Chronic Obstructive Pulmonary Disease

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COPD AND THE PERIPHERAL CIRCULATION

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease that affects the respiratory tract, produces persistent airflow limitation, and may eventually cause breathlessness and inadequate oxygenation. It is one of the most common conditions seen by physicians, occurring throughout the world. It is a major cause of death and disability in adults. Smoking causes most cases of COPD, but other factors, such as air pollution, occupational exposure to injurious material, and infections contribute to the occurrence and progression of the disease. Abstinence from smoking will stop COPD, but will not reverse the condition. However, new ways of treating COPD patients who have the disease at varying levels of severity are continually being reported.

These new therapies include agents with improved efficacy and fewer side effects; new methods of drug administration; and more novel methods of drug administration developed from recent studies of the cellular and subcellular mechanisms underlying COPD, and from investigations of the respiratory muscles and neurons.

The main function of the respiratory system is the transfer of O_2 and CO_2 from the body to the atmosphere. This process is vulnerable to injury at many points. Gas exchange takes place in alveoli, which are encased in muscular bellows driven by neurons in the medulla. The supply of air to the alveoli depends on the motion of these bellows. Air and blood are conveyed to the alveoli by a branching system of delicate and rather compliant tubes that enlarge and shrink with the movement of the bellows. Because the bellows themselves are mounted on the extremities, gas exchange must continue as the extremities move and must remain compatible with the changing metabolic demands created by contraction of the muscles that power the extremities. Breathlessness occurs when the metabolic demands of these muscles are not satisfied. The air brought into the lungs is contaminated with chemicals and microbes that can injure them, but elaborate defenses are in place in the respiratory tract to filter and remove these dangerous elements. In addition, white blood cells in the blood (e.g., polymorphonucleocytes, macrophages, and lymphocytes), which secrete antibodies and enzymes, can be mobilized in times of need to defend the respiratory tract. However, the defensive reactions themselves, unless controlled, can lead to lung injury.

COPD is the disease that most frequently produces long-term derangements in gas transfer. Although emphysema and bronchitis are the commonest forms of COPD, a number of other diseases, such as asthma, bronchiectasis, and cystic fibrosis, can also affect airway caliber and produce airflow limitation. Because these diseases differ considerably in their treatment and prognosis from emphysema and bronchitis, it is important to accurately diagnose them and distinguish them from COPD. This may be difficult at times, because the effects of neither emphysema nor bronchitis are anatomically uniform, and thus each can cause the patient to present with a wide range of symptoms and functional abnormalities.

Humans differ in their susceptibility to respiratory injury. For example, only about 15 per cent of smokers develop significant airflow limitation. This range in vulnerability can be partially attributed to a genetic basis. Molecular techniques promise to provide accurate methods for detecting individuals who are particularly likely to develop respiratory injury, and they offer hope for the development of techniques that can compensate for genetically based increased susceptibility.

Because levels of CO_2 and O_2 are important to the operation of all organs and not just to the lungs, severe COPD can have serious systemic effects, affecting the heart, kidneys, and brain, and ultimately most organs of the body. Conversely, diseases of the heart, kidney, and brain can exacerbate the effects of COPD on the respiratory system and further worsen gas exchange.

COPD is a treatable illness. There are many possible interventions that can help to prevent progression of the disease and relieve the adverse consequences of COPD. These include regimens that promote health, such as improved nutrition, physical training, and methods to relieve psychological stress. But there are also specific measures to widen airways, accelerate ciliary action, relieve the effects of inadequate oxygenation on the heart and pulmonary vasculature, and correct acid-base balance. Although it may not be possible to completely restore the airways and the alveoli to their normal state, carefully planned treatment will benefit most patients with COPD.

This volume brings together contributions from experts in different disciplines and is intended to present a comprehensive view of COPD, its causes, prevention, effects on the body, and current therapy. Each chapter presents a different facet of the disease and its relation to other diseases.

In addition to thanking the contributors, we would particularly like to acknowledge here the unflagging assistance of Ms. Anne W. Miller in all aspects of compiling and editing the contributions to this volume, and without whose help this book would never have reached completion.

