



Prostate Pathology

Peter A Humphrey, MD, PhD



*To my wife Kay, with love, for her tolerance of stolen time
and for allowing transformation of rooms in our house into rooms dedicated to the book,
and to my wonderful children Tom and Jen.*

■

Prostate Pathology

Peter A Humphrey, MD, PhD

*Professor of Pathology and Immunology
Division of Surgical Pathology
Department of Pathology and Immunology
Washington University School of Medicine
St Louis, Missouri*

■



American Society for Clinical Pathology
Chicago

■

Publishing Team

Erik Tanck (production)
Terri Horning (production)
Erica Haratsaris (production)
Joshua Weikersheimer (consulting publisher)



Copyright © 2003 by the American Society for Clinical Pathology.
All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the publisher.

Printed in Hong Kong

05 04 03 02 01 5 4 3 2 1

■

Preface viii**Acknowledgments ix****CHAPTER 1****Prostate Gland Development and Anatomic Structure 2**

- [1.1] Introduction to Prostate Gland Location and Function **3**
- [1.2] Historical Perspective of Anatomy and Concepts of Lobes and Zones **3**
- [1.3] Embryology and Development **3**
- [1.4] Maldevelopment **5**
- [1.5] Adult Prostate Anatomy **7**
- [1.6] Prostatic Tissue Ectopia **22**

CHAPTER 2**Prostatic Tissue Handling and Sampling 30**

- [2.1] Cytologic Specimens **32**
- [2.2] Core Needle Biopsy **32**
- [2.3] Transurethral Prostatectomy (TURP) **40**
- [2.4] Open Suprapubic or Retropubic Simple Prostatectomy (Enucleation) Tissue **44**
- [2.5] Radical Perineal and Retropubic Prostatectomy **44**
- [2.6] Cystoprostatectomy **51**
- [2.7] Postmortem Examination of the Prostate **51**

CHAPTER 3**Fine Needle Aspiration Biopsy of the Prostate 58**

- [3.1] The Cells **59**
- [3.2] Benign Diseases of the Prostate **62**
- [3.3] Malignant Diseases of the Prostate **64**
- [3.4] Variants of Prostatic Carcinoma **68**

CHAPTER 4**Inflammation and Infection 76**

- [4.1] Clinical Prostatitis **77**
- [4.2] Clinical Bacterial Prostatitis **77**
- [4.3] Histologic Acute Inflammation **78**
- [4.4] Clinical Chronic Bacterial Prostatitis **80**
- [4.5] Clinical Chronic Abacterial Prostatitis (Inflammatory) **80**
- [4.6] Histologic Chronic Inflammation **80**
- [4.7] Clinical Chronic Abacterial Prostatitis (Noninflammatory), or Prostatodynia **86**
- [4.8] Granulomatous Prostatitis **86**
- [4.9] Vasculitis **94**
- [4.10] Infections Prostatitis: Additional Types **94**

CHAPTER 5**Atrophy 100**

- [5.1] Classification **101**
- [5.2] Pathologic Features **101**
- [5.3] Differential Diagnosis **109**
- [5.4] Biological Significance **111**

CHAPTER 6**Metaplasia 114**

- [6.1] Squamous Cell Metaplasia **115**
- [6.2] Transitional Cell Metaplasia **119**
- [6.3] Mucinous Metaplasia **121**
- [6.4] Paneth Cell–Like Metaplasia **122**
- [6.5] Nephrogenic Metaplasia (Adenoma) and Stromal Metaplasia **123**

CHAPTER 7**Hyperplasia 126**

- [7.1] Incidence **127**
- [7.2] Etiology **127**
- [7.3] Pathogenesis **127**
- [7.4] Clinical Features **128**
- [7.5] Usual Nodular Epithelial and Stromal Hyperplasia **129**
- [7.6] Basal Cell Hyperplasia **140**
- [7.7] Cribriform Hyperplasia **144**
- [7.8] Mesonephric Remnant Hyperplasia **145**
- [7.9] Verumontanum Mucosal Gland Hyperplasia **147**

CHAPTER 8**Atypical Adenomatous Hyperplasia (Adenosis) 154**

- [8.1] Atypical Adenomatous Hyperplasia (Adenosis) **155**
- [8.2] Sclerosing Adenosis **162**

