OCCUPATIONAL LUNG DISORDERS

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with a foreword by

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Foreword

The hazard of inhaling silicious material into the lungs has existed so long as man has required stone for building. The industrial revolution triggered an explosion in the demand for coal and steel and the hazard to health of those providing the raw materials and the manufactured products which transformed the world in the nineteenth century, was accepted at first with fatalism. The plight of many of these workers was gradually appreciated as the nation's social conscience was roused towards the end of the century.

The study of industrial diseases has always presented special difficulties and these have tended to isolate this branch from the common run of general medicine. Not only has detection of the exact nature of the damaging agents often proved extremely difficult when complex industrial processes involve multiple exposures, but conflicting pressures from both management and workers have often hindered and complicated scientific investigation. These understandable attitudes have not been eased by the additional pressures introduced by legislation and compensation.

Lack of understanding about occupational disease cannot, however, be excused entirely on these grounds and it is certainly due in large part to the complexity of the scientific problems themselves.

Understanding occupational medicine involves knowledge far beyond the training of most medical graduates and includes the study of geology, chemistry, and biochemistry, and a detailed understanding of a very wide range of industrial and engineering processes. Even within the field of medicine the range of skills is great and requires expert knowledge of radiology, pathology, epidemiology, physiology and immunology.

In the face of these far-reaching demands it is not surprising that the subject of occupational medicine has been left to the experts and the gulf between them and the general clinician has remained wide. The situation has been aggravated by the dearth of readable textbooks.

Against this background, it is particularly valuable to have a succinct and up-to-date account of occupational lung disease which is relevant to present-day industrial processes, which summarizes selectively the basic information necessary for intelligent understanding and at the same time approaches the problem from the viewpoint of the practising physician.

Dr Raymond Parkes has had first-hand experience both as clinician and in the special field of pneumoconiosis with the Pneumoconiosis Medical Panels in Cardiff and London: with this he has been able to bring together success-

fully the mysteries of industrial pulmonary disease and the clinical manifestations and natural history as it affects the patient.

He discusses in detail many of the newer conditions now being recognized, with the increasing use of new materials the hazards of which are only just being realized. He has also included a discussion of the increasing number of lung diseases relating to organic dusts as well as those relating to noxious fumes and gases: the pathogenesis of these, depending so often on immunological factors, is opening up a new era in occupational medicine.

Disorders relating to environmental factors are perhaps above all others susceptible to control and prevention. An authoritative but readable account of occupational pulmonary disease is therefore of extremely practical importance to doctors in all branches of medicine who have to deal with the working population of our industrialized island.

Cardiothoracic Institute, London M. TURNER-WARWICK

Preface

This book aims to be a reasonably comprehensive and up-to-date study of occupational disorders of the lung. It has been designed principally with the general, chest and industrial physician, and the postgraduate student of occupational medicine in mind; but I hope it will also be of value to the radiologist, pathologist, thoracic surgeon and to the general medical practitioner in industrial areas. Although the contents of Chapters 1, 4 and 5 will be known to readers in some of these categories I believe that they may be of value to others as they include many of the basic facts necessary to a proper understanding of the disorders described in the rest of the book.

Occupational lung disorders are important not only because they may give rise to respiratory disability but because of the diagnostic difficulties they often cause (especially when a worker has moved out of the area or from the country where the occupational exposure occurred), prognostic and therapeutic uncertainties, and because the increasing complexity of the materials and methods of modern technology multiplies potential risks—a point which has relevance to developing as well as to old-established industrial countries. Furthermore, in recent years, a heightened interest in these problems has been occurring throughout the world.

All these disorders can be conceived of as a confrontation between the lungs and all their resources, on the one hand, and inhaled mineral, chemical or organic aerosols, on the other; accordingly they should be regarded as being within, and not outside, the fold of thoracic and general medicine. Therefore, the book is concerned primarily with their medical features *vis-à-vis* the relevant occupational hazards some of which, indeed, have ceased to exist in recent years—although many folk who bear their stigmata survive—while *pari passu* new risks have arisen and increased. But for an accurate diagnostic assessment of individual cases or the study of groups of workers exposed to a particular hazard the physician may need to seek the expert knowledge of the geologist, geochemist, physicist, chemist, immunologist, engineer, occupational hygienist, factory manager or epidemiologist; in short, interdisciplinary collaboration is invaluable, if not essential. However, the techniques of dust sampling and control, ventilation, protective clothing, codes of practice and other aspects of hygiene are only briefly discussed in these pages as they not only lie outside my competence but constitute a book in themselves. Reference is made in the appropriate places to sources of this information. Important extrapulmonary disease in the

form of the tumour malignant mesothelioma of the parietal pleura and peritoneum is necessarily included in Chapter 9.

