Amin Y. Barakat
Editor

Renal Disease in Children

Clinical Evaluation and Diagnosis

With a Foreword by Roscoe R. Robinson

Amin Y. Barak
Editor

Renal Disease in Children

Clinical Evaluation and Diagnosis

With a Foreword by Roscoe R. Robinson

With 70 Figures in 108 Parts and 95 Tables

Springer-Verlag
New York Berlin Heidelberg
London Paris Tokyo Hong Kong

Amin Y. Barakat
Clinical Professor of Pediatrics
Division of Pediatric Nephrology
Georgetown University School of Medicine
Washington, DC 20007, USA

(formerly Associate Professor of Pediatrics, Division of Pediatric Nephrology, and Director, Child Kidney Disease Prevention Program, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA)

Cover: The color of the kidneys in the cover drawing resembles that of the precious stone jade, and a form of it, called *nephrite,* is said to have been worn as amulets by American Indians to protect themselves against kidney disease and calculi.

Library of Congress Cataloging-in-Publication Data
Renal disease in children: clinical evaluation and diagnosis/Amin Y. Barakat, editor; with a foreword by Roscoe R. Robinson.
p. cm.
Includes index.
ISBN 0-387-97036-3
1. Pediatric nephrology. I. Barakat, Amin Y.
[DNLM: 1. Kidney Diseases—in infancy & childhood. WS 320 R392]
RJ476.K5R437 1989
618.92'61—dc20
DNLM/DLC 89-19664

Media conversion by Impressions, Inc., Madison, Wisconsin.
Printed and bound by Arcata Graphics/Halliday, West Hanover, Massachusetts.
Printed in the United States of America.

9 8 7 6 5 4 3 2 1

ISBN 0-387-97036-3 Springer-Verlag New York Berlin Heidelberg
ISBN 3-540-97036-3 Springer Verlag Berlin Heidelberg New York

To my wife, Amal,
and children, Rana, Nadim, and Zena

Foreword

The clinical specialty of adult nephrology has enjoyed spectacular growth during the past three decades. Such a statement is no less true for pediatric nephrology. This book stands in quiet testimony to that fact. Practitioners of pediatric nephrology are now concerned with the diagnosis and treatment of young patients with a widened spectrum of primary and secondary diseases of the kidneys and urinary tract, hypertension and disorders of water, electrolyte and acid-base metabolism. Their science, deriving from an exciting blend of physiology, morphology, pathology, immunology, biochemistry, microbiology, genetics and pharmacology, must also include an understanding of human developmental biology—an insight that colleagues who practice adult nephrology require to a somewhat lesser extent.

Dramatic, continuing advances in our understanding of the pathogenesis, pathophysiology, diagnosis and treatment of kidney diseases has led to a cascade of books and monographs on various aspects of the subject. Nevertheless, in view of the clear emergence of pediatric nephrology as a distinct medical specialty, it is most appropriate that a practical book, which focuses almost exclusively on approaches to the evaluation and diagnosis of young patients with kidney disease and related disorders, should appear. In that sense this book is unique. It provides an easily accessible, practical compendium or guide to the clinical investigation of all facets of kidney disease in children. Its special and unique emphasis is directed toward various approaches to the evaluation of such patients and the interpretation of associated laboratory or radiographical data. It avoids extensive discussion of disease mechanisms, pathophysiology or therapy. As an aid to diagnosis, the book will be particularly useful to those who participate in the daily care of children with disturbances of renal structure or function, whether the readers be students, house officers, family physicians, general pediatricians or pediatric nephrologists.

The editor and the authors have brought forth a volume that is easily read. It reflects a timely, highly useful and wonderfully concise, yet comprehensive view of an integrated and practical approach to the nephro-

logical evaluation of children and adolescents. The book can serve as an introduction to diagnostic pediatric nephrology for students or as a ready bedside reference for the more experienced practitioner. The authors are noted and experienced clinicians whose individual contributions have been blended together by the editor in such a manner as to minimize unnecessary overlap and duplication among the various chapters. A clear and refreshing approach of practical utility without sacrifice of scholarship is a major hallmark of the text. The narrative progresses logically and sequentially from introductory chapters dealing with relevant diagnostic methods through later sections that offer descriptive approaches to the study of specific disorders. Timely and special reminders are conveyed in the three concluding chapters: 1) prenatal evaluation is useful and important to the diagnosis of certain types of kidney or urinary tract abnormalities; 2) early diagnosis and treatment are essential determinants of successful outcome in many circumstances and 3) clinical practice will be influenced increasingly by the use of sophisticated information systems and their clinical databases as we approach and enter the twenty-first century.

