OFFICE DIAGNOSIS AND MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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PREFACE

The term "Chronic Obstructive Pulmonary Disease" (Lung Disease, Airway Disease, Airflow Disease), or COPD is widely used to describe a syndrome in which the major symptom arises from difficulty in moving air through the intrathoracic airways. The term is useful and descriptive shorthand, but unfortunately it serves to conceal the fact that within this syndrome there are a number of different diseases, of different etiology and prognosis that require different treatment. There is a danger that the label COPD attached to a patient may lead to a standard therapeutic approach, which denies him specific and valuable therapy, while he suffers through forms of treatment that have no value.

It is not possible to design rational therapy for any individual unless his disease is carefully defined. In the process of defining and understanding the disease mechanism, it often becomes clear that many conventional and widely-used methods of treatment are not only of no possible benefit, but actually may be harmful. In many cases of COPD, good treatment is not available at the present state of knowledge, but it is important that valueless treatment be withheld.

The initial assessment of each case is usually made in the office setting. The patient may present at any stage of the illness, from the earliest stages, when diagnosis is difficult

because of the paucity of signs, to the more advanced stages of respiratory failure, when diagnosis is hidden by an excess of signs. In nearly all cases, however, the underlying disease processes may be sorted out accurately by the simple and time-honored methods of history taking, physical examination, and chest radiography. Access to a pulmonary function laboratory is useful, but not essential; the laboratory helps to confirm clinical impressions, to quantitate disability, and in a few carefully chosen cases, to advance diagnosis, usually by special methods. Other laboratory tests are seldom useful in diagnosis, although obviously valuable in staging, management, and exemplary care.

I would like to express my appreciation to Miss Jacqueline Heda who prepared all the line illustrations for the book.

Toronto, Canada Geoffrey M. Davies

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CHAPTER 1 DEFINITIONS

The more frequent types of generalized obstructive airflow diseases are classified in this chapter, together with some explanation of the underlying pathology. In order to understand the mechanisms of disease, it is necessary first to define a few commonly used, or misused, terms.

Bronchus (Fig. 1–1). A bronchus is an airway having plates of cartilage in its wall. In the normal lung these airways also contain mucous glands, which secrete a mixture of acid and neutral mucopolysaccharides, together with a dilute electrolyte solution.

Trachea (Fig. 1–1). The trachea is a bronchus formed of hoops of cartilage, the posterior wall being unsupported. This structure continues into the main bronchi. The membranous wall may invaginate if the intrathoracic pressure is raised, and this may lead to some airflow obstruction.

Bronchiolus (Fig. 1–2). A bronchiolus is any airway distal to the last plate of cartilage, its wall being unsupported. In the normal lung, these airways contain no mucous glands, the small amount of mucus present comes from goblet cells.

The number of generations of each type of airway varies with the length of the segment. In a long segment (e.g., posterior basal) there may be as many as 24; in a short segment (e.g., medial segment, right middle lobe), as few as 15. Of these, a little more than half are bronchi.

