Primary Neoplasms of the Lung*

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The amazing variety of primary neoplasms of the lung and the frequency with which they are encountered is appreciated more widely now than at any other period in the history of medicine. They were once thought by clinicians to be rare pathological curiosities, their antemortem diagnosis next to impossible, and treatment of them so unsatisfactory as to make a careful search for them a waste of time and effort.

Now that extirpation of these tumors has become a relatively safe practice, and thoracic surgery is generally available in most sections of the country, there is more reason for all physicians to be interested in their detection and early recognition. This fact, with the ever increasing use of community-wide mass x-ray surveys, has caused the discovery of more and more of these potentially fatal neoplasms at a stage in which a cure is possible. It has also disclosed that many of the chronic or persistent infectious diseases of the lungs are due to bronchial occlusion by tumors which are amenable only to corrective surgery.

The following pages contain an outline of the various types of primary neoplasms to be found in the lungs, a description of the means of their detection, and a discussion of the possibilities for their treatment.

Pathology

All of the several primary pulmonary neoplasms, with the probable exception of alveolar cell carcinoma, have their origin in the bronchial tissues. They vary in malignancy from those which are apparently benign to some which are classified as Grade II according to their cellular characteristics. However, almost all of the so-called benign growths have been reported to undergo malignant changes at one time or another, so that one finds it difficult to be reassured in regard to any intrapulmonary tumor's harmlessness because of its behavior or apparent benignancy.

The following is a list of the pathologic types of primary neoplasm in the lung found in the records of our own hospitals (John Gaston Hospital and Baptist Memorial Hospital), and gleaned from the literature:

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1. Bronchiogenic Carcinoma.
2. Bronchial Adenoma and Cylindroma ("Mixed Tumors").
3. Hamartoma and Chondroma.
4. Lipoma.
5. Fibroma.
6. Hemangioma.
7. Myoblastoma.
8. Sarcoma and Fibrosarcoma.
10. Superior sulcus (Pancoast's) tumor.

Tuberculoma is not a true neoplasm, though it must be considered in any differential diagnosis of a mass lying within the lung, and will not receive detailed consideration as a primary neoplasm.

**Bronchiogenic Carcinoma**

Bronchiogenic carcinoma has been classified by Jaffe into four types according to the site of origin: 1) the central or hilar type which has its origin in a main bronchus, 2) the intermediary type originating in a bronchus of the third, fourth or fifth order, 3) the peripheral type which has its beginning in a bronchus near the pleura, and 4) the diffuse type.

Microscopically, these tumors possess a large degree of pleomorphism. However, certain cell types do predominate, and this has lead to a more widely used classification by Fried based upon the cellular composition of the tumor.

1. Squamous cell carcinoma:
   a) keratinizing,
   b) non-keratinizing,
   c) oat cell,
   d) anaplastic.
2. Adenocarcinoma:
   a) simple,
   b) papillary,
   c) mucocellular.
3. Round Cell Carcinoma.

Other pathologists include round cell carcinoma and anaplastic squamous cell carcinoma in the classification of undifferentiated carcinoma.

Though the frequency of each type varies somewhat in the published series in the literature, approximately 75 per cent of bronchial carcinomas are of the squamous cell type, 12 per cent adenocarcinoma and other types 13 per cent according to Fried.

In our series and in the Memorial Hospital series, squamous cell
carcinoma comprises approximately 40 per cent, adenocarcinoma
20 per cent and undifferentiated carcinoma 40 per cent.

The gross appearance of a bronchial carcinoma is that of an
opaque, yellowish-white, firm and irregular mass invading the
lung in broad sheets. Occasionally, however, the mass appears
to be encapsulated, rounded, and sharply demarcated from the
surrounding tissues, giving the gross appearance of a benign tumor.
In the course of the advance of the carcinoma in the lung there
is produced a fibrous tissue stroma, especially in squamous cell
carcinoma, which holds the carcinoma cells together with distinct
intercellular bridges (prickle cells).

Study of resected specimens reveals that the carcinoma tends
to extend along the adjacent submucosal tissue of the bronchus
for considerable distances beyond the limits of visible or palpable
tumor; as much as 2 cm. in the case of adenocarcinoma and 1.5 cm.
in squamous cell carcinoma.

In an estimated 15 per cent of cases of carcinoma of the bron-
chus the tumor outgrows its blood supply and with the help of
aerobic and anaerobic organisms develops central necrosis. The
detritus may be evacuated through a bronchus and produce a
large cavity which frequently contains a fluid level upon x-ray
examination, and closely resembles ordinary pyogenic lung abscess.

Changes may take place in pulmonary tissue which is not
actually invaded by tumor. Partial bronchial occlusion results in
an obstructive emphysema that frequently produces bullae which
may reach large proportions and which may rupture, resulting in
spontaneous pneumothorax. More often, atelectasis of a lobe or
an entire lung develops, complicated by pneumonitis and obliterat-
ing bronchiolitis with resulting bronchlectasis and lung abscess.

Metastases by the lymphatic and hematogenous routes are most
common, and a bronchial carcinoma may also spread by direct
extension into contiguous structures. Ochner and De Bakey an-
alyzed 2,570 collected cases and found metastases to the regional
lymph nodes in 75.9 per cent; liver 34.4 per cent; bones 24.4 per
cent; adrenal glands 17.6 per cent; kidneys 16 per cent; brain 14.6
per cent; heart and pericardium 10 per cent; and pancreas 5.1
per cent.

In 100 cases Jaffe found regional lymph node metastases in all
but two patients.

Pleural effusions, frequently sero-sanguinous, are commonly
found late in the course of the disease. The value of cell blocks
prepared from centrifuged pleural exudate should be stressed. In
as high as 94 per cent of cases in which carcinoma of the lung is
present and complicated by effusion positive evidence of carci-
noma cells in the pleural fluid will be found.
Mixed Tumors of the Lung

There is a group of bronchial tumors which was once thought to be benign and which is characterized by slow growth, and has a cellular structure which for long periods of time lacks the indications of malignancy. These tumors protrude into the lumen of the bronchus, usually present a smoothly rounded surface covered with normal appearing epithelium, and surface erosion is rare. Microscopically, the bronchial epithelium often is shown to have undergone squamous metaplasia and beneath this is a layer of fibrous tissue of varying thickness within which lies the main portion of the tumor. The predominating cells are usually small round cells with scanty cytoplasm and darkly staining nuclei in which mitotic division is rarely seen. The resemblance to fetal pulmonary alveoli is very striking, and the majority of these tumors were once loosely classified as bronchial adenomata.

