D.H. Dail S.P. Hammar
Editors

PULMONARY PATHOLOGY

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David H. Dail and Samuel P. Hammar
Editors

Pulmonary Pathology

With a Foreword by Herbert Spencer

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and 72 Color Plates

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Foreword

The exponential increase in knowledge in all branches of science, including pathology, has resulted in an avalanche of scientific literature which is now too extensive for most people to digest. This certainly applies to the field of pulmonary pathology. One has only to reflect on the better understanding of many disease processes and the description of many new diseases in the lung in the last 40 years to appreciate these changes. For this reason alone, a summary of the present knowledge is both essential and timely.

Pathology is undergoing a metamorphosis, with new diagnostic methods employing antibodies and other newly developed techniques to make diagnoses more precise. Until recently, these new techniques have largely been research tools, but are now being applied to day-to-day practice in diagnostic pathology laboratories. These new techniques offer exciting potential approaches to some of the as yet unsolved problems of pulmonary pathology.

Pulmonary Pathology, written by multiple authors working in their respective areas of interest, is intended to provide the reader with up-to-date information. In the years ahead, new lung diseases will be discovered, some of which may still be confused with classical diseases of great antiquity. For example, during the 1970s, Legionella pneumonia has been separated from pneumococcal lobar pneumonia, with which it was almost certainly confused in the past.

Although some of the conditions discussed in this book are uncommon or even rare, ignorance of these rare diseases is no longer acceptable. Pathologists involved in day-to-day practice are expected to have knowledge of ongoing advances in their field. This book provides a reference work that details the more important advances in pulmonary pathology. It is hoped the reader will be stimulated to review some of the fine original contributions cited here.

London

HERBERT SPENCER

Preface

It is humbling to approach a growing body of knowledge and recognize the many individuals who have helped mold our current concepts. Many have played a role with their hard work and ingenious concepts. At any time, some leaders evolve who are able to synthesize known parts and reach beyond their components to conceive the whole. An exceptionally few are extraordinary in these pursuits. These individuals are usually constantly wondering why something is different, or why it is similar. They are busy assembling the clues. The same individuals are usually able to describe their findings carefully and couch their hypotheses with appropriate wisdom.

This book is dedicated to two such leaders in the field of diagnostic pulmonary pathology. We feel they rightly deserve to be called "the fathers of modern pulmonary pathology."

Dr. Averill A. Liebow was born in Austria, and moved to the United States as a young man. He worked at Yale University and the University of California at San Diego. He is most noted for his many careful descriptions of new diseases in the lung. These were often accompanied by appropriate acronyms. He and his close associates helped to describe chronic eosinophilic pneumonia (CEP), bronchocentric granulomatosis (BCG), pulmonary alveolar proteinosis (PAP), desquamative interstitial pneumonia (DIP), giant cell interstitial pneumonia (GIP), interstitial pneumonia with bronchiolitis obliterans (BIP), and lymphoid interstitial pneumonia (LIP). He and his associates also described small chemodectoma-like bodies, sclerosing hemangiomas, plasma cell granulomas (PCG), pulmonary hyalinizing granulomas (PHG), benign clear cell "sugar" tumors, and intravascular bronchioloalveolar tumors (IVBAT). The spectrum of vasculitis was of particular intrigue to Dr. Liebow, and the entities of limited Wegener's granulomatosis, lymphomatoid granulomatosis (LYG), and necrotizing sarcoid granulomatosis (NSG) were described by him. He and his associates helped to characterize classical Wegener's granulomatosis, usual interstitial pneumonia (UIP), diffuse alveolar damage (DAD), pulmonary histiocytosis X (PHX), lymphangioleiomyomatosis (LAM), and various vascular changes in the lung. Many of Dr. Liebow's papers remain today as classic descriptions. He would not publish a new entity until enough cases were accumulated to describe a reasonable spectrum of that particular disease. Yet when it was time for the definitive publication, having completed the conceptualization of these diseases so thoroughly, Dr. Liebow would often offer the distinction of the first authorship to others.

Dr. Liebow had his "bottom drawer" where an unusual case was placed, awaiting a companion or two, then four or more. He loved his consultation work because it gave him the challenge he enjoyed so much. He also relished teaching, and one of his favorite teaching audiences was medical students, with whom he dealt with great compassion and fatherly guidance.

Herbert Spencer was born and worked in England, most recently at St. Thomas' and St. Mary's Hospitals. He taught frequently and eloquently at all levels. His many articles on topics in pulmonary pathology have greatly contributed to our understanding of disease processes. He did much work on surface proliferations in the lung, including those related to cancer. He enjoyed trying to make sense of the assorted surface lesions in bronchi and bronchioles. He suggested the name "pulmonary blastoma" to indicate the similarity of these lesions to those in the kidney. He published reports on many other conditions in the lung, such as

hypertensive vascular changes and rheumatoid effects. Professor Spencer more recently summarized his extensive experience with the plasma cell granuloma–histiocytoma complex, and added a large series of sclerosing hemangiomas to the literature.