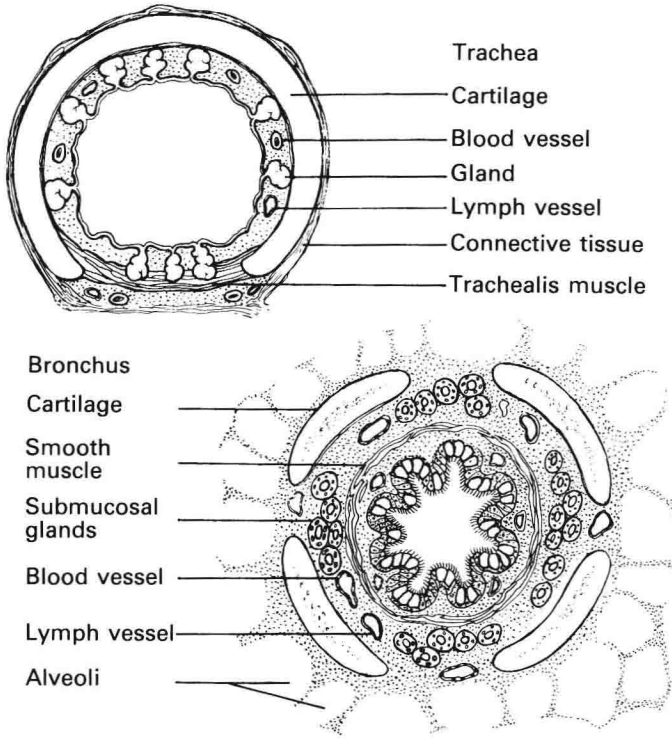

Fig. 1–1. Bronchus and trachea in cross section.

Terminal Bronchiolus. This is the smallest and most distal bronchiolus with an intact and uninterrupted respiratory epithelium. Each supplies a portion of lung tissue called an acinus.

Respiratory Bronchiolus (Fig. 1–2). This is a short, quickly branching airway within the acinus lined by respiratory epithelium interrupted by alveolar outpouchings. About 40% of the alveoli arise from this system. There are 5 to 8 generations of respiratory bronchioli within each acinus.

Alveolar Duct. This is an airspace within the acinus from which alveoli open, with no well-defined structure.

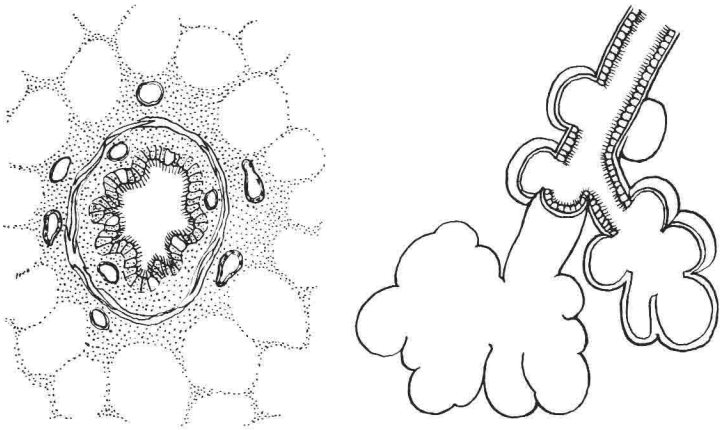

Fig. 1–2. Bronchiolus and respiratory bronchiolus.

Acinus. This is the portion of lung supplied by a terminal bronchiolus, and is the fundamental lung unit. There are some 15,000 acini in the lungs.

Alveolus. The alveolus is a blind-ending sac, lined by surfactant solution to stop it from collapsing from its own surface tension. Its wall consists of a double layer of structural cells enclosing a small space nearly filled by pulmonary capillaries. Each alveolus is about 200 μ in diameter and there are about 300 million in the young adult's lung. Alveoli atrophy with age, so that in a healthy 70-year-old there are less than 100 million.

Respiratory Epithelium. The airway tree is lined with ciliated columnar epithelium lying on a layer of basal cells, which are the parent cells. These lie in turn on a basement membrane. There are many other cells within the epithelial layer, notably the goblet cells, which secrete some of the mucus, and the APUD cells of neural crest origin, which may be the source of small cell tumors. The epithelium of the bronchi is pitted by rows of orifices of mucous gland ducts.

CLASSIFICATION

Within the group of diseases causing generalized airflow obstruction and known as COPD, there are several distinct entities, some well defined, some poorly defined. A suggested classification is as follows:

1. Diseases of Bronchi
   a. "Inflammatory"—chronic bronchitis
   b. Obliterative—bronchitis obliterans
   c. Reactive—asthma

2. Diseases of Bronchioli
   a. "Inflammatory"—chronic bronchiolitis and bronchiolitis obliterans
   b. Inflammatory but Specific—cystic fibrosis
   c. Reactive—asthma

3. Disease of the Lungs
   a. Emphysema

In addition, there are a few unusual diseases of the airways that cause multiple localized bronchial obstructions, such as amyloid disease and bronchostenotic sarcoidosis. These conditions will not be discussed.