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PATHOLOGY OF CHRONIC AIRFLOW OBSTRUCTION

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Airflow may be obstructed in the lung at several different sites, and at each site various lesions may be present. In any one patient there may be a combination in site, type, and severity of lesion.[108] It is thus a serious error to think that patients with chronic airflow obstruction can be neatly classified as having "chronic bronchitis," "small airways disease," or "emphysema." In many patients, perhaps the majority, the obstruction may be dominantly at one site; in a minority it may be limited to one site. In general, a wide spectrum of airway and parenchymal lesions is present in patients with symptomatic chronic airflow obstruction. For example, chronic productive cough (chronic bronchitis) increases in frequency as emphysema gets more severe; some 90% of patients with severe emphysema have chronic productive cough.[151]

RELEVANT NORMAL AIRWAY ANATOMY

For convenience of classification, it is appropriate to consider three major sites of chronic airflow obstruction: the large airways or bronchi, the small airways or bronchioles, and the gas-exchanging part of the lung, which is known as the acinus. Bronchi, by definition, are those airways that have cartilage in their walls, and they usually also have mucus-secreting glands deep into the surface epithelium. The important quantitative aspects of bronchi include that they have a modest number of generations (about four to ten, with a mean of seven), their length averages about 10 cm, and their total cross-sectional area increases from 2 cm^2 at the tracheal carina to 10 cm^2 where they terminate.[161] Another feature is that bronchi contain much smooth muscle, although proportionately this is less than in the succeeding airways. These are the membranous bronchioles that do not have cartilage in their walls, nor do they exchange gas since they have no alveoli in their walls. The number of divisions of airways in different bronchiolar pathways varies greatly.

In airways that traverse a long distance from the main bronchus to the periphery—axial pathways—there may be up to 25 bronchial and bronchiolar generations. An example of such a pathway would be to the parenchyma of the posterior basal segment. Other pathways have only a short distance to traverse, such as to the parenchyma of the medial aspect of the lung and these have as few as 10. These are known as spiral pathways.

The average summed length of bronchioles is approximately 1.8 cm and the total cross-sectional area increases from about 13.9 cm^2 to 281 cm^2.[161] The increase in total cross-sectional area of bronchioles has the important consequence that normally bronchioles contribute relatively little resistance to flow in the lungs. At one time it was thought that bronchioles contributed only 10% to 20% of total airflow resistance.[57] This had the important corollary that severe disease could be present in the bronchioles without making a serious impact on total flow resistance. The often-quoted example is that if half of the peripheral airways were obliterated, their resistance would double, but this would increase total airway resistance by only about 20%. Later data have suggested that resistance in the small airways probably contributes about 40% of total resistance[61, 68, 163]; this is in keeping with the model of asymmetric dichotomy of airways used for the quantitative data quoted here.[62] Weibel's model of symmetric dichotomy[164] produces data more consistent with the very low level of peripheral airway resistance first mentioned. This difference of opinion is of more than theoretic interest. The very low level of airflow resistance first quoted led to the notion that standard tests of pulmonary function, such as the forced expiratory volume in one second (FEV_1), might be normal in the presence of extensive peripheral airways disease. This possibility led to the proliferation of "tests of small airway function." The higher estimate of normal peripheral airway resistance suggested that these tests are of little relevance and that the FEV_1 adequately reflects abnormalities in peripheral airways.

CHRONIC AIRFLOW OBSTRUCTION AND MORPHOLOGIC CORRELATES

The term chronic airflow obstruction (CAO) is not intended to replace the term chronic obstructive pulmonary disease and has a different meaning. Chronic airflow obstruction is a simple physiologic abnormality, chronic diminished loss of expiratory flow defined in a particular way. Chronic obstructive pulmonary disease replaced the older term "chronic nonspecific lung disease," which comprised those conditions that are often, but not always, associated with CAO.[25] These conditions include chronic bronchitis, emphysema, bronchiolitis, bronchiectasis, asthma, and now rare but specific entities, such as rheumatoid bronchiolitis.

This chapter attempts to correlate various morphologic abnormalities in bronchi, bronchioles, and the acinus with chronic airflow obstruction (Table 1–1). Difficulty with interpretation of data should be recognized. Structural-functional correlations have been done mostly in three types of studies: (1) cases of patients with documented severe CAO, (2) lungs obtained at surgery for lung cancer, and (3) lungs subjected to post-mortem functional tests. Patients with lungs from the second group often have no CAO and seldom have more than