ADVANCES IN CARDIOPULMONARY DISEASES

VOLUME I

Selected Lectures from the 1961 Series of Postgraduate Courses Presented by the Council on Postgraduate Medical Education of the AMERICAN COLLEGE OF CHEST PHYSICIANS

ADVANCES IN CARDIOPULMONARY DISEASES

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Preface

RAPID ADVANCES IN MEDICINE call for critical review and assessment of available pertinent knowledge from time to time. This consideration has brought about a series of Postgraduate Courses sponsored annually by the Council on Postgraduate Medical Education of the American College of Chest Physicians, under the chairmanship of J. Winthrop Peabody, Sr., M.D.

From the wealth of new information presented at the Courses given in Chicago, Denver, Los Angeles, New York City and Philadelphia in 1961, a collection of representative lectures is being made available in this volume. As we see it, this book is bound to fill a gap between the teaching clinician and medical men interested in scientific progress as it applies to daily practice.

The philosophy of these lectures has been to appraise thoroughly current methods, to analyze new procedures and to evaluate new drugs and techniques with detached objectivity. With this in view, the presentations have been strengthened by the large clinical experience and sound judgment of the contributing authors and seasoned by their ingenuity and originality.

The material of this book has been prepared by leading specialists in pulmonary diseases, cardiology, thoracic and cardiovascular surgery, and pediatrics. There is a precise description of the pulmonary circulation and gas exchange at rest and on exertion. This is augmented by lucid discussion of lung function in pulmonary edema, bronchospasm, atelectasis, collagen diseases, fibrosis, sarcoidosis and obstructive emphysema. In another chapter, data are given relative to functional abnormalities of the lung, together with methods for their accurate measurements. The latter is correlated with specific and adjunct therapeutic procedures.

Pediatric subjects are considered in chapters which deal with infant resuscitation and with respiratory distress syndrome of the newborn (hyaline membrane disease).

Air pollution in its relation to the respiratory tract and the cardiovascular system is assayed in considerable detail. Due attention has been given to occupational as well as to general environmental hazards.

The increasing prevalence of obstructive emphysema prompted ample discussion of this subject. Pathomorphologic and pathogenetic aspects of its various forms are covered. Recent advances in its treatment have been appraised on the basis of vast personal experience and much original pioneering work of the contributing authors.

The alarming increase in the incidence of lung cancer has deemed it appropriate to include chapters on the diagnosis and treatment of this disease, as well as on the role of certain occupations in carcinogenesis.

A highly instructive chapter deals with pulmonary alveolar proteinosis, thesaurosis secondary to inhalation of hair spray, cholesterol pneumonitis, pulmonary eosinophilic granuloma, pulmonary hemosiderosis, diffuse bronchiolectasis (muscular cirrhosis of the lung), diffuse lymphangitic metastasis, Caplan's syndrome and other intriguing items.

In other chapters which cover cardiologic subjects, particular attention is given to arrhythmias, their diagnosis and differential diagnosis by ECG and phonocardiography. Also, there is thorough discussion of the symptomatology, physical manifestations, diagnosis, treatment and prognosis of dissecting aneurysm of the aorta, and nonpenetrating injuries of the heart and great vessels. Moreover, there is a critical review and casuistic illustration of modern methodology of open heart surgery in congenital, obstructive cardiac lesions. Too, there is an objective appraisal of the cardiovascular effects of occupational exposure to toxic substances.

Practical pointers are listed relative to the differential diagnosis and treatment of diaphragmatic hernias, with the author's illustrated case reports.

The importance of inhalation therapy, including IPPB and the use of aerosols with bronchodilators, detergents, enzymatic agents and antibiotics, is emphasized in various chapters.

In closing, we wish to say that the lecturers' methods and styles of presentation have been retained throughout the text so as to reflect their individual hallmarks and images as teachers and clinicians.

It is hoped that this book will serve as a useful guide in diagnosis and treatment as well as in the rehabilitation of the cardiopulmonary cripple.