In practice, the commonly encountered conditions are: chronic bronchitis, bronchitis obliterans, asthma (early onset, late onset), cystic fibrosis, and emphysema.

Chronic bronchiolitis, as a distinct entity, is not well recognized, probably because of the difficulty in diagnosis. It accompanies chronic bronchitis, and may be present in some industrial pulmonary diseases (e.g., asbestosis, and grain-workers' lung), but at this time does not merit separate discussion. The problems encountered in diagnosing bronchiolar disease are mentioned under "Bronchiolitis Obliterans," in this chapter.

PATHOLOGY AND PATHOGENESIS

Chronic Bronchitis

Chronic bronchitis is a disease of unknown etiology. It occurs more frequently in men, in city dwellers, and in temperate climates, and most often in heavy smokers. It may occur particularly in certain industrial settings and localities. It may occur in nonsmoking country-dwelling females, but is rare.

The accepted definition concentrates on the excessive mucus production; chronic bronchitis is diagnosed when sputum is coughed up for more than three months of two successive years. This focuses attention on the mucous glands and goblet cells, and is useful clinically, but chronic bronchitis may be present without mucus production, especially in *ex*-smokers.

Pathologically there is hypertrophy and hyperplasia of the mucous glands; that is, they are larger and more numerous, and extend into the larger bronchioli. The bronchi are narrowed, inflamed, and superficially ulcerated. There is patchy loss of respiratory epithelium, with denuded basal epithelium and areas of squamous metaplasia. The surface of the airways is pitted with dilated and ectatic mucous gland ducts. In other areas the mucosa is swollen and velvety, or hyperemic and fragile. There is an excess of mucus in the larger airways, which is detached from the surface with difficulty. Airway smooth muscle is hypertrophied and the airways are hyperreactive, often closing down on coughing. The bronchioli are also affected, showing inflammation, plugging, and sometimes obliteration. The alveolar tissue is not directly affected.

Because total airway cross section is least in the large airways, encroachment on the lumen is most important at large airway levels, especially in the region of the segmental and lobar bronchi. Involvement of large numbers of small airways is less obvious because of the considerably greater cross section (at terminal bronchiolar level, about 400 times that of the trachea). In the presence of bronchitis, bronchiolitis is difficult to diagnose.

While the mucus in chronic bronchitis is sometimes infected, infection is not an etiologic factor. Some patients run the entire course of bronchitis without ever having an infection. Bacterial infection of the mucus is a complication of chronic bronchitis.

Bronchiectasis (Bronchitis Obliterans)

Bronchiectasis is present when the normal distal tapering of a bronchus does not occur, and there is actual airway widening, usually locally. Ectasia is actually a secondary phenomenon and does not reflect the true pathology, which is total occlusion of the bronchus.

In allergic aspergillosis, local ectasia of a bronchus may follow local airway damage by the fungus-containing plug. After the plug has been cleared, a bronchogram may show a short segment of dilated airway, with normal airways proximal and distal (Fig. 1–3). The effect of this lesion on function is

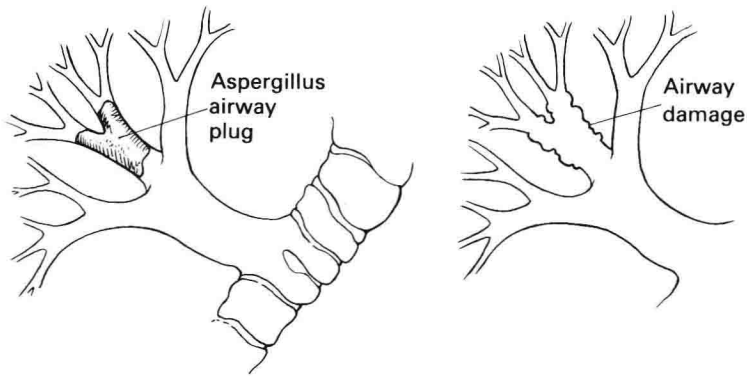

Fig. 1–3. Local airway damage in allergic aspergillosis.

trivial. In some cases the distal airway remains plugged and becomes obliterated, which is serious and leads to troublesome symptoms.

