

Calcium Metabolism and Growth During Early Treatment of Children With X-Linked Hypophosphatemic Rickets

The authors administered calcitriol (20 to 40 ng/kg/d) in 2 divided doses and phosphate 40 to 60 mg/kg/d in 5 divided doses to 8 infants (1 male) with X-linked familial hypophosphatemic rickets (XLHR). This syndrome is a result of an inactivating mutation in *PEX*, a gene that encodes an endopeptidase whose substrate may be the elusive "prephosphatonin." The subjects ranged in age from 3 to 12 weeks at diagnosis and initiation of therapy and were followed for 1 to 4 years.

Treatment led to a decline to normal or nearly normal serum concentrations of alkaline phosphatase and urinary excretion of hydroxyproline, but little rise in serum phosphate concentrations. Secondary hyperparathyroidism developed occasionally, usually when phosphate intake exceeded 50 mg/kg/d. Nephrocalcinosis (grades 1 and 2) appeared in 3/8 infants without compromise of renal function. The infants grew reasonably well, with lengths maintained within the normal ranges in 6/8 patients at the conclusion of the study (see Figure). Genu varum developed in 3 children while genu valgum developed in 1. The authors conclude that early treatment with calcitriol at a daily dose of at least 30 to 40 ng/kg and phosphate at a maximal daily dose of 40 to 50 mg/kg improves mineral metabolism and seems to minimize severe growth delay and leg deformities.

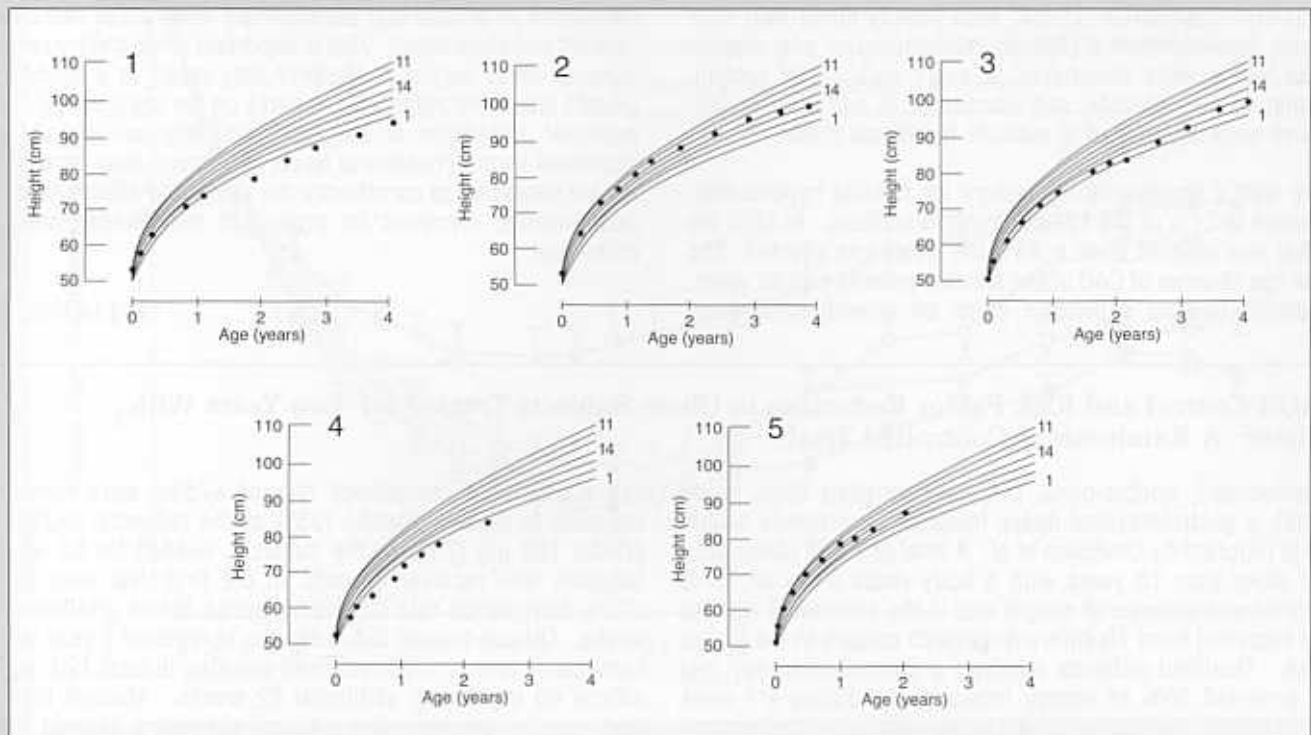
Editor's comment: Most children with XLHR have significant retardation of linear growth and deformities of the lower extremities despite administration of appropriate therapy with calcitriol and phosphate. In many instances this is the result of noncompliance with the arduous therapeutic regimen of multiple daily doses of phosphate. Treatment is not only difficult but also hazardous, with distressingly frequent periods of hypercalciuria (leading to nephrocalcinosis), hypercalcemia, and secondary hyperparathyroidism that necessitate frequent chemical and radiographic monitoring.

Several investigators have reported the beneficial effects of rhGH on the growth of children with XLHR. The experience of this writer with rhGH also has been encouraging and has seemingly made the management of calcitriol and phosphate dosing less difficult. The identification of "phosphatonin" is awaited as it may offer a more specific therapeutic (and hopefully less toxic) agent for this illness than is now available.

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Kruse K, et al. *Eur J Pediatr* 1998;157:894-900.

Figure
Growth Charts of 5 Study Patients With XLHR Treated the Longest With Phosphate and Calcitriol



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