

Editor's Comment: *It is striking that such financial analyses are now needed to justify growth screening, a fundamental tenet of pediatric care. However, as highlighted by this paper, many of the considerations remain elusive. What is the optimal height cut-off to identify likely pathology? What is the optimal screening paradigm? Serial height measurements will capture cases of growth deceleration before they become severe enough to cross the single height cut-off for pathology, but how frequent and how many are needed to balance improved sensitivity with increased cost? What is the actual cost of missed or delayed diagnoses and how are QALYs estimated, especially since the impact of short stature on quality of life remains so controversial? And what about the cost of height monitoring itself? Height*

measurements in the United States are performed as part of routine pediatric well child care,² and the cost of a stadiometer spread across the patient population is so negligible that it seems virtually free. The only real cost is the time to accurately measure the child and plot the measurements on the appropriate growth chart. With the increasing pressures to expedite patient flow faster and faster, time may be the most expensive aspect of growth screening.

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References

1. National Screening Committee. Child health sub-group report: growth disorders. Leeds: National Screening Committee; 2004.
2. American Academy of Pediatrics Policy Statement - Committee on Practice and Ambulatory Medicine. Pediatrics. 2000;105:645.

Histrelin Subdermal Implant in Central Precocious Puberty

This important article describes efficacy and safety data related to the use of a single annual subcutaneous implantation of a gonadotropin-releasing hormone analogue (GnRHa) to induce pituitary gonadotropin suppression in children with central precocious puberty. Histrelin provides a continuous slow release at an average rate of 65 µg/d of GnRHa. Its use as a single yearly implant has previously been shown to effectively suppress LH, FSH and testosterone secretion in adult males with prostate cancer.^{1,2} This report is the first in children with precocious puberty.

The procedure of implantation will require more detailed examination with wider clinical use. A pediatric surgeon is required to perform this procedure and in this study, local or general anesthetic or sedation was used. There is no comment about any practical difficulties with the implantation in terms of interference with daily activities such as sports and recreation, or whether the implant became dislodged in some patients.

Eugster EA, Clarke W, Kletter GB, et al. Efficacy and safety of histrelin subdermal implant in children with central precocious puberty: A multicenter trial. J Clin Endocrinol Metab. 2007;92:1697-704.

Editor's Comment: *The data on sex steroid, LH and FSH evaluation are impressive and clearly show that effective suppression of gonadotrope function occurs for 12 months after a single subcutaneous implantation. The choice of patients may need to be individualized and an implantation technique which avoids general anesthetic would clearly be preferable. Longer term studies to assess recovery of the pituitary-gonadal axis following discontinuation of treatment are important. This first report in children is encouraging and may eliminate the discomfort of monthly or three-monthly injections as currently practiced.*

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References

1. Schlegel PN, Kuzma P, Frick J, et al. Urology. 2001;58:578-82.
2. Chertin B, Spitz IM, Lindenberg T, et al. J Urol. 2000;163:838-44.

Hypogonadotropic Hypogonadism—Mutations and Phenotypes

Isolated hypogonadotropic hypogonadism (IHH) has been associated with mutations in 7 genes to date (Table). The products of the genes encoded by *KAL1*, *FGFR1*, *PROK2*, *PROKR2*, and *NELF* assist in the regulation of neural movement within the CNS—particularly the migration of olfactory and gonadotropin releasing hormone (GnRH)-containing neurons from the olfactory placode during early embryogenesis. Mutations in these genes result in abnormalities of GnRH secretion and the reproductive endocrine system (delayed adolescence, hypogonadotropism) and the sense of smell (hyposmia, anosmia), and those afflicted often display other neurologic (bimanual synkinesia) and somatic (renal agenesis) anomalies. These traits

are transmitted in an autosomal dominant manner often with incomplete penetrance and substantial inter- and intrafamilial variability in clinical manifestations. Mutations of *GPR54* limit release of GnRH while those of the *gonadotropin-releasing hormone receptor (GNRHR)* impair its function at the gonadotroph membrane. These disorders are transmitted in an autosomal recessive manner and are not associated with other specific clinical or anatomic abnormalities.

Intrigued by the variable clinical manifestations of IHH, Pitteloud and colleagues examined the genotype of 2 families in which single gene defects thought to have resulted in IHH had been previously identified. In pedigree #1, a 21-year-old male with IHH and