He is a source of stimulation to all who hear him talk, read his works, or have the pleasure of sharing consultations with him. As an open and honest individual, Professor Spencer would often begin his consultations on difficult lung lesions by a statement similar to "I don't know with certainty what this difficult lesion is, but here are some of my thoughts."

His ability to clearly summarize a large amount of literature has been well demonstrated in his outstanding and now classic text, *Pathology of the Lung*. Unaided by coauthors, he nurtured this treatise through four editions—the first in 1962, the latest in 1985. Professor Spencer is a gentleman who always has time to listen and share. In his spare time, he also authored a textbook on tropical pathology, so as not to become lazy between editions of his lung book. He wisely stated, "You never really know about a subject unless you write about it." His semiretired status means he works "a little less." We feel privileged to have Professor Spencer share with us some of his reflections on the growth of modern pulmonary pathology in the Foreword he has so kindly prepared for this book.

The immensity of Professor Spencer's job as solo author of *Pathology of the Lung* became apparent when we began to organize this text. We first thought a comprehensive book might be done by 2 authors, then thought that maybe 5 quite capable souls could do it, and finally decided on a team of 34. Our goal in creating this book was to offer a practical guide to the growing body of literature in pulmonary pathology. We wished it to be reasonably complete, yet easily read.

Pathologists should not work in a vacuum. The patient, whose various tissue and cell specimens we examine, has given much more information to his clinician in the form of history, physical examination, and laboratory test results than is present on the usual tissue request slip received with a specimen in the pathology laboratory. In many cases, it is important that the pathologist be aware of the clinical differential diagnoses and the various physical examination findings and laboratory tests used to arrive at these proposed diagnoses. Likewise, various radiographic studies examining the lungs and mediastinal structures in three dimensions and sectional planes are often critical in making a correct diagnosis and accurate clinical-pathological correlation. In addition, it is not uncommon for pathologists to have only cytologic specimens to make a diagnosis. For these reasons, we include three chapters toward the end of the book that are devoted to cytologic, radiographic, and clinical correlations of lung diseases.

We acknowledge our limitations. Most importantly, the majority of us have limited access to many fine articles in foreign languages, whatever those languages might be. All too often we over-bias our reviews to those articles published in our language, in this case English. We fully appreciate how many significant contributions are in other languages, and we have attempted to include some of these, but know we have sadly missed a significant number. Even within the English literature, we are also quite sure we have missed giving appropriate credit to some investigators. In these cases, we ask for your understanding. Please be assured this was not done with ill intent.

Our contributors have tolerated admirably the many deadlines and details imposed on them. The luxury of time is evasive. We appreciate the extra energy put into producing manuscripts during the course of a busy day or under the handicap of limited resources.

In preparation for this work, many people have helped in many ways. Some are credited in the following section on contributors' dedications and acknowledgements, but many have worked in the background, providing case material, follow-up, searching questions, and secretarial, laboratory, and photographic help. Others have reviewed and advised, and otherwise molded our contributions. We express our appreciation to all these individuals.

There are a few individuals who could always be counted on when problems arose. We wish to give special thanks to three of these individuals: S. Donald Greenberg, John A. Blackmon, and Frederic B. Askin. These individuals were always willing to listen and to make valuable suggestions when sudden crises arose.

We would like to specially acknowledge the many contributions made to pulmonary pathology by the late Charles B. Carrington. References to his many works are given throughout this book. We will sadly miss his future contributions, but are greatly appreciative for what he has given us in the field of pulmonary pathology.

Seattle

DAVID H. DAIL
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Individual Authors' Dedications and Acknowledgments

Often in a multi-contributor book, individual authors do not have a chance to express appreciation to those who have been important to them in both their personal lives and in the composition of their chapters. Such an opportunity is given here.

Dedications

Chapter 1/D.H.D.—Margie, Kim, and Holly Dail

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Color Plates to Chapters 1–19

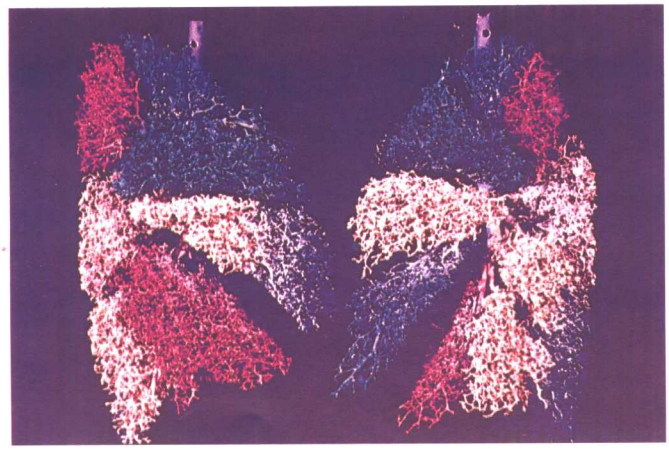

Plate 2–I. Injection corrosion cast with segments colored. (Courtesy of A.A. Liebow Pulmonary Collection, San Diego)

