Lorenzo D'Antiga
Editor

Pediatric Hepatology and Liver Transplantation

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Lorenzo D'Antiga
Paediatric Hepatology, Gastroenterology and Transplantation
Hospital Papa Giovanni XXIII
Bergamo
Italy

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To Martina, the sun of my life,
and to our children Francesco, Mattia, Anna and Maddalena
who make our days full of joy, projects and hope for the future

To Mum and Dad†
so trustful and proud, since the very beginning

To my brothers
Luca, who, as a young employee, made my studies at the Medical School affordable,
Alvise† and Angelo, always supportive during my career,
and Maria Giovanna†, who passed away at 4 months of age from an unknown liver disease

To my mentors
Lucia, Giorgina, Anil
and many others I am still learning from

To all doctors who take tender care of the sick ones
and consider it a privilege

Foreword

Paediatric hepatology has gone from obscurity to a status of specialty in its own merit over the span of seven decades. Though jaundice in babies and children had been occasionally reported in the past, liver disorders in childhood were considered extremely rare and almost always lethal. The real burden of paediatric liver disease was first recognised in the late 1950s and became a focus of attention only in the 1960s and 1970s.

Visionary men, like Morio Kasai, Daniel Alagille and Alex Mowat, put paediatric hepatology firmly on the map of paediatrics by the 1970s, recognising the importance of concentrating expertise in specialised centres, in order to elucidate physiopathological mechanisms, with consequent improved management and outcome for children with liver disease. This has resulted over a relatively short period of time in a vortex of new information, including the discovery of several causes of juvenile liver disease, leading not only to successful specific managements, but also to a better understanding of the liver physiology, based on the discovery of the deleterious effect of genetic defects affecting synthesis, transport and function of proteins manufactured by the liver.

In parallel, grew the awareness that liver disorders of adulthood can affect children as well, but that in children they present important differences, which need to be taken into account for successful treatment, examples of these conditions being autoimmune liver disease, viral hepatitides and acute liver failure.

Despite improved knowledge, the prognosis of paediatric liver disease remained severe for decades, with mortality rates between 50 and 60% within a few years from diagnosis for many conditions, until the advent of liver transplantation as a standard mode of treatment for children with end-stage liver disease in the early 1990s, which rapidly led to long-term survival rates of over 95%.

Current tasks are to clarify the physiopathological mechanisms of those juvenile liver diseases that remain without a recognised cause, to perfect medical management to avoid transplantation—including isolated hepatocyte or gene therapy—and to overcome the problems of rejection and long-term complications for those patients who need a liver transplant.

D'Antiga's *Pediatric Hepatology and Liver Transplantation* stems from the Editor's ambitious aim to provide a comprehensive, practical and up-to-date description of paediatric liver disorders and their management, spanning from historical notes, liver anatomy and physiology, to the discovery of new conditions and their management, to liver transplantation, to the peculiarities in children and adolescents of liver disorders that affect also adults.

This textbook will be highly valuable not only to gastroenterologists, paediatric hepatologists and transplant surgeons, but also to medical students, residents and adult physicians looking after patients with liver disease, as improved knowledge and management of hitherto lethal paediatric liver conditions has led to survival into adulthood and transition to adult services.

Lorenzo D'Antiga's aim was ambitious: the result excellent.

Giorgina Mieli-Vergani
London, UK

Preface

The liver may be considered "a timid, clever and resilient organ", because of its circulation enclosed between two capillary beds and the hidden excretion in the middle of the digestive tract, its pivotal role in human metabolism and its resistance to suffering if not to the exhaustion of the reserves. These intrinsic features and the relative rarity of hepatic disorders in infancy make liver disease in children a narrow and rather unknown field.

The liver goes through a perinatal immaturity phase during which it is prone to insults of various kinds but then matures and acquires the silent and stable control of most of the functions of body homeostasis and intermediate metabolism. The reasons why the functions and the diseases of the liver are still little known, and the expertise is prerogative of few specialized centres, probably reside in the lack of non-invasive tests allowing to understand the punctual state of health of this organ.

The purpose of this book is to try shedding some light on this field, spreading the experience made in the major international centres of paediatric hepatology and transplantation. Indeed the strength of this work stands on the contribution of the greatest experts working in the field all over the world, who kindly agreed to grant their expertise preparing a chapter of this book. It has been a great pleasure and honour having a prompt acceptance from persons I consider the top experts in various hepatology subspecialties and from whom I keep learning. Once again I experienced that friendship and mutual respect is a key component of any team project.

