

**Editor's Comment:** *These authors presented some truly encouraging information for endocrinologists to share with their patients with TS. Indeed hormone replacement therapy is associated with normal uterine development while the age of starting hormone replacement therapy is not a critical factor. Thus those women with TS who wish to participate in oocyte donation programs should be encouraged to do so or may be encouraged to do so with reasonably good assurance that their uterus should*

*be capable of sustaining a normal pregnancy. As the authors noted, their study could have unexpected biases due to its cross-sectional nature.*

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#### References

1. Doerr HG, Bettendorf M, Hauffa BP, et al. Hum Repro. 2005;20:1418-21.
2. Karnis MF, Zimon AE, Lalwani SI, et al. Fertil Steril. 2003;80:498-501.

## GH Treatment Effects on Body Composition in SGA

The use of growth hormone (GH) therapy in small for gestational age (SGA) children with short stature, now approved and licensed both in the US and Europe, requires critical appraisal. Body composition in childhood may be affected by alteration of fetal growth. SGA infants who show catch-up growth tend to become obese and may be at risk for metabolic syndrome in adult life. However, SGA children who remain short are thin and have a low BMI and possibly compromised bone mineral density. The group of 25 SGA subjects (birth weight and current height  $<-2$  SD) reported in this study were prepubertal and randomized to receive either GH therapy ( $n=16$ ) or act as untreated controls for 3 years and then start GH therapy ( $n=9$ ). Heights in both groups were  $<-2$  SD and the daily GH dose was 1 mg/m<sup>2</sup> body surface area.

Clinical characteristics were comparable in the 2 groups. In the untreated subjects lean body mass (LBM) decreased during the 3 years ( $P<0.01$ ) contrasting with the GH-treated group which showed catch-up increase of LBM. When the untreated subjects started GH, their LBM SDS also increased significantly. Therefore GH therapy, in the dose described, induced catch-up of LBM. However percentage body fat decreased in the GH-treated subjects. Bone mineral density SDS

measured by DEXA increased significantly in the GH-treated group compared to the untreated subjects.

Willemsen RH, Arends NJ, Bakker-van Waarde WM, et al. Long-term effects of growth hormone (GH) treatment on body composition and bone mineral density in short children born small-for-gestational-age: six-year follow-up of a randomized controlled GH trial. Clin Endocrinol (Oxf). 2007;67:485-92.

**Editor's Comment:** *These findings are of interest, but their clinical relevance remains uncertain. The anabolic effects of GH on muscle bulk and bone mineralization are demonstrated, as is its lipolytic effect. However the benefit to the child of these changes is difficult to assess. Is the improvement in BMD really going to prevent development of osteoporosis and increased fracture risk in adult life? The answers are unknown. Is the reduced LBM in the untreated short SGA child actually a disadvantage to the child? Again we are not certain. However, in this report the carefully studied longitudinal changes in body composition which occur during GH therapy are useful in documenting the anabolic and lipolytic effects of GH in short SGA children.*

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## Widespread Monoallelic Expression of Human Autosomal Genes

With certain exceptions, it is generally assumed that maternally and paternally-derived copies (alleles) of each gene are expressed at comparable levels in humans. The first exception is inactivation of most of the genes residing on the X-chromosome in females—so called X-inactivation. Half of the cells in an embryo on average randomly inactivate the paternal X chromosome and half inactivate the maternal X chromosome around the time of implantation. The second exception involves imprinting of autosomal genes, such as IGF-2, on a parent-of-origin basis. A third exception is a small group of autosomal genes that are subject to random monoallelic expression; these include genes encoding odorant receptors, T cell receptors, interleukins, and natural killer cell receptors. There is new evidence that monoallelic expression of autosomal genes may be

much more extensive than previously believed.

Gimelbrant et al exploited the growing number of single nucleotide polymorphisms (SNPs) and advances in gene chip (array) technology to survey allele-specific transcription of about 4,000 genes in lymphoblastoid cell lines from 3 individuals. They took advantage of the observation that once a cell decides to express one of 2 alleles, the clonal descendants of this cell continue to express the selected allele. Since lymphoblastoid cells are polyclonal, they were able to derive clonal B cell lines using single-cell cloning.

To perform the genome-wide screen for monoallelic transcription, the investigators developed protocols to distinguish polymorphic allele expression based on detection of SNPs in nuclear RNA, which is enriched in intronic RNA, where most SNPs associated