CHAPTER 9**Unusual Benign Conditions 166**

- [9.1] Pigment Disorders: Melanosis, Blue Nevus, and Ochronosis **167**
- [9.2] Amyloid in the Prostate **169**
- [9.3] Collagenous Spherulosis **169**
- [9.4] Postoperative Spindle Cell Nodule **170**
- [9.5] Endometriosis **171**
- [9.6] Extramedullary Hematopoiesis **171**
- [9.7] Teratoma **171**
- [9.8] Cowper's Glands **172**

CHAPTER 10**Pseudoneoplastic Lesions 176**

- [10.1] Pseudoneoplastic Lesions of Prostate 177
- [10.2] Pseudoneoplastic Lesions of Extraprostatic Tissues 177

CHAPTER 11**Prostatic Intraepithelial Neoplasia 182**

- [11.1] History of Diagnostic Terminology 183
- [11.2] Clinical Presentation 183
- [11.3] Incidence of PIN in Core Needle Biopsies 184
- [11.4] Incidence of High-Grade PIN in TURP Chips and Simple (Open) Prostatectomies 184
- [11.5] Incidence of High-Grade PIN in Whole Prostate Glands 185
- [11.6] Histologic Diagnosis of PIN 186
- [11.7] Low-Grade PIN 186
- [11.8] High-Grade PIN 188
- [11.9] Follow-up and Clinical Management of High-Grade PIN 203
- [11.10] PIN Reporting 205
- [11.11] PIN as Precursor 205
- [11.12] Summary 210

CHAPTER 12**Focal Glandular Atypia 218**

- [12.1] FGA in Needle Biopsy 219
- [12.2] FGA in TURP Chips and Simple Prostatectomy Specimens 224

CHAPTER 13**Clinical Aspects of Prostatic Carcinoma, With Histopathologic Correlations 226**

- [13.1] Etiology 231
- [13.2] Clinical Presentation 234
- [13.3] Natural History and Mortality 241
- [13.4] Treatment 245

CHAPTER 14**Adenocarcinoma 258**

- [14.1] General Approach 259
- [14.2] Diagnosis of Adenocarcinoma in Needle Core Biopsy 275
- [14.3] Diagnosis of Adenocarcinoma in Transurethral Resections and Open Prostatectomies 289
- [14.4] Diagnosis of Adenocarcinoma in Radical Prostatectomy Specimens 294
- [14.5] Diagnosis of Prostatic Adenocarcinoma in Locally Advanced and Metastatic Disease 311

CHAPTER 15**Grading of Prostatic Carcinoma 338**

- [15.1] History 339
- [15.2] World Health Organization (Mostofi) System 340
- [15.3] Gleason System 340
- [15.4] Grading in Metastatic Deposits 355
- [15.5] Grading After Radiation and Hormonal Therapy 355
- [15.6] Grade Progression 356
- [15.7] Prognosis and Grade 356

CHAPTER 16**Staging of Prostatic Carcinoma 376**

- [16.1] TNM AJCC/UICC Staging Classification 377
- [16.2] Clinical Staging 378
- [16.3] Pathologic TNM Staging 379
- [16.4] Pretreatment Models of Pathologic Stage 381
- [16.5] Stage Relationships with Pathologic Findings 382
- [16.6] Stage and Patient Outcome 382
- [16.7] Experimental Staging Procedures 384
- [16.8] Reporting of Pathologic Stage 385

CHAPTER 17**Variants of Prostatic Carcinoma 390**

- [17.1] Prostatic Ductal Adenocarcinoma 391
- [17.2] Mucinous (Colloid) Adenocarcinoma 400
- [17.3] Signet-Ring Carcinoma 403
- [17.4] Adenosquamous and Squamous Carcinomas 406
- [17.5] Basaloid and Adenoid Cystic "Carcinomas" 408
- [17.6] Transitional Cell (Urothelial) Carcinoma 410
- [17.7] Small Cell Carcinoma 414
- [17.8] Sarcomatoid Carcinoma (Carcinosarcoma) 419
- [17.9] Others 422

