LUNG FUNCTION

ASSESSMENT AND APPLICATION IN MEDICINE

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PREFACE TO THE SECOND EDITION

In the last few years there has been a notable advance in our understanding of lung ventilation–perfusion relationships including regional function. There have also been steady if less spectacular developments in other aspects of the subject; these have included the mechanisms and consequences of airway closure, the role of the lung and of the chest wall in the control of breathing, the physiology of exercise, ethnic differences in lung function, aspects of acid–base balance and lung function in different medical conditions. There have also been improvements in instrumentation.

These advances are reflected in the present edition of *Lung Function*, which also includes 23 new diagrams and 10 new tables. In addition, some of the original diagrams have been redrawn or new material added; the charts illustrating normal values have been rearranged and extended and many references have been replaced by more recent contributions. The book retains its character as a combined theoretical text and practical manual, which it is hoped will continue to be of use to all who have an interest in the function of the lung, in particular to postgraduate students and physicians with an interest in thoracic and industrial medicine and all those who are concerned with the practical assessment of lung function.

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Mr R.T.Harris has prepared the photographs, Mr V.Lewis the large lung sections and Mr G.Berry the nomograms showing normal values in subjects of European descent, Miss M.Gregory and Miss A.M.Hall have sought out errors in the references and in the text, Miss M.D.Blick has prepared the manuscript and Mrs C.J.John the figures. Their skill, diligence and good humour have been of very great assistance. Any omissions or errors which remain in the book I acknowledge as my own and I cordially invite suggestions from readers as to how these may be put right.

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CHAPTER I

INTRODUCTION

THEME

The lung is the organ of external respiration whereby oxygen and carbon dioxide are exchanged between the body and the surrounding air. The function of the lung impinges upon consciousness partly through movement of the chest wall which is under voluntary control; this is related to the requirement for speech and to the use of the arms. Consciousness of the need for respiratory effort gives rise to breathlessness which occurs during exercise and in states of high emotion. It is also a feature of damage to the lung by a wide range of agents and may occur as a compensatory process in disease of other organs.

The overall function of the lung is dependent on that of the brain and spinal cord, the skeletal musculature, the circulation and the organs and tissues which influence the composition of the blood. The intrinsic function of the lung is a consequence of its structure and may be analysed at all levels of complexity by application of the techniques of physiology, biophysics, biochemistry and other sciences. The apparent simplicity of the lung, its accessibility and interest to research workers in different disciplines and the need for optimal function in a number of circumstances have stimulated research from many points of view. The requirements of military aviation and industrial and clinical medicine in particular have led to the development and application of new tools of great versatility and convenience. The techniques of electron microscopy, immunology and pathology, though they still have much to contribute, have also been used to good advantage. The outcome is an understanding of the function of the lung which, although incomplete, is probably more comprehensive than for any other organ.

It is now possible to present an integrated account in which each aspect of function is related in a simple manner to the physical characteristics and physiological responses of lung tissue. Due to the technical developments, the function of the lung may also be assessed simply and logically and with a reasonable prospect that the results from different laboratories will both agree and be interpreted similarly. The time has now come to consolidate these advances in a new book about the lung.

ABOUT THIS BOOK

This book summarizes current concepts of the function of the lung, including the control of respiration and the factors limiting exercise. The function is described in terms of structure and of the techniques by which it may be assessed at rest and on exercise. For this purpose the terminology that is employed and the equipment and its manner of use are described in detail together with other information of use to those setting up a laboratory. The results of assessment in normal subjects at different stages of life and the syndromes of abnormal lung function, with the circumstances in which they occur, are also described. There is a full account of oxygen therapy and an outline of other treatment. The bibliography contains a high proportion of recent references; these are chosen for their present usefulness and are subdivided into sections to which the attention of readers is drawn at the ends of chapters. By this arrangement the book provides both a theoretical text on the function of the lung and practical instruction in the performance of tests, the interpretation of the results and their application to healthy and disabled subjects. It is likely to be of use to practitioners and their colleagues in many branches of medicine as well as to students of physiology and human biology and those working for higher medical degrees. The chapters are relatively self contained, so readers may begin with those which interest them most; in most instances they will wish to obtain a balanced view by starting at or near the beginning.

EARLY STUDIES OF LUNG FUNCTION

The founders of experimental physiology are Erasistratus (*c.* 280 B.C.) and Galen (131–201) who between them demonstrated the role of the diaphragm as a muscle of respiration, the origin and function of the phrenic nerve and the function of the intercostal and accessory muscles. The function of the diaphragm was further explored by da Vinci (1452–1519) who observed that during inspiration the lung expands in all directions following the movement of the thoracic cage. The collapse which follows puncture of the pleura was described by Vesalius (1514–1564).