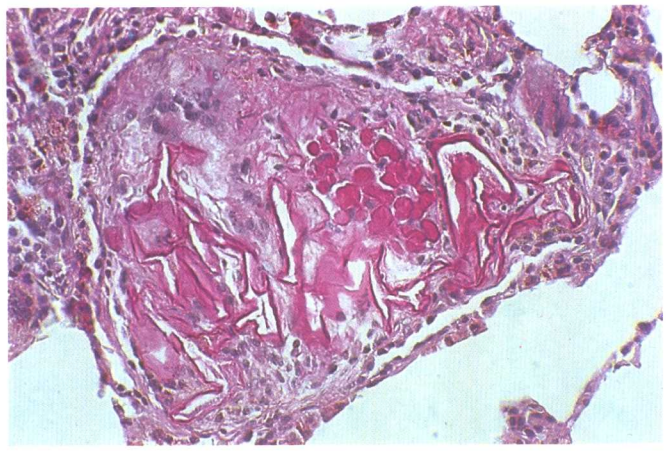

Plate 5–I. PAS stain of aspirated bean, with round starch cells and crumpled cellulose walls. PAS × 400.

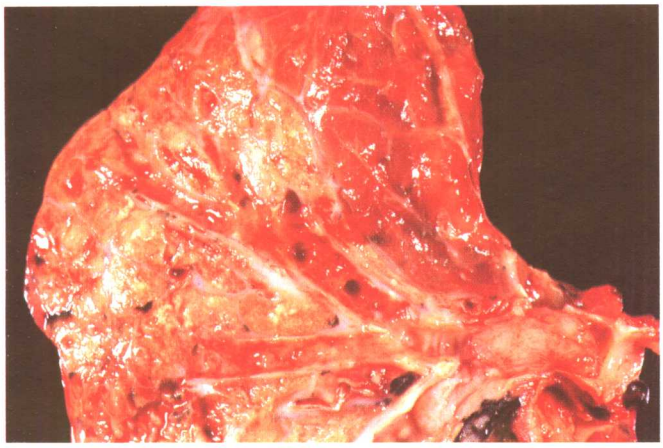

Plate 5–II. Endobronchial squamous carcinoma has produced a golden "post obstructive" pneumonia.

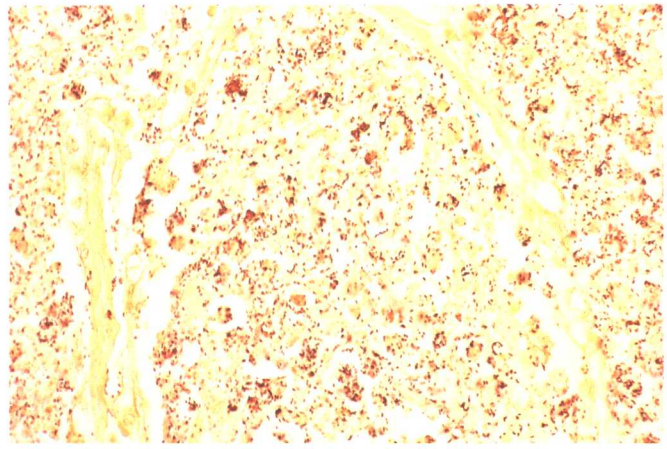

Plate 6–I. *Legionella pneumophila* organisms in alveoli. Dieterle method × 400.

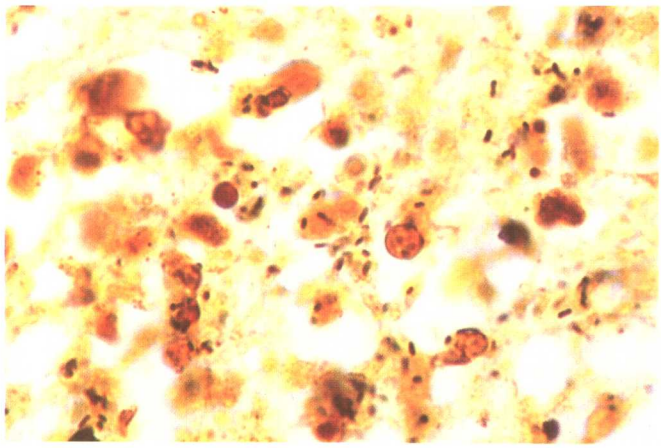

Plate 6–II. *Legionella pneumophila* at high power. Steiner & Steiner × 1000.

