Respiratory Physiology

—*the essentials*
2nd edition

John B. West, M.D., Ph.D.

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Preface

This book is primarily written as a core course for medical students and is based on lectures given in the School of Medicine of the University of California San Diego. A modern understanding of how the lung works is becoming increasingly important in the management of patients with pulmonary disease so it is hoped that this succinct account will also be useful to internists, anesthesiologists and paramedical personnel such as inhalation therapists.

If there is any bias in this book it is that the chief business of the lung is gas exchange. This shows in the first chapter and the arrangement of the succeeding ones. No apology is made for this emphasis; indeed it is astonishing how little attention is given to gas exchange in some traditional accounts of pulmonary function. On the other hand, other aspects such as the control of ventilation are sometimes given an undue amount of space and I have tried to achieve a better balance here. A final chapter has been added on the application of pulmonary physiology to the testing of lung function though this need not be regarded as part of a core course.

A text such as this must necessarily be eclectic and I have drawn extensively on the work of others. References to individual papers are not included in the text but there is a list of articles for additional reading. The book is illustrated with an unusually large number of diagrams because their value as teaching aids seems especially great in this area. In addition a set of audiotapes with slides is available to supplement this book.*

Several colleagues have read part or all of the manuscript and suggested improvements. They include Drs. D. D. Fanestil, Y. C. Fung, S. Lahiri, P. T. Macklem, R. A. Mitchell, S. Permutt and P. D. Wagner, and I am indebted to them. Of course any remaining shortcomings are my responsibility and I welcome constructive criticism from readers.

A frustrating aspect of writing such a brief text is that so many fascinating areas of respiratory physiology cannot be alluded to at all. My only consolation is that overburdened students and busy physicians will appreciate the conciseness and the limited objectives. An additional hope is that some students will be encouraged to read wider and seek out some of the interesting adjacent areas such as the comparative physiology of respiration.

Preface to the Second Edition

The temptation to enlarge this little book in its second edition is great but has been successfully resisted. The section on metabolic functions of the lung has grown but that on ventilation-perfusion relationships has been pruned. The chapter on control of ventilation has been largely rewritten. Some reviewers have argued that the book should include a discussion of the lung's defense system. My own feeling is that this subject is better taught in the context of pathophysiology and it is, therefore, covered in the companion volume (West, J. B. *Pulmonary Pathophysiology—The Essentials*. Baltimore: Williams & Wilkins, 1977).

* Available from Audio Visual Medicine, 850 Third Avenue, New York, N.Y. 10022.

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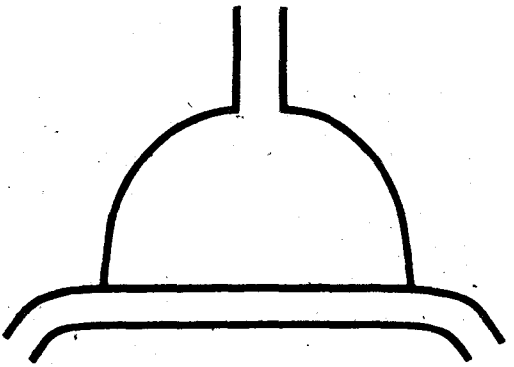

chapter 1

Structure and Function

how the architecture of the lung subserves its function

The lung is for gas exchange. Its prime function is to allow oxygen to move from the air into the venous blood and carbon dioxide to move out. The lung does other jobs too. It filters toxic materials from the circulation, metabolizes some compounds and acts as a reservoir for blood. But its cardinal function is to exchange gas, and we shall therefore begin at the blood-gas interface where the gas exchange occurs.

