

# Neonatal Hematology

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**Third Edition**

Edited by

**Pedro A. de Alarcón**

**Eric J. Werner**

**Robert D. Christensen**

**Martha C. Sola-Visner**

# Neonatal Hematology

## Pathogenesis, Diagnosis, and Management of Hematologic Problems

### Third Edition

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**Pedro A. de Alarcón**

University of Illinois College of Medicine

**Eric J. Werner**

Children's Specialty Group, Children's Hospital of  
The King's Daughters and Eastern Virginia Medical School

**Robert D. Christensen**

University of Utah Health and Intermountain Healthcare

**Martha C. Sola-Visner**

Boston Children's Hospital and Harvard University



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## Foreword

Previous editions of *Neonatal Hematology: Pathogenesis, Diagnosis, and Management of Hematologic Problems* have included a chapter by Dr. Howard Pearson on the history of pediatric hematology. Sadly, Dr. Pearson passed away in 2016. The editors of this third edition have once again chosen to include Dr. Pearson's Historical Review as the opening chapter of this text. Its relevance to the practice of hematology remains undiminished. We honor the memory of Dr. Pearson in this Foreword by sharing some insights on his life, as he was one of the truly iconic figures in the discipline of pediatric hematology.

Howard Allen Pearson, one of seven children, was born in Panama just six days after the stock market crash of 1929. The Canal Zone was an American possession, isolated from the country of Panama, in a sense a totally socialistic system run by the US government and relatively immune from the financial impact of the great depression. His father was an accountant with the Panama Canal Company, which managed the affairs of the Panama Canal. Except for contracting malaria at age one, Howard had what for the time was a healthy early childhood. His experiences, at times comical, growing up in Panama were shared with his grandson, Matthew, who prepared his grandfather's Oral History which is archived at the American Academy of Pediatrics History Center [1]. His sense of humor shines through in that oral history where it is recorded that he once remarked: "Since the Canal Zone was an American possession, it was officially American soil. So, if I really wanted to, I could have become President; but I decided not to."

The Pearson family returned to their origins in Lynn, Massachusetts in 1939. Howard quickly became a standout among his peers. In his own words he was something of a leader in high school, doing very well academically. He was president of his graduating class of some 500 students,

a member of the National Honor Society, and a winner of the Harvard Book Award. He was also an Eagle Scout with more than 40 merit badges, gaining skills that likely served him well many years later when he was Medical Director of The Hole in the Wall Gang Camp for children with serious diseases. After graduation from high school, it was off to college, in Howard's case, Dartmouth, a school he selected mostly because a close friend was headed there. He worked his way through Dartmouth babysitting for 25 cents an hour and getting free meals by hiring on to open the college dining room each morning at 6:00 a.m. Howard's \$200/year academic scholarship fell far short of Dartmouth's \$600/year tuition.

During Howard's first week as an undergraduate, the Dean of Dartmouth Medical School, Dr. Rolf Syversten, interviewed Howard as a possible candidate for later admission to the medical school. In those days, one could start medical school with only 36 months of college credits. Because of that interview, Howard was guaranteed an acceptance to Dartmouth Medical School to start three years hence. He ultimately graduated Dartmouth College magna cum laude and elected to Phi Beta Kappa while in medical school.

Howard entered Dartmouth Medical School in the fall of 1950. The school, now named the Audrey and Theodor Geisel School of Medicine at Dartmouth, was quite small at the time. His matriculating class consisted of just 24 students, almost all of whom had been Dartmouth undergrads. Shortly after starting medical school, Howard married Anne Livingston. He had met his future wife when they were both working at the Craigville Inn on Cape Cod. A year after they were married, the couple's first child was born. As Dartmouth was only a 2-year medical school, Howard, along with 20 of his classmates, transferred to Harvard Medical School to complete his

## Foreword

MD degree. In his Oral History, Howard recalls the family's struggles with finances. With two children to be cared for, there was little regular income. He would donate blood every 2 to 3 months for \$25 and worked filing X-rays for 75 cents an hour in the radiology department at Peter Bent Brigham Hospital.

Graduating from Harvard Medical School in 1954, and with a family to support, Dr. Pearson chose to take a rotating internship and pediatric residency as a naval officer at the National Naval Medical Center in Bethesda. Unlike those in civilian residencies, those training as military officers received a reasonable salary. While still a resident, his first manuscript as a senior author was published. This was a report of a child with Diamond–Blackfan syndrome. The patient was the first child in the United States to be successfully treated with adrenocorticotropin hormone.