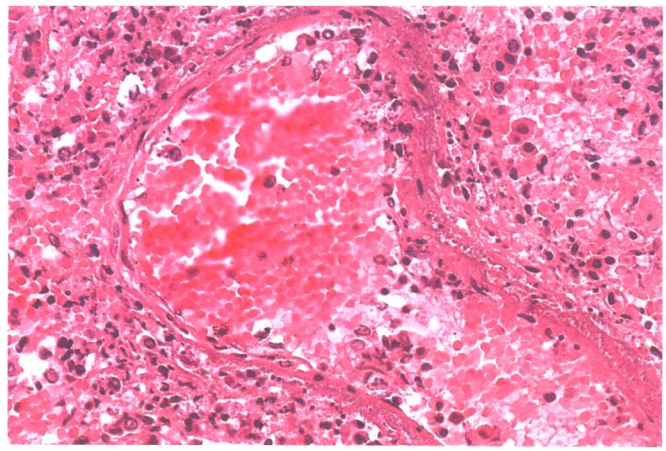

Plate 6–III. *Pseudomonas aeruginosa* vasculitis. H&E × 400.

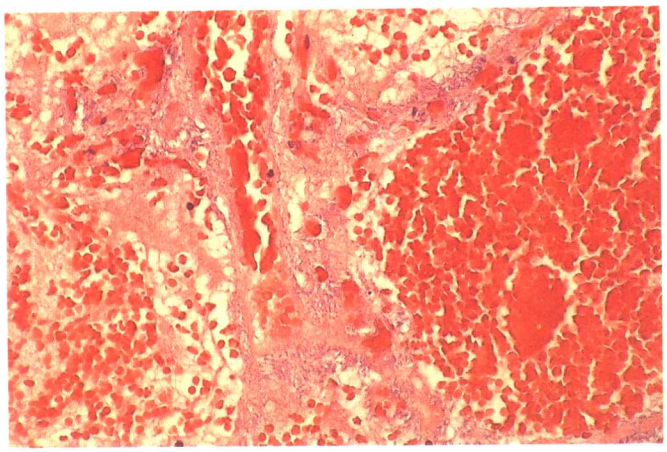

Plate 6–IV. Pseudomonas infiltrating alveolar septa produces a blue color. H&E × 400.

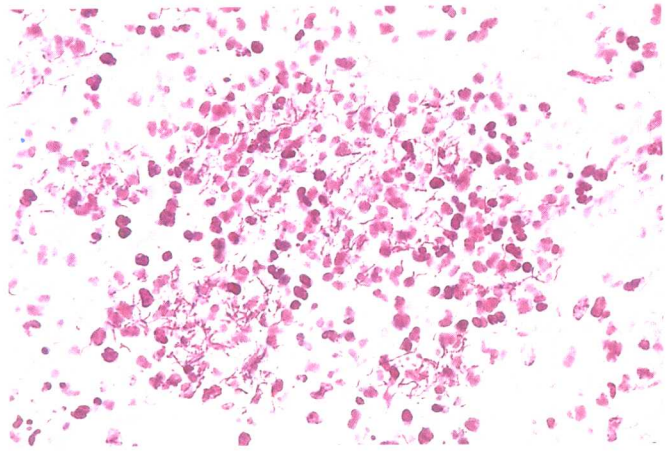

Plate 6–V. *Nocardia asteroides* on tissue Gram stain. Brown & Brenn × 400.

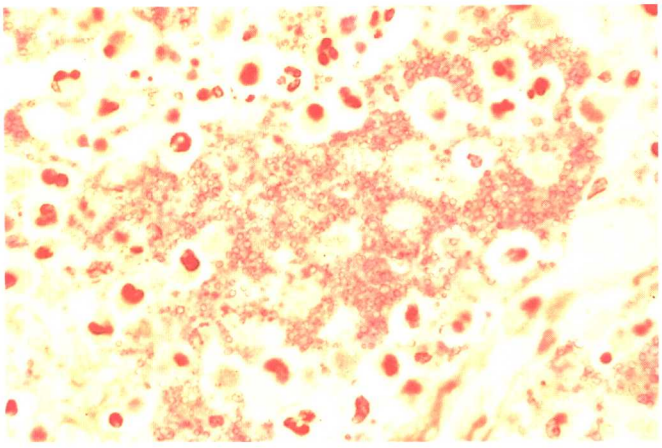

Plate 6–VI. Pneumonia plague with massive number of Gram-negative bacteria. Brown & Hopps × 650.

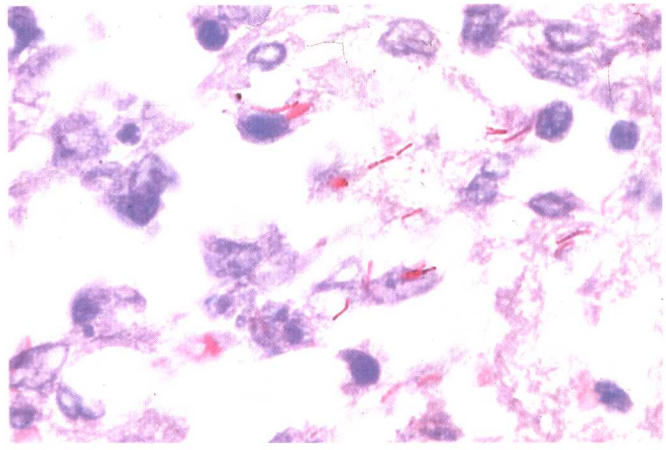

Plate 7–I. *Mycobacterium tuberculosis.* Ziehl-Neelson × 1000.