This writer takes great pride in the fact that both pediatric and adult nephrology are alive and well at Vanderbilt University Medical Center. The appearance of this book offers one more bit of evidence that this is so. The twelve Vanderbilt contributors and their valued colleagues from other institutions can be congratulated on the quality of their effort.

Nashville, Tennessee — Roscoe R. Robinson

Preface

Our fundamental knowledge in nephrology has advanced significantly in the past three decades. Thanks to basic research, we are now closer to understanding the pathophysiology and molecular basis of many renal diseases as well as the transport, metabolic and endocrine functions of the kidney. DNA linkage has made possible the identification of autosomal dominant polycystic kidney disease, Lowe's oculocerebrorenal syndrome and Wilms' tumor-aniredia complex. Identification of the gene in polycystic disease and possibly in other genetic diseases of the kidney is imminent.

The clinical workup and diagnosis of patients with renal disease, however, continue to be the main concern of physicians and practicing nephrologists. Physicians caring for children should be familiar with the clinical aspects of acid-base and electrolyte disturbances, proteinuria, hematuria, urinary tract infection, glomerular and tubular diseases, acute and chronic renal failure, hypertension and renal involvement in systemic disease. They should be able to initiate the workup on a child with renal disease, interpret urinalysis and other laboratory findings and know when to refer a patient to a pediatric nephrologist.

The purpose of this book is to provide pediatricians, family physicians, nephrologists, urologists, residents, clinical fellows and medical students with a complete compendium on the clinical evaluation of renal disease in children. The book is meant to be a desk reference and a bedside manual for all those managing children with kidney problems, to help them in the diagnosis of disease and the interpretation of relevant clinical laboratory data. It is not designed to be a textbook. The depth and detail of the different chapters vary according to the complexity of the subject discussed. The versatility of the material presented makes this book equally useful to the specialist consultant, the generalist and the house officer.

The book covers pediatric nephrology problems classified by mode of investigation (urinalysis, imaging, kidney biopsy, etc.) or presentation (hematuria, proteinuria, urinary tract infection, renal failure, etc.). De-

tailed discussions of pathophysiology and management of different renal conditions have been omitted to save space, and to concentrate on workup and diagnosis. Pathophysiology and therapy are sometimes briefly presented to the extent that they have an impact on the workup. Other disciplines that contribute to the diagnosis of renal disease, such as pathology and urology, are also presented. Prenatal diagnosis, prevention and use of the computer in renal disease are briefly discussed. Many tables, algorithms and formulas are included to assist the reader in the differential diagnosis and workup.

Because of space limitations, an exhaustive list of references is not provided; rather, a limited number of specific references and a few general key ones are included to allow the interested reader to pursue certain problems in depth. Formulas and reference intervals are also referenced. Extensive cross-referencing avoids repetition and redundancy. A detailed appendix includes 1) reference intervals, 2) formulas used in the diagnosis and treatment of various renal conditions, 3) nomograms and 4) a table of over 400 conditions and syndromes associated with renal involvement, which presents main clinical features, renal abnormalities and inheritance. This table will help the practicing physician and consultant to identify the nature of renal involvement for different conditions.

The editor would like to thank Doctors Iekuni Ichikawa, Robert C. MacDonnell, Jr., Valentina Kon and Aida Yared of the Division of Pediatric Nephrology, Vanderbilt University Medical Center for reviewing parts of the manuscript, and Doctor Marshall Summar for his help with the art work. Special thanks also go to the staff of Springer-Verlag for their help and support.

I owe a great debt to the contributing authors who spent much time and effort in this endeavor to help physicians provide better care to children with kidney disease.

AMIN Y. BARAKAT

Contributors

BILLY S. ARANT, JR., M.D.
Professor and Director, Division of Pediatric Nephrology, University of Texas Southwestern Medical Center at Dallas, Dallas, TX 75235-9063, USA

AMIN Y. BARAKAT, M.D., F.A.A.P.
Clinical Professor of Pediatrics, Division of Pediatric Nephrology, Georgetown University School of Medicine, Washington, DC 20007, USA

JEAN-PIERRE DE CHADARÉVIAN, M.D.
Professor of Pediatrics (Pediatric Pathology), Temple University School of Medicine and Director, Department of Anatomical Pathology, St. Christopher's Hospital for Children, Philadelphia, PA 19133, USA

JAMES C.M. CHAN, M.D.
Professor and Vice-Chairman, Department of Pediatrics and Director, Division of Pediatric Nephrology, Children's Medical Center, Medical College of Virginia, Richmond, VA 23298-0498, USA

RUSSELL W. CHESNEY, M.D.
Le Bonheur Professor and Chairman, Department of Pediatrics, The University of Tennessee Memphis College of Medicine, Le Bonheur Children's Medical Center, Memphis, TN 38103, USA

