PROSTATE CANCER

DIAGNOSIS AND CLINICAL MANAGEMENT



Prostate Cancer

Diagnosis and clinical management

Prostate Cancer

Diagnosis and clinical management

EDITED BY

Ashutosh K. Tewari M.D., M.Ch.

Ronald P. Lynch Professor of Urologic-Oncology
Director
Center for Prostate Cancer
Weill Cornell Medical College and New York Presbyterian Hospital
Director
LeFrak Center of Robotic Surgery, NYPH
Weill Cornell Medical College
New York Presbyterian Hospital
New York, USA

Peter Whelan Ms, FRCS

Community Urologist, Leeds, UK Emeritus Consultant Urological Surgeon Pyrah Department of Urology St. James's University Hospital Leeds. UK

John D. Graham FRCP, FRCR

Consultant in Clinical Oncology Beacon Centre Musgrove Park Hospital Taunton Somerset, UK Director, National Collaborating Centre for Cancer Cardiff, UK



This edition first published 2014 © 2014 by John Wiley & Sons, Ltd.

Registered office: John Wiley & Sons, Ltd, The Atrium, Southern Gate, Chichester,

West Sussex, PO19 8SQ, UK

Editorial offices: 9600 Garsington Road, Oxford, OX4 2DQ, UK

The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

111 River Street, Hoboken, NJ 07030-5774, USA

For details of our global editorial offices, for customer services and for information about how to apply for permission to reuse the copyright material in this book please see our website at www.wiley.com/wiley-blackwell

The right of the author to be identified as the author of this work has been asserted in accordance with the UK Copyright, Designs and Patents Act 1988.

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, except as permitted by the UK Copyright, Designs and Patents Act 1988, without the prior permission of the publisher.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names, service marks, trademarks or registered trademarks of their respective owners. The publisher is not associated with any product or vendor mentioned in this book. It is sold on the understanding that the publisher is not engaged in rendering professional services. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

The contents of this work are intended to further general scientific research, understanding, and discussion only and are not intended and should not be relied upon as recommending or promoting a specific method, diagnosis, or treatment by health science practitioners for any particular patient. The publisher and the author make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of fitness for a particular purpose. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of medicines, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each medicine, equipment, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. Readers should consult with a specialist where appropriate. The fact that an organization or Website is referred to in this work as a citation and/or a potential source of further information does not mean that the author or the publisher endorses the information the organization or Website may provide or recommendations it may make. Further, readers should be aware that Internet Websites listed in this work may have changed or disappeared between when this work was written and when it is read. No warranty may be created or extended by any promotional statements for this work. Neither the publisher nor the author shall be liable for any damages arising herefrom.

Library of Congress Cataloging-in-Publication Data

Prostate cancer (Tewari)

Prostate cancer : diagnosis and clinical management / edited by Ashutosh K. Tewari, Peter Whelan, John Graham.

p. ; cm.

Includes bibliographical references and index.

ISBN 978-1-118-34735-5 (pbk.)

I. Tewari, Ashutosh, editor of compilation. II. Whelan, Peter, 1947– editor of compilation.

III. Graham, John, 1955- editor of compilation. IV. Title.

[DNLM: 1. Prostatic Neoplasms-diagnosis. 2. Prostatic Neoplasms-therapy.

Patient Care Management. 4. Prostate-pathology. 5. Prostate-surgery. WJ 762]
 RC280.P7

616.99'463-dc23

A catalogue record for this book is available from the British Library.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

2013034289

Cover image: back drop © author Ch 03; inserts © author Ch 05 Cover design by Meaden Creative

Set in 9.5/13pt Meridien by Aptara Inc., New Delhi, India

Contents

Contributors, vii

Preface, x

- 1 Prostate Cancer Epidemiology, 1

 Annie Darves-Bornoz, Joe Park, and Aaron Katz
- 2 Diagnosis and Screening, 16 Yiannis Philippou, Harveer Dev, and Prasanna Sooriakumaran
- 3 Understanding the Histopathology, 34 *Jon Oxley*
- 4 Markers in Prostate Cancer, 49 *Philippa J. Cheetham*
- 5 Imaging, 72 *Jonathan Richenberg*
- 6 Counseling the Patient with Newly Diagnosed Prostate Cancer, Stage by Stage, 116 Nicholas James Smith and William Richard Cross
- 7 Active Surveillance in the Management of Low-Risk Prostate Cancer, 136 *L. Boccon-Gibod*
- 8 Radical Surgery, 145 *Adnan Ali and Ashutosh Tewari*
- 9 Radiation Therapy in the Management of Prostate Cancer, 170 *J. Conibear and P.J. Hoskin*
- 10 Novel Therapies for Localized Prostate Cancer, 191

