

MICROALBUMINURIA BIOCHEMISTRY, EPIDEMIOLOGY AND CLINICAL PRACTICE

Microalbuminuria, the abnormal urinary excretion of albumin, is recognised as an important independent marker of both renal and cardiovascular disease, particularly in diabetes mellitus. This volume is the only comprehensive and up-to-date review of the relevance of microalbuminuria to health and disease. It covers the pathophysiology and epidemiology of microalbuminuria, methodology of laboratory assessment, as well as a discussion of the non-specific nature of microalbuminuria in less well-recognised clinical situations. This is the first book to deal in detail with the treatment of microalbuminuria in diabetic and non-diabetic subjects.

It will provide an essential source of reference and a guide to clinical practice for diabetologists, endocrinologists, cardiologists, renal physicians and clinical biochemists.

DR PETER WINOCOUR trained in diabetes and endocrinology in Manchester and Newcastle and has published numerous articles on dyslipidaemia, hypertension and nephropathy, particularly in diabetes mellitus. Born in Glasgow on 2nd December 1956, he trained at the University of Glasgow and has served as a committee member of the British Hyperlipidaemia Association. His MD thesis was on the subject of metabolic control and complications in insulin-dependent diabetes mellitus. He is Consultant Physician at the Queen Elizabeth II Hospital, Welwyn Garden City, and Honorary Senior Lecturer at the Royal Free Hospital School of Medicine, London.

DR SALLY MARSHALL graduated with first class honours in biochemistry from the University of Glasgow in 1975, and with MB ChB in 1978. Her MD, for a thesis on microalbuminuria in diabetes, was awarded in 1990. She has published numerous articles on diabetes, particularly on several aspects of diabetic nephropathy. She has served as a committee member of the European Diabetic Nephropathy Study Group and is currently Chairman of the Professional Advisory Committee of the British Diabetic Association. She is Reader in Diabetes in the University of Newcastle upon Tyne, and Honorary Consultant Physician in the Royal Victoria Infirmary NHS Trust.

MICROALBUMINURIA

Biochemistry, epidemiology and clinical practice

PETER H. WINOCOUR

*Consultant Physician, Queen Elizabeth II Hospital, Welwyn Garden City,
Honorary Senior Lecturer, Royal Free Hospital School of Medicine*

and

SALLY M. MARSHALL

*Reader in Diabetes Medicine, Department of Medicine, University of Newcastle upon Tyne,
Honorary Consultant Physician, Royal Victoria Infirmary, Newcastle upon Tyne*

Foreword by

K. G. M. M. ALBERTI

CAMBRIDGE
UNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom
One Liberty Plaza, 20th Floor, New York, NY 10006, USA
477 Williamstown Road, Port Melbourne, VIC 3207, Australia
314-321, 3rd Floor, Plot 3, Splendor Forum, Jasola District Centre, New Delhi - 110025, India
79 Anson Road, #06-04/06, Singapore 079906

Cambridge University Press is part of the University of Cambridge.

It furthers the University's mission by disseminating knowledge in the pursuit of education, learning and research at the highest international levels of excellence.

www.cambridge.org

Information on this title: www.cambridge.org/9780521457033

© Cambridge University Press 1998

This publication is in copyright. Subject to statutory exception and to the provisions of relevant collective licensing agreements, no reproduction of any part may take place without the written permission of Cambridge University Press.

First published 1998

A catalogue record for this publication is available from the British Library

ISBN 978-0-521-45703-3 Paperback

Cambridge University Press has no responsibility for the persistence or accuracy of URLs for external or third-party internet websites referred to in this publication, and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.

.....

Every effort has been made in preparing this book to provide accurate and up-to-date information which is in accord with accepted standards and practice at the time of publication. Although case histories are drawn from actual cases, every effort has been made to disguise the identities of the individuals involved. Nevertheless, the authors, editors and publishers can make no warranties that the information contained herein is totally free from error, not least because clinical standards are constantly changing through research and regulation. The authors, editors and publishers therefore disclaim all liability for direct or consequential damages resulting from the use of material contained in this book. Readers are strongly advised to pay careful attention to information provided by the manufacturer of any drugs or equipment that they plan to use.

