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Textbook of Pathology

病理学

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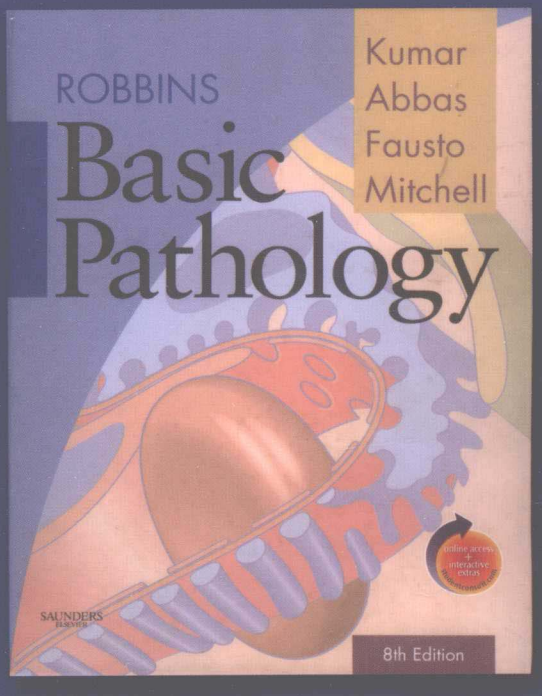
《Robbins基础病理学》第8版英文改编版



北京大学医学出版社

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北京大学医学出版社
Peking University Medical Press

图书在版编目（CIP）数据

病理学：英文／（美）翟启辉，周庚寅主编. －北京大学医学出版社，2009.
ISBN 978-7-81116-486-2

Ⅰ. 病… Ⅱ. ①翟…②周… Ⅲ. 病理学－医学院校－教材－英文 Ⅳ. R36

中国版本图书馆CIP数据核字 (2009) 第061109号

北京市版权局著作权合同登记号：图字：01-2008-2964

Robbins Basic Pathology, 8th Edition
ISBN-13: 978-1-4160-2973-1
ISBN-10: 1-4160-2973-7

Authorized English Adaptation from English language edition published by the Proprietor.
978-981-272-211-9
981-272-211-4
Elsevier (Singapore) Pte Ltd.
3 Killiney Road, #08-01 Winsland House I, Singapore 239519
Tel: (65) 6349-0200, Fax: (65) 6733-1817
First Published 2009
2009年初版

病理学

主　　编：翟启辉　周庚寅
出版发行：北京大学医学出版社（电话：010-82802230）
地　　址：（100191）北京市海淀区学院路38号 北京大学医学部院内
网　　址：http://www.pumpress.com.cn
E - mail：booksale@bjmu.edu.cn
印　　刷：北京圣彩虹制版印刷技术有限公司
经　　销：新华书店
责任编辑：张凌凌　　责任校对：杜悦　　责任印制：郭桂兰
开　　本：889mm×1194 mm　1/16　印张：30.5　字数：1216千字
版　　次：2009年8月第 1 版　2009年8月第1次印刷
书　　号：ISBN 978-7-81116-486-2
定　　价：99.00元

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改编版前言

为使医学教育和国际逐步接轨，双语教学在我国医学院校已推行多年，但至今仍然缺乏被广泛认可的教科书。自编的教材受英语水平的限制，语言表达上往往不尽人意。

Robbins Basic Pathology 是在全世界深受欢迎并被广泛采用的权威性教学用书，其立足前沿的理论知识、独特精致的编写风格、严谨规范的专业术语、图文交融的编排方式，无一不受到广大医学生和病理学工作者的推崇和青睐。是美国医学生学习病理学的首选教材，病理医师资格考试的必读用书，也是我国中文病理教材编写的主要参考书。

*Robbins Basic Pathology*原版的国际版和影印版已在国内销售，但由于价格依然偏高，某些内容与中国的教学习惯不完全吻合，尚难作为病理学教科书广泛应用。基于该书在国际上的影响力及我国的医学教育现状，北京大学医学出版社决定与ELSEVIER公司联合对该书进行改编。其目的是在不改变原书风格和基本内容的前提下，通过改编、精编和缩编使其内容和编排顺序符合中国的教学习惯。贴近前沿、贴近临床、贴近我国的教学实际是本书改编的主要宗旨。

本书依据*Robbins Basic Pathology*的最新版第8版进行改编。在改编过程中，对本书的内容进行了删节、调整和适当补充，个别章节有较大的更新和改动。同时，在内容上兼顾了临床医学及其他相关专业和不同学制的需求。因此本书可用作临床医学、口腔、公共卫生专业的五年制、七年制、八年制和留学生的双语教学用书，也可作为病理医生和进修生的重要参考书，以及作为执业医师资格考试的复习用书。