Many national and international experts—who are acknowledged in a later page—in various fields have given me their unstinted and invaluable help in the preparation of the book but if it contains any shortcomings or inaccuracies these are to be attributed to me and not to them.

At this point it is fitting to pay tribute to Dr Anthony Caplan—with whom I have been privileged to be associated for some years both as colleague and friend—who unmasked the association of atypical behaviour and unusual radiographic appearances of coal pneumoconiosis in coal-miners with rheumatoid arthritis; for this observation and his subsequent elaboration of it has undoubtedly given a strong impetus to the recognition and investigation of the part which may be played by immunological reactions to inhaled agents which has implications far beyond his original discovery, not only in regard to other types of pneumoconiosis, but in lung disease unrelated to occupation. As Parkes Weber wrote some years ago, 'For one common disease or syndrome there are several rare ones, the study of any one of which can help scientific progress as much as the study of a common one.'* The full fruits of Caplan's observations still remain to be harvested.

Finally, I wish to express my gratitude to Professor Margaret Turner-Warwick for contributing the Foreword; and also to Dr J. Watkins-Pitchford, Chief Medical Adviser (Social Security) Department of Health and Social Security, for encouraging this work to go forward to publication, although I should make it clear that opinions expressed throughout the book do not necessarily reflect the views of the Department.

* Parkes Weber, F. (1946). *Rare Diseases and Some Debatable Subjects*, p. 7. London; Staples Press.

London W. RAYMOND PARKES

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I am grateful, too, to Weidenfeld (Publishers) Ltd. (London) for permission to reproduce a short excerpt from *The Origin of Life* by the late Professor J. D. Bernal (1967). Acknowledgements accompany the tables and figures derived from the work of other authors.

Lastly, I am especially thankful to my wife for her forbearance during the long gestation of the book and for much typing and other help in its preparation.

W. R. P.

Abbreviations

ACGIH American Conference of Governmental Hygienists
ANF antinuclear factor
DAT differential agglutination test
FEV forced expiratory volume
FEV_1 forced expiratory volume in one minute
FRC functional residual capacity
FVC forced ventilatory capacity
HDI hexamethylene diisocyanate
IgA (E, G, M) immunoglobulin A (E, G, M)
MAC maximum allowable concentration
MDI diphenylmethane diisocyanate
NDI naphthalene diisocyanate
PEFR peak expiratory flow rate
PVP polyvinyl-pyrollidone
RF rheumatic factor
RV residual volume
SCAT sheep-cell agglutination test
TDI toluene diisocyanate
T_L lung gas transfer
TLC total lung capacity
TLV threshold limit value
UDS unit density sphere
VC vital capacity
WL working level
WLM working level month

Units and quantities

Å ångström(s) (10^{-10} m)
g gramme(s)
in inch(es)
kg kilogramme(s)
l litre(s)
m metre(s)
m^2 square metre(s)
m^3 cubic metre(s)
(*similarly mm^2 and mm^3, square and cubic mm*)
MeV mega electron volt(s)
mmHg millimetres of mercury pressure (torr)
mppcf million particles per cubic foot
*nm nanometre(s) (10^{-9} m)
*μm micrometre(s) (10^{-6} m)
ppm parts per million

* The use of the terms 'mμ' and 'millimicro' is discouraged by the BSI and other bodies as is that of the terms 'μ' and 'micron' for micrometre.

Contents

1—Introductory Considerations

I. TERMINOLOGY

To begin with, it is necessary to have a clear idea of what we mean by 'pneumoconiosis' because a variety of general definitions and descriptions have been current—and still are—since Zenker coined the term in 1867. In some cases their form has been conditioned by the compensation standards of various countries and is then rarely scientifically adequate. There are some authorities today who advocate outright rejection of the term but, as it has been in use for more than a century, this is hardly practical and the necessity of defining and classifying pneumoconiosis from the medical standpoint, cannot be avoided. As Card (1967) has written: 'That the concept of disease is a mental construct and belongs logically to the class of useful fictions should not blind us to its practical utility. If we accept this mode of analysis of our experience and we wish to diagnose, that is, assign a group of data to a particular disease, we must be able to define the disease.'