CHAPTER 18**Unusual Prostatic Neoplasms 430**

- [18.1] Adenomas 431
- [18.2] Soft Tissue (Stromal) Tumors 432
- [18.3] Hematolymphoid Neoplasms 441
- [18.4] Miscellaneous Neoplasms 446
- [18.5] Secondary Neoplasms 446

CHAPTER 19**Treatment Effects 456**

- [19.1] Surgery **457**
- [19.2] Hormonal Therapy **457**
- [19.3] Radiation Therapy **464**
- [19.4] Chemotherapy **468**
- [19.5] Miscellaneous Therapies **469**
- [19.6] Medical Therapy for BPH **469**
- [19.7] Minimally Invasive Therapy for BPH **469**
- [19.8] Experimental Prostate Cancer Therapy **470**

CHAPTER 20**Malignant Neoplasms Mistaken for Benign Conditions 478****CHAPTER 21****Molecular Biology of Human Prostatic Carcinoma: Clinical and Pathologic Implications 480**

- [21.1] DNA Content (Ploidy) **481**
- [21.2] Chromosomal Alterations **482**
- [21.3] Tumor Suppressor Genes **487**
- [21.4] Oncogenes **489**
- [21.5] Androgen Receptor **490**
- [21.6] DNA Methylation **491**
- [21.7] Cell Proliferation and Cell Death (Apoptosis) **491**
- [21.8] Gene Expression Profiling and Proteomics **494**

CHAPTER 22**Seminal Vesicles 506**

- [22.1] Embryology and Development **507**
- [22.2] Normal Anatomy **507**
- [22.3] Cysts **511**
- [22.4] Inflammation and Infection **512**
- [22.5] Calcification and Calculi **512**
- [22.6] Amyloid Deposits **512**
- [22.7] Hyperplasia **513**
- [22.8] Primary Benign Neoplasms **513**
- [22.9] Primary Neoplasms of Indeterminate (or Low) Malignant Potential **515**
- [22.10] Primary Malignant Neoplasms **515**
- [22.11] Secondary Neoplasms **516**

CHAPTER 23**Prostatic Urethra 522**

- [23.1] Congenital Anomalies **523**
- [23.2] Urethritis and Infection **524**
- [23.3] Infarcts and Fibrosis **525**
- [23.4] Urothelial Metaplasias **526**
- [23.5] Prostatic Urethral Epithelial Polyps **530**
- [23.6] Urothelial Hyperplasia **531**
- [23.7] Benign Neoplasms **531**
- [23.8] Dysplasia **532**
- [23.9] Malignant Neoplasms **533**

INDEX 540

“Prostatic cancer is a rare affection”

—Sir Henry Thompson in *The Diseases of the Prostate*, 1883

■

Preface

No longer. Prostate cancer is now the most common noncutaneous malignancy diagnosed in men in the United States. Worldwide it is the third most common male cancer. Prostate diseases are common afflictions of men: clinical prostatitis and benign prostate hyperplasia (BPH) are especially prevalent disorders. In the last 15 years, due in part to demographic shifts and public awareness, and also to widespread clinical use of serum prostate specific antigen in efforts to detect prostate cancer early, there has been an astonishing increase in the number of prostate needle biopsies performed to assess for prostate cancer presence. Indeed, it is estimated that in 2002 some 750,000 prostate needle biopsies were performed in the United States. In this context the concept for a genuinely comprehensive book on pathology of the prostate originated.