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Oxygen Transport or Transfer in the Lung*†

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OXYGENATION OF THE BLOOD in the lung may be impaired at sea level on air breathing primarily because of: (1) abnormalities for diffusion in the pulmonary membrane or (2) the perfusion of blood through poorly or nonventilated lung areas, where some type of ventilation blockage (partial or complete) prevents the inspired air from getting down to all the perfused alveoli. It is estimated that there are over 700 million alveoli in the lung where air can come in contact with capillary blood. All of the alveoli are not open at any one time, as with a deep breath more alveoli may be opened up, and poorly ventilated alveoli may be improved as compared to rest. The mean alveolar P_{O_2} is around 100 mm. Hg, breathing air at sea level pressure, and the arterial blood coming from the left side of the heart has a P_{O_2} around 95 mm. Hg (a mean alveolar-arterial P_{O_2} difference of 5 mm. Hg), and this arterial P_{O_2} level corresponds to an arterial blood oxygen saturation of the hemoglobin of 96% or more in the presence of normal ventilation-perfusion relationships. Oxygen diffuses across the pulmonary membrane to combine with hemoglobin (oxyhemoglobin) in the pulmonary capillaries since there is a higher head of pressure for oxygen in the alveoli

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as compared to the blood in the capillaries. The oxygen molecules move from a region of higher concentration to a region of lower concentration (diffusion). The pulmonary membrane includes everything through which oxygen must diffuse from the air in the alveoli to combine with the hemoglobin in the red blood cells, namely: the lining membrane of the alveoli, the capillary lining membrane, the interstitial fluid between the alveolar and capillary membrane, the plasma and the outer membrane layer of the red blood cell. In order for oxygen to diffuse across the pulmonary membrane and provide a normal hemoglobin saturation, the inspired air has to get down to all the alveolar areas with a capillary blood supply.

SURFACE AREA FOR GAS EXCHANGE

The surface area of the respiratory alveoli has been estimated, if flattened out, to be from 75 to 100 square meters in man (about the size of a tennis court). Wilson *et al.*[1] report the ratio of the average cross-sectional area involved in diffusion to thickness of the respiratory membranes as 15–21 meters per micron. By virtue of the large surface area of exposure, the passage of the red blood cells through the pulmonary capillaries affords a maximal diffusion area for the oxygen to contact the hemoglobin. The thin pulmonary capillaries have been described as virtually hanging in space, thus providing the large surface area of contact for gas exchange for oxygen with the hemoglobin, as the red blood cells flow by in single file. The pulmonary bed provides very little tissue support of the capillaries, with most of the surface of the vessel available for gas exchange exposed to atmospheric pressure. The intimate contact of oxygen and hemoglobin as provided by the large alveolar surface area is necessary if all of the hemoglobin is to be converted to oxyhemoglobin on air breathing in the time exposed as the erythrocytes flow by, for once beyond the capillaries the piling up of red blood cells (four to five million per cubic millimeter) offers a mechanical barrier to complete saturation of all the hemoglobin, even though the oxygen tension of the plasma be adequate or even somewhat elevated.

ARTERIAL BLOOD REFLECTS GAS EXCHANGE IN LUNGS

The measurement of the arterial blood oxygen saturation in a systemic vessel (such as the brachial artery) reflects changes occurring in the lungs and, in conjunction with analysis of the expired air, permits

an evaluation of the type of changes which may be present in the lung. Arterial blood is the only type of blood of value in determining the gas exchange. The saturation of the hemoglobin with oxygen is normally 96–98% at sea level on air breathing, both at rest and with exercise. The slight reduction results from venous admixture in the passage of the blood through the lungs and heart. The normal mean arterial partial pressure of oxygen (Po_2) is 95 mm. Hg at sea level as measured by direct tension techniques, either the Riley bubble method or the Clark electrode. Wilson *et al.*[1] report that the normal average oxygen tension in the capillaries is 4.0 mm. Hg less than in the pulmonary alveoli, and that 0.01 of the blood flow through the lung normally does not perfuse oxygenating capillaries.

HEMODYNAMIC DIFFERENCES IN THE PULMONARY CIRCULATION, REST AND EXERCISE

The blood flow through the lung takes the path of least resistance, and selective diversion of the flow of blood occurs in regions with high vascular resistance as compared with areas with less resistance. Many patients with extensive lung disease as revealed by the chest roentgenogram, have surprisingly good arterial blood oxygen saturations at rest,[2] as the blood flow is diverted through the better ventilated and perfused areas. However, with mild exercise, gross abnormalities in the arterial blood oxygen saturation may be revealed with the increased cardiac output and the loss of the selective diversion of flow. In the evaluation of the blood gas exchange for oxygen or if significant hypoxia be present, the exercise measurements are frequently of greater importance than the resting. Rest and exercise represent two different hemodynamic situations even in the same individual, and studies on both aspects are necessary to obtain the essential information in pulmonary function evaluation.

