



**Karolinska
Institutet**

Institutionen för Molekylär Medicin och Kirurgi

LONG-TERM FOLLOW-UP OF PRENATALLY DEXAMETHASONE- TREATED CHILDREN AT RISK FOR CONGENITAL ADRENAL HYPERPLASIA

AKADEMISK AVHANDLING

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av

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ABSTRACT

Congenital adrenal hyperplasia (CAH) is a disorder of steroid genesis affecting approximately 1:10 000 children and leading to increased levels of androgens during foetal life and subsequent virilization of external genitalia in affected girls. However, prenatal virilization can be eliminated by antenatal dexamethasone (DEX) treatment. To be fully effective, DEX treatment has to be started in the 6–7th postmenstrual week and continued until the results of the prenatal diagnosis are available at gestational week 11–12. This means that 7 out of 8 fetuses (boys and unaffected girls) are treated unnecessarily during early gestation. CAH-affected girls are treated to term.

We performed a long-term follow-up of children treated in Sweden during the years 1985–1995, and 26 of the 40 treated individuals participated in the study. The control group consisted of 35 sex- and age-matched healthy children.

In general, the DEX-treated children were as well adjusted as the controls (Studies I and II). There were no between-group differences in major cognitive measures such as IQ, learning and memory. Parents reported that the DEX-treated children performed just as well at school as the controls. However, in a test of verbal working memory (WM), significantly lower results were observed in CAH-unaffected short-term treated children. The CAH-affected children did not differ from the control group, probably owing to small sample size and, consequently, low power. The verbal WM was correlated with the children's self-perception of difficulties in scholastic ability, another measure in which CAH-unaffected children differed from the controls. In measures of temperament, psychopathology and well-being, parents reported generally as good health in the DEX- exposed group as in the control group. The only difference was an observed increase in sociability in DEX-exposed children. In the children's self-ratings, however, increased social anxiety was observed. This difference was significant in CAH-unaffected short-term-treated children.

In order to study gender role behaviour (Studies III and IV), we developed a new instrument, the Karolinska Inventory of Gender Role Behaviour (KI-GRB), which was evaluated in an additional group of 180 school-age children. The underlying dimensions of the inventory were described by the factor structure and the KI-GRB subscales were also associated with sex-specific cognition. In prenatally DEX-exposed, CAH-unaffected boys, more neutral behaviours were observed, while in girls no group differences emerged after controlling for site of residence. A similar pattern was found when CAH-affected children were included in the analyses

In summary, these studies indicate that prenatal DEX treatment of CAH may have negative effects on certain aspects of cognitive and affective development, as well as affect gender role behaviour.