Howard received permission from the navy to accept a fellowship with Dr. Louis Diamond, Chief of Hematology at the Children's Hospital in Boston. He had met Dr. Diamond when he was a medical student at Harvard. Dr. Diamond is considered the “Father of Pediatric Hematology.” The first generation of his trainees have been called “Diamond Chips.” Howard was one of these “chips,” along with Frank Oski, Lawrence Naiman and many others. If there were a 23andMe™ profile of pediatric hematologists in the United States, several score would find their training heritage linked back to Dr. Diamond in some way, including many contributors to this book.

Following his fellowship in Boston, Dr. Pearson returned to Bethesda, and for 4 years was Assistant Chief of the pediatric service under Dr. Thomas Cone, a consummate academic pediatrician, geneticist, historian and author. Much of Howard's later interests in the history of medicine likely can be traced to his relationship with Dr. Cone. When his military obligation was completed in 1962, Howard accepted a faculty position at the recently completed University of Florida Medical School in Gainesville where he established the Pediatric Department's first Division of Pediatric Hematology. He developed an interest in sickle cell disease and in animal models of human disorders. He was the first to show that dwarf cows with snorter's disease have the animal equivalent of the human Hurler's syndrome. Unfortunately, there are no videos of him performing a bone marrow on an affected cow, or

later a lion suspected of having the same disorder. His early years in Gainesville were extraordinarily productive and his efforts were recognized by moving from the rank of assistant professor to full professor in just 6 years. During his time in Florida, Howard became the perennial author of the chapter on hematology in Nelson's *Textbook of Pediatrics*. Dr. Waldo Nelson would later claim that by selecting Howard at such a young age to author that chapter, he had made him world famous.

By 1969, the Pearson family was ready to return to New England. Dr. Pearson was offered and accepted the opportunity to establish the first Division of Pediatric Hematology and Oncology at Yale. He later said that he never expected to stay in New Haven forever, but he remained on faculty well into his 80s and along the way, became chair of the Yale University School of Medicine's Department of Pediatrics. He won teaching awards and much kudos for establishing a truly collegial interaction with the community pediatricians in New Haven, an interaction that had fallen along the wayside over the years at Yale. Although his publications can be numbered in the many scores, perhaps the ones that have received much attention are his descriptions of the entity called functional asplenia (1969) and the “born again spleen” (1978), both of which were published in the *New England Journal of Medicine*. These and similar clinical reports cemented his reputation as one of the keenest minds in clinical research. It was he who also recognized that subjects with thalassemia could be identified and screened for simply by looking at their red blood cell indices. It is said that this single observation resulted in a marked reduction in the numbers of children being born with thalassemia major.

As his 12-year tenure as Chair of Pediatrics at Yale was ending, a friend of Paul Newman's stopped in to see Dr. Pearson to talk about a project Mr. Newman had envisioned, a summer camp for children with cancer. The camp was to be called “The Hole in the Wall Gang Camp” after the bunch of outlaws in Newman's film, *Butch Cassidy and the Sundance Kid*. Howard subsequently convinced Newman that the camp should also accept children with thalassemia, sickle cell disease, hemophilia, and other serious blood diseases. With a US\$10 million gift from Paul Newman, along with other contributions, the camp opened within a year. Howard

became its medical director. Reflecting on his work with Newman, years later Howard commented “I never dreamed in 1986 that the Camp would become such an important place in my life for such a long time” [1]. More than 1,000 youngsters were served each year during his time as medical director. Following his retirement as the camp’s medical director in 2005, Howard remained as its medical consultant, volunteer physician, and member of its board of directors.

Dr. Pearson’s influence and prominence extended well beyond New Haven. He held leadership positions in many professional societies. In 2002, he was named the recipient of the prestigious Howland Award. He was the President of the American Academy of Pediatrics during the important period when the Academy’s statement on the relationship between sleep position and sudden infant death was published. Because of his long-standing interest in medical history he was called upon to write the histories of the American Pediatric Society, the American Academy of Pediatrics, and the American Board of Pediatrics. Howard was a key figure in establishing an historical archive for the American Academy of Pediatrics, an archive now called the Pediatric History Center.

Only at age 84 did Dr. Pearson turn over the keys to his office at Yale, devoting his time to writing and The Hole in the Wall Gang Camp (see Fig. 0.1). He remarked that:

As I look back from the perspective of having far more time behind me than ahead of me, I probably spent too much time, including nights and weekends, on my own work and my career rather than my family. I really have no hobbies except an obsession with crossword puzzles. I do at least one crossword a day, and when I finish, I say to myself, “Another day without Alzheimer’s!”

