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LEON KOREN, M  
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# THE PEDIATRIC CLINICS OF NORTH AMERICA

New Frontiers in Pediatric Drug Therapy

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New Frontiers in Pediatric Drug  
Therapy

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

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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.<sup>39, 51, 63, 74</sup> 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,<sup>16</sup> 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.<sup>37, 68</sup> 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.<sup>22, 61</sup>

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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