I am also particularly grateful for having the chance to deepen my experience in the field of education I have always been very fond of. In that respect the attempt of this work is to give a comprehensive (although certainly incomplete) scenario of what a physician involved in the care of paediatric liver disease might face, opening the lens of the camera to a wide angle, and helping the reader place information within the broader topic of child health and global health. For this reason the first chapter, taking advantage of the World Health Organisation data, focuses on the relevance of liver disease worldwide, both in adults and in children. Part III is entirely devoted to paediatric liver disease in continents having different epidemiology and standards of care, appearing less frequently in the current literature but certainly taking care of the largest proportion of children with liver disease in the world. Another novelty of this book is the balanced examination of both paediatric liver disease and liver transplantation, discussed in the first two parts, since these topics are inherently related, given that most chronic liver disorders eventually require organ replacement. Several chapters are dedicated to emerging issues in the field, such as long-term graft dysfunction, quality of life and transition to adult care, but also to newly developed strategies to manage our patients, such as next-generation sequencing testing, cell and gene therapy.

My wish is to provide a helpful tool for a range of practitioners looking after children with liver disease, from residents making their first approach to paediatric liver disease through to specialists working in transplantation centres. I really hope this book can contribute to the care of children with liver disease.

Bergamo, Italy — Lorenzo D'Antiga

The Editor would be pleased to receive from the readers any suggestion aimed to improve the next edition of this book. Please send your precious comments to the following mailing address: dantiga.book@gmail.com.

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Editor and Contributors

About the Editor

Lorenzo D'Antiga is a Paediatric Hepatologist and Gastroenterologist working in Italy. His current position is Director of Child Health and of the Paediatric Liver, GI and Transplantation Unit of the Papa Giovanni XXIII Hospital of Bergamo. He trained as a Paediatrician at the University of Padua and as a Paediatric Hepatologist in the United Kingdom at King's College Hospital London. He has worked as Consultant Gastroenterologist and Hepatologist as well as Paediatric Intensivist, specializing in organ failure and transplantation. ESPGHAN member for 15 years, he contributed to the field of paediatric hepatology with publications, scientific presentations and invited lectures. He has been member of the Council of the ESPGHAN as Education Secretary (till 2014) and Member of the Education Committee of the UEG (till 2014). He serves as Senior Associate Editor for *Journal of Pediatric Gastroenterology and Nutrition* and as Associate Editor of *Liver Transplantation*.

Contributors

R. Agazzi Interventional Radiology, Department of Diagnostic Radiology, Hospital Papa Giovanni XIII, Bergamo, Italy

Henrik Arnell Department of Paediatrics, Karolinska University Hospital and CLINTEC, Karolinska Institutet, Stockholm, Sweden

Alastair Baker Paediatric Liver Centre, King's College Hospital, London, UK

Ulrich Baumann Liver Unit and Small Bowel Transplant, Birmingham Women's and Children's Hospital, Birmingham, UK

Hannover Medical School, Hannover, Germany

Pietro Betalli Department of Paediatric Surgery, Papa Giovanni XXIII Hospital, Bergamo, Italy

Rishi Bolia Department of Pediatric Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

Alberto Burlina Division of Inherited Metabolic Diseases, Reference Centre Expanded Newborn Screening, Department of Woman's and Child's Health, University of Padova, Padova, Italy

Stefania Camagni Department of Organ Failure and Transplantation, Hospital Papa Giovanni XXIII, Bergamo, Italy

Valeria Casotti Paediatric Hepatology, Gastroenterology and Transplantation, Hospital Papa Giovanni XXIII, Bergamo, Italy

Michele Colledan Department of Organ Failure and Transplantation, Hospital Papa Giovanni XXIII, Bergamo, Italy

Laura Cristoferi Division of Gastroenterology, Department of Medicine and Surgery, University of Milan-Bicocca, Milan, Italy

International Center for Digestive Health, University of Milan-Bicocca, Milan, Italy

Daniel D'Agostino School of Medicine, USAL University, Buenos Aires, Argentina

Division of Pediatric GI and Hepatology, Pediatric Liver and Intestinal Transplantation Program, Hospital Italiano, Buenos Aires, Argentina

Department of Pediatric, Hospital Italiano, Buenos Aires, Argentina

Lorenzo D'Antiga Paediatric Hepatology, Gastroenterology and Transplantation, Hospital Papa Giovanni XXIII, Bergamo, Italy

Mark Davenport Department of Paediatric Surgery, King's College Hospital, London, UK

Dominique Debray Pediatric Liver Unit, Reference Center for Biliary Atresia and Cholestatic Genetic Diseases, Hôpital Necker-Enfants Malades, Paris, France

