

# Liver Disease in Children

Fourth Edition





# **Liver Disease in Children**

# **Fourth Edition**

Edited by

# Frederick J. Suchy, MD

Chief Research Officer and Director,
Children's Hospital Colorado Research Institute, Children's Hospital Colorado;
Professor of Pediatrics and Associate Dean for Child Health Research,
University of Colorado School of Medicine, Aurora, CO, USA

# Ronald J. Sokol, MD

Professor and Vice Chair of Pediatrics;
Section Head, Gastroenterology, Hepatology and Nutrition;
Director, Colorado Clinical and Translational Sciences Institute; and Arnold Silverman MD Chair in Digestive Health,
University of Colorado School of Medicine and Children's Hospital Colorado, Aurora, CO, USA

# William F. Balistreri, MD

Director Emeritus

Pediatric Liver Care Center; Medical Director Emeritus, Liver Transplantation;
Dorothy M. M. Kersten Professor of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition,
Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, USA





# CAMBRIDGE UNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom

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/9781107013797

Fourth edition © Cambridge University Press 2014 Third edition © Cambridge University Press 2007 Second edition © Lippincott, Williams & Wilkins 2001 First edition © Mosby 1994

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 edition first published 1994 Second edition first published 2001 Third edition first published 2007 Fourth edition first published 2014 Reprinted 2015

Printed in Spain by Grafos SA, Arte Sobre Papel, Barcelona

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

 $Library\ of\ Congress\ Cataloging-in-Publication\ Data$ 

Liver disease in children. – Fourth edition / edited by Frederick J. Suchy, MD, chief research officer, and director, The Children's Hospital Research Institute, Children's Hospital Colorado, professor of pediatrics and associate dean for Child Health Research, University of Colorado School of Medicine, Aurora, CO, USA, Ronald J. Sokol, MD, professor and vice chair of pediatrics, section head, Gastroenterology, Hepatology and Nutrition, director, Colorado Clinical and Translational Sciences Institute; and Arnold Silverman MD, chair in digestive health, University of Colorado School of Medicine and Children's Hospital Colorado, Aurora, CO, USA, William F. Balistreri, MD, director emeritus, Pediatric Liver Care Center, medical director emeritus, Liver Transplantation, and Dorothy M. M. Kersten, professor of pediatrics, Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, USA.

pages cm

ISBN 978-1-107-01379-7 (Hardback)

 $\begin{array}{lll} {\rm 1.\ \ Liver-Diseases.} & {\rm 2.\ \ Pediatric\ \, gastroenterology.} & {\rm I.\ \, Suchy,\ \, Frederick\ \, J.,\ \, editor} \\ {\rm of\ \, compilation.} & {\rm III.\ \, Sokol,\ \, Ronald\ \, J.,\ \, editor\ \, of\ \, compilation.} \\ {\rm William\ \, F.,\ \, editor\ \, of\ \, compilation.} \end{array}$ 

RJ456.L5L575 2014

618.92′362-dc23 2013021438

ISBN 978-1-107-01379-7 Hardback

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**

List of contributors		vii
Preface	xi	

# Section I — Pathophysiology of pediatric liver disease 1

- 1 **Liver development** 1 Yiwei Zong and Joshua R. Friedman
- Functional development of the liver 10 Frederick J. Suchy
- Mechanisms of bile formation and cholestasis 24 Nikita A. Gupta and Saul J. Karpen
- 4 Acute liver failure in children 32 Robert H. Squires and Estella M. Alonso
- 5 **Cirrhosis and chronic liver failure** 51 Evelyn K. Hsu and Karen F. Murray
- 6 **Portal hypertension** 68 Benjamin L. Shneider
- Laboratory assessment of liver function and injury in children 88
   Vicky Lee Ng

