

2nd Editor's comment: Long sought but heretofore undiscovered, the elusive bioinactive GH molecule has now been identified in 1 patient. Previously, many patients have been suspected of having a biologically inactive, but immunologically active, GH (Kowarski et al, 1978; Valenti et al, 1985; Hayek et al, 1978; Bright et al, 1983; and others). However, with the technology of the 1970s and 1980s, it was not possible to prove that such a syndrome exists. Isoelectric focusing, studies of gene structure, and the interest and expertise of these authors have made

the suspected syndrome a fact. They clearly demonstrated that the proband synthesized and secreted an atypical form of GH that was able to bind with high affinity to the extracellular domain of the GH receptor, was unable to initiate signal transduction, and inhibited the biologic effects of native GH. The failure of the father with the same heterozygous mutation to express this phenotype demands further consideration.

Allen W. Root, MD

Effects of Recombinant Human Growth Hormone (rhGH) Treatment in Intrauterine Growth-Retarded Preterm Newborn Infants on Growth, Body Composition and Energy Expenditure

The investigators from Amsterdam administered rhGH (1.0 IU/kg or 0.33 mg/kg/d) to 7 preterm infants (mean gestational age, 30.4 weeks) with IUGR (mean birth weight, 938 g) beginning at 7 days of age and continuing until achieved weight was 2,000 g (34 to 68 days of treatment). When compared with an untreated control group of IUGR preterm infants, there was no effect of rhGH on: time to doubling of birthweight; increments in body weight, length, and head circumference; ponderal index; serum glucose or insulin values; skin-fold thicknesses; total body water; or energy expenditure. The authors concluded that administration of rhGH had no effect on growth or energy metabolism in preterm infants with IUGR.

Editor's comment: Despite some problems with the applicability to IUGR preterm infants of the utilized methodology¹, the data are of interest because they indicate that even exceedingly high doses of rhGH cannot positively affect the growth or metabolism of such children. Whether such therapy can have adverse effects is unknown at present. The findings also indicate the need to search for growth factors other than rhGH (perhaps insulin-like growth factor 2, insulin, etc) that may be of benefit to IUGR preterm infants. The utility of rhGH in preterm infants with appropriate growth for gestational age has yet to be assessed.

Allen W. Root, MD

van Toledo-Eppinga L, et al. *Acta Paediatr* 1996;85:476-481.

1. Wollmann H, et al. *Acta Paediatr* 1996;85:398-400.

Prenatal Diagnosis of 45,X/46,XX Mosaicism and 45,X: Implications for Postnatal Outcome

Prenatal diagnosis of chromosomal abnormalities is available for families who have an option whether to continue the pregnancy. Twelve patients with 45,X/46,XX mosaicism were diagnosed prenatally by amniocentesis and subsequently evaluated at 3 months to 10 years of age. All have had normal linear growth. Four had anomalies, including esotropia and ptosis (1); labial fusion (1); atrial septal defect (1); and urogenital sinus, dysplastic kidneys, and hydrometrocolpos (1). The patient with ophthalmologic abnormalities is mentally delayed. None would have warranted karyotyping for clinical suspicion of Turner syndrome. These 12 were compared with 41 45,X/46,XX patients diagnosed postnatally. The prevalence of 45,X/46,XX mosaicism is 10-fold higher among amniocenteses than in series of postnatally diagnosed individuals with Turner Syndrome, which suggests that most individuals with this karyotype escape detection and that an ascertainment bias exists toward those with clinically evident abnormalities. The authors note that the phenomenon of a milder phenotype for the prenatal group is similar to that observed for 45,X/46,XY individuals diagnosed prenatally. The

authors emphasize that prenatal counseling for 45,X/46,XX in the absence of such ultrasound abnormalities as hydrops fetalis should take into account the expectation of a milder phenotype than that of patients ascertained postnatally. The same does not hold true for 45,X diagnosed prenatally.

Koeberl DD, et al. *Am J Hum Genet* 1995;57:661-666.

Editor's comment: This presentation provides important information for genetic counseling. One should not be too discouraging when discussing the expectations of a fetus when a 45,X/46,XX karyotype or a 45,X/46,XY karyotype is reported. Many of these 45,X/46,XX children will be phenotypically normal and possibly may end up with a 46,XX karyotype. The 45,X cell line may sometimes disappear, although that was not investigated in this study. This comment is made because the prevalence of 45,X/46,XX mosaicism is 10-fold higher among amniocenteses data than in series of postnatally diagnosed individuals with Turner syndrome.

Judith G. Hall, MD