ROBERT B. ETTENGER, M.D.
Professor of Pediatrics and Director, Pediatric Renal Transplantation Program and Transplantation Immunology Laboratory, UCLA School of Medicine, Los Angeles, CA 90024, USA

LEONARD G. FELD, M.D., PH.D.
Associate Professor of Pediatrics, SUNY at Buffalo School of Medicine and Chief, Division of Pediatric Nephrology and Director, Children's Kidney Center, Children's Hospital of Buffalo, Buffalo, NY 14222, USA

ROBIN A. FELDER, PH.D.
Assistant Professor of Pathology and Associate Director, Clinical Chemistry and Toxicology, University of Virginia Health Sciences Center, Charlottesville, VA 22908, USA

ROBERT D. FILDES, M.D.
Assistant Professor of Pediatrics, Division of Pediatric Nephrology and Director, Pediatric End-Stage Renal Disease Program, Georgetown University School of Medicine, Washington, DC 20007, USA

AGNES FOGO, M.D.
Assistant Professor of Pathology and Pediatrics, Vanderbilt University School of Medicine, Nashville, TN 37232, USA

JOHN W. FOREMAN, M.D.
Associate Professor of Pediatrics, Medical College of Virginia, Richmond, VA 23298, USA

RAYMOND M. HAKIM, M.D., PH.D.
Associate Professor of Internal Medicine and Director of Clinical Services, Division of Nephrology, Vanderbilt University School of Medicine, Nashville, TN 37232, USA

MANFRED HANSMANN, M.D.
Professor of Obstetrics and Gynecology, University of Bonn, University Women's Hospital, 5300 Bonn, FRG

RICHARD M. HELLER, M.D.
Professor of Radiology and Radiological Sciences and Pediatrics, Vanderbilt University School of Medicine, Nashville, TN 37232, USA

IEKUNI ICHIKAWA, M.D.
Professor of Pediatrics and Director, Division of Pediatric Nephrology, Vanderbilt University School of Medicine, Nashville, TN 37232, USA

PHILIPPE JEANTY, PH.D., M.D.
Assistant Professor of Radiology and Radiological Sciences, Vanderbilt University School of Medicine, Nashville, TN 37232, USA

ROBERT D. JEFFS, M.D., F.R.C.S.(C)
Professor and Director, Division of Pediatric Urology, The James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, MD 21205, USA

PEDRO A. JOSE, M.D., PH.D.
Professor of Pediatrics, Physiology and Biophysics and Director, Division of Pediatric Nephrology, Vice-Chairman, Department of Pediatrics, Georgetown University School of Medicine, Georgetown Children's Medical Center, Washington, DC 20007, USA

GAD KAINER, M.B., B.S., F.R.A.C.P.
Visiting Scholar, Department of Pediatrics, Medical College of Virginia, Richmond, VA 23298, USA

BERNARD S. KAPLAN, M.D.
Professor of Pediatrics, University of Pennsylvania and Director of Pediatric Nephrology, Children's-Hospital of Philadelphia, Philadelphia, PA 19104, USA

SANDRA G. KIRCHNER, M.D.
Professor of Radiology and Radiological Sciences, Vanderbilt University School of Medicine, Nashville, TN 37232-2675, USA

VALENTINA KON, M.D.
Assistant Professor of Pediatrics, Division of Pediatric Nephrology, Vanderbilt University School of Medicine, Nashville, TN 37232, USA

ROBERT L. LYNCH, M.D., PH.D.
Associate Professor, Division of Pediatric Nephrology, St. Louis University School of Medicine, St. Louis, MO 63104, USA

ROBERT C. MACDONELL, JR., M.D.
Associate Professor of Pediatrics and Medicine, Assistant Professor of Surgery, Vanderbilt University School of Medicine, Nashville, TN 37232, USA

MITSURO NAKANO, M.D., PH.D.
Visiting Scholar, Department of Pediatrics, Medical College of Virginia, Richmond, VA 23298, USA

ZOE L. PAPADOPOULOU, M.D.
Professor of Pediatric Nephrology, University of Ioannina, Greece, and Director, Division of Pediatric Nephrology, Saint Sophia Hospital, Thessaloniki, Greece

ROSCOE R. ROBINSON, M.D.
Professor of Medicine and Vice-Chancellor for Health Affairs, Vanderbilt University Medical Center, Nashville, TN 37232, USA

ROBERT C. ROCK, M.D.
Associate Professor and Director, Department of Laboratory Medicine, The Johns Hopkins Hospital, Baltimore, MD 21205, USA

JUAN RODRIGUEZ-SORIANO, M.D.
Chairman, Department of Pediatrics, Hospital Infantil de Cruces, Cruces, Bilbao, Spain

