

**Editor's comment:** The results are reassuring to physicians treating short children with chronic renal insufficiency with rhGH. Data from this study do not suggest a negative effect of such pretransplant therapy. Mean height scores in the treated group at baseline and 60 months posttransplant were  $-1.92$  and  $-1.90$ , as compared with the control group at  $-1.88$  and  $-2.10$ . Thus, gains made in height were not lost. This article and an accompanying article by Haffner et al (N Engl J Med 2000;343[13]:923-930) provide

significantly helpful and reassuring information regarding the safety and effectiveness of treating children with rhGH. The reader also is referred to a lead article in GGH (Vol. 12, No. 4, p 49) titled, "Recombinant Human Growth Hormone Therapy for Children With Chronic Renal Insufficiency: An Update 1996," which addressed the subject of rhGH treatment in chronic renal insufficiency.

William L. Clarke, MD

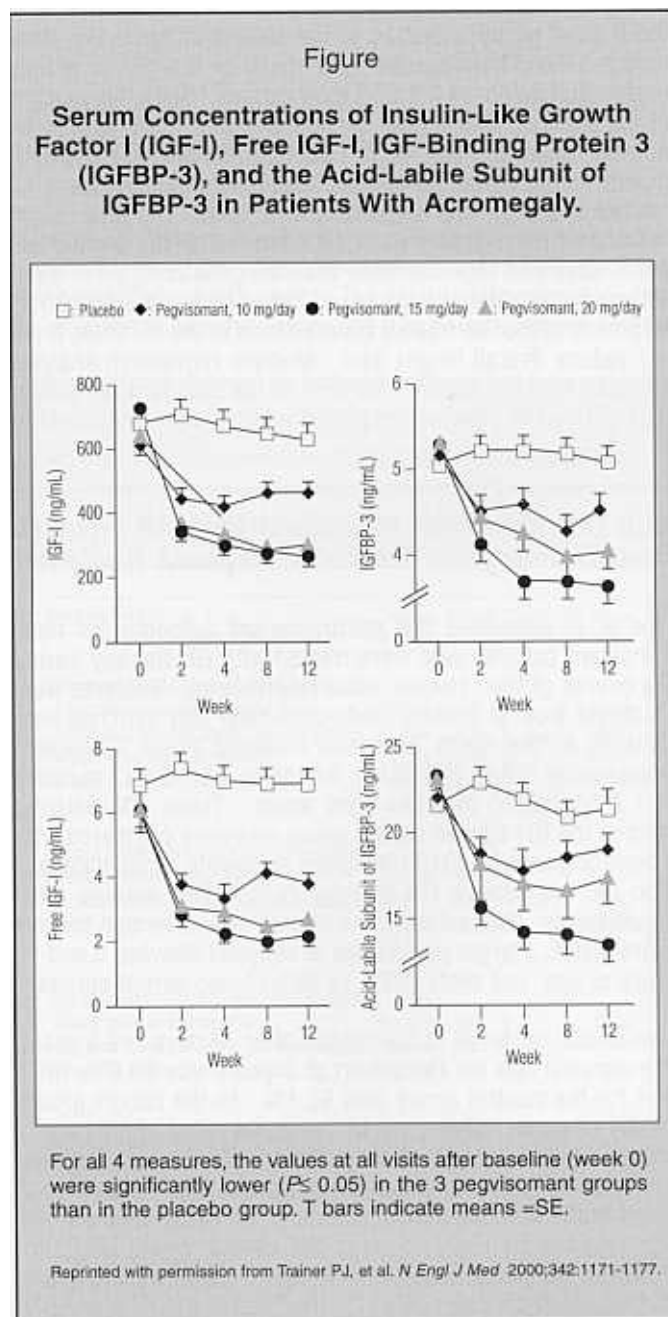
## Treatment of Acromegaly With Pegvisomant, a Genetically Engineered Human Growth-Hormone Receptor (hGHR) Antagonist

The present investigators report the beneficial effects of a GH receptor (GHR) antagonist in adults with acromegaly. Genetic engineering has permitted development of a mutated GH molecule with replacement of 9 amino acids that increases its affinity for one of the binding sites on the receptor and abolishes binding to the second site, thereby preventing functionally correct dimerization of the receptor. Polyethylene glycol polymers, which are covalently bound to a protein, are stated to be pegylated, thus, the name pegvisomant. Since the GHR is unable to dimerize, signal transduction is inhibited, leading to decreased IGF-I production.

In short-term (12-week) studies, 112 acromegalic adult subjects who had failed previous treatment (surgery and/or radiation and/or dopaminergic agonists, but not long-acting analogues of somatostatin) were divided into 4 groups, including a control group and 3 groups receiving different doses of pegvisomant. IGF-I concentrations (Figure) fell in a dose-dependent manner. Symptoms of GH excess ameliorated as there were significant decreases in soft tissue swelling, diaphoresis, and fatigue. The score for total symptoms and signs of acromegaly decreased significantly in all groups receiving the drug. As expected, serum concentrations of GH increased substantially during treatment in the patients who received 15 or 20 mg of pegvisomant. Anti-GH antibodies were noted in 5 patients but were without physiologic consequence. No patient had a significant change in tumor volume during the study. One patient had alterations in liver function while receiving this agent. No serious adverse effects were otherwise noted. The long-term consequences of the elevated GH concentrations remain to be determined.

