Color Atlas and Text of Pulmonary Pathology

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This book is dedicated to the memory of S. Donald Greenberg, MD,
one of the pioneers of modern lung pathology and academic father to many of us.

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Preface

We have attempted to compile a comprehensive atlas covering common, rare, and newly described lung diseases, both neoplastic and nonneoplastic, in one volume. Topics are organized into sections, chapters, parts, and subparts for ready accessibility. Although diseases are designated according to the most current classification schemes, topics are divided into chapters, parts, and subparts based on their histopathologic distinctiveness, a more intuitive approach for the practicing pathologist. Our objective is to provide a format of color figures and handy lists of diagnostic features that provide clear-cut essentials for diagnosis undiluted by other types of information that can be obtained from other sources when necessary. Our goal for the practicing pathologist is to expedite timely and accurate diagnosis when signing out cases. For students, residents, fellows, and specialty Board applicants, this same format facilitates rapid, comprehensible study of all topics in lung pathology. The use of gross pathology, cytopathology, and histopathology figures and tables in this book allows a multidimensional approach to pathologic diagnoses. We have attempted to illustrate common nonspecific findings, false positive features, and potential diagnostic traps that the practicing pathologist may encounter so that these can be distinguished from specific diseases.

This book was conceived as a tribute to our mentor, one of the outstanding pioneers of modern lung pathology in the 1960s, '70s, and '80s, Dr. S. Donald Greenberg. Dr. Greenberg spent most of his career at Baylor College of Medicine in the Texas Medical Center in Houston and worked closely with community and academic physicians throughout Texas. Above all else, Dr. Greenberg was highly respected as an inspiring teacher to students, housestaff, and practicing pathologists and clinicians, both in the community and in the university, and he received many teaching awards during his career. Therefore, a practical atlas of lung pathology that would be useful to students, housestaff, and practicing pathologists and clinicians, both community based and university based, was felt to be the best tribute to Dr. Greenberg's legacy.

Because of the logistics, it was not possible to include all of Dr. Greenberg's many protégés and students as contributors to this book, so an editorial staff composed of lung pathologists of the Houston-Galveston area plus one of Dr. Greenberg's first protégés, Dr. Carlos Bedrossian, was organized. In addition to the editors, other faculty from the Houston-Galveston area contributed to this book, as did those lung pathologists who came as Visiting Professors to the Texas Medical Center during the time when the book was in preparation.

Our hope is that this book represents a culmination of Dr. Greenberg's work through those who learned from him.

Philip T. Cagle, MD
2-17-2004

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Section 1

Normal Cytology and Histology

1 Bronchus

- Alvaro C. Laga
- Timothy Allen
- Philip T. Cagle

The airways of the lung are tubular or pipelike structures that conduct air through their lumens. The airways branch into tubes or pipes of increasingly smaller diameter, with larger bronchi dividing into smaller bronchi that branch into smaller bronchioles, which eventually lead into the air sacs or alveoli, where gas exchange occurs. The airways are accompanied by branches of the pulmonary artery that approximate their diameters in cross section.

Bronchi are conducting airways more than 1 mm in diameter. Multiple plates of cartilage in their walls prevent their collapse, permitting them to vary in caliber. In addition to their larger caliber, the histologic features that distinguish bronchi from bronchioles (see Chapter 2) are the presence of respiratory epithelium (pseudostratified ciliated columnar epithelium), bronchial seromucinous glands, cartilage plates, and smooth muscle. There are approximately 9 to 12 generations of bronchi. The left and right mainstem bronchi branch from the trachea at the carina and enter the left lung hilum and right lung hilum, respectively. The left mainstem bronchus is longer and narrower, and it has a greater angle than the right mainstem bronchus. The right upper lobe bronchus branches off the right mainstem bronchus before it enters the hilum. The mainstem bronchi branch into the lobar bronchi, which in turn branch into the segmental bronchi of the bronchopulmonary segments, which in turn branch into generations of smaller bronchi.

Histologic Features:

Histologically, the bronchus consists of a central lumen lined by a mucosa consisting of respiratory epithelium; a submucosa consisting of connective tissue containing bronchial seromucinous glands, capillaries, and lymphatics; a muscularis consisting of smooth muscle; and a connective tissue adventitia that contains lymphatics.