BLOOD-GAS INTERFACE

Oxygen and carbon dioxide move between air and blood by simple diffusion, that is, from an area of high to low partial pressure* much

* The partial pressure of a gas is found by multiplying its concentration by the total pressure. For example, dry air has 20.93% O_2. Its partial pressure (P_{O_2}) at sea level (barometric pressure 760 mm Hg) is $20.93/100 \times 760 = 159$ mm Hg. When air is inhaled

as water runs downhill. Fick's law of diffusion states that the amount of gas which moves across a sheet of tissue is proportional to the area of the sheet but inversely proportional to its thickness. The blood-gas barrier is exceedingly thin (Figure 1.1) and has an area of between 50 and 100 square meters. It is therefore well suited to its function of gas exchange.

How is it possible to obtain such a prodigious surface area for diffusion inside the limited thoracic cavity? By wrapping the small blood vessels (capillaries) around an enormous number of small air sacs called alveoli (Figure 1.2). There are about 300 million alveoli in the human lung, each about ⅓ mm in diameter. If they were spheres† their total surface area would be 85 square meters but volume only 4 liters. By contrast, a single sphere of this volume would have an internal surface area of only 1/100 square meters. Thus the lung generates this large diffusion area by being divided into myriads of units.

Gas is brought to one side of the blood-gas interface by *airways* and blood to the other side by *blood vessels*.

AIRWAYS AND AIR FLOW

The airways consist of a series of branching tubes which become narrower, shorter and more numerous as they penetrate deeper into the lung (Figure 1.3). The trachea divides into right and left main bronchi which in turn divide into lobar, then segmental bronchi. This process continues down to the terminal bronchioles which are the smallest airways without alveoli. All these bronchi make up the *conducting airways*. Their function is to lead inspired air to the gas exchanging regions of the lung (Figure 1.4). Since the conducting airways contain no alveoli and therefore themselves take no part in gas exchange, they constitute the *anatomic dead space*. Its volume is about 150 ml.

The terminal bronchioles divide into respiratory bronchioles which have occasional alveoli budding from their walls. Finally, we come to the alveolar ducts completely lined with alveoli. This alveolated region

into the upper airways, it is warmed and moistened and the water vapor pressure is then 47 mm Hg, so that the total dry gas pressure is only 760 − 47 = 713 mm Hg. The P_{O_2} of inspired air is therefore 20.93/100 × 713 = 149 mm Hg. A liquid exposed to a gas until equilibration takes place has the same partial pressure as the gas. For a more complete description of the gas laws see the Appendix.

† The alveoli are not spherical but polygonal. Nor is the whole of their surface available for diffusion (see Figure 1.1). These numbers are therefore only approximate.