He also said that he came from a generation that emphasized time commitment and hard work as the essential ingredients for success and that he could not remember many days when he had gone to work reluctantly. That’s a pretty good epitaph.



**Fig. 0.1** Dr. Howard Pearson at the Hole in the Wall Gang Camp (Source: Hole in the Wall Gang Camp News, available at <https://bit.ly/2YWnyKG>)

Within the pages of this edition of *Neonatal Hematology* you will recognize how Dr. Pearson’s commitment to hard work produced a voluminous quantity of clinical studies that form the basis for much of how we now provide care to infants and children with serious blood disorders. Read on.

James A. Stockman III MD

Reference

- 1. American Academy of Pediatrics. Pediatrics History Center: Oral history. Howard A. Pearson MD. Available online at <https://bit.ly/2Yrgy9A>.



## Preface

Since the last edition of this book, there have been many advances on the diagnosis and management of neonatal hematological and oncological conditions. Particularly, the ability to perform genomic analysis continues to improve and it has become more and more affordable. This ability has made possible the diagnosis of many rare disorders that prior to these advances were difficult or impossible to diagnose. Technological advances have also made it possible for physicians caring for the newborn to provide care to smaller and smaller newborns. The growth of information technology has made it possible to have an immense amount of data, literally at your fingertips. In the chapters that follow we have attempted to bring this complex matrix of information to the practicing physicians caring for newborns, and yet, remain true to the purpose of this book to provide practical information, to be a “how-to” more than a “why” book. We have continued with the order of chapters from the second edition, beginning with introduction and historical perspective. We follow with the two chapters on the development of the hematopoietic system, specifically the pathophysiology of the hematopoietic and immunological systems, the essence of blood. The remainder of the book presents practical approach to white cell disorders, red cell disorders, platelet disorders, coagulation abnormalities, transfusion medicine, neonatal oncology and manifestations of systemic disorders. Each section devoted to one of the major three cell lines begins with a practical algorithms-driven approach to the disturbance of that particular cell line. We have brought together immunologists, infectologists, hematologist/oncologists, transfusion medicine experts, and neonatologists from both sides of the Atlantic to provide you with up-to-date yet practical information for the care of our smallest of patients. We have brought along a new generation of authors so that we can continue the devotion and enthusiasm

for this field of our mentors Doctors Frank A. Oski, J. Laurence Naiman, and Gerald Rothstein who helped us develop a passion for the field.

As in the previous edition, we asked Dr. James A. Stockman III to provide a foreword for the book. For this edition, we asked him to highlight the contributions to our field made by Dr. Howard A. Pearson a giant in pediatric hematology who recently died. Dr. Pearson was a contributor to the book as author and mentor. He always shared his knowledge; he was a true gentleman and a friend. He will be sorely missed. As Dr. Pearson had written the chapter on the historical perspective of the field of neonatal blood disorders in our previous edition, we asked Dr. Stockman to provide such a chapter for this edition. Attesting to the breadth of Dr. Pearson’s knowledge, after reviewing the chapter in the previous edition, Dr. Stockman told us, “I cannot add any meaningful information to Howard’s chapter. Can you just reprint the chapter?” Thus, after asking permission from our publisher, we elected to print, unchanged, the historical perspective authored by Dr. Howard A. Pearson.

For this edition, we have also added our colleague Dr. Martha Sola-Visner to the editorial group and brought in many new generation authors. Lastly, we thank our families who have supported us during the countless hours of editing the book, specifically our spouses (Alice, Jill, Wendy, and Gary), our children and grandchildren (Alessandro and Katie, Tessa and Travis, Lucas, Audrey, Jacob and Caroline, Abby and Josh, Andrew and Henry, Elizabeth, Grant, Amelia, Elsa, Ansel, Louisa, Atticus and Cosette, and Veronica and José). Without their understanding we could never have completed this text. We hope that you find the book helpful in your day-to-day practice.

# Contributors

**James A. Stockman III, MD**

Retired President  
American Board of Pediatrics  
Chapel Hill, NC

**Pedro A. de Alarcón, MD**

William H. Albers  
Professor and Head, Department of Pediatrics,  
University of Illinois College of Medicine, Peoria,  
IL, USA

**Eric J. Werner, MD**

Division of Pediatric Hematology/Oncology,  
Children’s Specialty Group, Children’s Hospital  
of The King’s Daughters, Professor of Pediatrics,  
Eastern Virginia Medical School, Norfolk, VA,  
USA

**Robert D. Christensen is Director of  
Neonatology**

Research at Intermountain Healthcare and  
Professor of Pediatrics, University of Utah  
HEALTH, Salt Lake City, UT, USA.