However, the stroma in some cases is dominated by cells of mesoblastic origin including smooth muscle, hyaline cartilage, fat and sometimes even bone. This fact lead Graham and Womack to designate these tumors in 1938 as “mixed tumors of the lung.”

Much credit belongs to Graham and Womack for clarifying both the histology and the histogenesis of these mixed tumors of the bronchus. In accordance with their views, two groups of tumors arise as a result of the failure of the bronchial bud to develop into the normal arrangement of adult tissues. The first group contains those “in which mesodermal elements predominate.” The second group is that in which “the entodermal or epithelial elements are dominant.” The former group includes such tumors as chondroma, osteoma, lipoma, fibroma, angioma, myxoma and (in their malignant phase) sarcoma. The second group consists chiefly of adenomas and cylindromas.

Just what proportion of these tumors undergoes malignant change is not known at present. Graham and Womack, Anderson, Chamberlain, Goldman, and others have reported such cases that emphasize the potential malignant qualities of these neoplasms. There is general agreement that most surgically removed specimens reveal only local invasion of pulmonary tissue and occasional regional lymph node involvement. The five-year survival rate of patients from whom such tumors showing local invasion have been removed is between 80 and 90 per cent, indicating that their malignancy is relatively slight when compared with that of bronchiogenic carcinoma. It is felt that observation for several decades will be necessary before the final survival rate following their resection will be known.

Goldman recently reported two cases of the mixed tumor type
which ended in death. Endoscopic removal and irradiation therapy was followed later by recurrence of the tumor, in one case at the bifurcation of the trachea. He states that after a period of six years of observation and treatment "there is no doubt that a mixed tumor type of adenoma had become a highly malignant carcinoma, nor is there any doubt that if this neoplasm were seen only at postmortem and without the biopsy six years earlier, it would have been diagnosed as an undifferentiated bronchiogenic carcinoma."

Bronchial adenoma and cylindroma are presented in another paper in this issue.

Hamartoma and Chondroma

Hamartoma and chondroma of the lung belong to a group of tumors of the bronchus which are relatively benign. Histologically, these tumors consist of normal epithelial and mesodermal bronchial tissue cells which in their development have become distorted in their pattern, resulting in an abnormal mixing and arrangement of these tissues. Many of these tumors have been called chondromas because of the predominance of cartilage, but other tissue elements are present and thus they are not pure chondromas. The term "hamartoma" is more generally used.

Grossly these tumors are white or light gray and are sharply demarcated from the surrounding lung. The cut surface appears lobulated and calcium is frequently scattered throughout the tumor. Its size varies from that of a black-eyed pea to one that fills the entire hemithorax. In 26 of 30 cases Hickey and Simpson found that the tumor was subpleural; in the remaining four cases it was near the hilum of the lung. In the vast majority of cases the extension of the tumor is extrabronchial, although a few cases have been reported in which polypoid endobronchial hamartomas consisted of epithelium, fat, smooth muscle, cartilage and bone, with cartilage the predominant element in most cases. Multiple islands of cartilage surrounded by perichondrium are frequently found and portions of this cartilage have often undergone calcification. Fat is found scattered in these tumors in approximately one-half of the reported cases. Epithelial elements are frequently present, often giving rise to mucous cysts. In some cases the epithelial lining of these cysts is ciliated. Malignant changes in these tumors rarely occur.

Lipoma, Fibroma, Hemangioma and Myoblastoma

Lipoma, fibroma, hemangioma and myoblastoma may be classified as variants of the mixed type of bronchial tumor in which a specific type of cell of mesothelial origin predominates.

The lipomas are often pedunculated, smooth, round and covered
with normal mucous membrane. Microscopically, the lesion consists of lobules of mature fat cells with a delicate fibrous tissue stroma. In the case described by Watts, no muscle, cartilage or bone was present. Mature fat cells do appear in varying proportions in others of the so-called benign tumor groups in which different cellular types are dominant. The lipomas apparently arise from adipose tissue normally present in the bronchial walls.

Although all reported lipomas are histologically benign, because of bronchial occlusion serious and even fatal suppuration distal to them may occur.

Fibromas were found by Lindgren to represent about 9 per cent of the so-called benign bronchial tumors in his review of this subject, but many of them showed varying proportions of fat, muscle and angiomatoso tissue indicating their close relation to the mixed tumor group. Instances of malignant change were found.

Hamangiomas of the bronchus have been reported occasionally, and one in our experience was a smoothly rounded tumor projecting into the lumen of the right lower lobe bronchus covered by normal mucous membrane. Blood channels were large and diffusely irregular with a light fibrous tissue stroma surrounding them. No evidence of malignant change was observed.

Kramer in 1939 reported a pedunculated and apparently benign tumor in the right lower lobe bronchus which he characterized as a myoblastoma.

**Sarcoma and Fibrosarcoma**

Sarcoma and fibrosarcoma of the lung are extremely rare and appear most frequently in children and young adults. Many of the reported cases have proved upon review to be undifferentiated or anaplastic bronchiogenic carcinoma. In our own hospitals three such sarcoma cases were found in the past ten years, and review of the tissue specimens by Dr. Douglas Sprunt* resulted in their re-classification as anaplastic carcinoma.

Stout has done much to clarify this subject. He accepts as true fibrosarcomas only those tumors composed of fibroblasts which produce collagen and reticulum fibers, the latter being wrapped around the cells in a characteristic fashion. Collagen may be absent in the more undifferentiated fibrosarcomas. By eliminating all cases which did not fulfill his criteria, Stout could accept only six cases previously published in the literature as being true fibrosarcomas.

Womack and Graham cite the extremely interesting case of a pneumonectomy performed for an invasive tumor of the right

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upper lobe. Upon microscopic examination the epithelial and connective tissue had both become malignant. The epithelial elements were extremely anaplastic, rapidly growing, and with numerous mitotic figures. "The stroma was extremely cellular, with spindle-shaped cells whose nuclei showed evidence of rapid growth with numerous mitotic figures." This is an outstanding example of a tumor that Graham believes would have been called an adenoma had it been seen early, before its malignant transformation. They designate this tumor as a "carcinoma-sarcoma."