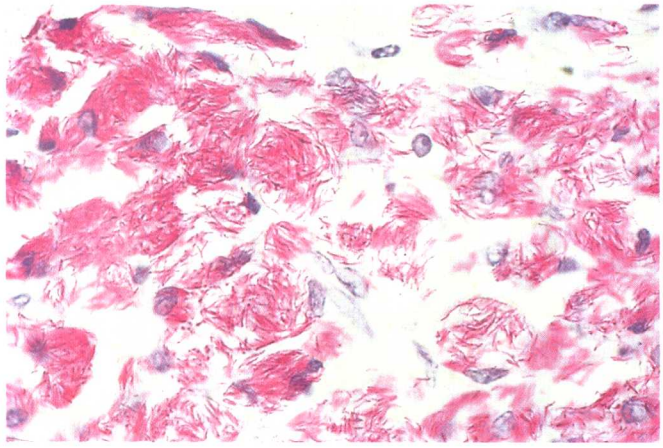

Plate 7–II. *Mycobacterium avium-intracellulare.* Ziehl-Neelson × 1000. PAS stain would appear identical.

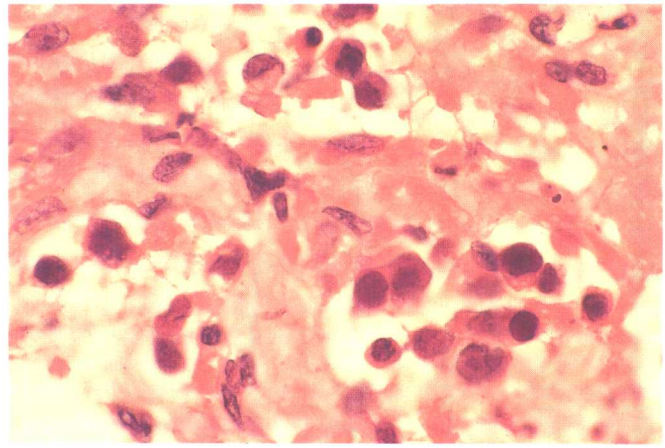

Plate 9–I. Densely basophilic adenovirus intranuclear inclusions with "smudge" cell effect. (see Fig. 9–1) H&E × 250.

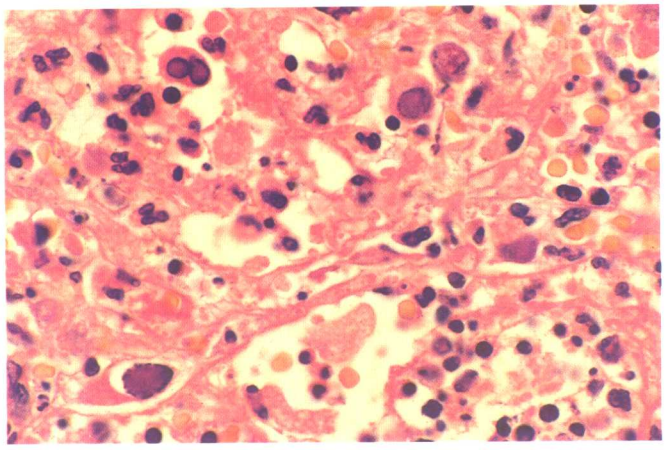

Plate 9–II. Eosinophilic intranuclear herpes simplex inclusions virtually fill entire nucleus. (see Fig. 9–10). H&E × 250.

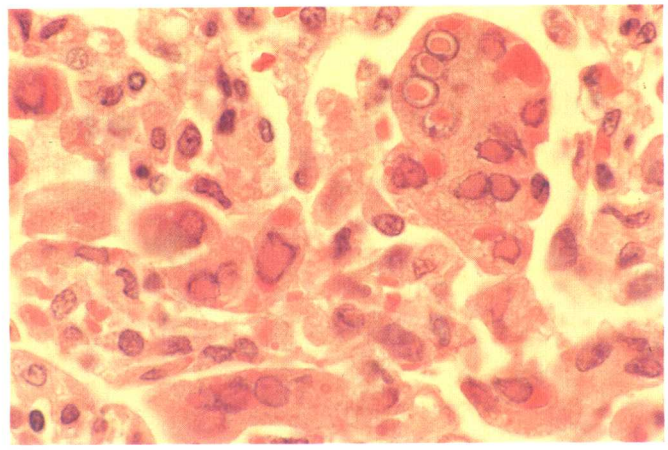

Plate 9–III. Multinucleate measles cells, with intranuclear and cytoplasmic inclusions (see Fig. 9–13). H&E × 250.