# Section II – Cholestatic liver disease 101

- 8 **Approach to the infant with cholestasis** 101 Amy Feldman and Frederick J. Suchy
- 9 Medical and nutritional management of cholestasis in infants and children 111 Andrew P. Feranchak, Frederick J. Suchy, and Ronald J. Sokol
- 10 **Neonatal hepatitis and congenital infections** 140 Philip Rosenthal
- Biliary atresia and other disorders of the extrahepatic bile ducts 155
   William F. Balistreri, Jorge A. Bezerra, and Frederick C. Ryckman
- Neonatal jaundice and disorders of bilirubin metabolism 177Mark Bartlett and Glenn R. Gourley

- 13 **Familial hepatocellular cholestasis** 199 Frederick J. Suchy, Shikha S. Sundaram, and Benjamin L. Shneider
- 14 Alagille syndrome 216Binita M. Kamath, Nancy B. Spinner, and David A. Piccoli
- 15 **Intestinal failure-associated liver disease** 234 Jason Soden and Ronald J. Sokol
- Disease of the gallbladder in infancy, childhood, and adolescence 247
   Frank W. DiPaola and James E. Heubi

# Section III – Hepatitis and immune disorders 265

- 17 **Hepatitis A and hepatitis E virus infection** 265 Philip Rosenthal
- 18 **Hepatitis B virus infection** 276 Mei-Hwei Chang
- 19 Hepatitis C virus infection 295Maureen M. Jonas
- 20 **Autoimmune hepatitis** 311 Nanda Kerkar and Cara L. Mack
- 21 **Sclerosing cholangitis** 322 Alexander G. Miethke and William F. Balistreri
- 22 **Drug-induced liver disease** 341 Eve A. Roberts
- 23 **Liver disease in immunodeficiencies** 370 Nedim Hadžić

# Section IV – Metabolic liver disease 387

24 Laboratory diagnosis of inborn errors of metabolism 387Piero Rinaldo



#### Contents

- 25 **α<sub>1</sub>-Antitrypsin deficiency** 400 David H. Perlmutter
- 26 **Cystic fibrosis liver disease** 419 Meghana Sathe and Andrew P. Feranchak
- 27 **Inborn errors of carbohydrate metabolism** 435 Rana F. Ammoury and Fayez K. Ghishan
- 28 Copper metabolism and copper storage disorders 465Ronald J. Sokol
- 29 **Iron storage disorders** 493 Michael R. Narkewicz and Peter F. Whittington
- 30 **Heme biosynthesis and the porphyrias** 509 Robert J. Desnick, Manisha Balwani, and Karl E. Anderson
- 31 **Tyrosinemia** 526 Grant Mitchell, Pierre A. Russo, Josée Dubois, and Fernando Alvarez
- 32 Lysosomal storage disorders 546T. Andrew Burrow and Gregory A. Grabowski
- 33 **Disorders of bile acid synthesis and metabolism** 567 Kenneth D. R. Setchell
- 34 Inborn errors of fatty acid oxidation 587Melanie B. Gillingham and Robert B. Steiner
- 35 **Mitochondrial hepatopathies** 603 Ronald J. Sokol
- 36 **Non-alcoholic fatty liver disease in children** 631 Rohit Kohli, Kevin E. Bove, and Stavra A. Xanthakos
- 37 **Peroxisomal diseases** 649 Paul A. Watkins and Kathleen B. Schwarz

38 **Urea cycle disorders** 664 Derek Wong and Stephen Cederbaum

# Section V – Other considerations and issues in pediatric hepatology 673

- Bacterial, parasitic, and fungal infections of the liver 673
   Donald A. Novak, Gregory Y. Lauwers, and Richard L. Kradin
- 40 **Systemic disease and the liver** 694 Kathleen M. Campbell
- 41 **Fibrocystic liver disease** 710 Ronen Arnon, Maureen M. Jonas, Antonio R. Perez-Atayde, and Frederick J. Suchy
- 42 **Tumors of the liver** 728 Dolores López-Terrada and Milton J. Finegold
- 43 Liver transplantation in children: indications and surgical aspects 760
   M. Kyle Jensen, Maria H. Alonso, Jaimie D. Nathan, Frederick C. Ryckman, Gregory M. Tiao, and William F. Balistreri
- 44 Liver transplantation in children: post-transplant care 773
   Estella M. Alonso and Riccardo A. Superina