Alveolar Cell Carcinoma

Alveolar cell carcinoma has attracted a great deal of interest recently because the preponderance of evidence makes us classify this malignant pulmonary neoplasm as multicentric in origin. It is also known as pulmonary adenomatosis and is histologically similar to the virus disease of sheep known as jagstzelt disease. These facts lead to an interesting bit of speculation in regard to the possible role of virus infections in the production of carcinoma.

The fundamental feature of alveolar cell carcinoma is the definite reproduction of alveolar structure. The malignant cells lining the alveoli are dark-staining, tend to be polygonal and have abundant eosinophilic cytoplasm. The cells are frequently in multiple layers, and the alveoli are often filled with these obviously malignant cells which show frequent mitoses. Malignant areas are separated grossly and microscopically by normal parenchyma, with masses and cords of wildly growing cells in a fibrous tissue stroma in the more malignant cases. A single lobe may be involved, or all lobes may be involved simultaneously with a diffuse distribution of discrete nodules which become coalescent as the growth progresses.

Metastases occur by way of the lymphatic channels to the regional lymph nodes and occasional distant metastases have occurred.

The Superior Sulcus Tumor (Pancoast's Tumor)

The superior sulcus tumor (Pancoast's tumor) is not a pathologic entity in itself but is the syndrome of a tumor which involves the cervical sympathetic chain and brachial plexus, and produces local bone destruction. In five of Pancoast's original cases no pathologic diagnosis was made, but his description of the others was compatible with the various types of bronchogenic carcinoma. Other types of neoplasm, however, have produced the same syndrome, such as the sympathoblastoma and carcinoma of the thymus. In our experience, and in that of others, neurofibromas have likewise fulfilled the criteria of a so-called Pancoast tumor.
Diagnosis

The index of suspicion on the part of the patient's physician is the most important single factor in the diagnosis of any primary lung tumor. These tumors occur frequently enough so that almost any busy practitioner will see two or three annually. Some of them are “silent” and are discovered only upon routine x-ray films made upon apparently healthy people, but there are certain cardinal symptoms which will arouse suspicion in the minds of alert practitioners in a large number of cases.

Cough, although a symptom common to many disorders of the respiratory tract, becomes significant when it changes in character. Pain, or a sensation of discomfort, in the chest is commonly experienced. Dyspnea on exertion is present as atelectasis develops or pleural fluid forms. Wheezing, remarkably similar to asthma and often relieved by adrenalin, results from partial bronchial occlusion and disappears as total occlusion ensues. Hemoptysis, particularly blood streaked sputum, is a valuable suspicion-arouser. Hoarseness, or weakening voice, in the absence of an intrinsic laryngeal lesion indicates invasion of, or pressure upon, the recurrent laryngeal nerve. Rheumatism, a form of pulmonary osteoarthropathy, frequently is associated with pulmonary neoplasm. And finally, persistent or recurring pulmonary injection, frequently vulgarly called “virus pneumonia,” should ring a bell to awaken any suspicion not previously aroused.

In our experience the advent of an increasing array of antibiotics is anything but an advantage to the patient with a primary neoplasm of the lungs. It takes longer now for a physician to systematically give each agent a thorough trial, and the temporary benefit experienced by the patient as his infection is subdued may allay suspicion of a tumor for surprising periods of time (Case 1).

Once a tumor of the lung is suspected, an orderly examination is indicated and the suggested outline is designed to reveal the diagnosis as early as possible in the series of examinations and with the minimum of expense to the patient:

1. Complete physical examination.
2. Fluoroscopy.
3. Laboratory,
   Blood counts and differential smear,
   Blood sedimentation rate,
   Sputum for tumor cells, tuberculosis, or fungus.
4. X-ray films of the chest,
   Postero-anterior and lateral projections,
   Diagonals (if needed).
5. Bronchoscopy,
   Biopsy,
   Bronchial lavage for cellular studies.
7. Laminagrams (or Bucky grid films).
8. Angiograms.
9. Surgical exploration (or biopsy of peripheral nodes).

Carcinoma of the bronchus is the most frequently encountered primary tumor of the lungs and is therefore the first to be suspected and sought out. Fortunately, most of the other primary neoplasms will be revealed in the course of an attempt to prove or disprove the presence of a carcinoma.

Diagnosis of a bronchiogenic carcinoma is often rendered difficult because of the associated pulmonary infection produced by interference with bronchial drainage. The clinical and x-ray pattern may be indistinguishable from tuberculosis (Case 2), even to cavity formation. Interstitial pneumonitis and abscesses often complicate the picture, and the diffuse infiltrating type of carcinoma closely resembles fungus infections in its clinical and roentgenologic manifestations. To further complicate the diagnosis, non-pathogenic Monilia are often found in the sputum, as are acid-fast forms of saprophytic actinomycetes.

The physical examination will often fail to reveal direct signs of a tumor in the chest, but indirect evidence can frequently be detected in the form of wheezing, or from signs of atelectasis, pneumonitis, suppuration or pleural fluid. A complete history and physical examination, meticulously carried out, is of importance to detect primary tumors elsewhere in the body to which the lung neoplasm may be secondary, and to reveal evidence of extension or metastases from a primary lung neoplasm outside of the lung itself.

The physical examination should include a particularly careful search for enlarged lymph nodes in the supraclavicular fossae, axillae and abdomen. In fact, the entire body should be palpated for nodules. A recent patient of ours was spared an exploratory operation by the discovery of a small pea-sized subcutaneous metastatic node on the anterior chest wall. In the eyes one may find a contracted pupil or a ptosis of the lid, part of a Horner's syndrome indicating involvement of the lower cervical sympathetic ganglia. The larynx may show impaired motion of one vocal cord which indicates invasion of, or pressure upon, one recurrent laryngeal nerve, even before marked changes in the voice take place. The genitals and prostate deserve attention because the former may be the site of origin of a single metastatic tumor in the lungs
which otherwise resembles a primary growth (solitary metastasis of a seminoma, for instance), and the latter occasionally gives rise to diffuse metastatic carcinoma in the lungs. The extremities must be inspected and palpated for evidence of pulmonary osteoarthropathy (clubbing, etc.) and for primary tumors of bone which may produce solitary pulmonary metastases resembling primary neoplasms.