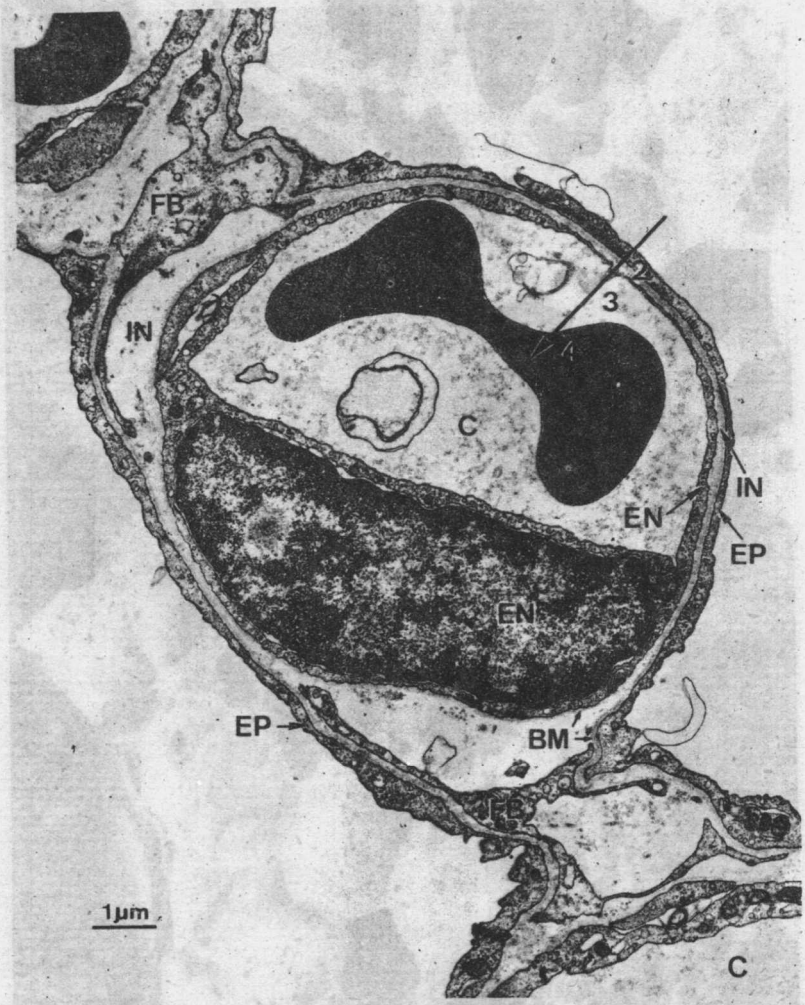

Figure 1.1. Electron micrograph showing a pulmonary capillary (*C*) in the alveolar wall. Note the extremely thin blood gas barrier of less than 0.5 microns. The arrow indicates the diffusion path from alveolar gas to the interior of the erythrocyte (*EC*) and includes the layer of surfactant (not shown in the preparation), alveolar epithelium (*EP*), interstitium (*IN*) capillary endothelium (*EN*) and plasma. Parts of structural cells called fibroblasts (*FB*), basement membrane (*BM*) and a nucleus of an endothelial cell are also seen. (From Weibel, E. R. *Respirat. Physiol. 11:* 54, 1970.)