VENTILATION-PERFUSION RELATIONSHIPS IN CHRONIC PULMONARY DISEASE

In chronic pulmonary disease there are four major types of impairment in the ventilation-perfusion relationships: (1) ventilation but no perfusion or impaired perfusion at the capillary level, (2) diffusion defect in the pulmonary membrane as the primary significant factor, (3) perfusion in the capillaries, but impaired alveolar ventilation and (4) perfusion in the capillaries but no alveolar ventilation.

Ventilation with Perfusion Impaired

Hypoxia is not produced in the first type consisting of alveoli which are normally ventilated but not perfused, or with the pulmonary blood flow markedly diminished, as results from fibrosis, thrombosis and other causes. However, the individual has to move air in and out of the non-perfused alveoli, increasing the work of breathing from which no benefit is derived. Also, the individual is unable to expand the pulmonary vascular bed and increase the pulmonary blood flow in a normal manner with mild exertion. The alveoli which are ventilated but not perfused actually constitute an increase in the dead space and decrease lung ventilation efficiency, as the percentage of oxygen extracted from the inspired air breathed is less. If the above type of defect was the only abnormality present, the arterial blood oxygen saturation would be normal.

Diffusion Defect in Pulmonary Membrane

The second type of abnormality consists of a generalized condition of increased resistance for the diffusion of oxygen through the pulmonary membrane, and this aspect represents the primary significant factor. A higher head of pressure is required to get the oxygen through the pulmonary membrane, so that the mean alveolar P_{O_2} of 100 mm. Hg (normal at sea level on air breathing) is inadequate to elevate the mean arterial P_{O_2} up around the normal value of 95 mm. Hg, and a significant reduction results in the arterial blood oxygen saturation. On air breathing, the mean arterial P_{O_2} may be as low as 55 mm. Hg or even less, especially with exercise (such a lowering would give an alveolar-arterial P_{O_2} difference of 45 mm. Hg). If a high oxygen breathing mixture (such as 32% oxygen increasing the inspired P_{O_2} by over 70 mm. Hg) is inhaled, the diffusion defect would be corrected immediately, as the head of pressure for oxygen in the alveoli is increased more than the mean alveolar-arterial P_{O_2} difference of 45 mm. Hg which exists on air breathing.

The use of high levels of graded oxygen breathing (30–40% oxygen) will not alter the structural characteristics of the alveolar-capillary membrane. Thus, it is not necessary to use 100% oxygen breathing to test for a primary diffusion defect. On the other hand, breathing a low oxygen mixture (such as 17% oxygen and decreasing the inspired P_{O_2} by over 25 mm. Hg) in a primary diffusion defect will markedly increase the hypoxia present, especially with exercise.

PERFUSION WITH IMPAIRED ALVEOLAR AERATION.

The third type of abnormality consists of poorly ventilated alveoli, where air gets in and out of the alveoli with difficulty due to some type of narrowing of the bronchi or the alveolar ducts, such as produced by edema, bronchospasm, fibrosis, atelectasis, mucus and secretions with or without infection. Even foreign substances such as iodized oil may produce a similar effect.[3] In the third type, the mean partial pressure of oxygen of 100 mm. Hg on air breathing at sea level is not maintained in the poorly ventilated alveoli, but may be reduced to 40 or 50 mm. Hg or more. The blood in the pulmonary capillaries perfusing the poorly ventilated alveoli can pick up oxygen only in proportion to the partial pressure of the oxygen in the poorly ventilated alveoli, and in the above case the maximal value for the P_{O_2} would be about 35–45 mm. Hg.