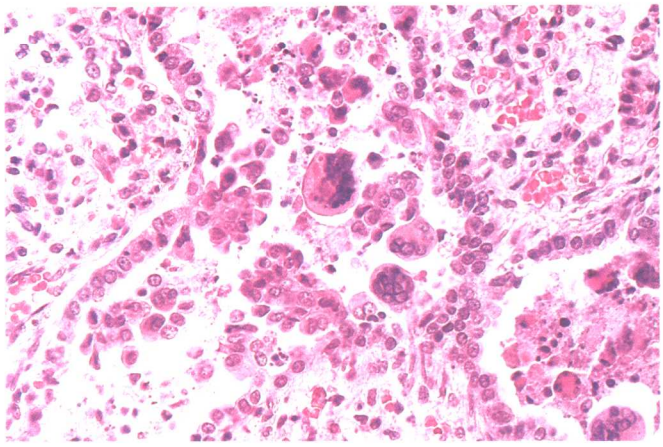

Plate 9–IV. RSV multinucleate cells in a child. Note eosinophilic cytoplasmic inclusion (see Fig. 9–14). H&E × 100.

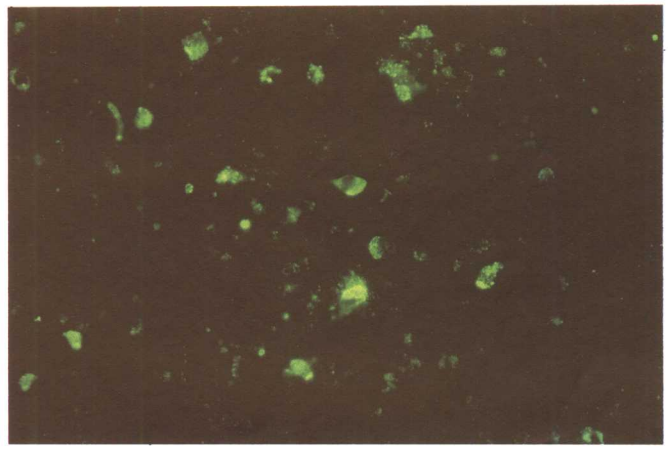

Plate 9–V. RSV indirect immunofluorescence on nasal aspirate. H&E × 125.

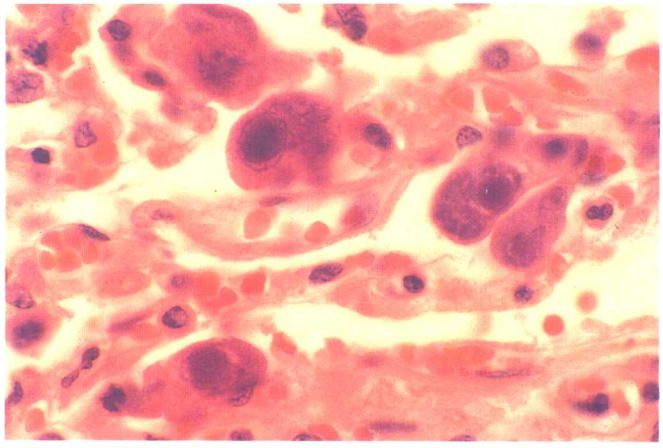

Plate 9–VI. Three CMV infected cells with typical intranuclear and cytoplasmic inclusions (see Fig. 9–20). H&E × 250.

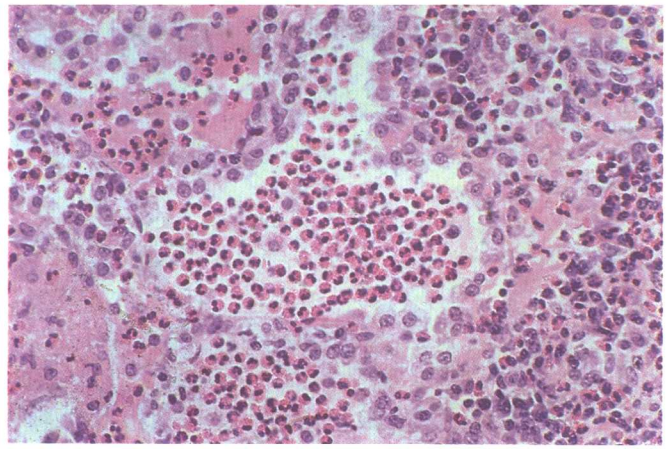

Plate 13–I. Eosinophilic leucocytes flood alveolus in eosinophilic pneumonia. H&E × 250.