- Bronchial lumens are lined by pseudostratified ciliated columnar epithelium (respiratory epithelium) that rests on a basement membrane; the pseudostratified appearance consists of nuclei of cells arranged as if they are layered one upon another in different strata when actually the bases of all the cells are touching the basement membrane.
- Ciliated columnar epithelial cells make up the majority of the cells of the bronchial epithelium (mucosa); cilia arise from terminal bars in the apices of these cells and project into the bronchial lumen, where they participate in the mucociliary escalator by push-

ing the layer of mucin lying over the bronchial lumen surface cephalad; also present in lesser numbers are goblet cells (columnar cells containing apical mucin), basal cells, and neuroendocrine (Kulchitsky) cells.

- Beneath the surface epithelium is the submucosa, which contains loose connective tissue with longitudinally arranged elastic fibers; bronchial glands (mucous glands) are seromucinous glands with ducts opening into the bronchial lumen present within the submucosa.
- Cartilage plates and smooth muscle bundles lie beneath the mucosa and submucosa.
- Bronchus-associated lymphoid tissue (BALT) consists of lymphoid tissue aggregates in the bronchial submucosal tissue equivalent to the mucosa-associated lymphoid tissue (MALT) of the gastrointestinal tract.

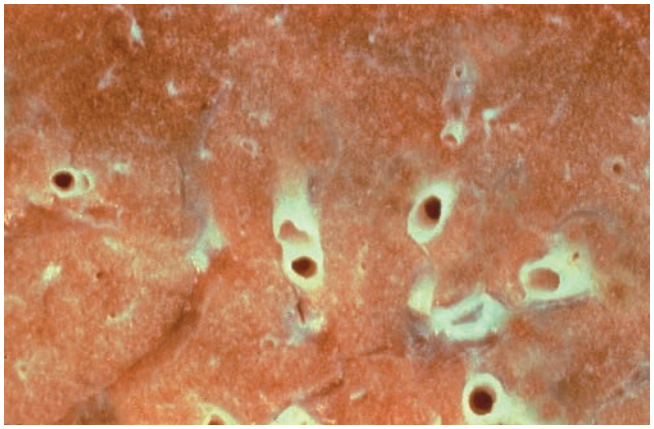

Figure 1.1 Gross figure of normal lung shows spongy tan lung parenchyma, interspersed bronchi, and pulmonary arteries forming bronchovascular bundles.

Figure 1.2 Bronchial wall with respiratory epithelium lining the lumen surface and underlying submucosal connective tissue containing a seromucinous gland with its duct connecting to the lumen surface and a cartilage plate.

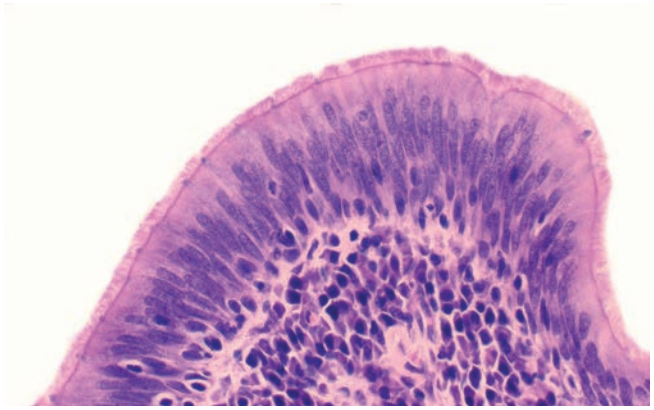

Figure 1.3 Ciliated pseudostratified columnar epithelium shows nuclei arranged as if they are lying in different layers or strata, giving a pseudostratified appearance, but in actuality the bases of all of the cells are touching the basement membrane; the surface of the columnar cells shows cilia arising from terminal bars, which form a dense line between the cell apical surfaces and the overlying cilia; there is an infiltrate of lymphocytes and plasma cells in the submucosa.

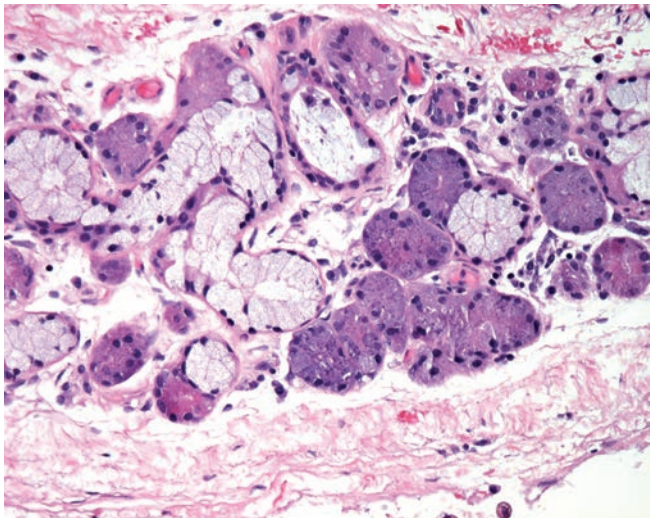

Figure 1.4 Bronchial glands are seromucinous glands in the submucosal connective tissue composed of both serous and mucinous acini.