本书编委均来自教学第一线，在双语教学和教材编写方面均具有丰富的经验。在繁重的病理教学、科研和诊断工作的同时，大家辛勤劳作，不遗余力地完成了初稿的编写；另有几位美国的病理学同道也参与了本书的编写。最后，又经美国的病理学专家翟启辉教授修改润色，反复斟酌，力求行文准确、简明易懂，体现原书的学术水平和语言风格。本书的编委会秘书陈方杰女士和山东大学病理学教研室的吴晓娟医师做了大量卓有成效的工作，山东大学病理学教研室的李丽、吴晓娟、项磊、张晓芳和桂婷参与了部分章节的二校，出版社的责任编辑也付出了辛勤劳动，在此一并表示感谢。另外，本书原版主编Kumar教授对本书的改编给予热情支持，并在百忙之中欣然作序，我们在享受其学术成果的同时，在此谨致由衷的谢意。

改编是双语教材编写的尝试和探索，疏漏和错误在所难免，愿广大病理学同道和学生在使用中不断提出宝贵意见，以期再版时不断完善。

翟启辉　周庚寅

2009年5月

Preface

I am pleased and honored to write the preface for *Robbins Basic Pathology* that has been specifically designed for use in China. Rather than translating *Basic Pathology* into Chinese, this book has been adapted in English so that medical students in China are exposed early in their education to the most widely used language for medical literature. It is my sincere hope that this will enhance the medical education of Chinese students.

Although the general organization of this edition will remain the same as in the US edition, special efforts have been made by the editors to make this book more suitable for Chinese medical students. Some of the chapters have been combined and material that is particularly relevant for Chinese students such as a discussion of avian influenza has been added. To provide maximal benefit to readers this edition will conform to the guidelines for the eight year medical school curriculum prescribed by the Chinese Ministry of Education. While the main focus will remain on basic pathology, appropriate advances in molecular pathology have also been integrated.

This book has been edited by leading Chinese pathologists and educators based in China and in the US, thus ensuring the highest standards as well as relevance for the Chinese medical students. I am grateful to all the distinguished colleagues for their willingness to undertake this important task.

Vinay Kumar

Contents

Introduction to Pathology

WHAT IS PATHOLOGY?

Literally translated, *pathology* is the study *(logos)* of suffering *(pathos)*. It is a discipline that bridges clinical practice and basic sciences, and it involves the investigation of the causes *(etiology)* of disease as well as the underlying mechanisms *(pathogenesis)* that result in the presenting signs and symptoms of the patient. Pathologists use a variety of molecular, microbiologic, and immunologic techniques to understand the biochemical, structural, and functional changes that occur in cells, tissues, and organs. Traditionally, the discipline is divided into general pathology and systemic pathology; the former focuses on the fundamental cellular and tissue responses to pathologic stimuli, while the latter examines the particular responses of specialized organs.

Pathology is divided into two main branches, Anatomical Pathology and Clinical Pathology. In America, pathologists often practice both anatomical and clinical pathology, a combination known as general pathology. Veterinary pathology is concerned with animal disease whereas Phytopathology is the study of plant diseases.

Anatomic Pathology. Anatomic pathology is a medical specialty that is concerned with the diagnosis of disease based on the gross, microscopic, and molecular examination of organs, tissues, and whole bodies (autopsy). Anatomical pathology is itself divided into subspecialties, the main ones being surgical pathology, cytopathology and forensic pathology.

Clinical Pathology. In our Chinese hospital system, we consider the clinical pathology as laboratory tests, and is not a part of pathology. However, in most of the other countries, clinical pathology is a medical specialty that is concerned with the diagnosis of disease based on the laboratory analysis of bodily fluids such as blood and urine, using the tools of chemistry, microbiology, hematology and molecular pathology. Clinical pathologists work in close collaboration with medical technologists. Clinical pathology is itself divided into subspecialties, the main ones being clinical chemistry, clinical hematology/blood banking and clinical microbiology.

HOW TO STUDY PATHOLOGY?

In this book, we first cover the principles of general pathology and then proceed to specific disease processes as they affect particular organs or systems.

The four aspects of a disease process that form the core of pathology are its cause (etiology), the mechanisms of its development (pathogenesis), the structural alterations induced in the cells and organs of the body (morphologic changes), and the functional consequences of the morphologic changes (clinical significance).

