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THE PEDIATRIC CLINICS OF NORTH AMERICA

New Frontiers in Pediatric Drug Therapy

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BENOIT BAILEY, MD, MSc, FRCPC, and
GIDEON KOREN, MD, ABMT, FRCPC, GUEST EDITORS

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GUEST EDITORS

BENOIT BAILEY, MD, MSc, FRCPC, Fellow, Division of Clinical Pharmacology and Toxicology, Department of Pediatrics, The Hospital for Sick Children, Toronto, Ontario, Canada

GIDEON KOREN, MD, ABMT, FRCPC, Professor, Division of Clinical Pharmacology and Toxicology, Department of Pediatrics, and Research Institute, The Hospital for Sick Children; and the Departments of Pediatrics, Pharmacology, and Medicine, University of Toronto, Toronto, Ontario, Canada

CONTRIBUTORS

MICHAEL R. ANDERSON, MD, Fellow, Division of Pediatric Critical Care, Department of Pediatrics, Case Western Reserve University School of Medicine, Rainbow Babies and Childrens Hospital, Cleveland, Ohio

BENOIT BAILEY, MD, MSc, FRCPC, Fellow, Division of Clinical Pharmacology and Toxicology, Department of Pediatrics, The Hospital for Sick Children, Toronto, Ontario, Canada

JEFFREY L. BLUMER, PhD, MD, Professor, Departments of Pediatrics and Pharmacology, Case Western Reserve University School of Medicine; and Chief, Division of Pediatric Pharmacology and Critical Care, Department of Pediatrics, Rainbow Babies and Childrens Hospital, Cleveland, Ohio

SYLVAIN CHEMTOB, MD, PhD, Departments of Pediatrics, Ophthalmology, and Pharmacology, Research Center of Hôpital Sainte-Justine, University of Montreal, Montreal, Quebec, Canada

ORNA DIAV-CITRIN, MD, Fellow, Division of Clinical Pharmacology and Toxicology, Department of Pediatrics, The Hospital for Sick Children, Toronto, Ontario, Canada

THOMAS W. FERKOL, MD, Assistant Professor, Division of Pediatric Pulmonology, Department of Pediatrics, Case Western Reserve University School of Medicine, Rainbow Babies and Childrens Hospital, Cleveland, Ohio

TERENCE R. FLOTTE, MD, Assistant Professor, Department of Pediatrics, and Assistant Professor, Department of Molecular Genetics and Microbiology, and Co-Director, Gene Therapy Center, University of Florida School of Medicine, Gainesville, Florida

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ORAL IRON CHELATION WITH DEFERIPRONE

Orna Diav-Citrin, MD, and Gideon Koren, MD, ABMT, FRCPC

Patients with refractory anemias, such as thalassemia major, who require regular red blood cell transfusions progressively accumulate iron. Each unit of red blood cells contains 200 to 250 mg of elemental iron and thus, patients on chronic transfusion programs accumulate approximately 0.5 mg/kg/day of iron. Tissue iron accumulation results in progressive organ dysfunction, leading to death if no iron-chelating therapy is initiated. Although transfusions sustain normal growth and development and improve the life expectancy of patients, they are complicated by the harmful consequences of iron overload because humans lack a physiologic mechanism for excreting excess iron.

Iron-chelating therapy for the management of transfusional iron overload was first introduced in the early 1960s.[39, 51, 63, 74] It is only since 1974, after the demonstration that it was possible to reduce the concentration of hepatic iron and arrest the progression of hepatic fibrosis in thalassemic patients with its long-term use,[16] that desferrioxamine gained acceptance as the standard form of therapy. Unfortunately, desferrioxamine is only effective when administered parenterally. Subcutaneous doses of 20 to 40 mg/kg/day for 8 to 12 hours resulted in iron excretion sufficient to produce a negative iron balance.[37, 68] Over the past two decades, several studies have demonstrated that regular desferrioxamine therapy ameliorates hepatic, cardiac, and endocrine dysfunction, improves growth and sexual maturation, and prolongs survival in iron-loaded patients.[22, 61]

Because of its high cost (approximately $40 US/2 g vial), desferrioxamine is not available in many countries where it is most needed. Even where it is available, many patients fail to comply with a regimen of prolonged subcutaneous infusions, especially during adolescence. Other problems with desferrioxamine therapy include its serious adverse effects. Intensive therapy in young

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From the Division of Clinical Pharmacology and Toxicology, Department of Pediatrics (ODC, GK), and Research Institute (GK), The Hospital for Sick Children; and the Departments of Pediatrics, Pharmacology, and Medicine, University of Toronto, Toronto, Ontario, Canada

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