

Dr. Blizzard critically analyzes the current thinking concerning the problem of when to perform reconstructive genital surgery in the patient with male pseudohermaphroditism assigned to the female gender.

In my opinion, he correctly rejects the extremist position that no reconstruction be undertaken until the patient herself can consent. Clearly, this approach will lead to great duress in the lives of the patient and her parents. (One can barely imagine the stress that a parent would be under in raising a child whose gender may change or that of the child who will surely learn at a surprisingly early age that her genitalia differ from those of other girls.) While each child must be considered individually, cliteroplasty during infancy and vaginoplasty at adolescence seem reasonable in my opinion once feminine gender has been assigned until the long-term efficacy of earlier vaginal reconstructive techniques have been evaluated.

Dr. Blizzard discusses the issue of intra-cultural differences in attitude toward the problem of intersex and the challenging question of whether all children with 46XX female pseudohermaphroditism should be reared as females.

His thoughtful and insightful comments are seconded by this writer, although my inclination is to rear all females with virilizing congenital adrenal hyperplasia as girls. Individualization of care and informed parental choice

are the keystones upon which management of the neonate with atypical external genitalia must be based.

Readers who wish to be brought up-to-date concerning some of the conundrums of intersex issues and what the current concepts are concerning intersex issues will benefit from Dr. Blizzard's commentary.

Blizzard RM. *Pediatrics* 2002;110(3):616-621.

Allen W. Root, MD

Dr. Blizzard's Comment: *Comments about one's commentary are not necessarily legitimate. However, I comment relating the above abstract and editorial comment by Dr. Root to the lead article in this issue by Dr. Sheri Berenbaum. Her studies and writings are always logical, intelligent, and scientifically based. In her article, Dr. Berenbaum demonstrates the applicability of my adjectives used to describe her approaches to solving the conundrums of intersex. I highly recommend each reader contemplate her description of the complexities in this field. Hopefully others will approach the conundrums of intersex in the same contemplative way as does she.*

Robert M. Blizzard, MD

Letter to the Editors:

In the December 2002 edition of *Growth, Genetics & Hormones* (Vol. 18. No. 4), two articles (Imaizumi K, et al. *Am J Med Genet* 2002;107:58-60; Kurotaki N, et al. *Nat Gen* 2002;30:365-366) were abstracted under the title *A Gene as a Major Cause of Sotos Syndrome Has Been Identified*. The authors are reported to state that the identification of a deletion or mutation of this mutated gene on chromosome 5 will sometimes help in the diagnosis of Sotos syndrome, etc. Both Dr. Judy Hall and Dr. William Horton gave cogent editorial comments.

However more recent evidence indicates that additional knowledge gained by Kurotaki and others should be considered by clinicians and investigators attempting to use identification of a deletion or mutation of this mutated gene (NSD1) to help in the diagnosis of Sotos syndrome. Specifically, at the ASHG meeting in October 2002, Kurotaki et al from Japan reported finding point mutations and deletions of the NSD1 gene in a large series of patients and Clech et al from Paris reported their findings in 39 patients. Only 14 were felt to have typical Sotos syndrome; four had a

NSD1 deletion of paternal origin. It had previously been suggested that based on similarity of the phenotypes, Sotos and Weaver syndromes might be allelic disorders. Rahman et al from the UK reported that >40% of patients with typical Sotos syndrome had intragenic mutations in NSD1 and 3 of 7 patients with Weaver syndrome had intragenic NSD1 mutations. In each of these series, patients with a combination of overgrowth and mental retardation, but without typical features of either Sotos or Weaver syndrome, were not found to have deletions or intragenic mutations of NSD1.

These reports collectively demonstrate that the majority of patients with typical Sotos and Weaver syndrome have intragenic mutations or deletions of NSD1, and thus, represent allelic disorders. However, the combination of overgrowth and mental retardation represents a heterogeneous phenotype in which only a portion is accounted for by abnormalities of NSD1.

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