Contents

<i>Preface</i>	<i>page</i> vii
<i>Foreword by Professor K. G. M. M. Alberti</i>	ix
1 Renal structure and physiology	1
2 Measurement and expression of microalbuminuria	11
3 Epidemiology and determinants of microalbuminuria in health	40
4 Microalbuminuria in diabetes mellitus	53
5 Microalbuminuria as a marker of endothelial dysfunction	97
6 Microalbuminuria, cardiovascular risk factors and cardiovascular disease	116
7 Microalbuminuria as a non-specific marker of disease	177
8 The management of microalbuminuria in diabetes mellitus and essential hypertension	191
<i>Index</i>	245

Preface

The interest in, and importance of, microalbuminuria is reflected in the exponential increase in the number of publications on the topic over the last few years. We recognised at commissioning of this book in 1993 that we were chasing a rapidly moving target. In persevering with this flood of literature our objective was to temper the enthusiastic discussion of microalbuminuria as a one-dimensional risk factor in diabetes and to broaden the discussion into other areas of general medicine. At the same time, we have tried to put the difficulties surrounding the measurement of microalbuminuria and the treatment of microalbuminuria in diabetes into an appropriate clinical context. We were also encouraged by the knowledge that such a book covering the broadest aspects of microalbuminuria had not previously been written.

Our interest in the subject has been stimulated over the last 15 years by our initially separately developed interests in Manchester and Newcastle, and subsequently by the opportunity to work together in George Alberti's powerhouse in the Department of Medicine, University of Newcastle upon Tyne from 1993 to 1997. The unplanned geographical splitting and conversion for one of us, from a University teaching post to a full-time National Health Service position, has added a touch of excitement regarding communication and ensuring that the manuscript is up to date. Modern technology has not totally alleviated these difficulties.

In addition to our undoubted gratitude to George Alberti, we would like to thank our many other colleagues and mentors who have provided stimulation and moral support over the last 15 years: Professor David Anderson, Dr Harold Cohen, Professor Paul Durrington, the late Dr John Ireland, Dr Rudy Bilous, Dr Jean Mcleod, Dr Carlo Catalano, Dr Steve Jones, Dr Martin Rutter, Dr Deepak Bhatnagar, Dr Laura Baines, Mrs Catherine White, Mrs Pat Shearing, Professor Philip Home, Professor Robert Wilkinson, Dr Trevor Thomas, and Professor Roy Taylor.

viii *Preface*

Finally we must acknowledge the patient and expert support from the staff of Cambridge University Press for bearing with us in times of chaos and confusion.

The book is dedicated to our families and friends who have borne the brunt of our frustrations in the preparation of this manuscript.

Peter H. Winocour
Welwyn Garden City
Sally M. Marshall
Newcastle upon Tyne

Foreword

The appearance of small amounts of albumin in the urine, which were less than those detected by conventional methods at the time but higher than normal, was first noted by Professor Keen and colleagues in the 1960s. Little further was done for 15 years until groups in London and Denmark started to look in more detail at urine protein excretion in people with diabetes. This intermediate grade of proteinuria between dip-stick detectable and normal was referred to as microalbuminuria – a totally inaccurate name but one that has stuck! Since then a vast amount of work has accumulated and many publications on the subject have appeared. Of particular interest is the fact that these small amounts of protein in the urine are associated not just with more rapid progression to end stage renal failure but with subsequent cardiovascular disease mortality and morbidity. Initially, studies focused on type 1 diabetes, but now there is much literature on type 2 as well, and increasing awareness of the relevance of microalbuminuria in non-diabetic renal and vascular disease.

For many physicians the amount of literature on microalbuminuria is overwhelming and hence tends not to be read. The present book by Drs Winocour and Marshall provides a succinct account of what we know about microalbuminuria, not just in relation to renal function but with regard to the broader aspects of diabetes. The book fills a large gap in the diabetes and renal literature. Importantly, the relevance of microalbuminuria in non-diabetic hypertension and other medical conditions is also examined. The book will, I hope, be of benefit to many people working in diabetes who would like to be updated but do not have time to hunt through voluminous tomes in dusty libraries or scan the Internet. It should be of particular interest to those working on complications in

x *Foreword*

diabetes, but will also appeal to students and generalists alike interested in glomerular and cardiovascular disease.

K.G.M.M. Alberti
President,
Royal College of Physicians, London