

**Problem behaviors:** The Child Behavior Checklist in its two versions, one for 2- to 3-year-old children, the other for the age group 4-18 years, was used. The pilot study had shown increased (internalizing) problem behaviors in DEX-treated children. In the current study, a few comparisons were significant, some favoring DEX-exposed children, some favoring controls. Overall, given the large number of comparisons, and the inconsistency and small effect sizes of significant findings, the evidence for the effects of prenatal DEX exposure on behavior problems is not convincing. **Gender-related behavior:** The Child Game Participation Questionnaire and the Child Behavior and Attitude Questionnaire were employed. If prenatal DEX exposure of female CAH fetuses interferes with the masculinization of their genitalia, does the same apply to the masculinization of the brain as indicated by later gender-related behavior? The initial analyses established, as expected, that CAH girls were significantly behaviorally masculinized in comparison to non-CAH girls, with much stronger masculinization in the more severe saltwasting (SW) form of CAH than the simple virilizing (SV) form, at least in the older age group. **Analyses for DEX effects** shows a slight but statistically significant reduction of masculinization in the total group of DEX-exposed CAH children, surprisingly not in the CAH girls alone, where the effect is weak, but also in the CAH boys. Further analyses are in progress. **Brain lateralization in terms of handedness:** Analyses are in progress. Overall, this project turned out to be markedly underfunded. We could compensate for the lack of funds in the data collection process by drawing into the study seven student volunteers without whom we would not have been able to be so successful in tracing families' changed addresses, in recruitment, and in follow-up calls. We underestimated even more the complexity of the data analysis and the time requirements. Unfortunately, given the skill level required, this shortfall cannot be made up by student volunteers. Therefore the data analysis and manuscript writing are not yet completed, but will continue for several more months. **Significance** Recent animal studies have raised concerns about possible adverse behavioral side effects of prenatal exposure to exogenous glucocorticoids. The test results of the current study do not support such concerns. **At the same time, initial findings in the gender domain suggest a reduction of behavioral masculinization which, if confirmed by the other analyses, might indicate lessened problems of gender adjustment that are seen in some girls with CAH.** Several articles are in preparation and a number of abstracts have been presented.<sup>8 9 10</sup>

## B. 11 $\beta$ -Hydroxylase Deficiency

1. **Prenatal diagnosis and treatment of 11 $\beta$ -hydroxylase deficiency** In the same family who had successful prenatal treatment in 1999 of 11 $\beta$ -hydroxylase deficiency, a subsequent pregnancy was prenatally diagnosed and treated. The fetus was diagnosed as a heterozygote unaffected female and prenatal treatment with dexamethasone was discontinued. Recently, in another family in which the proband is homozygous A331V, we performed prenatal diagnosis and prenatal treatment. The fetus is a homozygous normal male hence prenatal treatment was discontinued. Sequence analysis of some of the extended family members has been performed making prenatal diagnosis available when needed. This mutation (A331V) has been previously published.<sup>11</sup>
2. **Family studies:** We have identified two new families with 11 $\beta$ -hydroxylase deficiency. In the first family, DNA sequencing analysis of their *CYP11B1* gene has revealed that the twin probands are homozygous for the R384Q mutation (CGA to CAA) in exon 7. This mutation has been previously published by our institution.<sup>17</sup> The parents are both heterozygous for the mutation. In the second family, DNA sequencing revealed that the proband and her sib inherited a heterozygous paternal Q356X mutation (CAG to TAG) in exon 6 which has been previously published.<sup>12</sup> Both sibs inherited a heterozygous maternal G444D mutation (GGC to GAC) in exon 8, which has not been previously reported. *In vitro* expression studies will be performed with the G444D mutation to confirm that it is causative.

## C. Apparent Mineralocorticoid Excess