'Pneumoconiosis'—Proust's (1874) modification of Zenker's term 'pneumonokoniosis' (πνεύμων, lungs; κωηὶος, dust; ὁσις, state of)—just means 'dusty lung'. Thus, semantically, any dust-ridden state of the lungs or disease process resulting from it may legitimately be called pneumoconiosis. Now, while it is true that classification may be done in a variety of ways according to the purpose for which it is intended, the most appropriate method of definition and classification for medical purposes (having in mind the meaning of the word 'pneumoconiosis') rests upon morbid anatomical changes.

In this light, therefore, pneumoconiosis can be defined simply as *the presence of inhaled dust in the lungs and their non-neoplastic tissue reaction to it*. There are three key words here; dust, lungs, and reaction.

Dust

Dusts consist of solid particles of mineral or organic origin dispersed in air and, as such, are distinct from vapours, fumes and smoke (these terms are defined in Chapter 3), although all these categories are commonly embraced by the general term *aerosol*. Hence, by definition, pneumoconiosis does not include lung disorders due to inhaled aerosols other than dusts.

Lung

Strictly anatomically, 'lung' does not include the pulmonary (visceral) or

parietal pleura which is of different embryological origin from the lung; and so, primary pleural disease due to inhaled dust (for example, hyaline plaque formation and malignant mesothelial tumours attributed to asbestos dusts) should not be classified as pneumoconiosis.

Reaction

The lungs react to inhaled dust in a variety of ways which are discussed in Chapter 4 but, briefly, the reaction may be transient as, for example, in the case of the acute 'interstitial pneumonia' or granuloma formation of farmers' lung, or give rise to permanent reticulin proliferation or collagenous fibrosis.

To avoid misunderstanding at the outset it is important to emphasize that, by common consent among pathologists, 'fibrosis' means excessive production of collagen fibres (or scarring) and not an excess of reticulin fibres (*see* Chapter 4). Dusts which cause fibrosis are termed fibrogenic.

Both inorganic (mineral) and organic dusts may be classified according to the type of reactions they produce and individual diseases placed into these categories (Table 1.1).

TABLE 1.1

A CLASSIFICATION OF PNEUMOCONIOSIS WITH SOME EXAMPLES

Type of dust	*Lung reaction*	*Examples*
Inorganic (mineral)	No fibrosis—'inert' Local macrophage accumulation; little structural change; mild reticulin proliferation	Soot Iron (siderosis) Tin (stannosis) Barium (baritosis) Early stages of coal pneumoconiosis
	Sarcoid-like granuloma Foreign body granuloma	Beryllium disease Talc
	Collagenous fibrosis	Quartz and certain other forms of free silica (silicosis) 'Mixed dust' fibrosis Later stages of coal pneumoconiosis Asbestos (asbestosis) 'Talc' pneumoconiosis Beryllium disease
Organic (non-mineral) (e.g. antinomycete spores, avian and animal proteins	No fibrosis Transient 'interstitial pneumonia' or granuloma formation (acute extrinsic allergic alveolitis')	Farmers' lung Mushroom workers' lung Bagassosis Bird fanciers' lung
	Fibrosis Collagenous fibrosis (fibrosing 'alveolitis')	Farmers' lung Bagassosis Bird fanciers' lung

The foregoing definition of pneumoconiosis, it should be noted, embraces harmless as well as harmful changes in the lungs and in this book it refers both to dust accumulation and to dust-induced disease confined to the gas exchanging region of the lungs (that is, the acini—q.v. page 5) but which, in some instances (for example, farmers' lung), may also involve non-respiratory bronchioles.

Beryllium disease is a special case for, in addition to being a pneumoconiosis, it is also a systemic disorder and may be caused by fumes as well as dusts.

Because acute and chronic functional changes in the larger airways of the lungs caused by the inhalation of cotton and certain other vegetable dusts (that is, the 'byssinosis' group of diseases) are not associated with any characteristic morbid anatomical features, it is probably better not to classify them as 'pneumoconiosis' and, in accordance with common usage, this group is considered separately.