 Massimo Valerio, Mark Emberton, Manit Arya, and

 Hashim U. Ahmed

vi Contents

- 11 Posttherapy Follow-up and First Intervention, 211

 Ernesto R. Cordeiro, Anastasios Anastasiadis, Matias Westendarp,
 Jean J.M.C.H. de la Rosette, and Theo M. de Reijke
- 12 Managing Rising PSA in Naive and Posttherapy Patients, 230 George Thalmann and Martin Spahn
- 13 Diagnosis and Management of Metastatic Prostate Cancer, 245

 Bertrand Tombal and Frederic Lecouvet
- 14 New Therapies in Hormone Relapsed Disease, 265

 Carmel Pezaro, Aurelius Omlin, Diletta Bianchini, and
 Johann de Bono
- 15 End of Life Care in Prostate Cancer, 287 *John D. Graham*
- 16 The Long Perspective: Prostate Cancer as a Chronic Disease, 298

 Peter Whelan
- 17 The Future: What's in the Toolkit for Prostate Cancer Diagnosis and Treatment?, 313

 Norman J. Maitland

Index, 331

Color plate section can be found facing page 148

Contributors

Hashim U. Ahmed, FRCS(Urol.), BM, BCh, BA(Hons.)

MRC Clinician Scientist and Clinical Lecturer in Urology

Division of Surgery and Interventional Science, University College London, London, UK; and Department of Urology,

University College London Hospitals NHS Foundation Trust, London, UK

Adnan Ali, MBBS

Clinical Research Fellow Center for Prostate Cancer. Weill Cornell Medical College, New York Presbyterian Hospital, New York, NY, USA

Anastasios Anastasiadis, MD, FEBU

Fellow in Endourology and Laparoscopy Clinical Research Fellow EAU Section of Uro-Technology (ESUT), Academic Medical Center Amsterdam, The Netherlands

Manit Arya, MBChB, MD(Res), FRCS(Glas), FRCS(Urol)

Consultant Urological Surgeon Department of Urology, University College London Hospitals NHS Foundation Trust, London, UK: and Barts Cancer Institute, Queen Mary University London, London, UK

Diletta Bianchini, MD

Specialist Oncologist

Prostate Cancer Targeted Therapy Group and Drug Development Unit,

The Royal Marsden NHS Foundation Trust and

The Institute of Cancer Research, Surrey, UK

L. Boccon-Gibod, MD

Former Chairman and former head of surgery Department of Urology, CHU Bichat, Paris, France

Philippa J. Cheetham, MD

Attending Urologist Department of Urology, Winthrop University Hospital, New York, NY, USA

J. Conibear, MBBCh, BSc, MSc, MRCP, FRCR

Clinical Oncology Specialist Registrar Mount Vernon Cancer Center, Middlesex, UK

Ernesto R. Cordeiro, MD, FEBU

Fellow in Endourology and Laparoscopy Clinical Research Fellow Endourological Society, Academic Medical Center, Amsterdam, The Netherlands

William Richard Cross, BMedSci, BMBS, FRCS(Urol.), PhD

Consultant Urological Surgeon Department of Urology, St. James's University Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, UK

Annie Darves

Medical Student Stony Brook University and Winthrop University Hospital, New York

Johann de Bono, MD, FRCP, MSc, PhD, FMedSci

Professor of Experimental Cancer Medicine Prostate Cancer Targeted Therapy Group and Drug Development Unit, The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research,

Surrey, UK

Jean J.M.C.H. de la Rosette, MD, PhD

Chairman Department of Urology Chairman Clinical Research Office Endourology Society Executive Board Member Société Internationale d'Urologie Academic Medical Center, Amsterdam, The Netherlands

Theo M. de Reijke, MD, PhD, FEBU

Senior Staff Urology Department Academic Medical Center, Amsterdam, The Netherlands

Harveer Dev MA, MB BChir, MRCS

NIHR Academic Clinical Fellow in Urology Cambridge University Hospitals NHS Foundation Trust Cancer, Research UK Cambridge,