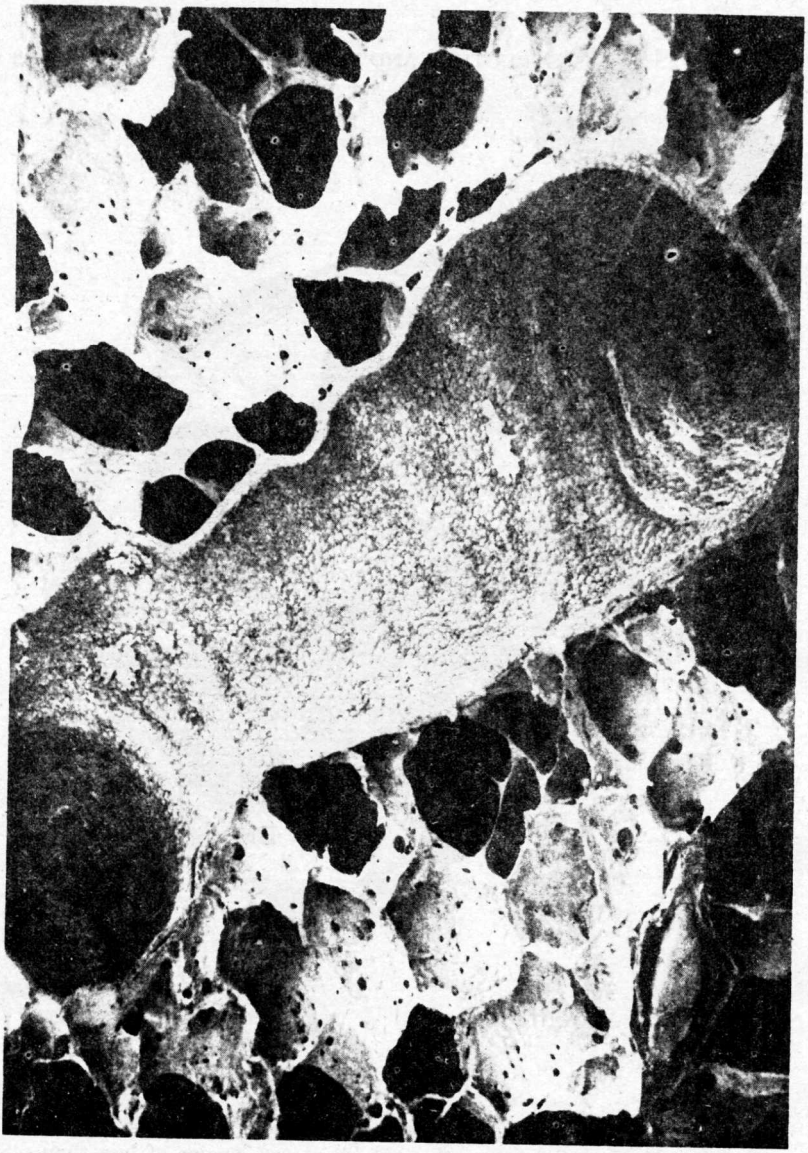

Figure 1.2. Section of lung showing many alveoli and a small bronchiole. The pulmonary capillaries run in the walls of the alveoli (Figure 1.1). The holes in the alveolar walls are the pores of Kohn. (Scanning electron micrograph by Nowell, J. A., and W. S. Tyler.)

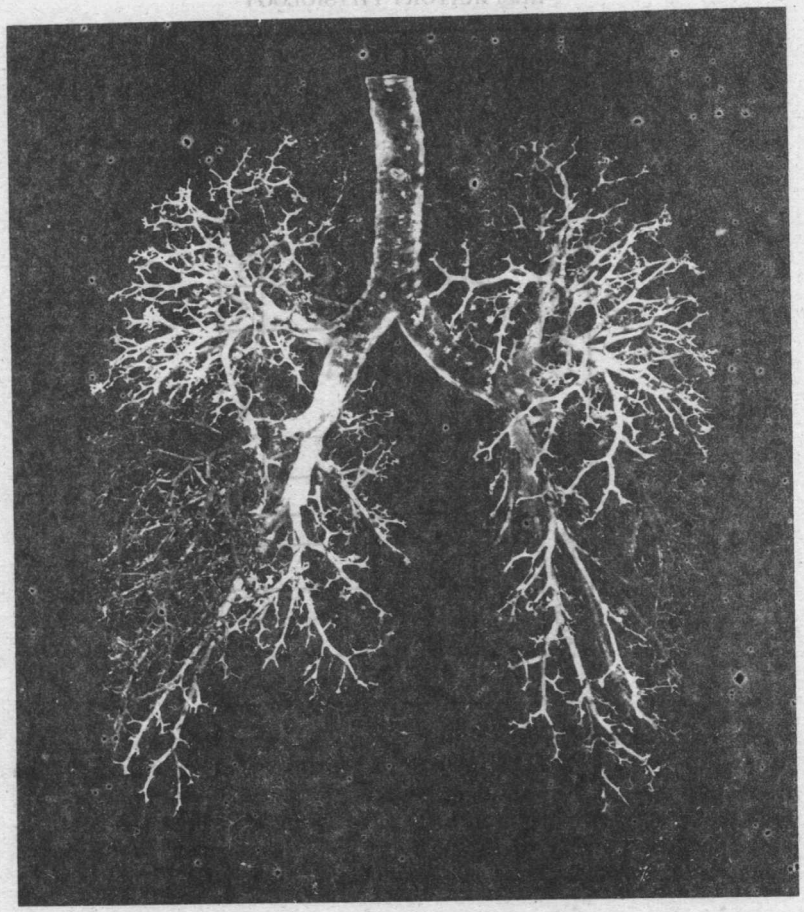

Figure 1.3. Cast of the airways of a human lung. The alveoli have been pruned away but the conducting airways from the trachea to the terminal bronchioles can be seen.

of the lung where the gas exchange occurs is known as the *respiratory zone*. The portion of lung distal to a terminal bronchiole forms an anatomical unit called the *primary lobule* or better, the *acinus*. The distance from the terminal bronchiole to the most distal alveolus is only about 5 mm but the respiratory zone makes up most of the lung, its volume being about 3000 ml.

During inspiration, the volume of the thoracic cavity increases and

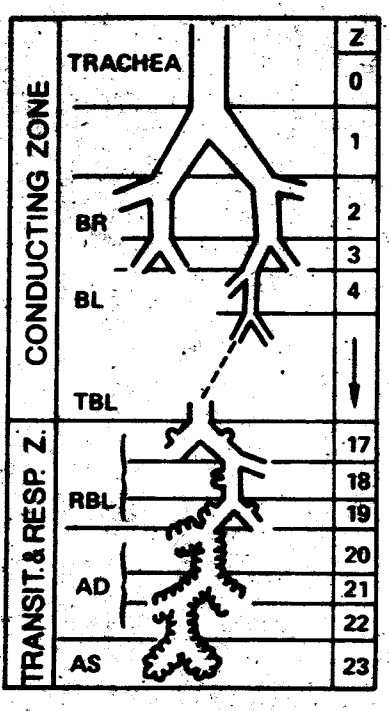

Figure 1.4. Idealization of the human airways according to Weibel. Note that the first 16 generations (*Z*) make up the conducting airways and the last 7 the respiratory zone (or the transitional and respiratory zone). *BR*, bronchus; *BL*, bronchiole; *TBL*, terminal bronchiole; *RBL*, respiratory bronchiole; *AD*, alveolar duct; *AS*, alveolar sac. (From Weibel, E. R. *Morphometry of the Human Lung*. Berlin: Springer-Verlag, 1963, p. 111.)

air is drawn into the lung. The increase in volume is brought about partly by contraction of the diaphragm which causes it to descend, and partly by the action of the intercostal muscles which raise the ribs, thus increasing the cross-sectional area of the thorax ("bucket handle action"). Inspired air flows down to about the terminal bronchioles by bulk flow like water through a hose. Beyond that point, the combined cross-sectional area of the airways is so enormous because of the large number of branches (Figure 1.5) that the forward velocity of the gas becomes very small. Diffusion of gas within the airways then takes over as the dominant mechanism of ventilation in the respiratory zone.

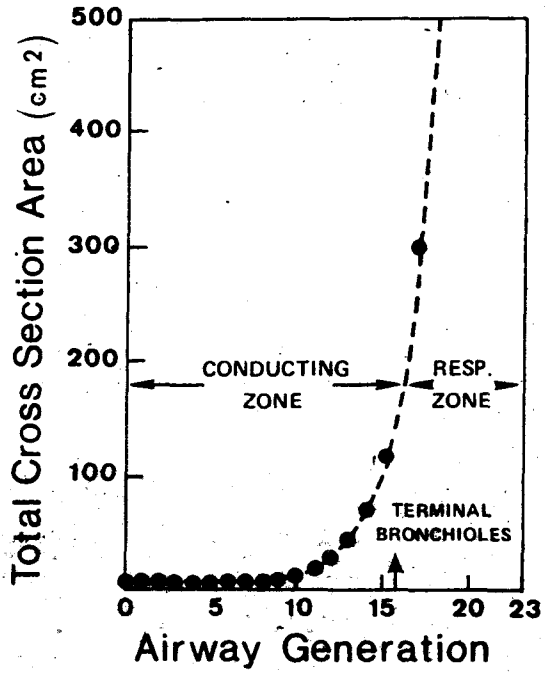

Figure 1.5. Diagram to show the extremely rapid increase in total cross-sectional area of the airways in the respiratory zone (compare Figure 1.4). As a result, the forward velocity of the gas during inspiration becomes very small in the region of the respiratory bronchioles and gaseous diffusion becomes the dominant mechanism of ventilation.

The rate of diffusion of gas molecules within the airways is so rapid, and the distances to be covered are so short, that differences in concentration within the acinus are virtually abolished within a second. However, because the velocity of gas falls rapidly in the region of the terminal bronchioles, inhaled dust frequently settles out there.

The lung is elastic and returns passively to its pre-inspiratory volume during resting breathing. It is remarkably easy to distend. For example, a normal breath of about 500 ml requires a distending pressure of less than 3 cm water. By contrast, a child's balloon may need a pressure of 300 cm water for the same change in volume.

The pressure required to move gas through the airways is also very

small. During normal inspiration, an air flow rate of 1 liter/sec requires a pressure drop along the airways of less than 2 cm water. Compare a smoker's pipe which needs a pressure of about 500 cm water for the same flow rate.

BLOOD VESSELS AND FLOW

The pulmonary blood vessels also form a series of branching tubes from the pulmonary artery to the capillaries and back to the pulmonary veins. Initially the arteries, veins and bronchi run close together, but toward the periphery of the lung, the veins move away to pass between the lobules, whereas the arteries and bronchi travel together down the centers of the lobules. The capillaries form a dense network in the walls of the alveoli (Figure 1.6). The diameter of a capillary segment

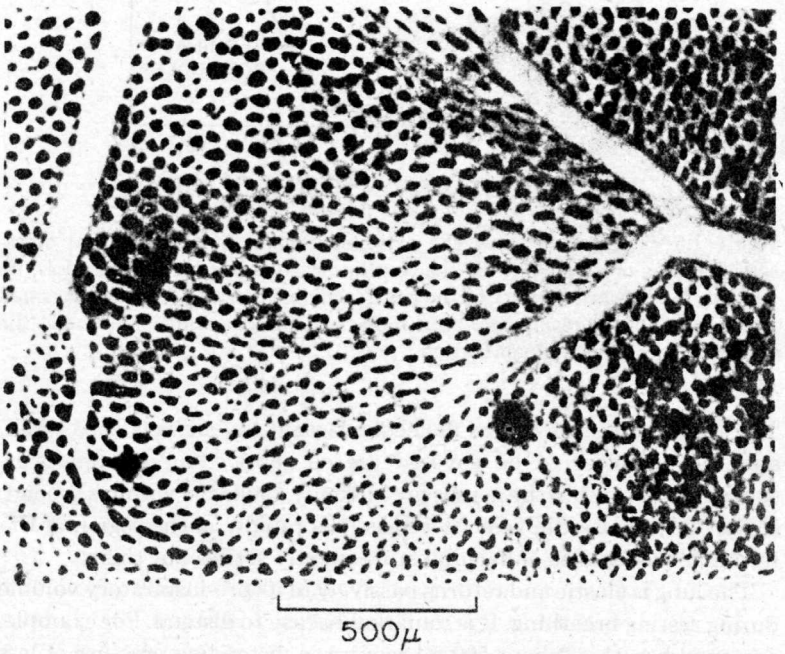

Figure 1.6. View of an alveolar wall (in the frog) showing the dense network of capillaries. A small artery (*left*) and vein (*right*) can also be seen. The individual capillary segments are so short that the blood forms an almost continuous sheet. (From Maloney, J. E., and B. L. Castle. *Respirat. Physiol.* 7: 150, 1969.)

is about 10 microns, just large enough for a red blood cell. The lengths of the segments are so short that the dense network forms an almost continuous sheet of blood in the alveolar wall, a very efficient arrangement for gas exchange. Alveolar walls are not often seen face on as in Figure 1.6. The usual microscopic cross-section (Figure 1.7) shows the red blood cells in the capillaries and emphasizes the enormous exposure of blood to alveolar gas with only the thin blood-gas barrier intervening (compare Figure 1.1).

The pulmonary artery receives the whole output of the right heart but the resistance of the pulmonary circuit is astonishingly small. A mean pulmonary arterial pressure of only about 20 cm water is required for a flow of 6 liters/min. (The same flow through a soda straw needs 120 cm water.)