TABLE 1.2

NUMBERS OF NEW CASES OF MAJOR TYPES OF PNEUMOCONIOSIS AND BYSSINOSIS IN SELECTED ATTRIBUTABLE INDUSTRIES DIAGNOSED IN THE UNITED KINGDOM BY THE PNEUMOCONIOSIS MEDICAL PANELS

Industry	*1951*	*1954*	*1957*	*1960*	*1963*	*1964*	*1966*	*1967*	*1968*	*1969*	*1970*	*1971*
Coal mining	3035	4449	3456	3279	2268	1213	937	741	765	624	773	623
Asbestos	15	31	56	29	67	83	114	168	128	134	153	145
Refractories	20	26	51	16	24	13	14	18	10	16	11	17
Pottery	135	345	233	50	76	65	27	31	30	31	29	25
Slate mining and splitting	34	21	27	43	38	69	51	23	42	38	40	1
All foundries	156	256	259	99	86	72	55	44	52	40	48	3
Cotton (byssinosis)	43	73	160	403	354	271	149	146	126	78	110	
Flax (byssinosis)	–	–	–	–	–	–	9	14	3	–	–	

From H.M. Department of Health and Social Security Annual Reports. London: H.M.S.O. Every third year selected up to 1963.

Improper terminology, which is sometimes encountered and should be avoided at all costs, is exemplified by the use of 'silicosis' as a general term for all forms of pneumoconiosis, and 'pneumoconiosis' as a synonym for coal pneumoconiosis.

During the past hundred years the incidence of silicosis and the pneumoconiosis of coal miners steadily increased in most major industrial countries until the 1950s, since when it has undergone a downward trend, while asbestosis has become increasingly more frequent, and disorders of the extrinsic allergic 'alveolitis' type (for example, farmers' lung) have only recently been properly recognized. These trends are reflected in Table 1.2 which shows newly diagnosed compensation cases in Britain. Figures such as these, of course, are crude in that they are selective. The Report of the Katowice Symposium (1968), however, indicates that similar trends are occurring in other major industrial countries. But in newly developing countries the hazards which cause some of these diseases have only recently arisen and, if not properly controlled, will lead to new endemic areas of pneumoconiosis.

In short, pneumoconiosis and other dust-induced diseases are an important medical problem from the standpoint of differential diagnosis, and in causing respiratory disability and, sometimes, premature death in certain occupations.

II. ANATOMY

Some familiarity with the basic features of lung anatomy and cytology is necessary for an understanding of the pathogenesis and behaviour of the different types of pneumoconiosis and other occupational lung diseases.

Lung airways

From the trachea downwards each branch of the airways divides progressively into two daughter branches the length and diameter of which are not necessarily uniform. The average diameter of daughter branches is smaller than

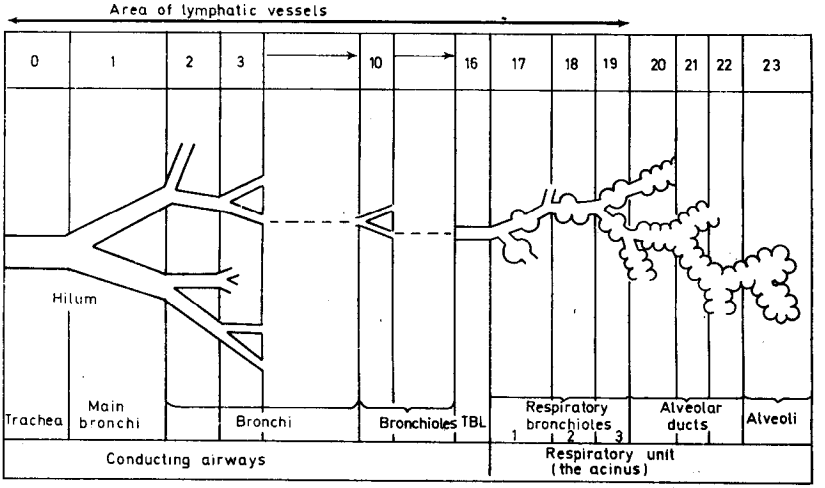

Figure 1.1. Conducting airways and respiratory unit (not to scale). The zones of the bronchi and bronchioles are truncated. The relative size of the respiratory unit is greatly enlarged; this is in fact about one-sixth of the distance from hilum to distal alveoli. Figures at the heads of the columns indicate the approximate number of generations from trachea to alveoli. (Modified, with permission, from Weibel, 1963)

that of the parent branch but, over the complete number of some twenty-three generations, the total cross-section and volume of the airways system increase progressively while the individual airways become smaller.

