises. There is no doubt that a patient will become greatly improved after the removal of a cancerous lung which contains an abscess or a considerable amount of infection. In other cases, however, in which infection is not a prominent feature there is some doubt as to how much palliation will be accomplished when tumor tissue in large amount is left behind. Also, there always remains the possibility of making the patient more uncomfortable if the bron-
chal stump breaks open because of some cancer tissue which prevents its healing. Of course, there will be a difference of opinion on this whole question. We find at the Barnes Hospital that in the majority of cases which we explore but do not remove the lung the conditions present, such as involvement of the great vessels, make the technical procedure of pneumonectomy impossible.

**SUMMARY**

1) Primary carcinoma of the lung has shown a remarkable increase in the last half century, to become perhaps the most frequent visceral carcinoma in the male sex.

2) Apparently some exogenous carcinogenic factor, inherent in our recent culture, must be responsible for this dramatic increase.

3) The possibility of cigarette smoking as one of the factors is briefly discussed.

4) Bronchiogenic carcinoma is no longer, as formerly, a hopeless condition. It is curable by total pneumonectomy if the surgeon gets the patient early enough.

**RESUMEN**

1) El carcinoma primitivo del pulmón ha demostrado un notable aumento en los últimos cincuenta años, para venir a ser probablemente el carcinoma visceral más frecuente en el sexo masculino.

2) Aparentemente algún factor carcinogénico, exógeno, inherente a nuestra cultura debe ser responsable de este dramático aumento.

3) La posibilidad de la influencia del fumar cigarrillos se discute brevemente.

4) El carcinoma bronquiológico ya no es como antes una condición desesperada. Es curable por la neumonectomía total si el cirujano toma a su cargo al enfermo tempranamente.

**REFERENCES**