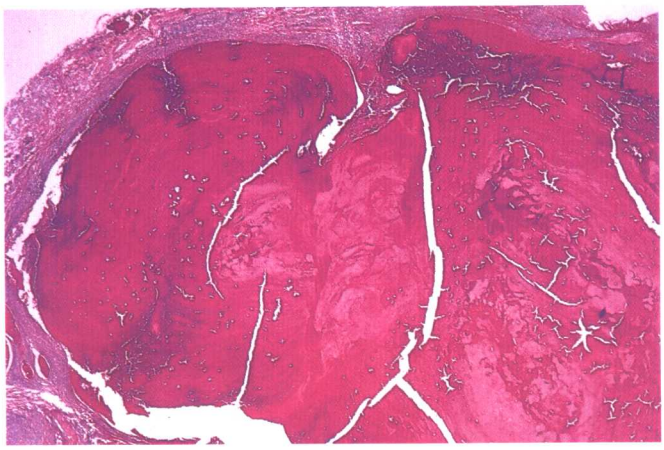

Plate 13–II. Inspissated mucus of mucoid impaction stains vividly. PAS × 25.

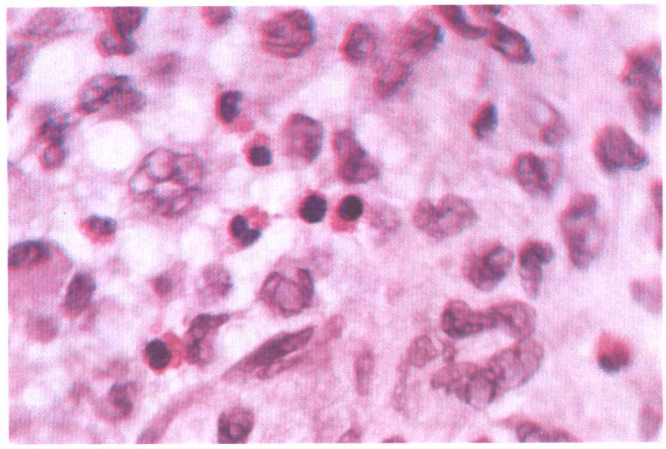

Plate 14–I. Note highly convoluted nuclei of pulmonary histiocytosis X cells. H&E × 550.

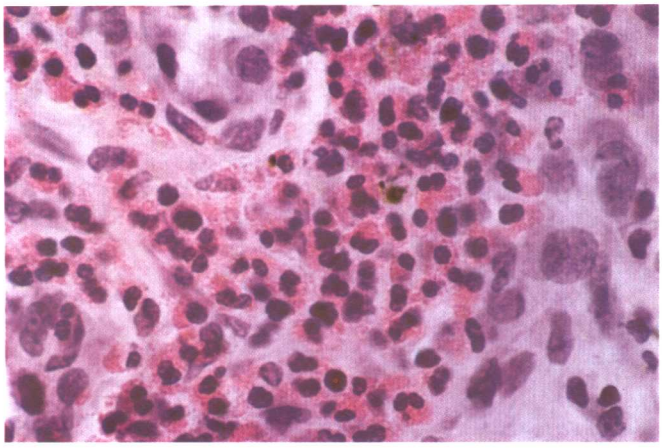

Plate 14–II. Eosinophils are focally increased in pulmonary histiocytosis X. H&E × 550.

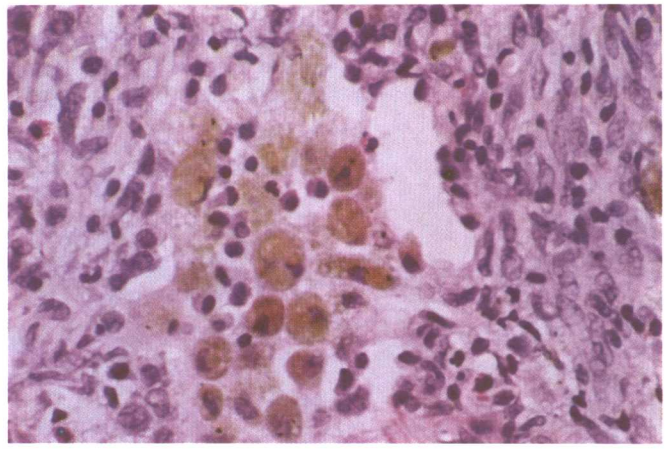

Plate 14–III. Tan-brown pigmented smoker's macrophages are common in pulmonary histiocytosis X. H&E × 330.

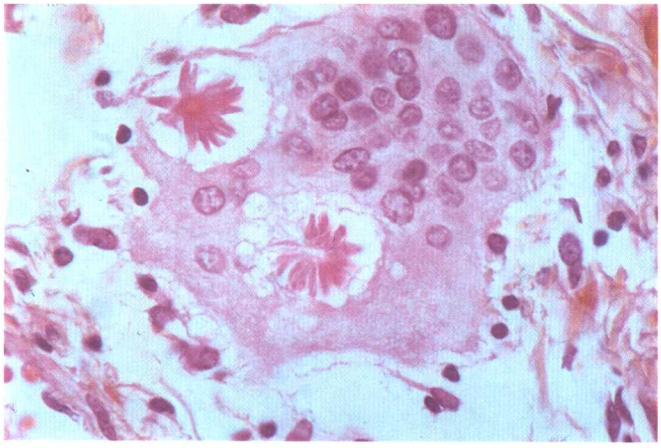

Plate 15–I. Two red asteroid bodies and halos are present in a multinucleate giant cell. H&E × 600.

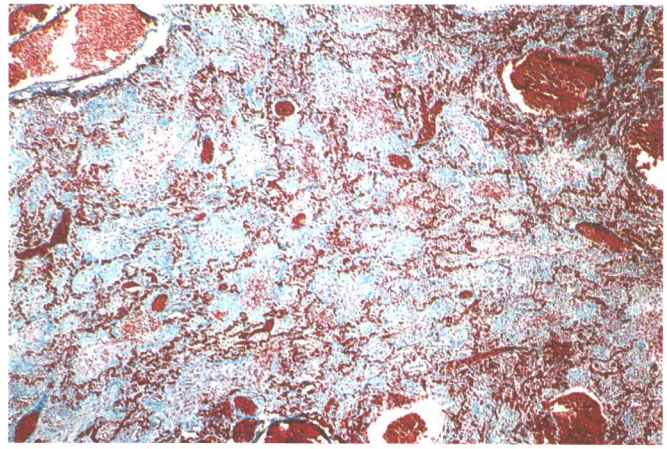

Plate 19–I. Fatal case of Paraquat poisoning. Alveoli are filled with collagen. Masson trichrome × 50 (Courtesy H. Spencer).

Contents

CHAPTER 1

Handling of Surgical Pathology Specimens

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The continuous development of new clinical, radiologic, surgical, and pathologic techniques highlights an ever-changing practice of pathology. With reference to many locations in the body, and certainly in the lung, the pathologist is being asked to be more diagnostic with smaller and smaller samples. Immunohistochemistry and other newer techniques entering diagnostic practice may lead to a diagnosis based on only a few cells. As in electron microscopy, the challenge will be to judge whether such samples are truly representative. Pattern recognition on tissue sections is still valuable, but is being supplemented, and in part replaced, with some of these newer techniques.

The history of change is clear in pulmonary pathology. Autopsy pathology allowed Laennec[1] in 1819, among his many other astute observations, to make some knowledgeable observations of pulmonary tuberculosis (see Chapter 7) and pulmonary edema (see Chapter 25).

Standard thoracotomies are now used only for therapeutic resections. The minithoracotomy for diffuse lung disease diagnosis was introduced by Klassen[2] in 1949. This technique involves entering the anterior fourth or fifth intercostal space and with slight modifications, has led the way to replacing a full thoracotomy for diagnostic purposes. Several variations of the minithoracotomy have been developed. One alternative approach is a mini-anterior thoracotomy through the second or third intercostal space (modified Chamberlain type).[3,4] Another alternative is with a slightly larger incision through the posterior auscultatory triangle that is not as large an incision as is the standard thoracotomy. Some advantages and disadvantages are inherent with each technique. In those done for more limited disease, compared to the greater choice of open biopsy sites in diffuse lung disease, the approach is usually dictated by the distribution of the disease.

The results from rigid bronchoscopy with generously sized biopsies were well outlined by the serial reports of Anderson of 13 patients in 1965,[5] 450 patients in 1972,[6] and 939 in 1978.[7] Rigid bronchoscopy is still used for excisions of central endobronchial lesions and to obtain bigger biopsies of difficult central lesions.

To better reach the upper lobes by the transbronchial route and to enter more distal bronchi, flexible fiberoptic bronchoscopy has been widely accepted in most countries. It was developed in Japan between 1964 and 1966 by Ikeda[7,8] and it was introduced in the United States in 1969. Its original smaller channel biopsy forceps has been replaced by a larger channel (2.6 mm) crocodile forceps allowing capture of samples in the range of 1 to 2 mm. Using the standard 5.2-mm external dimension flexible bronchoscope, Kovnat and associates[9] noted they could obtain direct cannulation of all third order, 74% of fourth order, and 38% of fifth order bronchi. They could directly visualize all fourth order, 86% of fifth order, and 56% of sixth order bronchi. Fluoroscopic guidance has helped localize the endoscope into the abnormal lung regions and, with experience gained from taking multiple biopsies, the limited invasiveness and relative safety of the flexible bronchoscope have made it the standard biopsy technique today.

Complications of this procedure in a large user survey conducted by Herf et al.[10] showed a 5.5% incidence of pneumothorax, a 1.3% incidence of greater than 50 ml of bleeding, and a mortality of 0.24%. A literature review by Zavala[11] found corresponding incidences of 4% pneumothorax, 9% hemorrhage (averaging 25–100 ml where specified), and a mortality of 0.23%, mostly