Andrea Dellostrologo Hepatology, Gastroenterology and Nutrition Unit, "Bambino Gesù" Children's Hospital, Rome, Italy

Anil Dhawan Paediatric Liver GI and Nutrition Center and Mowat Labs, King's College Hospital, London, UK

Fabiola Di Dato Department of Translational Medical Science, Section of Paediatrics, University of Naples Federico II, Naples, Italy

Angelo Di Giorgio Paediatric Hepatology, Gastroenterology and Transplantation, Hospital Papa Giovanni XXIII, Bergamo, Italy

Mortada H. F. El-Shabrawi Faculty of Medicine, Cairo University, Cairo, Egypt

Luca Fabris International Center for Digestive Health, University of Milan-Bicocca, Milan, Italy

Digestive Disease Section, Yale University, New Haven, CT, USA

Department of Molecular Medicine, University of Padua, Padua, Italy

Stefano Fagiuoli Gastroenterology, Hepatology and Transplantation, ASST Papa Giovanni XXIII, Bergamo, Italy

Sandy Feng Division of Transplantation, Department of Surgery, University of California San Francisco, San Francisco, CA, USA

Björn Fischler Department of Paediatrics, Karolinska University Hospital and CLINTEC, Karolinska Institutet, Stockholm, Sweden

Laura Fontanella Department of Organ Failure and Transplantation, Hospital Papa Giovanni XXIII, Bergamo, Italy

Akinari Fukuda Organ Transplantation Center, National Center for Child Health and Development, Tokyo, Japan

Maria Guido Department of Medicine—DIMED, Anatomic Pathology Unit, University of Padova, Padova, Italy

Gustavo Boldrini Division of Pediatric GI and Hepatology, Pediatric Liver and Intestinal Transplantation Program, Hospital Italiano, Buenos Aires, Argentina

Department of Pediatrics, Hospital Italiano, Buenos Aires, Argentina

Nedim Hadzic Kings College Hospital, London, UK

Steffen Hartleif University Children's Hospital Tübingen, Tübingen, Germany

A. Holvast Pediatric Hepatology, Beatrix Children's Hospital-UMCG, University of Groningen, Groningen, The Netherlands

Giuseppe Indolfi Meyer Children's University Hospital, Firenze, Italy

Raffaele Iorio Department of Translational Medical Science, Section of Paediatrics, University of Naples Federico II, Naples, Italy

Wojciech Janczyk The Children's Memorial Health Institute, Warsaw, Poland

Naglaa M. Kamal Faculty of Medicine, Cairo University, Cairo, Egypt

Mureo Kasahara Organ Transplantation Center, National Center for Child Health and Development, Tokyo, Japan

Chayarani Kelgeri Liver Unit and Small Bowel Transplant, Birmingham Women's and Children's Hospital, Birmingham, UK

Deirdre Kelly The Liver Unit, Birmingham Womens and Childrens Hospital and University of Birmingham, Birmingham, UK

Florence Lacaille Pediatric Gastroenterology-Hepatology-Nutrition Unit, Hôpital Universitaire Necker-Enfants Malades, University Paris Cité Sorbonne Paris Descartes Medical School, Paris, France

Lisa Licini Department of Pathology, Papa Giovanni XXIII Hospital, Bergamo, Italy

Simon C. Ling Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, ON, Canada

Department of Paediatrics, University of Toronto, Toronto, ON, Canada

Ines Loverdos Unidad de Gastroenterología, Hepatología y Nutrición pediátrica, Corporació Sanitària Universitària Parc Taulí. Sabadell, Barcelona, Spain

Maria Grazia Lucà Gastroenterology, Hepatology and Transplantation, ASST Papa Giovanni XXIII, Bergamo, Italy

Kathrin Ludwig Department of Medicine—DIMED, Unit of Pathology and Cytopathology, University Hospital of Padova, Padova, Italy

George V. Mazariegos UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, USA

Patrick McKiernan Division of Pediatric Gastroenterology Hepatology and Nutrition, Children's Hospital of Pittsburgh of UPMC and University of Pittsburgh, Pittsburgh, PA, USA

V. A. McLin Pediatric Gastroenterology, Hepatology and Nutrition Unit, Swiss Pediatric Liver Center, University Hospitals of Geneva, Geneva, Switzerland

Giorgina Mieli-Vergani MowatLabs, Paediatric Liver, GI and Nutrition Centre, King's College Hospital, London, UK

Federico Mingozzi Spark Therapeutic Inc, Philadelphia, PA, USA

Inserm, Évry, France

Genethon, Évry, France

Ellen Mitchell Division of Pediatric Gastroenterology Hepatology and Nutrition, Children's Hospital of Pittsburgh of UPMC and University of Pittsburgh, Pittsburgh, PA, USA