Fluoroscopy of the chest is valuable to show evidence of obstructive emphysema, a "lighting up" of a segment or lobe on expiration, when a bronchus is partially occluded by any of the primary tumors. It also is the only means of detecting paralysis of one side of the diaphragm when it exhibits paradoxical motion as the patient inhales sharply, which would indicate involvement of the phrenic nerve. Pleural fluid is readily detected and located for aspiration by means of the fluoroscope.

The total blood counts and differential white cell count are apparently unaffected directly by a primary neoplasm of the lungs, and changes are more often due to associated pulmonary infection present. Anemia, when present, is usually of the secondary or hypochromic variety in contrast to that found in carcinoma of the stomach. The blood sedimentation rate is usually elevated in the presence of malignant lung tumors and serves only to arouse suspicion of their presence, or to help confirm one's impression of their malignancy. Insufficient data are available as yet to establish the place of serological tests for malignancy in the diagnosis of pulmonary neoplasms, especially since tuberculosis frequently produces a false positive result.

Sputum examination for cancer is gaining in popularity as experience with the method is acquired in various medical centers and hospitals. Expectorated specimens may be smeared while fresh and examined by the technic of Papanicolaou, or bronchial washings may be obtained, centrifuged and imbedded for staining with hematoxylin and eosin. The bronchial lavage can easily be performed as an office procedure using ten cubic centimeters of a normal saline solution in the same manner as iodized oil is instilled for bronchograms, as described by Carr et al. Waddall identified bronchogenic carcinoma from sputum examinations in 84 of 100 patients, and others are reporting similar results.

The standard x-ray examination of the chest, while one of our most valuable aids in the detection of primary lung tumors, often fails to reveal the shadow of the tumor itself. Lateral views and often diagonal projections will show shadows behind the heart shadow or diaphragm which are not to be seen on the conventional film. Even then the evidence provided by the x-ray films may
only indirectly point to the presence of a tumor; atelectasis of a lobe or lobule, interstitial pneumonitis, an abscess, "virus pneumonia," apparent tuberculosis or pleural fluid.

Certainly absence of a tumor shadow is insufficient evidence upon which to rule out the existence of a lung tumor when symptoms or signs indicate the possibility of its presence. All too often an early carcinoma or other bronchial neoplasm casts no recognizable shadow on the x-ray film or is concealed by shadows of other structures.

When definite tumor shadows are seen on the x-ray films, it is impossible to identify with certainty the type of neoplasm which casts them. Bronchial carcinoma, as well as the less malignant tumors, may appear to be a discrete, sharply circumscribed intrapulmonary tumor which grows at an imperceptible rate and has the appearance of a benign tumor. Yet more of these circumscribed shadows are due to carcinoma, and malignant, than are due to adenomas, hamartomas and all the rest of the less malignant mixed tumors combined.

Bronchography is of value in demonstrating the presence of neoplasms in the bronchi, especially when they lie in the smaller bronchi beyond the visible range of bronchoscopy. A persistent filling defect on repeated examinations must be viewed as strong evidence in favor of a primary lung tumor.

Bucky grid films, laminagrams and angigrams are each useful under certain conditions to help delineate tumors from surrounding atelectasis or areas of infection, and to differentiate neoplasms from vascular anomalies or diseases.

Bronchoscopic examination of the patient suspected of having a primary neoplasm of the lung is absolutely indicated. A high proportion of lung tumors can be detected directly or indirectly by this means, and it is also necessary to help determine the probable operability of the patient's lesion.

About 40 per cent of all bronchial tumors originate within the visible portions of the bronchial tree where they can be seen directly through a standard type bronchoscope and a biopsy of them taken. Right angle and retrograde-viewing bronchoscopes, though not yet universally used, are improving this figure. Herbut and Clerf report positive biopsies obtained from 71 of 180 patients who had proved bronchiogenic carcinoma, or 39 per cent. Even a higher rate of positive diagnosis was obtained by them by examination of bronchial secretions in which they found cancer cells in 161 of the 180, or 89 per cent.

It must be emphasized that a single negative biopsy is insufficient to exclude the presence of a bronchial neoplasm. Normal
mucous membrane or granulation tissue often overlies the neoplasm so that multiple biopsies of various portions of the lesion may be required to yield an accurate diagnosis.

Additional bronchoscopic information of value is the site and extent of the tumor in its relation to the major bronchi and trachea, and evidence of extensive metastases to the mediastinal lymph nodes as shown by widening of the carina or fixation of the bronchial tree. At bronchoscopy the larynx likewise can be inspected directly for evidence of recurrent laryngeal nerve palsy.

One note of warning might be interjected here in regard to taking a biopsy through a normal and intact mucous membrane. Our own experience includes a case of hemangioma so biopsied, following which there was a profuse gush of blood which filled the bronchoscope and threatened to suffocate the patient until she was suspended in an inverted position over the edge of the operating table and the bleeding ceased spontaneously before exsanguination took place. On another occasion one of us ruptured a non-pulsating aneurysm of the aorta with the bronchoscope with immediate death of the patient. A catastrophe was recently averted when a protruding mass in the trachea was not biopsied because it was covered by normal mucosa, and an aneurysm of the innominate artery was found at exploration, although it was fully expected that a neoplasm would be found. (Angiograms had not been made).

Aspiration biopsy with a needle through the chest wall is intentionally omitted, since there are safer ways of arriving at the diagnosis of a neoplasm in the lung, and the danger of implanting carcinoma cells in the chest wall is pointed out by Dolley and Jones, and others.

Exploratory thoracotomy is now widely used in patients who present strong presumptive evidence of a primary neoplasm of the lung but whose preliminary examinations have failed to yield a positive diagnosis. It is used with the same degree of safety (and with less discomfort to the patient) as is exploratory laparotomy. To wait to see what develops in a patient who offers suggestive evidence of a pulmonary neoplasm is to let the opportunity for cure be forever lost in many instances. Even benign appearing tumors should be explored promptly because many of them are actually malignant, the majority of the others have malignant potentialities, they will eventually produce bronchial occlusion with suppurative complications, and even those most completely benign will (with continued growth) assume a size sufficient to crowd contiguous and vital structures with untimely death of the patient.
Treatment

Until Graham in 1933 performed the first successful pneumonectomy for bronchiogenic carcinoma, such a diagnosis was equivalent to a death sentence to the patient. The literature now contains increasing numbers of patients reported to be alive five or more years after pneumonectomy for carcinoma of the bronchus, and Graham's first case is still alive and well seventeen years later.