Institute Cambridge Biomedical Campus Cambridge, UK

Mark Emberton, FRCS(Urol.), FRCS(Eng.), MD, MBBS, BSc

Professor of Urology and Director, Honorary Consultant Urologist

Division of Surgery and Interventional Science, University College London, London, UK; *and* Department of Urology,

University College London Hospitals NHS Foundation Trust,

London, UK

John D. Graham, FRCP, FRCR

Consultant in Clinical Oncology Beacon Centre,

Musgrove Park Hospital,

Taunton,

Somerset, UK; and

Director, National Collaborating Centre for

Cardiff, UK

P. J. Hoskin, MD, FRCP, FRCR

Consultant in Clinical Oncology Mount Vernon Cancer Centre Northwood UK; and Professor in Clinical Oncology University College London

Aaron Katz, M.D.

Chairman of Department of Urology Winthrop University Hospital, New York

Frederic Lecouvet, MD, PhD

Division of Radiology, Cliniques universitaires Saint Luc, Institut de Recherche Clinique, Université catholique de Louvain, Brussels, Belgium

Norman Maitland, PhD

YCR Professor of Molecular Biology and Director Department of Biology, YCR Cancer Research Unit, University of York, York, UK

Aurelius Omlin, MD

Clinical Research Fellow Prostate Cancer Targeted Therapy Group and Drug Development Unit, The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research, Surrey, UK

Jon Oxley, BSc, MD, FRCPath

Consultant in Cellular Pathology Southmead Hospital, North Bristol NHS Trust, Bristol, UK

Joe Park

Medical Student Stony Brook University and Winthrop University Hospital, New York

Carmel Pezaro, MBChB, FRACP,

Clinical Research Fellow Prostate Cancer Targeted Therapy Group and Drug Development Unit, The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research, Sutton. UK

Yiannis Philippou MA(Cantab), MBBChir

Foundation Year 2 Department of Surgery, The Royal Marsden NHS Foundation Trust, Sutton, UK

Jonathan Richenberg, BM, BcH, MA, MRCP, FRCR (Hon. Sen. Lect.), BSMS

Consultant Radiologist Department of Imaging, Royal Sussex County Hospital, Brighton, UK

Nicholas James Smith, MBChB, FRCS(Urol.), PhD

Specialist Registrar Department of Urology, St. James's University Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, UK

Prasanna Sooriakumaran, MD, PhD, FRCSUrol, FEBU

Senior Fellow in Robotics and Urology
Honorary Consultant Urological Surgeon
Nuffield Department of Surgical Sciences,
University of Oxford,
Oxford, UK; and
Visiting Assistant Professor
Department of Molecular Medicine and
Surgery,
Karolinska Institute,
Stockholm, Sweden

Martin Spahn, MD

Associate Professor Senior Consultant Department of Urology, University Hospital Bern, Inselspital Anna Seiler-Haus, Bern, Switzerland

Ashutosh Tewari, MD, MCh

Ronald P. Lynch Professor of Urologic-Oncology Director Center for Prostate Cancer, Weill Cornell Medical College, New York Presbyterian Hospital; New York, NY, USA; and Director LeFrak Center of Robotic Surgery, Weill Cornell Medical College, New York Presbyterian Hospital, New York, NY, USA

George Thalmann, MD

Professor of Urology
Director and Chairman
Department of Urology,
University Hospital Bern, Inselspital Anna
Seiler-Haus,
Bern, Switzerland

Bertrand Tombal, MD, PhD

Professor of Urology Division of Urology, Cliniques universitaires Saint Luc, Institut de Recherche clinique, Université catholique de Louvain, Brussels, Belgium

Massimo Valerio, MD, FEBU

Clinical Research Fellow, PhD candidate
Division of Surgery and Interventional Science,
University College London, London, UK; and
Department of Urology
University College London Hospitals NHS
Foundation Trust,
London, UK; and
Centre Hospitalier Universitaire Vaudoi,

Peter Whelan, MS, FRCS,

Lausanne, Switzerland

Community Urologist, Leeds, UK Emeritus Consultant Urological Surgeon, Pyrah Department of Urology, St. James's University Hospital, Leeds, UK

Matias Westendarp, MD

Fellow in Endourology and Laparoscopy Clinical Research Fellow Academic Medical Center, Amsterdam, The Netherlands

Preface

With the advent of new drugs and innovative technologies with which to treat prostate cancer in the last few years, and the realization that over-diagnosis and hence overtreatment have been a feature of the recent past; it was felt timely to produce a short, comprehensive book on all aspects of prostate cancer, leaving the details for the expert to the many excellent contemporary monographs.