**Martha C. Sola-Visner, MD**

Associate Professor of Pediatrics,  
Division of Newborn Medicine, Boston Children’s  
Hospital and Harvard University School of  
Medicine, Boston, Massachusetts, USA

**Howard A. Pearson, MD**

deceased

**Amber M. D’Souza**

Assistant Professor, Department of Pediatrics,  
University of Illinois College of Medicine, Peoria,  
IL, USA

**Mervin C. Yoder, MD**

Professor of Pediatrics, Indiana University  
School of Medicine, Indianapolis, IN,  
USA

**Amy E. O’Connell, MD, PhD**

Instructor in Pediatrics, Harvard Medical School  
Attending Neonatologist, Boston Children’s  
Hospital Boston, MA, USA

**Angela E. Rivers MD, PhD**

Assistant Professor of Pediatrics, University of  
Illinois, Chicago

**William B. Slayton, MD**

Associate Professor of Pediatrics, Division of  
Pediatric Hematology/Oncology, Stop Children’s  
Cancer of Palm Beach Country Endworld Chair,  
University of Florida, Gainesville, FL, USA

**Amy E. Geddis, MD PhD**

Professor of Pediatrics, University of Washington  
Director, Bone Marrow Failure Program Seattle  
Children’s Hospital, Cancer and Blood Disorders  
Clinic

**Meera Srikanthan, MD**

Acting Instructor of Pediatrics, University of  
Washington Seattle Children’s Hospital, Cancer  
and Blood Disorders Clinic

**Katie Bergstrom, LGC, Licensed Genetics  
Counselor**

Seattle Children’s Hospital, Cancer and Blood  
Disorders Clinic

**Julie J. Kim-Chang**

Division of Pediatric Allergy, Immunology, and  
Pulmonary Medicine, Department of Pediatrics,  
Duke University School of Medicine, DUMC Box  
2644, Durham, NC 27710

**James L. Wynn, MD**

Assistant Professor of Pediatrics, Division of  
Neonatal-Perinatal Medicine, Department of  
Pediatrics, Vanderbilt University Medical Center,  
Nashville, TN, USA

List of Contributors

**Matthew A. Saxonhouse, MD**

Division of Neonatology, Atrium Health Levine Children’s Hospital, 1000 Blythe Blvd. Charlotte, NC 28203

**John W. Sleasman, MD**

**Robert A. Good**

Professor and Chief Medical Instructor, University of South Florida, Department of Pediatrics, all Children’s Hospital, 801 6th St. South, St Petersburg, FL

**Parul Rai, MD**

Instructor Department of Hematology St. Jude Children’s Research Hospital Memphis, TN

**Ewelina K. Mamcarz, MD**

Assistant Member Department of Bone Marrow Transplantation and Cellular Therapy St. Jude Children’s Research Hospital Memphis, TN

**Jane S. Hankins, MD, MS**

Associate Member Department of Hematology St. Jude Children’s Research Hospital Memphis, TN

**Pamela J. Kling, MD**

Professor, University of Wisconsin, Madison, WI, USA

**Mary Elizabeth Ross, MD, PhD**

Assistant Professor of Pediatrics, Division of Pediatrics Hematology/Oncology, University of Illinois College of Medicine, Peoria, IL, USA (no email)

**Stephen P. Emery, MD**

Associate Professor  
Divisions of Ultrasound and Maternal-Fetal Medicine  
Department of Obstetrics, Gynecology, and Reproductive Sciences  
University of Pittsburgh School of Medicine  
Pittsburgh, PA

**Jon F. Watchko, MD**

Associate Professor  
Professor Emeritus  
Division of Newborn Medicine  
Department of Pediatrics  
University of Pittsburgh School of Medicine  
Pittsburgh, PA.

**Bertil Glader, MD, PhD**

Lucile Packard Children’s Hospital Stanford, Palo Alto, CA Stanford University School of Medicine, Stanford, CA, USA

**Aditi Kamdar, MD**

Lucile Packard Children’s Hospital Stanford, Palo Alto, CA Stanford University School of Medicine, Stanford, CA, USA

**Ted S. Rosenkrantz, MD**

Professor of Pediatrics and Obstetrics, Division of Neonatal–Perinatal Medicine, University of Connecticut School of Medicine, Farmington, CT, USA

**William Oh, MD**

Professor of Pediatrics, Warren Alpert Medical School of Brown University, Attending Neonatologist, Women and Infants’ Hospital, Providence, RI, USA

**Emöke Deschmann, MD, MMSc, PhD**

Attending Neonatologist, Department of Women’s and Children’s Health, Division of Neonatology, Karolinska Institutet Department of Neonatology, Karolinska University Hospital, Stockholm, Sweden

**Patricia E. Davenport, MD**

Instructor of Pediatrics, Division of Newborn Medicine, Boston Children’s Hospital and Harvard University School of Medicine, Boston, MA, USA.