Bronchioles and Alveolar Ducts

2

- Alvaro C. Laga
- Timothy Allen
- Philip T. Cagle

Bronchioles are defined as conducting airways less than 1 mm in diameter that lack cartilage in their walls. Bronchioles are divided into two groups. The larger (average diameter 0.5–1 mm) terminal (membranous) bronchioles branch from the smallest bronchi and give rise to the smaller (average diameter 0.15–0.2 mm) respiratory bronchioles. The terminal (membranous) bronchioles only conduct air, similar to bronchi, whereas the respiratory bronchioles both conduct air and participate in gas exchange via the alveoli in their walls. The respiratory bronchioles branch into about two more generations of respiratory bronchioles with increasing numbers of alveoli in their walls and give rise to the alveolar ducts.

Terminal bronchioles (membranous bronchioles) are the most distal generation of bronchioles that do not contain alveoli. Terminal bronchioles have a simple columnar epithelium (bronchiolar mucosa) composed of ciliated columnar cells and nonciliated Clara cells, a layer of smooth muscle, and a connective tissue adventitia. Terminal (membranous) bronchioles lack cartilage, and seromucinous glands and goblet cells are generally not observed or are minimal in the normal bronchiolar mucosa. The terminal bronchiole leads into the acinus (a functional unit composed of the structures distal to a single terminal bronchiole—its respiratory bronchioles, alveolar ducts, and alveoli). A lobule is an anatomic unit consisting of the acini of 3 to 10 terminal (membranous) bronchioles that are bounded together by the interlobular septum. As with the bronchi, the bronchioles are accompanied by branches of the pulmonary artery of approximately the same diameter.

Respiratory bronchioles have a bronchiolar wall with simple columnar to cuboidal bronchiolar epithelium and alveoli budding from their walls. The alveoli budding from the bronchiolar walls increase in numbers the higher the generation of the respiratory bronchiole. In two-dimensional longitudinal sections of glass slides, respiratory bronchioles often appear to have a bronchiolar mucosa and wall on one side of their lumen and alveolar spaces on the opposite side of their lumen. Respiratory bronchioles represent the first generation of airways in which exchange of gases occurs.

Alveolar ducts are straight tubular spaces bounded entirely by alveoli and lead to alveolar sacs. They contain numerous outpockets of alveoli protruding from their lumens and lack bronchiolar mucosa or wall.

Histologic Features:

- Membranous (terminal) bronchioles are lined by ciliated simple columnar epithelium.
- Respiratory bronchioles consist of both simple columnar epithelium and alveoli.
- Alveolar ducts are spaces lined by alveoli.

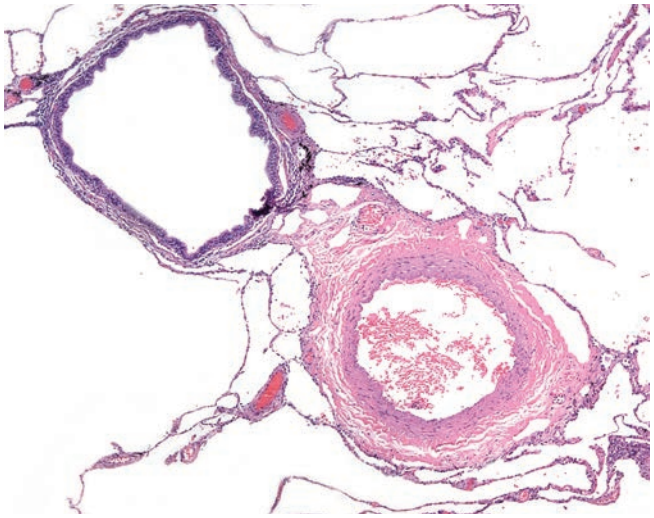

Figure 2.1 Cross section of a terminal (membranous) bronchiole with its lumen lined by simple ciliated columnar epithelium and an accompanying small muscular pulmonary artery.