The mortality rate incidental to a total pneumonectomy per se has been reduced to a level comparable to that of major abdominal operations. Technical advances in physiology, anesthesiology, blood banking, chemotherapy, antibiotic therapy and thoracic surgery have made invasion of the chest a safe and practical procedure. Accordingly, the mortality rate reported by any one surgeon will depend upon the extent of radical dissection he feels justified in performing.

The objectives of treatment of a patient with bronchiogenic carcinoma are two-fold. The primary desideratum is, of course, complete eradication of the neoplasm and can be accomplished only by means of surgery. When all examinations indicate that the carcinoma is confined to one lung, or to the lung and its regional lymph nodes, total pneumonectomy is the treatment of choice.

The second desideratum of treatment is that of palliation and amelioration of the patient's symptoms when a curative surgical procedure is impossible. This can be accomplished by means of either a limited or extremely radical resection intended to remove the source of the patient's symptoms, or by the use of nitrogen mustard (Methyl-bis) and/or deep x-ray irradiation. It becomes a matter of judgment on the part of the patient's physician which course will provide the individual patient with the longest life and the greatest freedom from discomfort.

Other palliative measures to be employed in cases with extensive and painful infiltration of the chest wall by carcinoma are multiple intercostal neurectomy, high chordotomy or cerebral lobotomy.

It is obvious that the number of patients who will be cured of bronchial carcinoma will depend upon the early recognition of the disease, and the number recognized in time for a curative resection is still distressingly small but improving. Brock in 1938 found only 4 of 106 patients with carcinoma of the bronchus who had no demonstrable extension beyond the limits of the lung. Overholt in 1940 reported 14 of 100 patients whose carcinoma proved resectable, and Churchill in the same year reported 17.4 per cent of 155 patients with carcinoma whose lesions could be completely removed. Ochsner and DeBakey performed resections
upon 195 of 548 patients, but only 57 of these were done with the expectation of a cure, a total of 10.4 per cent. It is encouraging to note that in Ochsner and DeBakey's report of 1948 there were 8 patients alive and well among those 36 who had resections more than five years previously, 22.2 per cent of the operated group and 1.5 per cent of the total number with a diagnosis of carcinoma of the bronchus. There were 12 additional living patients in the four year survival group who, if they all survive, would increase the number of five year survivals to 20 in the following year. Additional candidates for long term survival were to be found in the first, second and third year postoperative groups.

It is generally agreed that evidence of distant metastases from a bronchiogenic carcinoma such as are found in the axillary or supraclavicular lymph nodes, brain and liver, are definite indications of inoperability of the tumor. The majority of thoracic surgeons agree that pleural fluid in which neoplastic cells can be demonstrated is likewise a contraindication to surgery.

Evidence of recurrent laryngeal nerve paralysis, phrenic nerve paralysis, Horner's syndrome, brachial plexus involvement, and severe chest wall pain indicate that total extirpation of the carcinoma is unlikely, but do not contraindicate exploration, especially when a positive diagnosis of carcinoma has not been made. Each of these nerves has been found to be affected by pressure from relatively benign tumors, and even when direct invasion by carcinoma has taken place it is possible in many instances to perform a sufficiently radical dissection to relieve the patient of his distressing symptoms. One is likewise justified in performing a resection of a lobe or a lung in which suppuration is present and is the cause of the majority of the patient's symptoms, even when such a resection offers no reasonable hope of cure.

However, it is to be remembered that a person from whom a lung has been removed, particularly a patient in the older age group, is far from being a comfortable person. It is difficult to maintain the heart and mediastinum in the mid-line even with the use of air or plasma in the empty hemithorax, and the retraction of the mediastinum toward the operated side and over-distention of the remaining lung produces discomfort, and often dyspnea, which is continuous throughout the remainder of the patient's life, unless a secondary thoracoplasty is performed. One hesitates to perform a thoracoplasty upon a patient whose life expectancy is limited, adding thereby to the sum total of his discomfort.

For these reasons it is the firm conviction of this Group that resection should be performed: 1) when it offers a reasonable hope of cure or, 2) when it is directed at the alleviation of symp-
toms which are present or are likely to occur within the immediate future.

As has been pointed out by Skinner et al, it is important to the comfort and happiness of a patient with inoperable carcinoma to maintain as high a level of general health as possible. Particular attention is paid to his red blood cells and hemoglobin. He is given a high protein diet, often supplemented with a high protein drink formula, extra vitamins and iron. The following high protein drink formula has proved palatable and effective in helping to maintain blood protein levels, and may be served between meals as a drink or frozen into a sherbet with varying flavors:

6 egg whites,
6 tablespoonfuls skimmed milk powder,
[Starlac (Borden's) or commercial powder],
4 ounces Karo syrup,
6 ounces orange juice, or flavored to taste with chocolate, vanilla, spiritus frumenti, or other flavoring.

The use of nitrogen mustard (Methyl-bis) has produced marked benefit in the reduction of pain and improvement of bronchial drainage in 70 per cent of our cases. The initial experience reported by Skinner et al. has been confirmed in our subsequent observations. The Methyl-bis is given in 10 milligram doses, administered intravenously on four consecutive days. The affinity of Methyl-bis for young cells gives rise to its principle complication of repression of the formation of blood cells and platelets, so that blood counts at bi-weekly intervals following its use are indicated, as are transfusions whenever necessary.

The patient's infectious complications are controlled with the use of antibiotics and a bronchial drainage routine which includes 15 grains of ammonium chloride four times a day as an expectorant, postural drainage at least four times daily and a high fluid intake.

Deep x-ray therapy as applied for palliation and the relief of pain, usually following the course of Methyl-bis, is customarily reserved for such a time as it may be specifically needed.

The effectiveness of this palliative regime is demonstrated by the fact that numerous patients have been able to return to work for periods of a year to two and one-half years, requiring nothing stronger than codeine for occasional sedation up to a short time before their eventual deterioration and death.