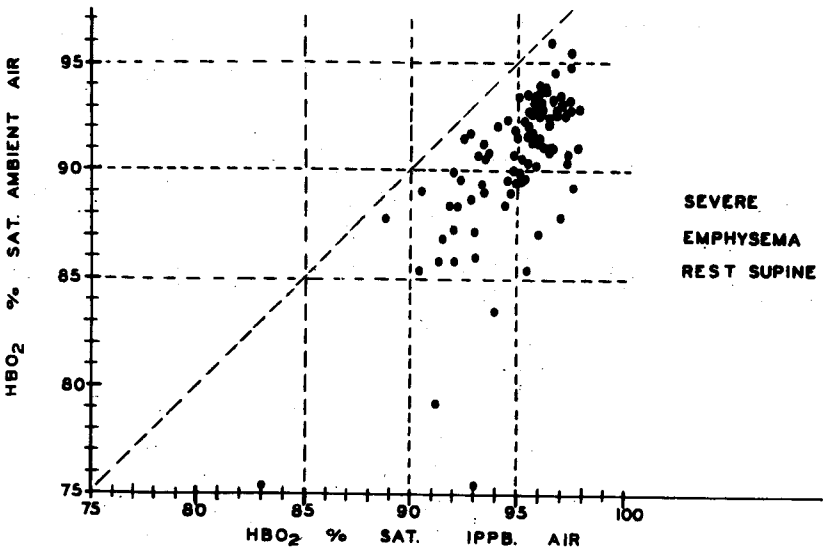

FIG. 1.—The arterial blood oxygen saturation in severe emphysema at rest was compared to changes produced by intermittent positive pressure breathing on compressed air. In every case, there was an improvement in the arterial blood oxygen saturation with the IPPB on compressed air only (no bronchodilators or oxygen). In a significant number of cases, the arterial blood oxygen saturation was normal, 96% or more on the IPPB on compressed air, and this would indicate the presence of many poorly ventilated areas which could be better ventilated with some assistance on inspiration. The IPPB provides a more uniform distribution of air for the poorly ventilated areas as compared to ambient breathing.

There is no diffusion defect in the pulmonary membrane in this type, rather a poor distribution of air to the alveoli with the oxygen getting across to the capillary blood in proportion to the partial pressure of oxygen in the various alveoli. If an individual with the above type of defect is given 32% oxygen to breathe, the high inspired P_{O_2} will eliminate the inequality of the ventilation and the arterial blood oxygen saturation will go up to a normal value of 97% or more. Also, with intermittent positive pressure breathing on compressed air only, in many of the poorly ventilated alveoli, the circulation of air is improved, increasing the mean alveolar P_{O_2} with a rise in the arterial P_{O_2} and blood oxygen saturation, in some cases to normal (Fig. 1). A similar response may be observed with voluntary deep breathing with a slow rate (9–10 per minute) and increased tidal volume, and in some cases the total minute ventilation may not be increased.[4]

Perfusion with No Alveolar Aeration

The fourth type of abnormality in ventilation-perfusion relationships consists of alveoli or lung areas completely cut off from the air supply, so that there is perfusion of blood but no ventilation, just the reverse of the situation of the first type, where there is ventilation but no perfusion. This type of abnormality actually constitutes a little right-to-left shunt, as the blood flows through these areas without contact with the air that is breathed in and out of the alveolar areas, and if this condition is extensive, severe hypoxia will be present. The use of 33% oxygen breathing in this type of case does not correct the hypoxia, especially with exercise, as the increased level of inspired oxygen (elevated P_{O_2}) does not get down to the areas where there is perfusion but no ventilation. The blood coming from the ventilated and perfused alveoli is already 100% saturated for oxyhemoglobin on air breathing. The increase in the amount of dissolved oxygen in the plasma is slight on 32% oxygen breathing as compared with air breathing and usually inadequate to obscure this small type of right-to-left shunt at the alveolar level. Intermittent positive pressure breathing will not improve the saturation, as the increased depth of breathing does not affect those areas which are perfused but not ventilated. The use of a low level of oxygen breathing (17% oxygen) in cases without significant emphysema also has very little effect (decreases the saturation about 1–2% less than obtained on air breathing and in the same range as observed in the normal), as the air does not get down to the areas which are perfused but not ventilated. However, at rest on 100% oxygen breathing, the arterial saturation