Etiology or Cause. The concept that certain abnormal symptoms or diseases are "caused" is as ancient as recorded history. For the Arcadians (2500 B.C.), if someone became ill, it was the patient's own fault (for having sinned) or the makings of outside agents, such as bad smells, cold, evil spirits, or gods. In modern terms, there are two major classes of etiologic factors: intrinsic or genetic and acquired (e.g., infections, nutritional, chemical, and physical). Knowledge or discovery of the primary cause remains the backbone on which a diagnosis can be made, a disease understood, or a treatment developed. The concept, however, of one etiologic agent to one disease—developed from the study of infections or single-gene disorders—is no longer sufficient. Genetic factors are clearly involved in some of the common environmentally induced maladies, such as atherosclerosis and cancer, and

the environment may also have profound influences on certain genetic diseases.

Virtually all forms of organ injury start with molecular or structural alterations in cells, a concept first put forth during the 19th century by Rudolf Virchow. We therefore begin our consideration of pathology with the study of the origins, molecular mechanisms, and structural changes of cell injury. Yet different cells in tissues constantly interact with each other, and an elaborate system of extracellular matrix is necessary for the integrity of organs. Cell-cell and cell-matrix interactions, contribute significantly to the response to injury, leading collectively to tissue and organ damage, which are as important as cell injury in defining the morphologic and clinical patterns of disease.

Pathogenesis. Pathogenesis refers to the sequence of events in the cellular or tissue response to an etiologic agent (the initial stimulus) to the ultimate expression of the disease. The study of pathogenesis remains one of the main domains of pathology. Even when the initial infection or molecular cause is known, it may be many steps removed from the expression of the disease. For example, to understand cystic fibrosis is to know not only the defective gene and gene product but also the biochemical, immunologic and morphologic events leading to the formation of cysts and fibrosis in the lung, pancreas, and other organs. Indeed, as we shall see throughout the book, the molecular revolution has already identified mutant genes underlying a great number of diseases. Nevertheless, the functions of the encoded proteins and how mutations induce disease are often still obscure. Thus, the study of pathogenesis has never been more exciting scientifically or more relevant to the development of new therapies.

Morphologic Changes. The morphologic changes refer to the structural alterations in cells or tissues that are either characteristic of the disease or diagnostic of the etiologic process.

Functional Derangements and Clinical Significance. The nature of the morphologic changes and their distribution in different organs or tissues influence normal function and determine the clinical features (symptoms and signs), course, and prognosis of the disease.

Pathology is a foundation for the clinical specialties. It involves many basic medical sciences such as anatomy, histology, embryology, physiology, biochemistry, molecular biology, microbiology and immunology. To attend lectures, lab session, clinical pathological conference, and observation of autopsy are the essential components of the learning and training process. How well you understand pathology is directly related to the success of the future medical profession.

DIAGNOSTIC AND RESEARCH TECHNIQUES IN PATHOLOGY

I. Human Pathology

A. Diagnostic Applications in Human Pathology

1. Autopsy. Autopsies are performed to determine the cause of death by examination of a cadaver, mainly in two situations: at the request of clinicians (with relatives' consent) to verify the cause of death, and to see whether the correct diagnosis was made in life and the appropriate treatment given, and at the request of the Coroner, usually during the investigation of criminal law cases and civil law cases in some jurisdictions. Those who specialize in autopsies are Forensic Pathologists. Forensic pathology is a critical component now in the criminal investigation.

2. Biopsy, Intraoperative Interpretation, and Resection

- *Biopsy.* a procedure where diseased tissue is removed from the body for laboratory examination to determine whether cancer or inflammation is present. A biopsy can be performed using a needle to extract a small piece of tissue or as a surgical procedure to remove a larger piece of tissue.
- *Frozen section.* a procedure done by the pathologist during an operation to give the surgeon an immediate answer as to whether a tissue is benign (non-cancerous) or malignant (cancerous).
- *Resection.* a procedure to remove an entire diseased area or organ (occasionally multiple organs) is often performed during the definitive surgical treatment of a disease where the diagnosis is already known or strongly suspected. In this case, the pathologist examines the removed tissue to (1) decide whether the previously-suspected diagnosis is correct, (2) investigate whether there were any unsuspected concurrent diseases, and (3) determine whether the entire diseased area was removed. Especially in the case of cancer, if there is any small area of disease remaining in the patient, another operation or further treatment is often necessary. One example of a resection is a mastectomy, where the specimen consists of the entire breast, plus the overlying skin and axillary lymph nodes.