MOUIN G. SEIKALY, M.D.
Assistant Professor of Pediatrics, Division of Pediatric Nephrology, University of Texas Southwestern Medical Center at Dallas, Dallas, TX 75235-9063, USA

ZIAD M. SHEHAB, M.D.
Clinical Associate Professor of Pediatrics, Section of Infectious Disease, Arizona Health Sciences Center, Tucson, AZ 85724, USA

JAMES E. SPRINGATE, M.D.
Assistant Professor of Pediatrics, Division of Pediatric Nephrology, Children's Hospital of Buffalo, Buffalo, NY 14222, USA

SHARON M. STEIN, M.D.
Fellow, Department of Radiology and Radiological Sciences, Vanderbilt University School of Medicine, Nashville, TN 37232, USA

MARSHALL SUMMAR, M.D.
Fellow, Division of Genetics, Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, TN 37232, USA

LETICIA U. TINA, M.D.
Associate Professor of Pediatrics, Division of Pediatric Nephrology, Georgetown University School of Medicine, Washington, DC 20007, USA

BRENT F. TREIGER, M.D.
Resident, The James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, MD 21205, USA

ELLEN G. WOOD, M.D.
Assistant Professor and Director, Division of Pediatric Nephrology, St. Louis University School of Medicine, St. Louis, MO 63104, USA

AIDA YARED, M.D.
Assistant Professor of Pediatrics, Division of Pediatric Nephrology, Vanderbilt University School of Medicine, Nashville, TN 37232, USA

Contents

1
Introduction to the Diagnosis of Renal Disease and Guidelines for Patient Referral

AMIN Y. BARAKAT

I. Introduction

Renal disease is a major cause of morbidity and mortality. The primary physician should be familiar with the modes of presentation of different renal conditions and should have a high index of suspicion for patients with asymptomatic disease. Early diagnosis of these conditions in children is important in the prevention of renal failure and end-stage renal disease.

II. Presentation of Patients with Renal Disease

Patients with renal disease may present with 1) signs and symptoms of renal disease, 2) abnormal urinalysis, 3) urinary tract infection (UTI), 4) glomerular disease, 5) tubular disease, 6) electrolyte and acid-base dis-

turbances, 7) decreased renal function, 8) hypertension, 9) congenital abnormalities of the kidney or urinary tract or 10) renal involvement in systemic disease. These complaints or findings should prompt a thorough history and physical examination including blood pressure determination (Chapter 2). A few simple laboratory and radiological studies may suggest the diagnosis or lead to a prompt referral. Often, renal diseases may be asymptomatic; therefore, a yearly urinalysis and blood pressure determination should be an integral part of routine medical care of children.

III. Signs and Symptoms of Renal Disease

Urinary symptoms such as frequency, urgency, dysuria, hesitancy and urinary retention may suggest UTI, obstructive uropathy or urinary calculi. Abdominal, loin or suprapubic pain may be present also.

Physicians should be familiar with the normal voiding pattern of children at various ages. The normal frequency and amount of urine at different ages are presented in Chapter 2 and Appendix I. Nocturnal *enuresis*, particularly the primary form, is associated with a positive family history, is usually idiopathic and initially requires no other investigation than a urinalysis and urine culture. Secondary and diurnal forms of enuresis, as well as enuresis beyond the age of 10 years, may require a renal sonogram (ultrasound) and voiding cystourethrogram. The physician should differentiate between *frequency* (usually suggesting UTI) and *polyuria*, which is the passage of larger amounts of urine than normal. Polyuria indicates a decrease in urine concentrating ability and may be seen in diabetes mellitus, diabetes insipidus and chronic renal failure. A random urine specific gravity (sp gr) of >1.020 rules out a urine concentration defect. A child with polyuria and decreased random urine sp gr should have a fasting sp gr or a water deprivation test (Chapter 12). Decreased concentrating ability with evidence of other renal disease may be due to chronic pyelonephritis, hydronephrosis, renal cystic disease or renal dysplasia, nephronophthisis-medullary cystic disease or sickle cell nephropathy. Referral to a pediatric nephrologist is necessary if these conditions are suspected.

It is important to keep in mind that renal disease in children may present in a subtle manner, and physicians should have a high index of suspicion of a renal cause for any child who fails to thrive or who has unexplained fevers, vague pains, gastrointestinal symptoms, anemia, acidosis, an abdominal mass, edema or hypertension. Physicians should be generous in performing urinalyses and urine cultures on children, particularly those below the age of five years, since UTI at this age often presents with signs and symptoms not related to the urinary tract. Younger children with a UTI may have a normal urinalysis and a urine culture is necessary to make the diagnosis. Children with a documented