

## Prenatal Treatment of Females With Congenital Adrenal Hyperplasia Due to 21-Hydroxylase

Congenital adrenal hyperplasia due to 21-hydroxylase deficiency has been well defined on a pathogenetic basis during the last few years. There are actually 2 genes linked to the HLA loci next to the C4B gene of the major histocompatibility complex on chromosome 6. Prenatal diagnosis is possible in the first trimester by chorionic villus sampling and DNA analysis or HLA linkage. Because congenital adrenal hyperplasia is the most common cause of female pseudohermaphroditism, the possibility of in utero therapy has been raised. This paper reports a pregnancy in which a female was recognized to be affected with the salt wasting form of congenital adrenal hyperplasia at 10 weeks of gestation. However, in order to suppress the adrenal, dexamethasone therapy had already been introduced during the eighth week. The child was born at term with minimal masculinization of her external genitalia in spite of being a severe salt loser.

The article summarizes the published total of 14 such cases of female infants who had been prenatally treated. Five newborn girls whose mothers received dex-

amethasone (starting between 5 and 8 weeks) had normal external genitalia. Five newborn girls whose mothers received hydrocortisone starting from 3 to 9 weeks had mild or partial virilization. Four female newborns whose mothers were treated with dexamethasone starting at 5 to 10 weeks had marked virilization.

It would appear that prenatal treatment has varying effectiveness. The reasons for this variation are not clear, but they may include familial variation in response to therapy, problems with transplacental passage of glucocorticoids, variations in maternal metabolism of glucocorticoids, variations in the clearance of exogenous glucocorticoids, fetal adrenal steroidogenic functional differences, and differences in the pituitary adrenal feedback mechanism.

Pang S, Pollack MS, Marshall RN, et al. *N Engl J Med* 1990;322:111-115.

**Editor's Comment**—This report demonstrates not only the power of DNA techniques to diagnose pre-

*natally, but also the problems with intrauterine therapy: The therapy needs to be started earlier than it is possible to diagnose the presence of the biochemical abnormality. Since chorionic villus sampling is not available until approximately 9 weeks, the process of masculinization would have started prior to our ability to make the diagnosis. In addition, the range of masculinization among treated fetuses makes it clear that we do not really understand individual differences in response or the processes that lead to masculinization. It is clear that additional cases need to be followed carefully and reported so that we may ultimately arrive at the best therapies both in utero and ex utero. Follow-up information is also needed on those infants who are treated early but found not to be affected females. The assumption is that no harm has been done, but we need to be sure. A prospective collaborative study is very much needed. Hopefully, those pediatric endocrinologists with a special interest in congenital adrenal hyperplasia will establish such a study.*

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