

RUBIN'S PATHOLOGY:

Clinicopathologic Foundations of Medicine
Fifth edition



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DEDICATION

We dedicate this book to our wives and families, whose love and support throughout this endeavor sustained us; To our colleagues, from whom we have learned so much; And to students everywhere, upon whose curiosity and energy the future of medical science depends.

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Pathology is the study of disease and its effects on the organism. This discipline is a prerequisite for rational medical therapeutics, and has its roots in the early attempts of scholars to understand how human disease begins, manifests and progresses. Celsus (25 BC–50 AD) was the first to describe the cardinal signs of inflammation: *tumor* (swelling), *rubor* (redness), *calor* (heat) and *dolor* (pain). However, deeper understanding of disease awaited several developments that did not occur for one and one half millennia.

The first major advance was the introduction of the necropsy by Antonio Benivieni (1443–1502). The modern approach to autopsy technique was pioneered by Carl Rokitansky (1804–1878) in Vienna. Among the most important applications of post-mortem examination is to elucidate the course of a disease in an individual patient, as manifest through its clinical symptoms and signs. Giovanni Morgagni (1682–1771) is credited with developing the concept of clinicopathologic correlation, which remain the foundation of our approach to the study of disease.

The compound microscope was invented in 1595 in Holland by Zacharias Jansen (1588–1631). In 1665, Robert Hooke (1635–1703) in England first coined the term “cell” after examining a piece of cork under a microscope. Nearly 200 years elapsed until the theory of the cell as the building block of all living organisms was enunciated by Matthias Schleiden (1804–1881) and Theodor Schwann (1810–1882). The theory was refined by Rudolf Virchow (1821–1902) to stipulate that all existing cells derive from previously existing cells, and pathologic reactions are, therefore, reactions of cells.

As the techniques used to study the human body in health and disease evolved from structural to mechanistic, diverse scientific disciplines have been at the forefront of medical progress, including physiology, biochemistry, biophysics, immunology, genetics and, more recently, molecular biology, genomics and proteomics. The approaches pioneered by investigators in these areas have been adopted as tools of the pathologist: cellular biochemistry, electron microscopy, immunostaining, flow cytometry, molecular probes and genetic analysis, to name a few. Thus, the coordinate evolution of biological research and pathology continues to provide new opportunities to understand and, hopefully, treat disease. The medical significance of seemingly arcane mutations or signaling pathways is increasingly evident, and with the advent of pharmacologic and genetic manipulation, continues to enter the realm of medical practice.

The basic function of Pathology in the medical curriculum and in medical practice has become less descriptive and more mechanistic and integrative. Pathology, as presented in this text, and as practiced in most medical schools, is in equal measure

morphology and pathophysiology. As such, this text seeks to relate clinical and histological manifestations of disease to their basic mechanisms.

The student arrives in the Pathology classroom having mastered the basic sciences of the medical curriculum: physiology, biochemistry, anatomy, molecular biology, etc. It is in the context of Pathology that a framework for future medical training is constructed, by integrating these subjects into the setting of a whole patient. Disease processes may be seen as injuring cells and impairing organ function, altering signaling cascades and cytokine production and upsetting the balance of electrolytes and cells in the blood. But Pathology breathes life into these analyses by focusing on the consequences of these abnormal processes for the human being.

In this context, this 5th edition of *Rubin's Pathology* presents Pathology as the clinicopathologic foundation of medicine, and endeavors to provide medical students and their instructors with a lucid discussion of basic disease processes and their effects on cells, organs and people. Significant advances in the understanding of basic pathophysiologic processes are incorporated into revised chapters on basic disease processes (Chapters 1–9) and specific organ pathology (10–30). Notable examples include new sections on proteasomal degradation, stem cells, diabetes and obesity, emerging infections and agents of biowarfare.

This edition also represents a transition in editorship. Emanuel Rubin, the founder and main Editor of this textbook for its first four editions, is now Consulting Editor. With deepest appreciation for Manny's contribution to this work and to our careers, and with the encouragement of the publishers, we have assumed editorial responsibility for this textbook. New contributors from many institutions have joined the distinguished roster of authors. We include for the first time ancillary learning materials: audio questions, on-line text and illustrations and case studies. Self-assessment and review is further available using the companion text *Review of Pathology*.

Pathology is a dynamic discipline. Any textbook such as this is a snapshot of an object in motion. It has been our goal to provide an authoritative instructional and reference text that accurately portrays the field in 2006–2007, both what is known and what remains to be explained. We hope that our students will share the excitement of discovery that we have been privileged to experience in our education and careers.

Raphael Rubin
David S. Strayer
Philadelphia
January, 2007



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