This book presents a practical histopathologic approach to diagnosis of prostatic disease. It also should provide a ready repository of information on prostatic diseases. We hope it will prove useful for practicing pathologists, pathology residents and fellows, urologists and genitourinary oncologists, radiologists, and clinicians and researchers interested in diseases of the prostate. The coverage extends from basic anatomy throughout embryology and developmental diseases through tissue sampling considerations, to the diagnosis of benign and malignant diseases (both common and uncommon) in the prostate. We explore diagnosis of prostatic disease in all tissue sample types, including fine needle aspirates (special thanks to Richard M. DeMay, MD), needle core biopsy, transurethrally resected prostatic chips, open (simple) prostatectomy tissues, radical prostatectomy tissue, and metastatic prostatic cancer samples. The emphasis in the book is on surgical pathology diagnosis and differential diagnosis, using gold standard H&E-stained sections as the foundation for diagnosis. As such, the book contains many hundreds of H&E images, in an effort to portray the diversity, heterogeneity, and spectrum of disease within the prostate gland. Particular attention has been paid throughout the book to pseudoneoplastic and pseudobenign conditions, which are frequently misdiagnosed but infrequently discussed adequately in pathology texts. Clinical presentations, gross findings, and the role of special studies, including relevant molecular biologic and genetic testing, are all integrated into the discussion of each disease entity. And while few molecular genetic tests are currently used in the diagnosis or prognostic stratification of prostate diseases, the useful possibilities of molecular medicine will be felt within the book; indeed, a full chapter (Chapter 21) discusses the molecular biology of prostate cancer.

Readers learn in many different ways, so the presentation comprises images, text, figures, quick reference tables and data-rich, larger tables. Quick reference tables allow for capture, at a glance, of essential facts—the book is “prehighlighted” in a very real sense. The larger tables are designed to satisfy those want more about specific studies culled from the world literature on specific diseases. We hope the book will be a resource for “reference mining”: a compendium of key references from all of the last century, and also for the years 2000–2003 of the new. Thus, both classical, historical papers, and the most recent, important publications are gathered (alphabetically) at the end of each chapter. Reference updating finally stopped only in February of 2003, one month prior to going to print. The ASCP Press deserves real praise for this often overlooked commitment to currency. We were able to incorporate numerous references from the year 2002, and several from the year of publication itself. We sought to impart the latest diagnostic information, including typing, Gleason grading, and staging of prostate cancer.

We will have succeeded when the book serves as an asset in the daily practice of diagnostic surgical pathology of the prostate, and again when it serves as the necessary consolidated source for otherwise difficult-to-find knowledge on the many diseases that affect the human prostate gland.

Peter A. Humphrey, Author

Joshua Weikersheimer, Consulting Publisher, ASCP Press

My deep appreciation goes to:

Joshua Weikersheimer, PhD, Consulting Publisher, ASCP Press, for his patience, wit, and wisdom

Mark R Wick, MD, for originating the concept of this book

Robin Vollmer, MD, a valued friend and collaborator, who inspired my interest in urological pathology

Pepper Dehner, MD, Professor and Director of Anatomic Pathology at Washington University Medical Center, who provided support and the freedom in the form of time (in the Lauren Ackerman model) that made the writing of this book possible

Emil Unanue, MD, Professor and Chairman, Department of Pathology and Immunology at Washington University School of Medicine, for creating a Department where academic pathology thrives

My colleagues in urology at Duke University and Washington University Medical Centers, including David Paulson, MD, Philip Walther, MD, PhD, William Catalona, MD, David Keetch, MD, Adam Kibel, MD, and Gerald Andriole, MD

Joel Picus, MD, of Medical Oncology, Washington University, for reviewing Chapter 13 on the clinical aspects of prostate cancer

Madeleine Kraus, MD, for the review and critique of the hematopathology section of Chapter 18

Mahul Amin, MD, David Grignon, MD, and John Srigley, MD, for discussions and work together on the Gleason grading system

Jeffrey Milbrandt, MD, PhD, for discussions on basic science aspects of the molecular pathogenesis of prostate cancer

Henry Royal, MD, Horacio Maluf, MD, John Srigley, MD, Tom Ulbright, MD, Patricia Troncoso, MD, Adriana Reyes, MD, Michael Kyriakos, MD, J Allan Tucker, MD, Robert Young, MD, Robert B Jenkins, MD, Hung Chiang, MD, Xiaopei Zhu, MD, John Pfeifer, MD, PhD, Daniel Niku, MD, Ganesh Devendra, MD, Gerald Dagleish, MD, and Mark Watson, MD, PhD, for slides, images, and figures

Margaret Chesney, for expert typing and perseverance

Erik Tanck, for care and skill in producing the book, and the ASCP Press Staff for careful work in handling the book

My parents Loren Humphrey, MD, PhD, and Janice Humphrey for continued support and encouragement throughout my medical career

Acknowledgments