**W. Beau Mitchell, MD**

Associate Professor of Pediatrics, Icahn School of Medicine at Mount Sinai, New York

**James B. Bussel, MD**

Emeritus Professor of Pediatrics, Professor of Pediatrics in Obstetrics and Gynecology, Weill Cornell Medical College, New York

**Kurt R. Schibler, MD**

Division of Neonatology, Children’s Hospital Medical Center, Cincinnati, OH, USA

**Thomas F. Michniacki, MD**

Clinical Assistant Professor of Pediatric Hematology/Oncology, Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI

List of Contributors

**Kelly Walkovich, MD**

Clinical Associate Professor of Pediatric Hematology/Oncology, Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI

**Manuela Albisetti, MD**

Division of Hematology, University Children’s Hospital, Zurich, Switzerland

**Paul Monagle, MBBS, MD, M.Sc, FRACP, FRCPA, FCCP**

Department of Haematology Royal Children’s Hospital Flemington Rd. Melbourne Victoria, Australia, 3052

**Gary Woods, MD**

Clinical Director, Pediatric Thrombosis Program Aflac Cancer and Blood Disorders Center, Children’s Healthcare of Atlanta Emory University School of Medicine, Atlanta, GA

**Cyril Jacquot**

Center for Cancer and Blood Disorders, Children’s National Hospital, Washington, DC, USA; Department of Pediatrics and Pathology, George Washington University School of Medicine and Health Sciences, Washington, DC

**Yunchuan D. Mo**

Center for Cancer and Blood Disorders, Children’s National Hospital, Washington, DC, USA; Department of Pediatrics and Pathology, George Washington University School of Medicine and Health Sciences, Washington, DC

**Naomi L. C. Luban, MD, FAAP**

Division Chief, Laboratory Medicine, Children’s National Hospital, Professor of Pediatrics and Pathology, George Washington University School of Medicine and Health Sciences, Washington, DC, USA

**Erin M. Guest, MD**

Division of Hematology/Oncology Director, Cancer Genomics Program, Children’s Mercy Hospital, 2401 Gillham Road, Kansas City MO 64108

**Catherine Garnett, MD**

PhD. Clinical Research Fellow, MRC Molecular Haematology Unit, Weatherall Institute of

Molecular Medicine, Headington, Oxford, OX3 9DS, United Kingdom

**Irene Roberts, MD**

Professor of Paediatric Haematology Oxford University Department of Paediatrics, Children’s Hospital and MRC Molecular Haematology Unit, Weatherall Institute of Molecular Medicine, Headington, Oxford, OX3 9DS, United Kingdom

**Alan S. Gamis, MD, MPH Professor**

Division of Hematology/Oncology Associate Division Director, Children’s Mercy Cancer Center Children’s Mercy Hospital, 2401 Gillham Road, Kansas City MO 64108

**Kevin F. Ginn MD, Assistant Professor**

Division of Hematology/Oncology Director, Pediatric Brain Tumor Program Children’s Mercy Hospital, 2401 Gillham Road, Kansas City MO 64108

**Jaszianne A. Tolbert, Assistant Professor**

Division of Hematology/Oncology and Clinical Pharmacology Director, Experimental Therapeutics in Pediatric Cancer Program Children’s Mercy Hospital, 2401 Gillham Road, Kansas City MO 64108

**Glenison Samuel, Assistant Professor**

Division of Hematology/Oncology Children’s Mercy Hospital, 2401 Gillham Road, Kansas City MO 64108

**J. Allyson Hays, Assistant Professor**

Division of Hematology/Oncology Director, Histiocytosis Program Children’s Mercy Hospital, 2401 Gillham Road, Kansas City MO 64108

**Nancy C. Chescheir, MD Clinical Professor**

Department of Obstetrics and Gynecology, Division of Maternal–Fetal Medicine, University of North Carolina School of Medicine, Chapel Hill, NC, USA

**Randall G. Fisher, MD Medical Director**

Division of Pediatric Infectious Diseases, Children’s Specialty Group; Children’s Hospital of the King’s Daughters, Eastern Virginia Medical School, Norfolk, VA, USA