3. Cytopathology. Cytology is the diagnosis of disease from individual cells, such as cervical smears or fluid from cysts. This is much faster to perform than histology, but has more limited diagnostic abilities. In general, cytology is used as a rapid screening test to determine whether something is malignant or not. Currently there are two major techniques to collect the material including exfoliative cytology, and fine needle aspiration (FNA) or

needle aspiration biopsy. Cell blocks can be prepared for additional stains to make an accurate diagnosis.

B. Basic Techniques Used in the Diagnosis

- *Gross observation* is the first and critical step to handle a specimen. The major tools are unaided eyes, ruler, and balance. The size, color, consistency of the lesion and its anatomic relationship with the adjacent normal tissue should be described and recorded. Sampling of the lesion and normal tissue is the essential component of the diagnostic process. Tissue sampling is irreversible; it requires systematic training and necessary skills from the pathology residents or pathologists.
- *Histopathology* is the diagnosis of disease by studying tissue samples. These range from tiny biopsies (for instance, from someone's stomach taken by endoscopy) to organs removed at an operation (e.g., a colon containing a cancer). From these specimens, we select areas to take sections from, which are stained and examined under a microscope.
- *Immunohistochemistry* or *IHC* refers to the process of localizing proteins in cells of a tissue section exploiting the principle of antibodies binding specifically to antigens in biological tissues. Immunohistochemical staining is widely used in the diagnosis of abnormal cells such as those found in cancerous tumors. Visualizing an antibody-antigen interaction can be accomplished in a number of ways such as immunoperoxidase and immunofluorescence. IHC techniques have been used since the 1940s. It is not only a critical and necessary diagnostic tool in surgical pathology, but it is getting more and more important in the patient prognosis and prediction to the therapeutic response to certain chemotherapy protocol.
- *Molecular pathology* is an emerging discipline which is focused on the study and diagnosis of disease through the examination of molecules within organs, tissues or bodily fluids. Molecular pathology shares some aspects of practice with anatomic pathology, clinical pathology, molecular biology, biochemistry, proteomics and genetics. It is a multi-disciplinary approach that encompasses the development of molecular and genetic techniques to the diagnosis and classification of human tumors, the design and validation of predictive biomarkers for treatment response and disease progression, the susceptibility of individuals of different genetic constitution to develop cancer, and the environmental and lifestyle factors implicated in carcinogenesis.
- *Personalized pathology* is an emerging concept that each specimen contains a molecular and genetic signature that is different from other specimens with similar morphological features. Traditionally, pathologists have used a series of morphologic techniques and relied on the microscopic appearance of resected tissues to determine a pathologic diagnosis and, with respect to neoplastic lesions, provide predictions of a biopsy or the potential clinical behavior that might be anticipated. With the introduction of the techniques of molecular biology in medicine, the role of the pathologist has changed. With the pathologist's unique perspective on disease processes and access to tissue specimens from the operating room, he or she has become a key player in the area of personalized medicine and the development of new approaches to diagnosis and translational research. With the help of personalized pathology, each patient can be treated with a specific protocol individually designed with the hope to optimize the effect and best possible therapeutical outcome.

II. Experimental Pathology

1. Animal Experiment

Experiments are performed on animal models which mimic human disease to investigate the etiologies, pathogenesis, and the behavior of certain diseases. Its major advantages are the flexibilities to design the study based on the aims, goals and hypothesis, which are not applicable in human bodies. Animals are used for pharmaceutical tests, such as the dose effect and dynamics which can accumulate tremendous amounts of data to prepare for the human clinical trials. Another example is the carcinogenesis mechanisms of certain substances that can be studied on animals, which are not ethically allowed on human beings. However, the data from animals can not be directly applied or translated to human patients. Careful translational evaluation is extremely important prior to designing a clinical trial.

2. Tissue and Cell Culture

Tissue culture is the method of keeping tissue alive and growing in vitro in a specialized media containing a rich mixture of essential amino acids, vitamins, and peptides, thus replicating conditions in which the tissue normally grows in an animal or human. Applications and uses of tissue culture in the biosciences are myriad and are growing exponentially.

WHAT DO PATHOLOGISTS DO?

Pathologists are physicians who diagnose and characterize disease in living patients by examining biopsies, resections or bodily fluid. They do not usually see patients directly; instead, they tell other doctors what disease their patient has, whether it is benign (nice) or malignant (nasty), and whether or not it is completely excised. Very few diagnoses