Treatment of the superior sulcus tumor of Pancoast deserves special mention because it is usually, but not always, a carcinoma of the bronchus which has extended beyond the limits of the lung. No reports have come to our attention which indicate that a patient has survived five years or more after surgical extirpation
of such a tumor when *carcinoma* was the etiological factor. However, it is now our opinion that these tumors should be explored because occasionally a neurofibroma is found producing the syndrome, even including bone erosion, and can be completely extirpated.

Palliation can also be afforded to some of these incurable patients whose tumor is carcinomatous by resecting the mass and at the same time performing an intercostal neurectomy. It is our practice to fulgurate any tumor tissue left behind, and one such patient of ours has now been working without pain for a period exceeding two years.

Hamartomas and chondromas are relatively benign so that when they are found upon exploration, as limited a resection as possible is indicated. In some cases they have been “shelled out” without sacrifice of lung tissue and in others a segmental resection of a portion of a lobe has proved adequate. Their usual peripheral location lends itself to this type of excisional treatment when suppuration and bronchiectasis are absent.

Lipomas which are pedunculated can be removed safely at bronchoscopy by means of the biopsy forceps and can be expected to be cured by this treatment. But when lipomas cause bronchial occlusion, exploration of the chest is indicated with their removal by bronchotomy if possible, or lobectomy if necessary to extirpate them completely and remove bronchiectatic and infected segments peripheral to them.

Fibromas and myoblastomas, being actually tumors with malignant potentialities, require excision with an adequate margin to assure their total removal, and lobectomy is usually necessary, or pneumonectomy if a main stem bronchus is the site of their origin.

Hemangiomas of the bronchus are similarly treated, although we have a patient (mentioned as the one whose biopsy was followed by severe hemorrhage) alive and well without symptoms seven years following a single course of deep x-ray irradiation.

Sarcomas and fibrosarcomas are treated following the principles laid down for any other malignant growth in the lungs; radical and complete extirpation if possible, together with a resection of the regional and mediastinal lymph nodes. The result of treatment in the true sarcoma group is discouraging, none of the six cases accepted by Stout having survived a five year period. None of the patients encountered in our own experience presented an operable tumor at the time they were seen and deep x-ray irradiation produced no appreciable improvement.

Treatment of alveolar cell carcinoma has been unsatisfactory in general, although Graham has mentioned a case in which lobectomy was performed with relief of symptoms for four years,
but eventual death occurred as the result of extension or recurrence in other lobes. In our own experience, a patient revealed alveolar cell carcinoma in a lobe removed for bronchiectasis, but died a few months later as the disease progressed (Case 4). There are no reports to our knowledge of x-ray irradiation having proved of material benefit to these patients and no series treated by Methyl-bis has been reported.

Case 1: Mr. B.J.A., age 51, white male. This patient's history is included to illustrate a rather large group of patients whose diagnosis is delayed unduly while the infectious complications are being treated by the entire gamut of chemotherapy and antibiotics.

C.C.: Fever, cough, sputum and weight loss beginning five months previously.

P.I.: About the First of September 1949, the patient began to be aware of a low grade fever, a gradually increasing cough with sputum, and an insidious weight loss. No acute illness was recalled. During the following months until January 20, 1950, the patient received treatment with a succession of antibiotics until all of them available on the market had been given a thorough trial. This resulted in some marked gain in the

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**Fig. 1, Case 1:** Mr. B.J.A. (Bronchiogenic carcinoma), October 6, 1949. The chest film suggests the presence of a pulmonary tuberculosis or “virus pneumonia” involving the upper two-thirds of the right lung, with a suggestion of some enlarged hilar nodules on this side. On the left there is some minimal infiltrate in the extreme apex—Fig. 2, Case 1: Mr. B.J.A., January 18, 1950. During the interval between these two films, this patient has had numerous antibiotics which have apparently brought about some improvement in the pneumonitis in the right lung. Some of this clearing may actually represent a contraction of the lobe rather than resolution. The right hilar mass is more definite at this time, and a bronchoscopic biopsy revealed the presence of an unclassified bronchogenic carcinoma with tracheal involvement. We see therefore that carcinoma patients can improve temporarily and deceptively with antibiotics.
patient's weight, but without full return of his strength. A mild cough persisted with sputum occasionally streaked with blood. Wheezing and dyspnea had developed in the meantime.

**P. H.:** The past history was essentially non-contributory.

**P. E.:** The patient was a poorly nourished white male appearing chronically ill. There was a subicteric tint of the skin with multiple pigmented nevi over the chest posteriorly, some of which appeared irritated and suggested the possibility of a malignant melanoma. The veins over the neck, chest and abdomen were distended.

Examination of the chest showed limited motion on the right with wheezes, rales and ronchi over the upper half of the right lung field.

The remainder of the general examination was not remarkable.

The laboratory reported the blood counts within normal limits and the blood sedimentation rate, corrected for cell volume, was elevated to 34 mm. in one hour.

X-ray films of the chest made on January 18, 1950 were compared with earlier outside films made in September 1949. There was noted considerable clearing of a diffuse infiltrate present in the upper third of the right lung, some of which may have represented a contraction of the lobe rather than a true resolution of the infiltrate. There was an increase in the size of the right hilar shadow and in the lateral view a density was visible about 5.0 x 8.0 cm. in diameter.

Fluoroscopic examination revealed the right diaphragm paralyzed and elevated and it exhibited paradoxical motion on sniffing.

Bronchoscopic examination on January 20, 1950 revealed a tumor at the lower end of the trachea which was granulomatous and partially obstructing the lumen of the trachea itself, leaving a lumen not over 5.0 mm. in diameter. Inspection beyond this point was impossible.

A biopsy was taken from the tumor in the trachea and was reported as bronchiogenic carcinoma, undifferentiated.

Because of the obvious tracheal involvement surgery was not recommended, but instead the patient was given a course of Methyl-bis intravenously which was followed by deep x-ray irradiation. Six weeks later the patient showed marked improvement of his wheezing and dyspnea, and the blood had disappeared from his sputum.

**Case 2:** Mr. G.S., age 45, white male. This case has been selected to illustrate the close clinical resemblance between some cases of carcinoma of the bronchus and pulmonary tuberculosis. All routine examinations indicated a diagnosis of pulmonary tuberculosis except for the absence of tubercle bacilli in the sputum.