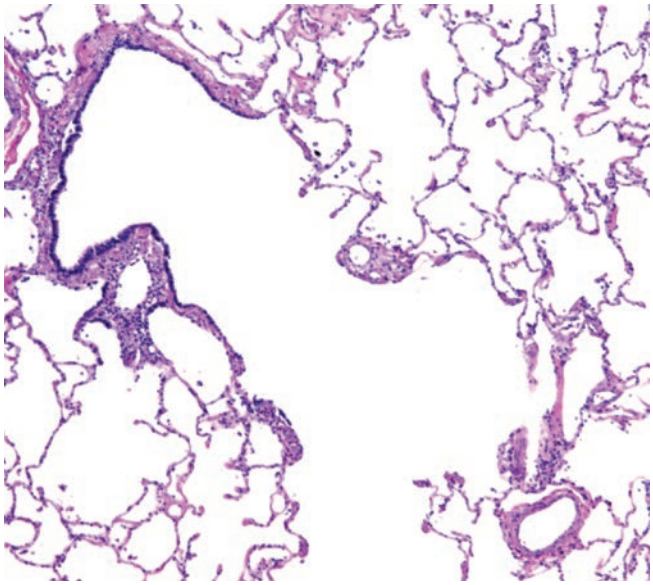

Figure 2.2 Longitudinal section of a terminal (membranous) bronchiole opening into a respiratory bronchiole; the latter consists of a bronchiole with alveoli budding from its wall, displaying simple columnar epithelium on one side of the lumen and alveoli on the other side.

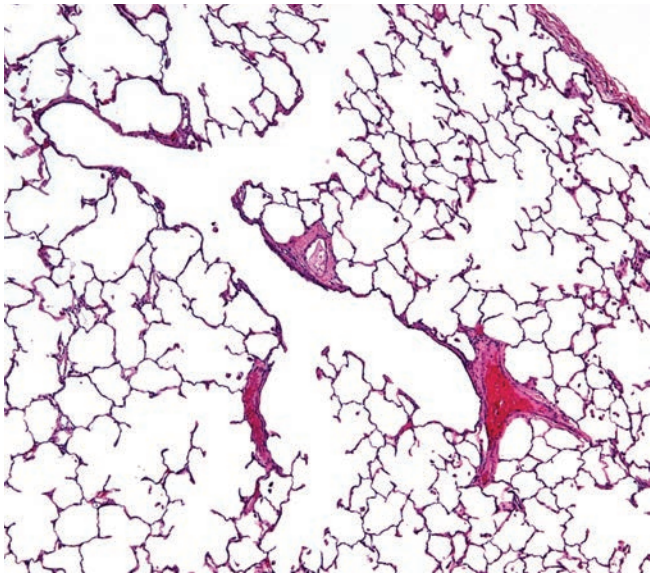

Figure 2.3 Longitudinal section of respiratory bronchiole (lumen lined by bronchiolar epithelium and alveoli) branching into alveolar ducts (lumens lined by alveoli only).

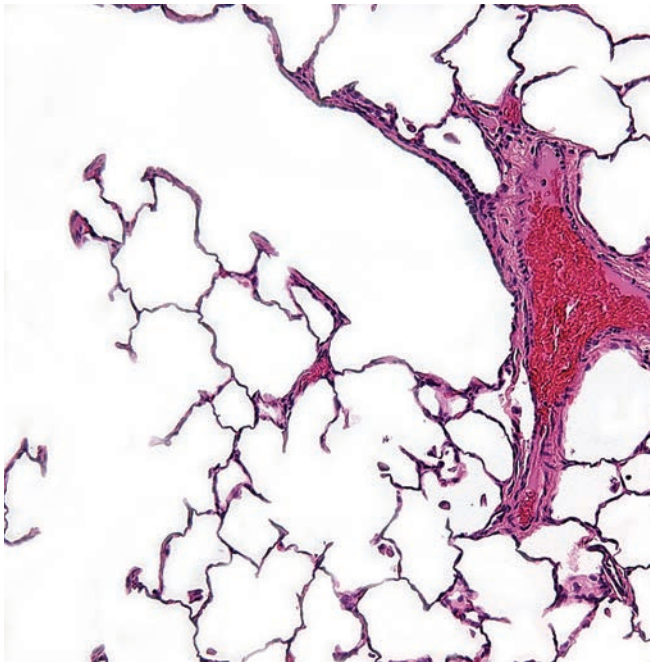

Figure 2.4 Higher power shows respiratory bronchiole lined on one side by simple columnar epithelium and alveoli on the other side; it is accompanied by a small arterial vessel.