The need for fresh air was recognized by Galen who believed it reacted with the blood in the left heart and arteries to produce the 'vital spirit'. The absence of a visible communication between the pulmonary artery and the pulmonary vein led him to suggest that blood passed through invisible pores between the two sides of the heart; he therefore failed to appreciate the true function of the lung. The barrier to the passage of the blood imposed by the interventricular septum was recognized by Ibn-al-Nafis (*c.* 1210–1289) and Servetus (1511–1553) who, separately, proposed that blood passes from the pulmonary artery through the lung to the pulmonary vein. The demonstration by Harvey (1578–1657) of the circulation of the blood through the lung and by Malpighi (1628–1694) of the proximity of the capillaries to the smallest air spaces prepared the way for a better understanding of lung function.

The role of ventilation in maintaining life was demonstrated by Vesalius who was able to restore the activity of the heart in an apnoeic dog by insufflating air into the trachea through a reed. Hooke (1635–1703) subsequently showed that the essential factor is the supply of fresh air which he allowed to escape through puncture holes in the pleura after the lung had been exposed. Boyle (1627–1691), and to a lesser extent Mayow (1643–1679), demonstrated that the constituent of air which supports combustion also supports life. Lower (1631–1691) further showed that the uptake of air in the lung causes the blood to change colour. These discoveries laid the foundations for subsequent studies of gas exchange but their importance was not immediately apparent. The confusion was such that on 22 January 1666, after a meeting of the Royal Society on the subject of respiration, Samuel Pepys wrote in his diary, 'it is not to this day known, or concluded on among physicians . . . how the action is managed by nature, or for what use it is'. Many who have attended more recent scientific meetings must have come to a similar conclusion.

THE PAST THREE HUNDRED YEARS

Summary

The information about the lung which was necessary for the birth of respiratory physiology was available by about the year 1667. Thereafter aspects of the subject developed at different rates, reflecting their immediate interest and the techniques which were available for their investigation. In general the mechanical and biochemical aspects have proved more amenable to investigation than the control mechanisms. The interval between the development and the application of techniques for assessment has usually been short; however, many techniques are of comparatively recent origin and it is only during the last decade that they have been applied extensively to the study of human variability, the effects of exposure to noxious substances and the effects of disease.

The stroke output of the lung bellows or vital capacity was the first index of function to be investigated. It was measured in 1679 and was a fully developed test by the year 1846. At this time there was interest in the mechanical properties of the lung but progress was slow in the absence of suitable techniques for measurement; these have been developed and applied mainly during the past thirty years. The history of the dynamic measurement of ventilatory capacity is only a little longer. The exchange of gas in the lung was studied intensively during the period beginning about 1890. At this time new techniques were used to lay the foundations for subsequent work. Fundamental concepts of the distribution of gas in the lung and the implications for gas exchange of the relationship between lung ventilation and perfusion were also formulated at this time; the development during the past few years of powerful new techniques has led to further exploration of this important aspect of function. Recently the physiological and pharmacological responses of lung tissue have also been the subject of intensive scrutiny.

The mechanism whereby respiration is controlled has been

investigated during the second half of the period under review. Much information has been obtained but has proved difficult to interpret. However, as a result of the long period of development, the concepts are broadly based and highly sophisticated; they are likely to be further elaborated during the coming decade.

The development of the main subdivisions of lung function is described in rather greater detail in the following paragraphs. These require of the reader some knowledge about the lung and should be read in conjunction with the chapters where the subdivisions are described.

Lung volume

The volume of air which a man can inhale during a single deep breath was first measured by Borelli (1679). Subsequent work established that this quantity in an average adult is about 200–300 in^3 (3·3–4·9 l) at ambient temperature. The need for a temperature correction was pointed out by Goodwyn (1788). Thackrah (1831) showed the volume of air to be less in women than in men and to be reduced amongst workers in flax and other occupations due to the inhalation of dust. The measurement was finally put on a quantitative basis by Hutchinson (1846). He defined the *vital capacity* as 'the greatest voluntary expiration following the deepest inspiration' and designed a spirometer for its estimation. He showed that the vital capacity is related to the height such that 'for every inch of height (from 5 ft to 6 ft) eight additional cu. inches of air at 60°F are given out by forced expiration'. He further showed that the vital capacity decreases with age and is reduced by excess weight and by disease of the lung. The measurement of the residual volume by a gas dilution method was first performed by Davy (1800).

Lung mechanics

The role of the elastic recoil of the lung in causing expiration was demonstrated by Donders (1849) who was the first to measure the retractive force. This work was extended by Cloetta (1913). At about the same time Rohrer (1915) was applying the concepts of Newtonian mechanics to explain the relationship between the force exerted by the respiratory muscles and the rate of air flow.

This approach was extended by his successors, Neergaard and Wirz (1927), using the pneumotachograph of Fleisch (1925). Neergaard also demonstrated the role of surface forces in the lung by comparing the relationship of the lung volume to the retractive force when the air in the lung was replaced by water. Knowledge of the visco-elastic properties of the lung was extended by Bayliss and Robertson (1939), Dean and Visscher (1941) and Rahn, Otis, Chadwick and Fenn (1946).

Breathlessness and ventilatory capacity

The relationship of the vital capacity to breathlessness was considered by Peabody (1915) who also compared the ventilation during the inhalation of carbon dioxide with that during exercise. The use of the forced vital capacity was advocated by Strohl (1919). The role of changes in lung distensibility in causing breathlessness was explored by Christie (1934). The maximum breathing capacity was introduced as a dynamic test of lung function by Jansen, Knipping and Stromberger (1932), who calculated the equivalent minute volume from the kymograph record of a forced vital capacity. The measurement was first made during maximum voluntary ventilation by Hermannsen (1933).

Blood chemistry and gas exchange in the lung

During the eighteenth century the role of the lung as an organ of gas exchange was obscured by the belief of Lavoisier (1777) and others that it was the site of combustion. This was disproved by Magnus (1837) who used an extraction technique to analyse the gases in the arterial and venous bloods. The use of such data for the calculation of cardiac output was proposed by Fick (1870), whilst the true site of oxidation was demonstrated by Pflüger (1872). The techniques for analysing gases were improved by Haldane and described in *Methods of Air Analysis* (1899); an improved method for determining the concentrations in the blood was described by Haldane and Barcroft (1902). The tonometer methods for measuring the blood gas tensions were developed by Bohr (1890) and Krogh (1910) and further technical advances were reported by Peters and Van Slyke in *Quantitative Clinical Chemistry* (1932). The application of these and other techniques to human arterial blood was made possible through the introduction by Hürter (1912) of the procedure of arterial puncture.

The relationship of the pressure to the content of oxygen in the blood was explored by Paul Bert and described in *La Pression Barométrique* (1878); in this he showed that the pressure and not the concentration of gases in the atmosphere is of physiological significance. The oxygen dissociation curve was described by Bohr (1904); with Hasselbalch and Krogh (1904), Bohr showed that its shape is greatly influenced by the coexisting tension of carbon dioxide. Further advances were made by Barcroft and summarized in *The Respiratory Function of the Blood* (1914). The dissociation curve for carbon dioxide was described by Christiansen, Douglas and Haldane (1914) and the chemical reactions were further explored by Hasselbalch, Hastings, Roughton, Sendroy, Stadie and others. Some of this work is described by L.J.Henderson in *Blood: a study in general physiology* (1928).

The exchange of gas across the alveolar capillary membrane was considered by Bohr (1890). He found that the tension of oxygen was sometimes higher in the arterial blood than in the alveolar gas and concluded that oxygen was secreted by the alveolar cells. The measurements were in error but the hypothesis was supported by Haldane and Smith (1896–98) who, during inhalation of gas containing carbon monoxide, obtained differences between the observed and expected tensions of carbon monoxide in the blood which could best be explained by the secretion of oxygen. This view was opposed by Krogh and Barcroft, who believed (correctly) that the transfer of oxygen took place solely by diffusion. The controversy led Bohr to develop his integration method for determining the mean tension of oxygen in the pulmonary capillaries and to calculate the diffusing capacity of the lung for carbon monoxide. It also stimulated physiological expeditions to high altitudes, including those to Pikes Peak, described by Douglas, Haldane, Y.Henderson and Schneider (1913), and Cerro de Pasco, described by Barcroft in his second edition of *The Respiratory Function of the Blood.* Studies of conditions at high altitude were also undertaken by Dill, Christensen and Edwards (1936), Houston and Riley (1947) and others.

The distribution of gas in the lung was considered by Zuntz (1882) who introduced the concept of deadspace; this was first measured at post mortem by Loewy (1894). The deadspace for carbon dioxide was measured during life by Bohr (1891) as well as by Haldane and others who used the method of sampling the alveolar gas devised by Haldane and Priestley (1905). By this method Douglas and Haldane (1912) showed that the deadspace increased with the depth of inspiration, but the magnitude of the increase was disputed by Krogh and Lindhard (1913–14) who sampled the end tidal gas. Part of the increase was believed by Haldane to represent ventilation of the alveolar ducts and atria where the ventilation per unit of perfusion (i.e. the ventilation–perfusion ratio) is probably higher than in the alveoli. Haldane, Meakins and Priestley (1918–19) considered the effect of this imbalance between ventilation and perfusion upon the composition of the alveolar gas and the arterial blood. The application of these concepts to patients with lung disease was described by Meakins and Davies in *Respiratory Function in Disease* (1925). The subsequent development of the techniques of bronchospirometry by Jacobaeus (1932), of cardiac catheterization by Cournard (1942) and of regional assessment using radioactive gases by Knipping (1955) has resulted in a very comprehensive picture of this aspect of lung function.

Control of respiration

Knowledge of the central nervous regulation of respiration stems from the observations of Legallois (1812) and Flourens (1824) that a lesion in a small area of the medulla oblongata causes cessation of breathing. The location of the respiratory region was defined with increasing precision by many workers, including Lumsden (1923) and Pitts, Magoun and Ranson (1939). At an early stage Hering and Breuer (1868) separately showed that the region receives, via the vagi, sensory information on the distension of the lung. This provides the basis for a mechanism of self-regulation whereby the inflation of the lung tends to terminate inspiration and to initiate expiration whilst deflation of the lung has the opposite effect. The nervous activity in the fibres of the vagi was studied by Adrian