We are privileged to have had an internationally known team of contributors ranging across the field. Aaron Katz and colleagues set the scene with the all important review of the epidemiology and natural history of the disease. Jon Oxley sets the contemporary context of histopathology; Philippa J. Cheetham gives us an exhaustive review of the current state of markers in this disease, whereas Jonathan Richenberg brings us up to date with imaging of the disease both locally and distantly. In an innovatory chapter, William Richard Cross reviews what informed consent means and the evidence we have, stage by stage, with which to advise our patients.

The management of localized disease is discussed from all aspects of possible therapies, starting with a discussion on active monitoring, a counterintuitive concept when dealing with cancer in not offering treatment immediately, and why it is valid in prostate cancer, by L. Boccon-Gibod. Ashutosh Tewari gives an authoritive description of surgical treatment, whereas P.J. Hoskin examines both external beam radiotherapy and brachytherapy to help us understand why, numerically, these are the most frequent treatments utilized. Hashim U. Ahmed and Mark Emberton review the role of emerging therapies to which they have contributed so much.

In linked chapters, Theo M. de Reijke, George Thalmann, and Bertrand Tombal, together with their colleagues, explore what options there are when definitive therapies appear to have failed. It is hoped that these, taken together with William Richard Cross's chapter, will allow all readers to reflect on the two important components of prostate cancer treatment:

evidence and timescale. Johann de Bono brings his immense experience and expertise to discuss the exciting developments of new therapies in this disease. Peter Whelan looks at the progress and lack of it, from the beginning of anatomical radical prostatectomy through the PSA era to the current day, whereas John D. Graham reminds us that this is a malignant disease with which we are dealing and some patients progress and some die from it. In a sensitive account, he sets out how our patients may be supported to have a "good death."

Finally, we thought it appropriate to ask a scientist, Norman Maitland, who has spent more than 30 years in this field, to give a scientific rather than a clinical take on future prospects.

We hope this book will prove useful to the experts to enable them to understand where other experts are "coming from," what their therapies have to offer, and what are these therapies' inevitable limitations to the generalist who can use this book to help guide patients through the bewildering options available, and sincerely to include the lay reader, both patient and their relatives. We hope that it will provide a comprehensive summary, an accessible narrative, and a starting point for discussions patients will have with their treating physicians.

Andrew von Eschenbach, a urologist and ex-director of the US National Institute of Cancer, stated that the hope was to turn prostate cancer into a chronic disease. This has largely been achieved in the current era with many men living a quarter or even a third of their lives after the diagnosis. We hope this book shows how this came about and how men can and must be persuaded to live out their lives as fully as possible, and that there are always options, and one will probably fit an individual's needs.

We are grateful to all at Wiley especially Oliver Walter who commissioned this volume, and to Kate Newell and Claire Brewer.

CHAPTER 1

Prostate Cancer Epidemiology

Annie Darves-Bornoz¹, Joe Park¹, and Aaron Katz²

¹Stony Brook University and Winthrop University Hospital, New York

United States—recent trends in incidence and mortality

Incidence

Prostate cancer is the most common non-skin cancer diagnosed among American males, affecting roughly one in six men (16.15%) over the course of their lifetime. Prostate cancer is also the second leading cause of cancer-related deaths in American men. According to the most recent data from the Surveillance Epidemiology and End Results (SEER) database, an estimated 241 740 men were diagnosed with prostate cancer and over 28 000 died of it in the United States in 2012 [1]. The incidence of prostate cancer spiked in the United States in the early 1990s because of the advent of more aggressive prostate-specific antigen (PSA) screening [2]. This was followed by a sharp decline from 1992 to 1995 during which incidence rates returned to a new baseline which remained approximately two and a half times the pre-PSA era rate, likely due to the fact that increased screening in prior years had successfully diagnosed much of the previously undetected prostate cancer patients in the population.

Mortality and survival

Most recent data show that mortality rates due to prostate cancer have been declining, with a 3.5% decrease between 2000 and 2009 [3]. In addition, 5-year survival rates have also been increasing, jumping from 76% between 1983 and 1985 to 98% between 1992 and 1998 [4]. While this staggering rise in survival and decline in mortality can in part be attributed

Prostate Cancer: Diagnosis and Clinical Management, First Edition.

Edited by Ashutosh K. Tewari, Peter Whelan and John D. Graham.

© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

²Department of Urology, Winthrop University Hospital, New York