Index 788

# **Contributors**

### Estella M. Alonso MD

Professor, Department of Pediatrics, Northwestern University, Chicago, and Director of Hepatology, Department of Gastroenterology, Hepatology and Nutrition, Children's Memorial Hospital, Chicago, IL, LISA

### Maria H. Alonso MD

Associate Professor of Surgery and Pediatrics, Department of Surgery, University of Cincinnati College of Medicine, Cincinnati, OH, USA

## Fernando Alvarez MD

Chief, Division of Gastroenterology, Hepatology and Nutrition, CHU Saint Justine Medical Centre, and Professor, Department of Pediatrics and Deaprtment of Microbiology and Immunology, University of Montreal, Montreal, Quebec, Canada

# Rana F. Ammoury MD

Assistant Professor, Department of Gastroenterology and Nutrition, Steele Children's Research Center, University of Arizona, Tucson, AZ, USA

# Karl E. Anderson MD FACP

Associate Director, General Research Center, and Director, Division of Human Nutrition, Department of Preventive Medicine and Community Health, University of Texas Medical Branch, Galveston, TX, USA

# Ronen Arnon MD

Associate Professor, Departments of Pediatrics, Hepatology and Surgery, Medical Director of Pediatric Hepatology and Liver Transplantation, Mount Sinai School of Medicine, New York, NY, USA

# William F. Balistreri MD

Director Emeritus, Pediatric Liver Care Center, Medical Director Emeritus, Liver Transplantation and Dorothy M. M. Kersten Professor of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, USA

# Manisha Balwani MD MS

Assistant Professor, Department of Genetics and Genomic Studies and Department of Medicine, Mount Sinai School of Medicine, New York, NY, USA

## **Mark Bartlett**

Fellow in Pediatric Gastroenterology, University of Minnesota, Minneapolis, MN, USA

#### Jorge A. Bezerra MD

Director, Pediatric Liver Care Center; Professor of Pediatrics, The William and Rebecca Balistreri Chair of Pediatric Hepatology, Division of Gastroenterology, Hepatology and Nutrition, University of Cincinnati College of Medicine and Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

## Kevin E. Bove MD

Professor, Division of Pediatric Pathology, University of Cincinnati Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

# T. Andrew Burrow MD

Assistant Professor of Clinical Genetics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

# Kathleen M. Campbell MD

Assistant Professor, Department of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition, University of Cincinnati College of Medicine and Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

# Stephen Cederbaum MD

Professor Emeritus, Psychiatry, Pediatrics and Human Genetics, University of California Los Angeles, Los Angeles, CA, USA

# Mei-Hwei Chang MD

Department of Pediatrics and Hepatitis Research Center, National Taiwan University Hospital, College of Medicine, Taipei, Taiwan

# Robert J. Desnick MD

Dean for Genetics and Genomic Medicine; Professor and Chairman Emeritus, Genetic and Genomic Sciences; Professor

vii

#### List of contributors

of Pediatrics; Professor of Oncological Sciences; and Professor of Obstetrics, Gynecology, and Reproductive Science, Mount Sinai School of Medicine, New York, NY, USA

#### Frank W. DiPaola MD

Clinical Fellow, Pediatric Gastroenterology, Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medial Center and University of Cincinnati College of Medicine, Cincinnati, OH, USA

### Josée Dubois MD

Professor of Medical Imaging, CHU Saint Justine Medical Centre, University of Montreal, Montreal, Quebec, Canada

# Amy Feldman MD

Fellow, Department of Gastroenterology, Hepatology and Nutrition, University of Colorado School of Medicine and Children's Hospital Colorado, Aurora, CO, USA

# Andrew P. Feranchak MD

Willis C. Maddrey MD Professorship in Liver Disease, Department of Pediatrics, UT Southwestern Medical Center and Children's Medical Center, Dallas, TX, USA

# Milton J. Finegold MD

Professor, Department of Pathology and Immunology and Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA

## Joshua R. Friedman MD PhD

Assistant Professor of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Division of Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA, USA

# Fayez K. Ghishan MD

Professor and Chair, Department of Pediatrics; Director of the Steele Children's Research Center, University of Arizona, Tucson, AZ, USA

# Melanie B. Gillingham PhD

Department of Molecular and Medical Genetics, Oregon Health and Science University, Portland, OR, USA

# Glenn R. Gourley MD

Professor, Department of Pediatrics, University of Minnesota, Minneapolis, MN, USA

# Gregory A. Grabowski MD

Professor of Pediatrics and Molecular Genetics, Biochemistry and Microbiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

# Nikita A. Gupta MD

Assistant Professor of Pediatric Gastroenterology, Emory University School of Medicine, and Pediatric Hepatologist, Children's Healthcare of Atlanta, GA, USA

#### Nedim Hadžić MD

Professor of Paediatric Hepatology, King's College Medical School, London, UK

#### James E. Heubi MD

Director, Clinical Translational Research Center, and Professor, Department of Pediatrics, Cincinnati Children's Hospital Medical Center and University of Cincinnati College of Medicine, Cincinnati, OH, USA

### Evelyn K. Hsu MD

Assistant Professor of Pediatrics, Division of Gastroenterology and Hepatology, Seattle Children's Hospital, University of Washington School of Medicine, Seattle, WA, USA

### M. Kyle Jensen MD MS

Assistant Professor of Pediatric Gastroenterology and Hepatology, University of Utah, Primary Children's Medical Center, Salt Lake City, UT, USA

#### Maureen M. Jonas MD

Senior Associate in Medicine, Division of Gastroenterology, Hepatology and Nutrition, Children's Hospital Boston, and Professor of Pediatrics, Harvard Medical School, Boston, MA, USA

# Binita M. Kamath MD MRCP

Assistant Professor, Department of Paediatrics, University of Toronto; Staff Physician, Division of Gastroenterology, Hepatology and Nutrition, Hospital for Sick Children, Toronto, Ontario, Canada

# Saul J. Karpen MD PhD

Emory University School of Medicine, Department of Pediatric Gastroenterology, Hepatology and Nutrition, Atlanta, GA, USA

# Nanda Kerkar MD

Associate Professor of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition, Pediatric Liver Disease/Liver Transplant Program, Mount Sinai School of Medicine, New York, NY, USA

## Rohit Kohli MBBS MS

Associate Professor, Department of Pediatrics, University of Cincinnati College of Medicine, and Co-Director, Cincinnati Children's Steatohepatitis Center, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

# Richard L. Kradin MD

Gastrointestinal Pathology Service and Department of Pathology, Massachusetts General Hospital; and Department of Pathology, Harvard Medical School, Boston, MA, USA

# Gregory Y. Lauwers, MD

Gastrointestinal Pathology Service and Department of Pathology, Massachusetts General Hospital; and Department of Pathology, Harvard Medical School, Boston, MA, USA

List of contributors

### Dolores Lopez-Terrada MD PhD

Professor of Pathology and Pediatrics, Baylor College of Medicine, Houston, TX, USA

#### Cara L. Mack MD

Associate Professor of Pediatrics, Section of Pediatric Gastroenterology, Hepatology and Nutrition, Digestive Health Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO, USA

# Alexander G. Miethke MD

Assistant Professor, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, University of Cincinnati College of Medicine, and Pediatric Liver Care Center, Children's Hospital Medical Center, Cincinnati, OH, USA

#### **Grant Mitchell MD**

Professor, Medical Genetic Division, Department of Pediatrics Saint Justine Medical Centre, University of Montreal, Montreal, Quebec, Canada

#### Karen F. Murray MD

Professor of Pediatrics, Division Chief, Gastroenterology and Hepatology, Seattle Children's Hospital, University of Washington School of Medicine, Seattle, WA, USA

# Michael R. Narkewicz MD

Professor of Pediatrics, Section of Gastroenterology, Hepatology and Nutrition, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO, USA

# Jaimie D. Nathan MD

Assistant Professor of Surgery and Pediatrics, Department of Surgery, University of Cincinnati College of Medicine, Cincinnati, OH, USA

# Vicky Lee Ng MD FRCPC

Associate Professor of Paediatrics, University of Toronto, and Medical Director, Liver Transplant Program, Division of Gastroenterology, Hepatology and Nutrition, SickKids Transplant Centre, Hospital for Sick Children, Toronto, Ontario, Canada

# Donald A. Novak MD

Department of Pediatrics, University of Florida, and Division of Pediatric Gastroenterology, Shands Hospital, Gainesville, FL, USA

# Antonio R. Perez-Atayde MD

Director of Speical Techniques and Staff Pathologist, Department of Pathology, Boston Children's Hospital and Harvard Medical School, Boston, MA, USA

# David H. Perlmutter MD

Physician-in-Chief and Scientific Director, Vira I. Heinz Professor of Pediatrics, and Chair, Department of Pediatrics,

University of Pittsburgh School of Medicine, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, USA

### David A. Piccoli MD

Chief, Division of Gastroenterology, Hepatology and Nutrition, Fred and Suzanne Biesecker Professor of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Children's Hospital of Pennsylvania, Philadelphia, PA, USA

### Piero Rinaldo, MD PhD

Professor of Laboratory Medicine and Pathology, Department of Laboratory Medicine and Pathology, Department of Laboratory Genetics, and Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN, USA

#### Eve A. Roberts, MD MA FRCP

Adjunct Associate Professor, Departments of Medicine, Paediatrics and Gastroenterology, University of Toronto, and Hepatologist, Division of Gastroenterology and Nutrition, Hospital for Sick Children, Toronto, Ontario, Canada

## Philip Rosenthal MD

Professor of Pediatrics and Surgery; Director Pediatric Hepatology Director Pediatric Clinical Research, Departments of Pediatrics and Surgery and the Liver Center, the University of California, San Francisco, CA, USA

# Pierre A. Russo MD

Chief, Anatomic Pathology, Children's Hospital of Philadelphia, Philadelphia, PA, USA

# Frederick C. Ryckman MD

Professor of Surgery and Pediatrics, Director of Pediatric Surgery Training Program, Pediatric Liver Care Center, Cincinnati Children's Hospital, Cincinnati, OH, USA

# Meghana Sathe MD

Assistant Professor, Department of Pediatrics, University of Texas Southwestern and Children's Medical Center, Dallas, TX, USA

# Kathleen B. Schwarz MD

Professor of Pediatrics, Johns Hopkins University School of Medicine, and Chief, Pediatric Liver Center, Johns Hopkins Hospital, Baltimore, MD, USA

# Kenneth D. R. Setchell PhD

Department of Pathology and Laboratory Medicine, Cincinnati Children's Hospital Medical Center and Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA

# Benjamin L. Shneider MD

Director, Pediatric Hepatology, Professor of Pediatrics University of Pittsburgh, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, USA



#### List of contributors

#### Jason Soden MD

Associate Professor, Department of Gastroenterology, Hepatology, and Nutrition, University of Colorado School of Medicine and Children's Hospital Colorado, Aurora, CO, USA

#### Ronald J. Sokol MD

Professor and Vice Chair of Pediatrics; Section Head, Gastroenterology, Hepatology and Nutrition; Director, Colorado Clinical and Translational Sciences Institute; and Arnold Silverman MD Chair in Digestive Health, University of Colorado School of Medicine and Children's Hospital Colorado, Aurora, CO, USA

# Nancy B. Spinner PhD

Professor of Pathology and Genetics, Chief, Division of Genomic Diagnostics, and Evelyn Willing Bromley Chair of Pediatric Pathology, Department of Pathology Perelman School of Medicine at the University of Pennsylvania, Children's Hospital of Pennsylvania, Pittsburgh, PA, USA

### Robert H. Squires MD

Clinical Director, Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital of Pittsburgh of UPMC, and Professor of Pediatrics, University of Pittsburgh, Pittsburgh, PA, USA

# Robert D. Steiner MD FAAP FACMG

Credit Unions for Kids Professor of Pediatric Research, Vice Chair for Research in Pediatrics, Department of Pediatrics, Medical and Molecular Genetics and Program in Molecular and Cellular Biosciences, Oregon Health and Science University, Portland, OR, USA