tends to be in the normal range of 99% or more in most cases, due to the increase in the amount of oxygen dissolved in the plasma on 100% oxygen breathing, almost 2 volumes per cent, and the Po_2 usually is over 400 mm. Hg. When small vessels are involved before the red cells are extensively piled up, one upon another, the high oxygen tension in the blood coming from the ventilated and perfused alveoli may oxygenate fully the hemoglobin perfused through the nonventilated areas when these small vessels come together.[5, 6] Once the red cells are stacked up, four to five million per cubic millimeter, there is an inadequate time and surface area for all the reduced hemoglobin to be changed to oxyhemoglobin; hence, on 100% oxygen breathing in a large right-to-left shunt, the brachial artery oxygen saturation is less than 95%. However, in small right-to-left shunts, at or near the capillary level, 100% oxygen may obscure or almost completely obscure this type of abnormality. The use of 30–40% oxygen provides an inspired Po_2 large enough to overcome a primary diffusion defect in the pulmonary membrane (so-called alveolar capillary membrane block) if that be the primary significant abnormality, but does not obscure the small right-to-left shunt, especially with exercise.

SEVERITY OF HYPOXIA EVALUATED FROM ARTERIAL SATURATION

When the rest or exercise arterial blood oxygen saturation is less than 96% on air breathing at sea level pressure, impairment in the oxygen transfer is present. The severity of the impairment depends on the extent of the lowering of the arterial blood oxygen saturation.[7] In general, a severe degree of hypoxia is present when the rest and exercise saturations are less than 92%, and a very severe degree with rest below 88% and with the exercise less than 85% at sea level on air breathing. A moderate degree of hypoxia is present when the saturation is between 92 and 94%. A saturation of 94–96% represents only a slight decrease. Accurate arterial blood oxygen saturations are essential for this type of classification and study. The arterial saturations were determined on the Van Slyke from oxygen contents and capacity measurements with duplicate checks on both. Oxygen capacity was also checked from the hemoglobin, using the Beckman DU spectrophotometer cyanmethemoglobin method. One Gm. of hemoglobin combines with 1.34 volumes per cent of oxygen. In addition, the saturation was measured on the (double scale) oximeter Cuvette (red-infrared) for whole blood, calibrated daily against the Van Slyke in each case. The arterial Po_2 was

determined by both the Riley oxygen bubble technique and the Clark electrode.

HYPOXIA PRESENT IN CHRONIC PULMONARY DISEASE

Arterial blood studies were done on a group of 137 cases of obstructive disease, 76 cases of both significant obstructive and restrictive and 83 cases with significant restrictive, but no emphysema as evaluated by lung volume measurements. A diagram of the average lung volume compartments in the above three groups of chronic pulmonary disease is given in Figure 2. The first group is the obstructive (emphysema), consisting of 137 cases in which the absolute volume of the residual air was above 200% in all cases (average 273%), and the ratio of residual air to total lung capacity above 50% in all cases (average 60%). The total lung capacity was increased and the total vital capacity decreased, although there existed wide individual variations in the latter. The average timed vital capacity for three seconds was 41% of the predicted normal vital capacity as compared to the observed total vital capacity, which was 67% of predicted. The maximal breathing capacity was decreased in a very pronounced degree. There was impaired mixing as measured by the nitrogen washout test employing the nitrogen meter with continuous recordings of each breath on oxygen breathing.

The second group consisted of 76 cases of both significant obstructive and restrictive disease (Fig. 2). There was pronounced prolongation of the rapid forced exhalation as revealed by the average timed vital capacity for three seconds of only 53% of predicted, as compared to the total vital capacity of 75% of the predicted normal. There was severe impairment in air distribution as evaluated by the nitrogen washout test with the nitrogen meter. The absolute volume of the residual air was increased in varying degrees with an average of 180% of predicted for the entire group. The ratio of residual air to total lung capacity was increased, with an average of 46% for the entire group. The average total lung capacity was 102% of predicted, although in some cases there was a significant decrease below the predicted value. In all cases, there was significant fibrosis as evidenced by the x-ray appearance, and in many of these cases a significant reduction in total lung capacity in spite of a marked increase in the absolute volume of the residual air.

In the third group, there was a restrictive condition present and the complete absence of emphysema as a significant factor. In most of these cases, the diagnosis was pulmonary fibrosis, although in a few cases (7) a diagnosis was made of sarcoidosis, pulmonary alveolar proteinosis and lupus erythematosus, either by scalene node biopsy, lung biopsy or