Giovanni Morana Division of Radiology, Treviso Regional Hospital, Treviso, Italy

Antonella Mosca Hepatology, Gastroenterology and Nutrition Unit, "Bambino Gesù" Children's Hospital, Rome, Italy

Andrès F. Muro Mouse Molecular Genetics Laboratory, International Center for Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy

Vicky Lee Ng The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

Emanuele Nicastro Paediatric Hepatology, Gastroenterology and Transplantation, Hospital Papa Giovanni XXIII, Bergamo, Italy

Valerio Nobili Hepatology, Gastroenterology and Nutrition Unit, "Bambino Gesù" Children's Hospital, Rome, Italy

Department of Pediatrics, Facoltà di Medicina e Psicologia, Sapienza University of Rome, Rome, Italy

Massimiliano Paganelli Pediatric Gastroenterology, Hepatology and Nutrition, Sainte-Justine University Hospital Center, Montreal, QC, Canada

Hepatology & Cell Therapy Laboratory, Sainte-Justine Research Center, Montreal, QC, Canada

Department of Pediatrics, Université de Montréal, Montreal, QC, Canada

Isabella Pellicioli Pediatric Intensive Care Unit, Hospital Papa Giovanni XXIII, Bergamo, Italy

Domenico Pinelli Department of Organ Failure and Transplantation, Hospital Papa Giovanni XXIII, Bergamo, Italy

Giusy Ranucci Department of Translational Medical Science, Section of Paediatrics, University of Naples Federico II, Naples, Italy

Nathalie Marie Rock Pediatric Gastroenterology, Hepatology and Nutrition Unit, Swiss Pediatric Liver Center, University Hospitals of Geneva, Geneva, Switzerland

Diana Sacchi Department of Medicine—DIMED, Anatomic Pathology Unit, University of Padova, Padova, Italy

Seisuke Sakamoto Organ Transplantation Center, National Center for Child Health and Development, Tokyo, Japan

Marianne Samyn Paediatric Liver, GI and Nutrition Centre, King's College Hospital NHS Foundation Trust, London, UK

Maria Camila Sanchez Division of Pediatric GI and Hepatology, Pediatric Liver and Intestinal Transplantation Program, Hospital Italiano, Buenos Aires, Argentina

Department of Pediatrics, Hospital Italiano, Buenos Aires, Argentina

Alberto Sanchez-Fueyo Institute of Liver Studies, King's College, London, London, UK

Mariateresa Sanseviero Hepatology, Gastroenterology and Nutrition Unit, "Bambino Gesù" Children's Hospital, Rome, Italy

Samantha Sarcognato Department of Medicine—DIMED, Anatomic Pathology Unit, University of Padova, Padova, Italy

Melanie Schranz Gastroenterology, Hepatology and Transplantation, ASST Papa Giovanni XXIII, Bergamo, Italy

Naresh Shanmugam Institute of Advanced Paediatrics, Dr. Rela Institute and Medical Centre, Chennai, India

Khalid Sharif Liver Unit and Small Bowel Transplant, Birmingham Women's and Children's Hospital, Birmingham, UK

S. Sironi Department of Diagnostic Radiology, Hospital Papa Giovanni XIII, Bergamo, Italy

Piotr Socha The Children's Memorial Health Institute, Warsaw, Poland

Aurelio Sonzogni Department of Pathology, Papa Giovanni XXIII Hospital, Bergamo, Italy

James E. Squires UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, USA

Anshu Srivastava Department of Pediatric Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

Mario Strazzabosco Division of Gastroenterology, Department of Medicine and Surgery, University of Milan-Bicocca, Milan, Italy

International Center for Digestive Health, University of Milan-Bicocca, Milan, Italy

Digestive Disease Section, Yale University, New Haven, CT, USA

Ekkehard Sturm University Children's Hospital Tübingen, Tübingen, Germany

P. Tessitore Department of Diagnostic Radiology, Hospital Papa Giovanni XIII, Bergamo, Italy

Roshni Vara Paediatric Inherited Metabolic Disease, Evelina Children's Hospital, London, UK

Silvio Veraldi Hepatology, Gastroenterology and Nutrition Unit, "Bambino Gesù" Children's Hospital, Rome, Italy

Diego Vergani MowatLabs, Institute of Liver Studies, King's College Hospital, London, UK

H. J. Verkade Pediatric Hepatology, Beatrix Children's Hospital-UMCG, University of Groningen, Groningen, The Netherlands

Jessica Woolfson The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada