LECTURE NOTES ON
RESPIRATORY DISEASE

WRITTEN AND ILLUSTRATED BY

R.A.L. BREWIS

THIRD EDITION

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PREFACE TO THE THIRD EDITION

The aims and structure remain the same as in the previous editions but the whole text has been reviewed and updated, and seventeen new figures have been added. As a result the book has become a little larger. There are two new chapters—on Defences of the Lung and Cystic Fibrosis—and there has been expansion elsewhere to include topics such as the flow–volume curve, bronchoalveolar lavage, combination chemotherapy of small-cell cancer, long-term oxygen therapy and improvements in aerosol administration. The emphasis remains clinical and biased towards the commoner conditions so that, compared with previous editions, the book has become rather more of a clinical handbook in some parts. This seems to me to reflect the needs of the students and young doctors that I come into contact with—as well as my own interests! I am grateful to the students, young doctors and to many others for stimulation and encouragement.

R.A.L.B.

Newcastle upon Tyne, 1985

PREFACE TO THE FIRST EDITION

The aim of this book is to present a concise review of respiratory disease. In addition to offering the medical student an alternative to attending lectures it is hoped that this book might provide the MRCP candidate with his basic minimum requirements in the respiratory field and the more mature general medical reader with a painless refresher course.

The emphasis throughout is on information which is useful and relevant to everyday clinical medicine. In reviewing pulmonary physiology and the assessment of pulmonary function all unnecessary complexities, symbols and equations have been avoided and attention has been focused on concepts and investigations which are in everyday use. A number of rare conditions receive little or no mention but the practical aspects of management of the commoner disorders are dealt with in some detail.

Numerous teachers, colleagues, students and patients have played a part in the development of my interest in respiratory disease but I owe a particular debt to Professor Jack Howell for opening my eyes to some of the special fascinations of the subject. I am grateful to Miss Veronica Downey for help with typing; without her watchful eye on my other commitments it would have been impossible to attend to the business of writing. I am grateful to Dr Martin Farebrother for reading parts of the manuscript and to Mr Per Saugman for his encouragement and courtesy. I hope to express my gratitude to my wife and family by seeing a little more of them.

R.A.L.B.

Newcastle upon Tyne, 1974

CONTENTS

	Preface to the Third Edition	vii
	Preface to the First Edition	viii
1	Review of Anatomy of the Lung	1
2	Review of Respiratory Physiology	11
3	Surface Tension and Alveolar Stability	32
4	Defence Mechanisms Protecting the Lung	36
5	The History—Symptoms of Respiratory Disease	41
6	Examination of the Chest	45
7	Pulmonary Function Tests and Blood Gases	60
8	Elements of Radiology of the Chest	90
9	Acute Respiratory Infection	100
10	Pneumonia	106
11	Tuberculosis	121
12	Bronchiectasis	137
13	Cystic Fibrosis	144
14	Lung Abscess	152
15	Asthma and Allergic Disorders of the Lung	155
16	Diffuse Lung Fibrosis	202
17	Sarcoidosis	214
18	Chronic Bronchitis, Airways Obstruction and Emphysema	221
19	Carcinoma of the Bronchus	244
20	Pulmonary Embolism and Pulmonary Hypertension	262
21	Pulmonary Oedema	278

22 Pneumothorax and Pleural Effusion 288
23 Trauma and the Lungs 299
24 Occupational Lung Disease 304
25 Drug-induced Lung Disease 316
26 Hypoxia and Oxygen Therapy 322
27 Multiple-choice Questions 332
Appendix: SI Units of Pressure 374
Further Information 375
Index 381

CHAPTER 1 / REVIEW OF ANATOMY OF THE LUNG

The essential function of the lung is exchange of oxygen and carbon dioxide between the blood and the atmosphere. This takes place by a process of molecular diffusion across the alveolar membrane. A very large surface area is necessary to achieve this gaseous exchange—in an adult man it is estimated that the surface area of the alveoli is about 60 square metres. The structure of the lung represents an evolutionary solution to the problems of accommodating this huge membrane, moving air and blood to and from its surfaces and protecting it from external insults.

Surface anatomy

The position of the lungs and some useful external landmarks are indicated in Fig. 1.1. A few points are worthy of special mention.

1 The apices of the lungs extend well above the clavicles.

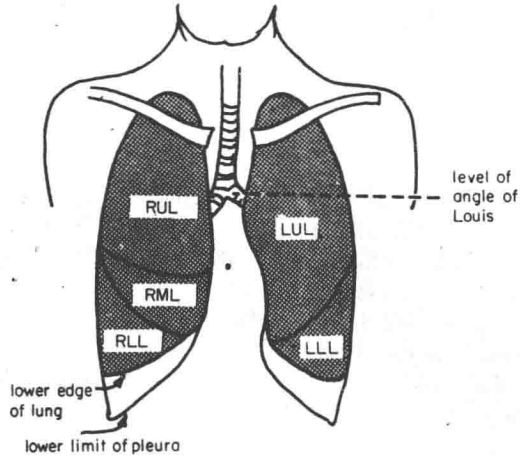
2 The posterior surface of the lungs extends further downwards than the anterior surface.

3 The upper lobes are situated *in front of* the lower lobes so that the lung immediately below the anterior chest wall is largely derived from the upper lobe and that beneath the posterior chest wall is mainly lower lobe.

4 The diaphragm, in its resting position, rises quite high into the thorax—a fact readily confirmed on any standard chest X-ray but commonly overlooked during examination of the patient.

Subdivisions of the lung

The lungs are divided into **lobes**—three on the right and two on the left—which are separated by slit-like invaginations of the pleural space. Each lobe has its own lobar bronchus. Each lobe is further subdivided by incomplete fibrous septa which extend inwards from the pleural surface into **bronchopulmonary segments**. Each bronchopulmonary segment is supplied by its own segmental bronchus and the usual arrangement of the segmental bronchi is shown in Fig. 1.2. Some pathological processes may be limited to particular segments which may be identified



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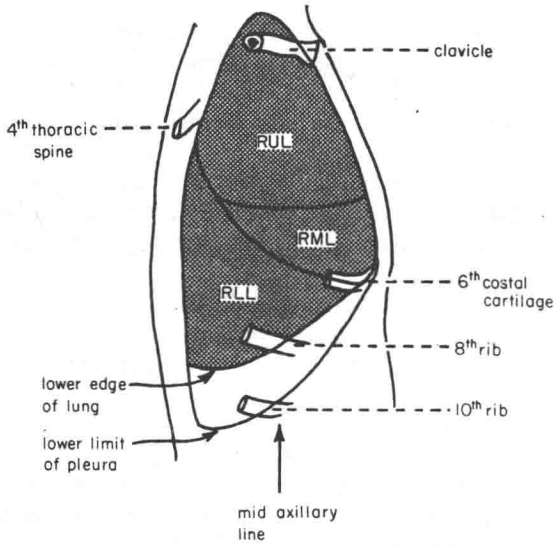

(b)

Fig. 1.1. ***Surface anatomy.*** **(a) Anterior view of the lungs. (b) Lateral view of right side of chest at resting end-expiratory position. RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.**

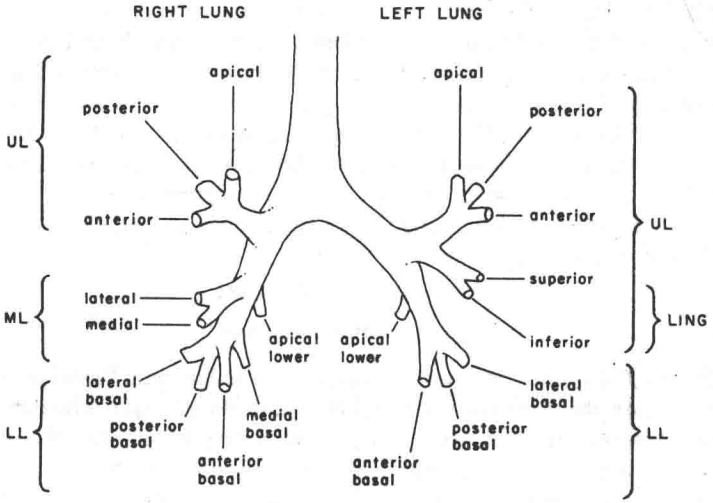

Fig. 1.2. *Diagram of bronchopulmonary segments.* UL, upper lobe; ML, middle lobe; LL, lower lobe; LING, lingula.

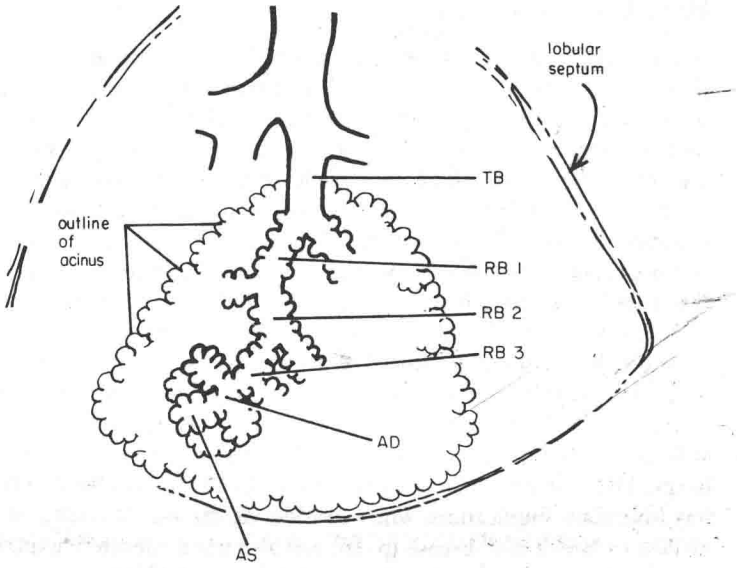

Fig. 1.3. *Diagram of the anatomy of the lobule.* The lobule lies within incomplete fibrous

radiologically. Smaller incomplete fibrous septa are present within each segment which outline individual **lobules**. Lobules are about 1 cm in diameter and of variable shape but generally they are pyramidal with the apex towards the bronchiole which supplies them. The anatomy of the lobule is illustrated in Fig. 1.3. Each lobule contains three to five **acini**, each supplied by a terminal bronchiole. Acini are sometimes visualized on the chest X-ray when they are filled with secretions or bronchographic contrast medium producing a blotchy appearance sometimes referred to as acinar pattern.

Branching of the airways

The trachea divides into two main bronchi. The left main bronchus is longer than the right and comes off at a more abrupt angle. The right main bronchus is more directly in line with the trachea so that inhaled material tends to enter the right lung more readily than the left. The main bronchi divide into lobar and then segmental bronchi as shown in Fig. 1.2. Further divisions occur in an uneven dichotomous fashion; that is, the branches at a division are not necessarily of the same size.

Bronchi and bronchioles

Bronchi are airways with cartilage in their walls. There are about 10 divisions of bronchi beyond the tracheal bifurcation. Smaller airways without cartilage in their walls are referred to as **bronchioles**. The term **respiratory bronchiole** refers to the peripheral bronchioles with alveoli in their walls. The bronchiole immediately proximal to the appearance of alveoli is known as the **terminal bronchiole**. The number of divisions between the bifurcation of the trachea and the terminal bronchiole varies between about 9 and 32. In general there are fewer branches to acini near the hilum and more branches to the peripherally-situated acini.

The total cross-sectional area of the airways increases at each subdivision so that it is enormously greater at, say, 14 divisions from the trachea than it is in the trachea itself (Fig. 1.4). This means that rate of airflow also diminishes strikingly as air penetrates more deeply into the lungs. This distribution of cross-sectional area and hence rate of airflow has important implications when considering the site of resistance to airflow in health and disease (p. 15) and also when considering mechanisms of deposition of inhaled particulate matter (p. 39).

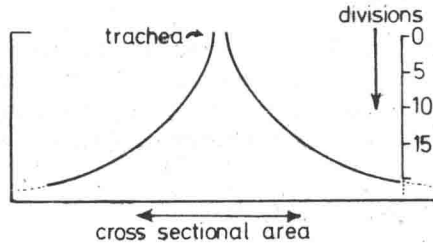

Fig. 1.4. *Diagrammatic representation of the increase in total cross-sectional area of the airways at successive divisions.*

Collateral ventilation

Holes in the alveolar walls known as pores of Kohn allow communication between parts of the lobule supplied by different respiratory bronchioles. There is a variable degree of communication at alveolar level between neighbouring lobules. Collateral ventilation through these communications is of importance in panacinar emphysema. In this condition they are increased in size and number as part of the parenchymal destructive process.

Pulmonary vasculature

Pulmonary artery

The pulmonary artery divides into left and right pulmonary arteries which provide branches accompanying the branches of the bronchial tree. The arteries accompanying bronchi are elastic but only have their muscular coats. The arteries accompanying bronchioles have well-developed medial muscular coats which become thinner peripherally. The arterioles accompanying terminal and respiratory bronchioles are thin walled and contain little smooth muscle.

Capillary network

The capillary network in the alveolar walls is very dense and provides a very large surface area.

Pulmonary venules

The pulmonary venules do not accompany the arterioles but drain laterally to the periphery of lobules and then pass centrally in the interlobular and intersegmental septa, ultimately joining to form the four main pulmonary veins which empty into the left atrium.

The bronchial circulation (Fig. 1.5)

Small bronchial arteries usually arise from the descending aorta and travel in the outer layers of the bronchi and bronchioles supplying the tissues of the airways down to the level of the respiratory bronchiole.

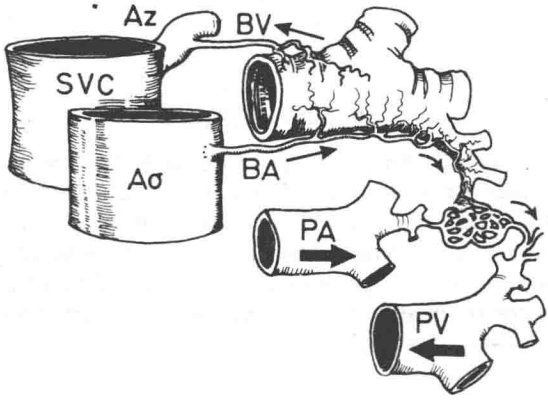

Fig. 1.5. *The bronchial circulation.* Three or more bronchial arteries (BA) arise from the aorta (Ao) and supply the bronchi down to the level of the terminal bronchiole. They also supply the vessel walls of pulmonary arteries (PA) and veins (PV). The bronchial supply to the large bronchi drains to the right atrium via bronchial veins (BV), the azygos or hemiazygos veins (Az) and the superior vena cava (SVC). Most of the bronchial arterial blood, however, drains to the left atrium via the pulmonary veins; there are plexuses linking the two circulations in the lung periphery.

Most of the blood drains into radicles of the pulmonary vein contributing a small amount of desaturated blood which accounts for part of the 'physiological shunt' observed in normal individuals. The bronchial arteries may be much enlarged in some diseases (e.g. severe bronchiectasis, pulmonary fibrosis).

Structure of the airways

Trachea

The trachea has cartilaginous horseshoe-shaped 'rings' supporting anterior and lateral walls. The posterior wall is flaccid and during coughing, when intrathoracic pressure is raised and the glottis opens, this soft posterior segment billows forwards reducing the lumen of the trachea to a U-shaped slit. This results in a high linear velocity of air-flow which produces a shearing effect, hastening the clearance of any excess of secretions. The trachea is lined with ciliated epithelium which contains goblet cells.

Bronchi

The bronchi have irregular plates of cartilage in their walls. Smooth muscle is arranged in spiral fashion internal to the cartilaginous plates and attached to them. The muscle coat becomes more complete distally as the cartilaginous plates become more fragmentary.

The epithelial lining is ciliated and includes goblet cells which become less numerous peripherally. Larger bronchi also have acinar mucus-secreting glands in the sub-mucosa. Hypertrophy of these glands is one of the more striking features of chronic bronchitis.

Bronchioles

The bronchioles have no cartilage in their walls. The muscular layer becomes progressively thinner peripherally but some strands of smooth muscle persist to the level of respiratory bronchioles and possibly beyond. Bronchial smooth muscle and bronchial innervation is considered on p. 157. The epithelium is made up of a single layer of ciliated cells with only very occasional goblet cells. A granulated cell known as the Clara cell appears in the wall of distal bronchioles and this cell is suspected of possessing secretory properties. It may contribute mucus to alveolar fluid making up the foundation of the mucous blanket which is propelled upwards by ciliary action.

Other cells are present in distal bronchioles which have a brush border. These are suspected of having a role connected with salt and water regulation of the fluid secretions passed upwards from the alveoli.

Ciliated epithelium

Ciliated epithelial cells possess about 200 cilia each 3–6 μm in length. Cilia beat with a whip-like action very rapidly (the beat frequency is about 20 per second), organized waves of contraction passing regularly from cell to cell. The structure of each cilium is complex. (Fig. 1.6).

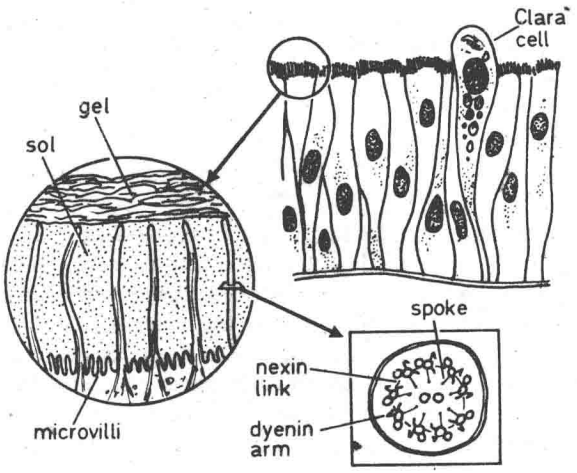

Fig. 1.6. *Ciliated epithelium in a bronchiole.* The cilia beat in the thin (sol) layer beneath the raft of sticky mucus (gel layer). The sol layer is about 5 μm thick and its water and electrolyte content is regulated by the brush border (microvilli) present on many cells. The main features of a cross-section of a cilium are shown in the rectangle. Cells are about 0.2 μm in diameter.

Normal cilia contain longitudinal tubules which are arranged as nine pairs of tubules in an outer circle with a pair of central tubules. The peripheral tubules are connected to each other by structures referred to as nexin links and to the central tubules by radial 'spokes'. One of each pair of outer tubules carries two additional links referred to as dyenin arms. These appear to be responsible for the contractile properties of the cilium. They are absent in some forms of the immotile cilia syndrome where there is gross deficiency of pulmonary mucociliary clearance.

Mucociliary clearance is discussed in Chapter 4.

Alveolar structure

Alveoli are about 0.1–0.2 mm in diameter and take up a variety of shapes depending on the arrangement of adjacent alveoli. The structure of the alveolar wall is represented diagrammatically in Fig. 1.7. The capillaries are completely lined by flattened endothelial cells resting on a complete basement membrane. The alveoli are completely lined by a layer of alveolar cells which are of two types.

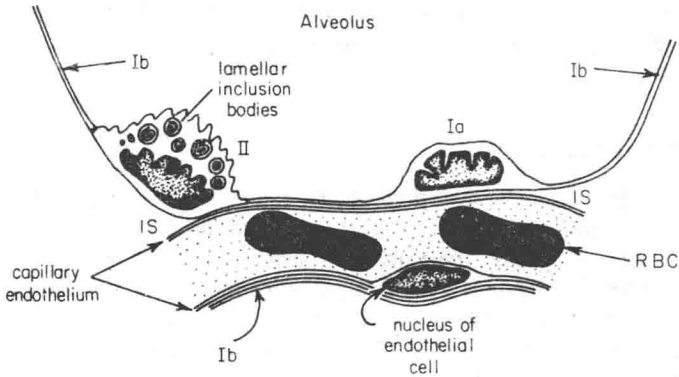

Fig. 1.7. *Structure of the alveolar wall as revealed by electron microscopy.* Ia, Type I pneumocyte; Ib, Flattened extension of Type I pneumocyte covering most of the internal surface of the alveolus. II, Type II pneumocyte with lamellar inclusion bodies which are probably the site of surfactant formation. IS, Interstitial space. RBC, red blood corpuscle. Pneumocytes and endothelial cells rest upon thin continuous basement membranes which are not shown.

Type I pneumocyte

These cells have extensive flattened processes which extend to cover most of the internal surface of the alveoli. Only the nuclei of these cells are evident on light microscopy.

Type II pneumocyte

These cells are less numerous and more globular than the type I pneumocytes. Electron microscopy reveals that these cells contain

bodies with a concentric lamellated structure. It is now generally agreed that these bodies are concerned with the manufacture or storage of surfactant and that the type II pneumocyte is the principal source of surfactant (p.32).

Alveoli contain phagocytic macrophages and other cells (p. 213).

Interstitial space

There is a potential space between the alveolar cells and the capillary basement membrane which is only apparent in disease states when it may contain fluid, fibrous tissue or a cellular infiltrate. It is continuous with the interstitial space surrounding bronchi and blood vessels (p. 280).

Lymphatic vessels

Lymphatic channels are present in the interstitial space. They accompany the bronchial tree at least as far as the level of the respiratory bronchioles and supply the walls of the airway as well as the pulmonary interstitium. Lymphatics are also found in the interlobular septa and are abundant beneath the pleural surface. Drainage of lymph is towards the intrapulmonary lymph nodes adjacent to the proximal bronchi (hilar lymph nodes) and thereafter to the mediastinal lymph nodes.