Bronchi are characterized by the presence of variable amounts of cartilage in their walls; the continuations of these airways without cartilage to the alveolar areas of the lung constitute the *bronchioles*. The last three or four (rarely, up to eight) generations of bronchioles which carry a variable number of *alveoli* (alveolus, a little hollow) in their walls are named *respiratory bronchioles* because they are capable of gas exchange. The *terminal bronchiole* is the last airway without alveoli before the first respiratory bronchiole (*Figure 1.1*). This diagram is not drawn to scale, the airways of the respiratory unit being shown disproportionally large by comparison with the conducting

airways, and the distance between generations 4 and 17 spans the greater length of the lung.

The lining of the airways as far as the terminal bronchiole consists of epithelial cells which are of pseudo-stratified, columnar and ciliated type; situated irregularly between them are mucus-secreting *goblet cells* opening to the surface. Goblet cells are plentiful proximally but become progressively fewer in number distally until, in the bronchioles, they are extremely scanty—at least in health.

Mucous glands are found only in bronchi and lie between the epithelium and cartilage. Their total volume is substantially greater than that of the goblet cells and it is likely that they produce the greater part of mucus secretion in health and disease (Reid, 1960). Increased activity is expressed by hypertrophy. This hypertrophy is the structural basis of chronic bronchitis, and the comparison of gland thickness to bronchial wall thickness is a valuable practical index of its presence and degree of severity (Reid, 1960). (Section V, this chapter.)

Secreted mucus spreads as an uneven layer on the cilia which possess an auto-rhythmic stroke directed proximally and advancing the layer in that direction; this process is often referred to as the 'ciliary escalator'. Although this is an efficient arrangement for removal of inhaled foreign particles it may be impaired or destroyed by some noxious agents, and excess mucus in chronic bronchitis may sometimes impose an undue burden upon the cilia.

The respiratory unit

The most distal respiratory bronchioles end in *alveolar ducts* which open into the *alveolar sacs* with clusters of alveoli (*Figure 1.1*). *Alveoli*, and their contained gas, are so closely in contact with the alveolar capillaries as to be integral with them.

The respiratory bronchioles, alveolar ducts and alveoli, therefore, comprise a respiratory unit—the *acinus* (a berry) (*Figure 1.1*). The size and shape of acini vary but they are from 0·5 to 1·0 cm in length.

Lobules consist of a variable number of respiratory units (from three to five) which may be partly bound by connective tissue; their shape and size are very variable.

Alveoli are, on average, about 0·15 mm in diameter, approximately 300 million in number (possibly more) and their total surface area, which is proportional to lung volume, of the order of 70 to 80 square metres (Weibel, 1968). This area is estimated to vary by about one-third between full expiration and inspiration with a range of values from approximately 30 to 100 square metres respectively (von Hayek, 1960). Obviously, therefore, the lungs possess great respiratory reserve. It appears that about 40 per cent of alveoli are located on the respiratory bronchioles and alveolar ducts (Pump, 1969).

There are small tubular communications—the accessory bronchiolo-alveolar communications of Lambert (1955)—between some terminal and respiratory bronchioles and neighbouring alveoli. These accessory air inlets, as they appear to be, probably contribute to collateral ventilation, and dust particles or dust-containing macrophages may be found in them and in contiguous alveoli.

Alveolar walls are composed of a number of differing cell types which are

variously responsible for gas exchange, disposal of inhaled foreign material, and immunological activity within the lung. Their appearance, distribution and relationships have been established by electron microscopy and six groups of cells can be distinguished morphologically in human lungs (Brooks, 1966). This is shown diagrammatically in *Figure 1.2.*

(1) *Type I Pneumocytes.*—Flat and extremely thin epithelial cells which form a continuous layer (about 0·2 μm thick away from their nuclei and invisible by light microscopy) over the alveolus apart from sporadic interruption by Type II pneumocytes. Both types of cell rest on a tenuous, but

