

inconsistencies were noted, the methods were comparable. The main advantage of the computerized method over the manual rating method is that it uses a continuous scale instead of an interval scale. This diminishes the error of the interpretation of maturity stages, as the difference of 1 interval stage in the rating of a particular bone may result in an increase of 0.3 bone age years. The 6b model was less time-consuming than the 13b model, and yielded acceptable readings of bone maturation. The main disadvantage of CASAS is the need for special equipment (hardware and software),

which increases the cost. The curves for bone maturation in TS girls and CTS children presented in this article will enhance our understanding of the dynamics of growth, whether spontaneous or in response to specific therapeutic modalities. The procedure has been technically described by Tanner and Gibbons (J Pediatr Endocrinol 1994;7:141-145), in an article that is highly recommended to those of you who wish to review the details of the system and its principles.

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Intranasal Administration of GHRP Hexarelin Accelerates Growth in Short Children

The investigators administered the growth hormone-releasing peptide (GHRP) hexarelin (His-D-2-methyl-Trp-Ala-Trp-D-Phe-Lys-NH₂) to 8 short prepubertal children (7 males, 1 female; 5.3 to 11.6 years of age). All subjects had normal growth hormone (GH) secretion (>10 ng/mL) in response to provocative stimulation as well as a substantial increase in GH concentrations (>20 ng/mL) following 1 intranasal inhalation of hexarelin (20 µg/kg). Hexarelin (60 µg/kg/dose) was administered intranasally 3 times daily while the children were recumbent. Mean growth rate increased from 5.3 ± 0.8 cm/y to 8.3 ± 1.7 cm/y during the first 6 to 8 months of therapy ($P < 0.001$). Skin-fold thickness declined and head circumference increased during therapy. Serum levels of insulin-like growth factor 1 (IGF-1), inorganic phosphate, and alkaline phosphatase increased during administration of hexarelin. No adverse local or systemic clinical or biochemical events were recorded during this treatment period. The authors concluded that, over the short term, intranasal hexarelin accelerates growth in short children with intact GH secretion.

Editor's comment: *The natural compound whose biologic activity is mimicked by the various synthetic GHRPs is unknown. GHRP acts through a somatotrope receptor that is separate from that for GH-releasing hormone (GHRH) and through a different intracellular signaling pathway (GHRH-adenylyl cyclase/cyclic adenosine monophosphate; GHRP-phosphoinositol). The primary site of action of the GHRPs may be within the hypothalamus rather than directly at the pituitary, as they are inactive in the absence of GHRH. GHRPs are active when administered intravenously, subcutaneously, intranasally, and orally. The present report demonstrates the short-term effects of GHRP administered intranasally. We may anticipate that these agents will also be active during short- and long-term oral administration. If experience demonstrates the safety and effectiveness of oral GHRP, yet another therapeutic agent may be available for the management of the carefully selected short, GH-sufficient child.*

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Laron Z, et al. *Clin Endocrinol* 1995;43:631-635.

Nondisjunction in Human Sperm: Evidence for an Effect of Increasing Paternal Age

It is well established that increased maternal age is associated with an increased risk of chromosomal trisomy in offspring, ie, the maternal age effect. In contrast, the existence of a paternal age effect has been controversial, with most epidemiologic evidence favoring the absence of such an effect. One of the difficulties has been separating paternal from maternal age effect.

Griffin et al have taken a different approach to the question of paternal age effect. They directly analyzed sperm. Sperm are normally monosomic; they contain only 1 copy of each autosome plus an X or a Y chromosome, ie, 23 X or Y. The authors used fluorescent in situ hybridization (FISH) to count the number of X, Y, and number 18 chromosomes in about 400,000

individual sperm from 24 men, ranging in age from 18 to 60 years. By using probes for both the X and Y chromosomes and chromosome 18, they could distinguish between disomy involving 1 chromosome and diploidy involving a whole complement of chromosomes. Moreover, in cases of disomy for the sex chromosomes, they could distinguish between nondisjunction that occurred during the first meiotic division, which would produce disomic sperm carrying both an X and a Y chromosome, and nondisjunction that occurred during the second meiotic division, which would produce disomic sperm carrying 2 X or 2 Y chromosomes. When such sperm fertilize normal ova, trisomic embryos would be produced containing 47,XXX, 47,XXY or 47,XYY chromosome complements.