The initial pathologic event in bronchiectasis, then, is bronchitis obliterans, often occurring early in life, especially in

the course of an acute bronchitic illness like pertussis or measles. Multiple mucous plugs form in the bronchi, and a small, sick child may not clear all of them. As the acute illness subsides, the child apparently returns to normal, but in some bronchi the plugs remain and eventually organize to leave fibrous obliteration of the bronchi. The lung distal to the blocks does not collapse as cross ventilation is extensive.

The child is then left with a number of blind-ending tubes, and as they are bronchi, mucus is constantly secreted into them. There is no airflow through the tubes to facilitate mucus clearance, but the mucus is still moved into the airstream, perhaps by cilial activity, or perhaps because children are active creatures who ventilate and move about doing somersaults or standing on their heads tipping the secretions out of the tubes. It is usually later on, often in early adult life, that the stagnant mucus becomes infected, and the next series of changes takes place. Chronic low-grade inflammation damages the mucosa, ulcerates the ciliated epithelium and stimulates more mucus secretion. The inflammation then involves the airway wall, which starts to bulge, and the typical sac-like structure of bronchiectasis is formed (see Fig. 1–4). This creates even more room for infected mucus to accumulate, and the symptoms of the disease follow.

Because the initiating illness is a generalized disease, the resulting bronchiectasis is also widespread and patchy, involv-

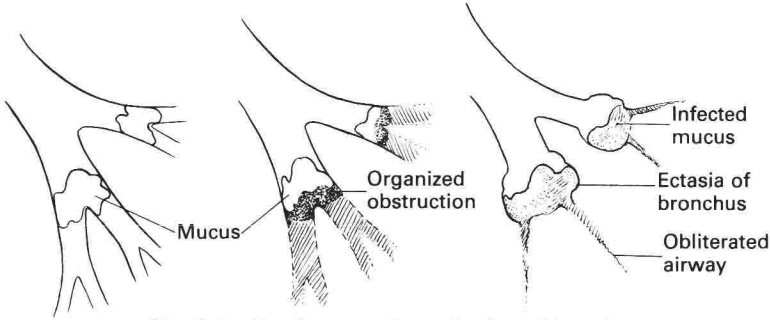

Fig. 1–4. Development of saccular bronchiectasis.

ing multiple segments of both lungs. It is therefore rarely that surgical resection of damaged lung is curative.

Bronchiectasis involving the lower portions of the lungs is always more troublesome, as the upper airways drain themselves whenever the patient sits or stands. The mucus in the dependent airways must be raised against gravity, and so is more likely to accumulate and become infected.

Other conditions may obliterate bronchi; these include destructive pneumonias in the adult and particularly pulmonary tuberculosis. Fortunately pulmonary tuberculosis usually affects the upper parts of the lungs, so that the resulting bronchitis obliterans may well be asymptomatic. Severe progressive pulmonary fibrosis may cause bronchiectasis in the late stages. Foreign bodies aspirated into the airways, if not rapidly cleared, may damage and obliterate the bronchi, and may occasionally damage only one portion of lung so that curative resection may be possible, but this is rare.

Primary tuberculosis may cause right middle lobar collapse in young people, the mechanism being tuberculous ulceration of the proximal part of the lobar bronchus by an invading hilar gland. If the lobe remains collapsed for a long time, as is often the case, the more distal bronchi may become damaged, so that when the tuberculosis eventually heals and the lobar bronchus reopens, the reexpanding lobe contains some obliterated airways. The secondary changes of bronchiectasis may follow, which is another unusual example in which the bronchiectasis may be expected to be localized.