**C. C.:** Hemoptysis five weeks previously.

**P. I.:** The patient complained of a spasmodic cough of fifteen or twenty years duration, and two years earlier had been studied at the Arkansas State Tuberculosis Sanatorium for two weeks where sputum examinations were negative for tubercle bacilli and where x-ray examinations apparently showed no active tuberculosis.

Two months before admission to the Baptist Memorial Hospital the patient had pneumonia, and approximately one week after recovering from this he raised one teaspoonful of blood in his sputum. The blood gradually disappeared and at the time of admission his sputum consisted of about one tablespoonful of clear mucus daily. Wheezing had appeared two months earlier and was constant, and the patient complained of easy
fatigue and only a fair appetite. He had no fever, no chest pain or night
sweats. Weight loss was moderate.

P. H.: The patient's only significant illnesses previously were five at-
tacks of pneumonia since 1916. There was no known tuberculosis contact.

P. E.: The patient was well developed and fairly well nourished with a
temperature of 99.0 degrees F., pulse 80, blood pressure 122/84. The gen-
eral examination was non-contributory except for a scar in the left pos-
terior axillary line where an old empyema had been previously drained.
The lungs were essentially normal to physical examination and no rales
were heard.

The chest x-ray films made on August 11, 1945 revealed in the right
lung a cavity measuring 2.5 cm. in diameter in the right infraclavicular
area. There was likewise a small amount of flocculent infiltration in the
first interpace peripherally. The left lung was clear. There was some
pulmonary emphysema revealed in both bases and the right costophrenic
angle was blunted while the left diaphragm was flattened and adherent
to the chest wall laterally. X-ray impression was chronic fibroid caver-
nous pulmonary tuberculosis, bilateral pulmonary emphysema, and pos-
tible tracheobronchial tuberculosis.

The laboratory reported the blood counts within normal limits and the
blood sedimentation rate corrected for cell volume at 15 mm. in the first
hour.

Because of the patient's wheezing a bronchoscopic examination was
performed on August 20, 1945 and some granulation tissue with an ulcer

FIGURE 3

CASE 2

FIGURE 4

Fig. 3, Case 2: Mr. G.S., July 11, 1945. The chest film here suggests a typical
pulmonary tuberculosis with a right infraclavicular cavity measuring about
4 cm. There is very little parenchymal reaction around the cavity, and there
is a suggestion of enlarged calcified nodes on the left. The final diagnosis in
this case was epidermoid bronchiogenic carcinoma, inoperable.—Fig. 4, Case 2:
Mr. G.S. Biopsy specimen from granulation tissue in the trachea under low
power reveals a fairly rapidly growing epidermoid carcinoma, Grade III. Num-
crous mitotic figures are seen and the individual cells vary greatly in size and
staining characteristics.
was found at the orifice of the right upper lobe bronchus. This granulation tissue extended up the right wall of the trachea about 1.0 cm. A specimen was removed with the biopsy forceps and revealed epidermoid carcinoma, Grade III.

Since the pathologic report did not agree with our clinical impression, the bronchoscopy was repeated September 8, 1945 and the fungating mass was now seen to be larger than before. It was attached along a broad base on the right wall of the trachea. Biopsy specimens were again removed and again revealed epidermoid carcinoma.

Because of the extensive tracheobronchial involvement no resection was undertaken and only palliative treatment was advised.

**Case 3:** Mrs. A.C.G., age 58, white female. This patient was first seen at the John Gaston Hospital on March 12, 1945.

**C. C.:** Fever, chest pain and a productive cough.

**P. I.:** In the hospital she had fever for three days, with some pain in the left costal margin. X-ray examination of the chest made the day after admission showed an increase in the hilar glands bilaterally with an area of consolidation at the left base. The patient was placed on one of the sulfa drugs. X-ray film of the chest on March 22, 1945 showed a decrease in the density. The discharge diagnosis was tonsillitis and acute interstitial pneumonitis. She was discharged home on April 5, 1945. She was re-x-rayed as an out-patient on April 14, 1945 which showed “post-pneumonic fibrosis.”

The patient was apparently free of symptoms until shortly before her second admission on February 4, 1947. At that time she was running a temperature of 104 degrees F., complaining of cough with a small amount of purulent sputum. There was some leukocytosis. X-ray findings on admission were reported as pneumonia of the left lower lobe. X-ray film on February 12, 1947 showed more extension and then on February 21, 1947 showed some clearing. She was discharged on February 24, 1947 with a diagnosis of bronchopneumonia.

The third admission was on June 7, 1947 at which time she was admitted complaining of fever, cough, sputum and pain in the left chest. X-ray examination on admission showed a patchy infiltrate at the left base. She was not running much fever at this time, and the diagnosis of primary atypical pneumonia was made. On June 13, 1947 an attempt was made to secure bronchograms by instillation of iodized oil, and some bronchiectasis was demonstrated in the left lower lobe. On June 17, 1947 the patient was bronchospected by the Ear, Nose and Throat Service, at which time only a slight increase in the mucus coming from the left lower lobe was seen. This sputum was examined for tumor cells but none were found. The patient was discharged home on June 21, 1947.

Her next admission was on February 8, 1948 when she was readmitted because of fever and chest pain. X-ray film on February 9, 1948 showed a moderate extension of the previously described infiltrate in the left lower lobe, and it was diagnosed as a bronchopneumonia. Subsequent films on February 15, February 22 and March 10, 1948 showed no change. Bronchograms were repeated on March 17, 1948 and showed a definite though moderate bronchiectasis apparently limited to the left lower lobe. The patient was bronchospected again on March 24, 1948, at which time the mucous membrane was seen to be reddened from the level of the vocal cords on down. There was a moderate amount of purulent sputum in both lower lobes, with an increased amount in the left lower lobe.
FIGURE 5 (CASE 3)

Fig. 5, Case 3: Mrs. A.C.G. (Alveolar Cell Carcinoma), March 13, 1945. This patient was repeatedly hospitalized for attacks of bronchopneumonia which always localized in the left lower lobe. It was during such an attack that this film was made and there is a definite infiltration in the left base with slight elevation of the left leaf of the diaphragm. The remainder of the lung fields is essentially clear.—Fig. 6, Case 3: Mrs. A.C.G., August 13, 1945. Bronchographic studies revealed the presence of a bilateral basal bronchectasis, most noticeable in the left lower lobe where there was irregularity in the diameter of the bronchi, with some widening and loss of finer branches. No bronchial obstruction was visualized.—Fig. 7, Case 3: Mrs. A.C.G., November 3, 1946. Another attack of "bronchopneumonia" again brought the patient to the hospital. Again the bronchopneumonia process was localized in the left lower lobe, but there was a somewhat differential distribution than on the film made three years previously. Suggestion of minute areas of infiltrate in the right base is also seen.
Fig. 8, Case 3: Mrs. A. G., December 21, 1948. A left-lower lobe resection was performed and the immediate post-operative course was in keeping with an adenomatous tumor. A careful pathological examination of the resected lobe revealed an adenomatous epithelial tumor. This is now classified as an adenocarcinoma.