Trainer PJ, et al. N Engl J Med 2000;342:1171-1177.

**Editor's comment:** Neurosurgical removal of GH-secreting pituitary adenomas has been and remains the primary mode of therapy for acromegaly. Medical treatment of hypersomatotropism has been reserved as secondary management; estrogens, dopaminergic agonists (bromocriptine, cabergoline), and short- and long-acting somatostatin analogues (depot preparations of octreotide and lanreotide) that impair GHRH release and inhibit its function at the somatotroph membrane have been employed to lower GH production and decrease IGF-I generation. The introduction of a GHR antagonist has expanded the therapeutic boundaries for this disease, which is so difficult to treat. In another study,



*Pegvisomant also lowered IGF-I concentrations and ameliorated symptoms in acromegalic subjects resistant to treatment with octreotide. Whether this GHR antagonist or later generations of GH antagonists will be useful in children is a matter for study. One hopes that such agents will not be employed to alter the growth of normally tall children, but its*

*use in other overgrowth syndromes will be of interest to explore in controlled settings.*

Allen W. Root, MD

Herman-Bonert VS, et al. Growth hormone receptor antagonist therapy in acromegalic patients resistant to somatostatin analogs. *J Clin Endocrinol Metab* 2000;85:2958-2961.

## Normal Growth Velocity Before Diagnosis of Celiac Disease

Celiac disease has been shown to result in nutritional growth retardation even in asymptomatic patients. However, there are instances in which this disease does not alter normal physical growth.

To evaluate height velocity of patients with confirmed celiac disease before and after diagnosis, anthropometric measurements were taken in 23 patients aged 0.1 to 10.66 years of age. All patients studied during the first 6 months of life showed normal growth velocity, and 6 of 10 patients showed normal growth velocity during the second 6 months of life. Ten of 12 patients between 1 and 2 years of age showed normal growth velocity and 7 of 9 patients aged 2 to 10 years also showed normal height velocity. The authors concluded that celiac disease could be present in children who are growing at a normal rate and that appropriate height and growth should not be factors that exclude the possibility of celiac disease.

Lejarraga H, et al. *J Pediatr Gastroenterol Nutr* 2000;30:552-556.

**Editor's comment:** *This paper is interesting as patients with confirmed celiac disease were followed longitudinally with reliable anthropometric data. While most of us have stressed the pres-*

*ence of short stature and delayed growth as 2 of the most important clinical manifestations of celiac disease, it is important to be aware of the existence of untreated patients who grow at normal rates. This paper clearly documents that this indeed occurs but is contrary to the usual clinical presentation. Normal growth found in patients with celiac disease requires an explanation. The length of the lesion in the small bowel could be a factor leading to normal or abnormal growth. In countries where the prevalence of celiac disease is high, clinicians should be alerted to the possibility of this disease in a normal, asymptomatic, short-statured child with a previous history of diarrhea or iron deficiency anemia.*

Fima Lifshitz, MD

**2nd Editor's comment:** *Unfortunately, the authors made only a minimal statement regarding the weight-to-height relationship. Twelve of the 23 patients had normal height and height velocity at diagnosis. Of all the children, 6 also showed normal weight increments before diagnosis. We can only assume that the phenomenon described occurs in children of normal weight for height and in children of low weight for height.*

Robert M. Blizzard, MD

## Nutritional Rickets in African-American Breast-Fed Infants

Kreiter and associates report the characteristics of infants and children diagnosed with nutritional rickets at 2 medical centers in North Carolina in the 1990s. Records of 30 children were reviewed; 57% of these presented in 1998 and 1999. All were black and all were breast-fed (average duration of breast-feeding, 12.5 months). Breast-feeding has increased significantly since 1988 (Figure) in North Carolina in both black and white women. Children older than 1 year had a history of poor intake of fortified cow's milk or other dairy products. The age of diagnosis ranged from 5 to 25 months, but one third presented at 12 months of age or younger. Sixty-three percent were diagnosed between April and October, some of the warmer spring/summer months in this southern area. As expected, presenting signs included skeletal abnormalities (n=16) such as bowing of the legs, flaring of the wrist, costochondral beading, fractures, failure to thrive (n=13), hypocalcemic tetany/seizures (n=2), and developmental delay (n=1). Length was <5th percentile in 17 of 26 of the infants (65%), and only 2 patients had a length >50th percentile. With the exception of 1 patient who had

recently begun vitamin D treatment, all patients had hypophosphatemia. Sixty percent had hypocalcemia, and 100% had elevations in alkaline phosphatase.

All of the children with rickets were breast-fed without vitamin D supplementation. A survey of 400 pediatricians in North Carolina revealed that 42% prescribed vitamin supplements for all breast-feeding infants, whereas 42% prescribed supplemental vitamins only for selected breast-feeding infants (ie, those with dark skin who are being exclusively breast-fed for more than 4 to 6 months or who are premature). The authors also note that the 1997 American Academy of Pediatric Policy Statement indicates that "vitamin D and iron need to be given before 6 months of age in selected groups of infants (vitamin D for infants whose mothers are vitamin D deficient or those infants not exposed to adequate sunlight)" but that no guidance is given as to how to test mothers for vitamin D deficiency.

Kreiter S, et al. *J Pediatr* 2000;137(2):153-157.