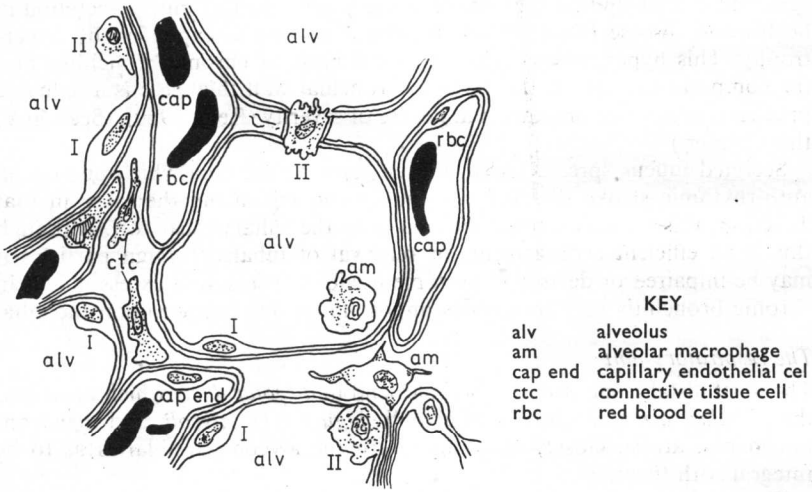

Figure 1.2. Diagram of the cells of the alveoli. (By courtesy of Dr R. E. Brooks and the Editor of American Review of Respiratory Diseases)

continuous, basement membrane composed of reticulin fibres (*see* Chapter 4). These cells are generally regarded as non-phagocytic but some doubt concerning this has been expressed (*see* Chapter 3).

(2) *Type II pneumocytes.*—Rounded or cuboidal epithelial cells set here and there in the alveolar walls; they are characterized by lamellated inclusions and may have mild phagocytic properties. They appear to develop from Type I cells, and most probably secrete surfactant.

(3) *Alveolar macrophages.*—These lie in contact with Type I cells or in small groups within the alveolus but are distinct from Type II cells. They contain a variable number of phagosomes (*see* Chapter 4) with ingested material. They apparently originate outside the lungs from precursor cells (promonocytes) in the bone marrow and from peripheral blood monocytes (that is, promonocyte→monocyte→macrophage) thus forming a distinct cell line (van Furth, 1970) to which the term 'mononuclear phagocyte system' has been given. They are actively mobile and phagocytic and the chief protagonists in the reaction of lungs to inhaled particles (*see* Chapter 4).

(4) *Endothelial cells.*—In the capillaries these rest on a basement membrane of reticulin. The capillaries, of course, contain the cellular elements of the blood.

(5) *Connective tissue cells.*—Fibroblasts.

(6) *Leucocytes and lymphocytes in the interalveolar septa.*—These are infrequent in the normal lung.

This arrangement—shown in the electron micrograph (*Figure 1.3*) of rat lung which is similar to human lung—provides intimate proximity of alveolar gas and capillary blood (gas/blood 'interface') and the opportunity for macrophages and, possibly to some extent, Type II pneumocytes to ingest exogenous and endogenous material (*see* Chapters 3 and 4). Cells containing dust migrate from the alveoli to the ciliary 'escalator' and are subsequently expelled in the sputum or into the bronchiolar lymph vessels from which they pass to regional lymph nodes (*see* Chapter 3).

Lung framework

The cellular elements of the lung are supported mainly by reticulin, elastic and collagen fibres. Reticulin fibres are the main support of alveolar walls which are reinforced by elastic fibres with collagen less well represented. As already stated, both basement membranes consist of reticulin fibres which are also found in the ground substance of the alveolar septa between the capillary and pulmonary epithelial cells.

The rest of the lung also has a framework of reticulin, collagen and elastic fibres.

Surface active agent (surfactant)

A substance which may be produced (at least in part) by Type II cells (Corrin, 1970) and reduces surface tension has been demonstrated in the alveoli (Pattle, 1955). It is a lipoprotein containing saturated dipalmitoyl lecithin which, *in vitro*, is one of the most stable surface active agents known; it has the unusual property of its surface tension rising when it is stretched and falling nearly to zero when compressed. Almost certainly this prevents the lung collapsing when its transpleural pressure is reduced (as in expiration) and allows alveoli of different sizes to remain open at the same transpleural pressure (Pattle, 1968).

There is as yet no evidence that alteration in its properties is involved in the pathogenesis of pneumoconiosis.

Blood supply

Pulmonary arteries conveying venous blood and bronchial arteries conveying arterial blood into the lungs are closely associated with the bronchi and all are enveloped by a common connective tissue sheath the *broncho-arterial bundle.*

Pulmonary arteries accompany the bronchi—although they branch more frequently—and do not become capillaries until they reach the respiratory bronchioles, at which point they form an increasingly rich plexus in intimate proximity to the alveolar epithelium so that only the thickness of the pulmonary epithelial cells, the two basement membranes and a fine tissue space separate alveolar gas from capillary blood (*Figure 1.3*). This thickness away from cell nuclei may be as little as 0·2 μm. The capillary surface area is equal to that of the alveoli, that is, some 70 to 80 square metres (Weibel, 1963).