Each red blood cell spends about a second in the capillary network and during this time probably transverses two or three alveoli. So

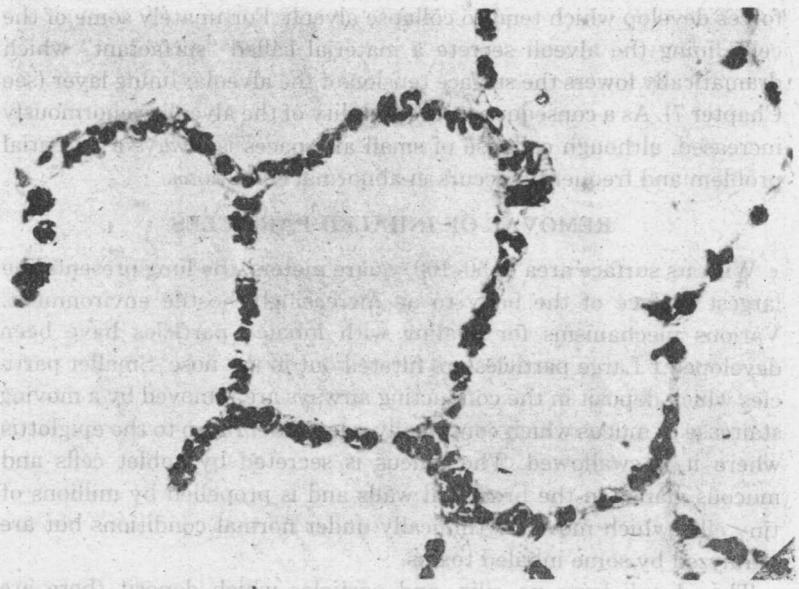

Figure 1.7. Microscopic section of dog lung showing capillaries in the alveolar walls. The blood-gas barrier is so thin that it cannot be identified here (compare Figure 1.1). This section was prepared from lung which was rapidly frozen while being perfused. (From Glazier, J. B., J. M. B. Hughes, J. E. Maloney, and J. B. West. *J. Appl. Physiol.* 26: 65, 1969.)

efficient is the anatomy for gas exchange that this brief time is sufficient for virtually complete equilibration of oxygen and carbon dioxide between alveolar gas and capillary blood.

The lung has an additional blood system, the bronchial circulation, which supplies the conducting airways down to about the terminal bronchioles. Most of this blood is carried away from the lung via the pulmonary veins. The flow through the bronchial circulation is a mere fraction of that through the pulmonary circulation, and the lung can function fairly well without it, for example, following lung transplantation.

To conclude this brief account of the functional anatomy of the lung, let us glance at two special problems that the lung has overcome.

STABILITY OF ALVEOLI

The lung can be regarded as a collection of 300 million bubbles each 0.3 mm in diameter. Such a structure is inherently unstable. Because of the surface tension of the liquid lining the alveoli, relatively large forces develop which tend to collapse alveoli. Fortunately some of the cells lining the alveoli secrete a material called "surfactant" which dramatically lowers the surface tension of the alveolar lining layer (see Chapter 7). As a consequence, the stability of the alveoli is enormously increased, although collapse of small air spaces is always a potential problem and frequently occurs in abnormal conditions.

REMOVAL OF INHALED PARTICLES

With its surface area of 50–100 square meters, the lung presents the largest surface of the body to an increasingly hostile environment. Various mechanisms for dealing with inhaled particles have been developed.‡ Large particles are filtered out in the nose. Smaller particles which deposit in the conducting airways are removed by a moving staircase of mucus which continually sweeps debris up to the epiglottis where it is swallowed. The mucus is secreted by goblet cells and mucous glands in the bronchial walls and is propelled by millions of tiny cilia which move rhythmically under normal conditions but are paralyzed by some inhaled toxins.

The alveoli have no cilia, and particles which deposit there are

‡ For a detailed description of the lung's defense system see *Pulmonary Pathophysiology—The Essentials*. by John B. West, Baltimore, Williams & Wilkins, 1977.