Fig. 9, Case 3: Mrs. A. G., April 22, 1949. This is now classified as an alveolar cell carcinoma.

Fig. 10, Case 3: A chest film, taken May 1, 1949, shows the presence of a large mass in the left-lower lobe. The mass is well circumscribed and exhibits growth characteristics of an adenocarcinoma. The mass is more extensive and exhibits growth characteristics of an adenocarcinoma. The mass is more extensive and exhibits growth characteristics of an adenocarcinoma.
Secretions were taken for study for tumor cells, and the report was obtained that the sputum contained "many fat-laden macrophages." The patient was discharged home again on March 27, 1948.

She was readmitted on October 10, 1948 with a diagnosis of a chronic interstitial pneumonitis and bronchitis. X-ray film on October 10, 1948 showed no change from the previous films. Because of the repeated bouts of pneumonia and the demonstrable bronchiectasis, the patient was transferred to the thoracic surgical service on October 24, 1948 with the idea of doing a lobectomy if possible. X-ray film on October 25, 1948 showed some extension of the infiltrative process. Patient was bronchoscoped on November 18, 1948 and a large amount of purulent sputum was seen in the left lower lobe bronchus. On November 29, 1948 the patient was taken to surgery and left thoracotomy was done. At that time the left lower lobe and the lingula of the left upper were found to be completely atelectatic. They were lightly attached to the surrounding structures by fibrinous adhesions which were easily divided. The lower lobe and lingula of the upper lobe were removed by the individual ligation technic, and the immediate postoperative condition of the patient was good. The remaining lobe on that side expanded without difficulty with the use of an intercostal tube and underwater seal. On December 1, 1948 the postoperative film showed satisfactory reexpansion of the left lung and a clear right lung. Subsequent films on December 6 and 13, 1948 showed that the lung fields were in a satisfactory state. The pathological report on the resected lung tissue was pulmonary adenomatosis. On January 7, 1949 x-ray examination of the chest showed some infiltrate in the upper lobe on the left and subsequent films showed that this process spread to the right base, as well as becoming more extensive on the left. About the middle of January 1949, the patient began to complain of some shortness of breath and began to raise large amounts of clear mucoid sputum. This amount of sputum gradually increased and the shortness of breath increased, in spite of bronchial drainage measures to help keep the bronchial tree clear. The patient was discharged home however February 26, 1949 with the family understanding that the pulmonary adenomatosis had already spread and the patient's eventual outlook was hopeless. The patient was followed in the out-patient department by periodic x-ray films which showed a gradual but progressive increase in the infiltrative lesions in both lungs. On April 5, 1949 the x-ray department asked permission to start some x-ray therapy to the chest to see if the spread of the adenomatosis could be checked, and the patient received 1,000 r through air to an anterior and posterior port over the left lung between April 5 and 14, 1949. There was no improvement in the patient's symptoms during this course of therapy.

The patient was admitted again to the John Gaston Hospital on April 25, 1949 because of the increasing shortness of breath and increase in sputum. There was no pain. Examination showed coarse rales over the left lung with dullness. Her course was one of gradual decease in strength. The patient continued to raise large amounts of clear mucoid sputum, as much as 500 cc. for 24 hours, and died on May 19, 1949. Permission for autopsy was not granted.

**SUMMARY**

The pathology, clinical diagnosis and treatment of the various primary pulmonary neoplasms is discussed.
A list of these tumors encountered in our practice and gleaned from the literature is presented and the principle pathologic characteristics of each is described. The actual or potential malignancy of almost all of them is emphasized.

An attempt is made to stimulate the physician’s suspicion of the presence of a bronchial or pulmonary neoplasm early in the disease, and a routine of examinations is proposed to reveal the diagnosis as early as possible. Special factors to be observed during the course of the examinations are mentioned. The manner in which carcinoma of the bronchus may simulate pulmonary tuberculosis or “virus pneumonia,” or be masked by associated pulmonary suppuration, is emphasized, and examination for bronchial neoplasms is urged before a long time is expended applying the many chemotherapeutic and antibiotic drugs.

The extent of resection necessary for the complete extirpation of the various primary pulmonary neoplasms is discussed, and measures to make life more endurable for those patients whose tumors are inoperable are described.

Illustrative case histories are presented, and one new case of alveolar cell carcinoma of the lung is reported.

RESUMEN

Se discute el diagnóstico anatomo-patológico, el clínico y el tratamiento de los tumores primarios pulmonares.

Se presenta una lista de los tumores encontrados en nuestra práctica y referidos en la literatura y se describen las características de cada uno. Se recalca la malignidad presente o la potencial de todos ellos.

Se intenta estimular la sospecha del clínico acerca de los tumores pulmonares, de manera temprana y se propone una serie de exámenes de rutina para ese diagnóstico oportuno. Se mencionan los factores especiales que se observan durante la investigación.

Se insiste en la manera como el carcinoma puede simular la tuberculosis pulmonar o la “neumonía de virus” y puede enmascararse por la supuración y se hace énfasis en la necesidad de investigar las neoplasias bronquiales antes de que transcurra mucho tiempo empleando las numerosas drogas químicas y antibióticas.

Se discute la extensión de la resección necesaria para la extirpación completa y se describen las medidas que han de tomarse para hacer la vida más duradera y soportable a los inoperables.

Se presentan historias clínicas demostrativas y se presenta un nuevo caso de carcinoma de células alveolares del pulmón.
REFERENCES