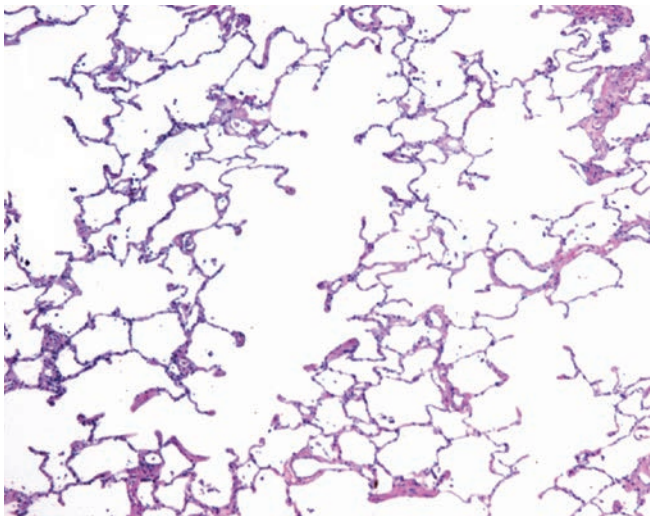

Figure 2.5 Alveolar duct consists of tubular space lined by alveoli and terminates in alveolar sacs.

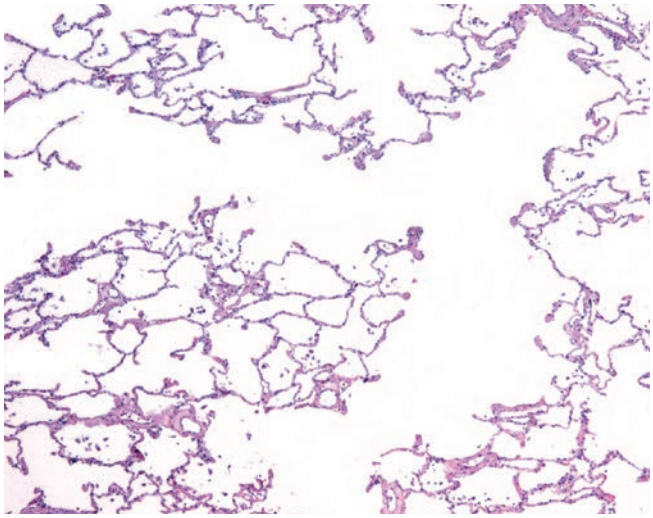

Figure 2.6 Alveolar ducts have walls composed of alveoli.

Blood Vessels and Lymphatics

3

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The pulmonary vasculature involved in gas exchange includes pulmonary arteries and arterioles that bring blood relatively low in oxygen and high in carbon dioxide from the heart to the gas exchange areas, alveolar capillaries where the gas exchange occurs, and pulmonary venules and veins that return oxygenated blood to the heart. Bronchial arteries and veins are part of the systemic circulation and provide oxygen and nutrients to the bronchi.

Pulmonary arteries branch into increasingly smaller vessels accompanying the bronchi and bronchioles, often with a common connective tissue sheath (bronchovascular bundle), and have a cross-section diameter approximately equal to that of the accompanying airway. Gas exchange occurs in capillaries in the alveolar septa, and venules merge into increasingly larger veins that return oxygenated blood to the heart. Veins are found in the interlobular septa and pleura.

The large branches of the pulmonary artery are elastic arteries, although the elastic fibers are more fragmented than in the aorta. The elastic pulmonary arteries give rise to the muscular pulmonary arteries that accompany the bronchioles. Arteries have two elastic lamina, but smaller arterioles often have only one elastic lamina. Veins also have only one elastic lamina. Histologic differentiation of venules from arterioles may be very difficult.

Lymphatic channels are found in the bronchovascular bundles, in the interlobular septa, along pulmonary veins, and in the pleura. Lymphatics are generally histologically inconspicuous. Certain diseases, such as sarcoidosis, tend to be distributed along lymphatics (lymphangitic distribution).

Histologic Features:

- Muscular pulmonary arteries have a tunica media of circularly oriented smooth muscle lying between internal and external elastic lamina.
- Pulmonary arteries have a thin tunica media compared to systemic arteries.
- Pulmonary veins have a single elastic lamina and gradually acquire a muscular media downstream.
- The tunica media of pulmonary veins consists of circularly oriented smooth muscle with interspersed elastic fibers.