As a rule, however, bronchiectasis is a widespread patchy disease affecting both lungs, and is not amenable to surgery.

Bronchiolitis Obliterans

A similar obliterative process may occur in bronchioli. These airways, however, do not secrete mucus in any quantity, being devoid of mucous glands. The damaged airways may give rise to no symptoms at all, and consequently the true incidence of this disease is not known; it is only when it is extensive that it may be clinically significant.

The history of the description of bronchiolitis obliterans is

interesting. In the early 1960s, McLeod, Swyer and James, independently sought the explanation for the radiologic condition of unilateral transradiancy, in which one lung looks darker than the other on chest radiographs. They found that the transradiant lung was smaller and failed to empty on expiration, indicating obstruction, but the bronchogram was apparently normal, although the contrast failed to pass into the distal airways. The pulmonary artery on the affected side was small, and at this point it was believed that hypoplasia of the pulmonary artery was the etiology. Pathologic investigation, however, showed extensive bronchiolar obliteration on the affected side, with emphysematous lung tissue. The true cause is bronchiolitis obliterans occurring in childhood during the stage of alveolar multiplication (effectively during the first three years of life), so that the affected lung shows maldevelopment of the alveoli in terms of number and the artery follows suit. Again the damaging disease is likely to be measles, pertussis, or severe viral bronchitis. As the underventilated lung is also underperfused, there is no mismatch and the child may have no obvious symptoms, although he has only one functioning lung.

It soon became clear that unilateral disease is the exception, and patchy bilateral involvement is more frequent. In the childhood disease, the patchy emphysematous changes may draw attention in later life, but if the obliteration occurs over the age of 5 years, the alveolar maldevelopment does not take place and diagnosis will be missed.

In the adult, acute viral illness may often cause acute bronchiolar inflammation, which usually subsides without permanent damage; however, sometimes there is obliteration of some airways. If this is extensive, lung function may be affected and the patient rendered permanently short of breath; sputum production is not a feature.

Acute exposure to certain toxic gases, such as chlorine, acid fumes, and smoke inhalation may damage the bronchioli and may possibly cause permanent obliteration, but this is hard to prove. The accompanying damage to the bronchi is often more dramatic and hides the bronchiolar disease.

Rarely an obliterated bronchiolus may dilate and become

ectatic. Because the wall does not contain cartilage and is more compliant, the ectatic sac may be large, often more than 1 cm in diameter.

Many pathologic studies have shown that chronic bronchiolitis is frequent and found in many lung diseases. It is invariably present in chronic bronchitis, for instance, but physiologically is overshadowed by the damage to the large airways. In pneumoconiosis, especially in asbestosis, the small airways may be the primary site of injury, and in pulmonary fibrosis of any cause, the bronchioli are affected early and profoundly.

Attention is turning more and more to the smaller airways, partly as early markers of pulmonary disease, and partly because of the role they must play in the redistribution of gas flow within the lungs. They prove to be peculiarly difficult to study, but progress is being made. Chronic bronchiolitis will eventually become a frequently diagnosed condition, whether it is present in isolation or part of a generalized inflammation of the airway tree.

Cystic Fibrosis

This autosomal recessive disease affects about 1 in 2000 live births. The literature is extensive, and I do not propose to review the theories of the pathogenesis. All exocrine glands are affected, with a failure to reabsorb sodium from the gland tubule, so that the pancreas, the intestinal mucosa, the salivary glands, the sweat glands, the bronchial glands, and the liver are affected. Diagnosis is confirmed by finding excessive amounts of sodium and chloride in the sweat.

In the lungs, the major effects are on the bronchioli and bronchi; chronic infection of the airways occurs at an early age. The most characteristic lesion is a bronchiolar abscess, a small pus-containing dilatation of an occluded bronchiolus, which occasionally dilates to a size of 1.5 to 2 cm, and then discharges leaving an empty cyst. Staphylococcus, and in later life, Pseudomonas are common pathogens, although other organisms are frequent as well.