# Frederick J. Suchy MD

Chief Research Officer, and Director, Children's Hospital Colorado Research Institute, Children's Hospital Colorado; Professor of Pediatrics and Associate Dean for Child Health Research, University of Colorado School of Medicine, Aurora, CO, USA

### Shikha S. Sundaram MD MSc

Assistant Professor of Pediatrics, Section of Gastroenterology, Hepatology and Nutrition, Children's Hospital Colorado and University of Colorado School of Medicine, Aurora, CO, USA

# Riccardo A. Superina MD

Professor, Department of Surgery, Northwestern University Feinberg School of Medicine, and Ann and Robert G. Lurie Children's Hospital of Chicago, Siragusa Transplant Center, Chicago, IL, USA

# Gregory M. Tiao MD

Attending Surgeon, Division of Pediatric General and Thoracic Surgery, Associate Professor of Surgery and Pediatrics, and, Surgical Director of Liver Transplantation, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

#### Paul A. Watkins MD PhD

Professor of Neurology, Johns Hopkins University School of Medicine, Kennedy Krieger Institute, Baltimore, MD, USA

#### Peter F. Whittington MD

Professor of Pediatrics and Medicine, Northwestern University Feinberg School of Medicine, and Director, Siragusa Transplantation Center, Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

# Derek Wong MD

Assistant Professor of Pediatrics, Division of Medical Genetics, David Geffen School of Medicine at University of California Los Angeles, CA, USA

# Stavra A. Xanthakos MD MS

Assistant Professor, Division of Gastroenterology, Hepatology and Nutrition, University of Cincinnati Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

## Yiwei Zong PhD

Associate Project Manager, Department of Strategic Management, China Resources, China



# **Preface**

Seven years have passed since the publication of the third edition of *Liver Disease in Children*. This text continues to be the premier, comprehensive reference on pediatric liver disease. Pediatric hepatology continues to grow and evolve as a distinct discipline and so it remains a challenge to provide comprehensive coverage without markedly increasing the length of this text. To keep the size of this textbook within limits, the number of references for each chapter has been limited to classical and the most relevant current citations. The editors felt that this was a reasonable compromise, since ready access to the literature is possible through resources such as PubMed.

We have appreciated the contributions of so many of our colleagues over the past two decades, but to ensure a fresh perspective and to involve experts who have emerged in the field, 11 of the chapters are written by authors contributing to this textbook for the first time. These contributors have provided particular expertise in areas such as liver development, autoimmune liver disease, intestinal failure-associated liver disease, fatty liver disease, and inborn errors of metabolism. There is also expanded coverage of liver transplantation.

As has been the case with its predecessors, this fourth edition presents a critical review of pediatric hepatology and its scientific underpinnings by recognized experts in the field. Major advances have occurred, notably in the understanding of liver development, molecular physiology of the liver and biliary tract, and molecular virology. Our ability to diagnose

and treat children with liver disease has continued to improve. Genome-wide association studies are defining new risk factors for disorders such as non-alcoholic fatty liver disease, hepatitis B and C infection, biliary atresia, hepatic malignancy, and autoimmune liver disease. The ability to diagnose previously enigmatic disorders or identify modifier genes through whole exome or whole genome sequencing is becoming more common. The correlation of phenotype with genotype is sometimes possible. Genetic determinants of liver fibrosis are also being identified. Variants in genes involved in drug metabolism, drug transport, and the immune response have been linked to the risk of some adverse drug reactions. Emerging technologies are bearing fruit as new therapeutics for liver disease and hepatic fibrosis are becoming available, and these will need detailed evaluation in children. There is increasing emphasis on the notion of personalized medicine in which thorough phenotyping of patients is correlated with a wealth of genomic data to better understand and treat our patients.

We are grateful to all of our contributing authors for their efforts in crafting the fourth edition of *Liver Disease in Children*. We are confident that it will remain an essential reference for all physicians involved in the care of children with liver disease.

Frederick J. Suchy MD Ronald J. Sokol MD William F. Balistreri MD