Congenital Adrenal Hyperplasia

Background

Congenital adrenal hyperplasia (CAH) is a group of disorders resulting from inherited defects in adrenal steroidogenesis. Classical CAH presents in the newborn period with virilization in female infants and with salt-wasting (with or without adrenal crisis) in both sexes. Non-classical CAH usually presents in later childhood with virilization. As CAH has considerable risk of mortality and morbidity, especially in the newborn period, newborn screening programs have been introduced in a number of countries. There is some evidence in the literature to suggest that a significant number of cases which have been detected by neonatal screening, especially in male infants, may be missed on clinical grounds alone. No data currently exist on the incidence of CAH in Australia.

Objectives

- To estimate the incidence of classical and non-classical CAH in Australia
- To compare case ascertainment during a trial period of newborn screening in NSW with case ascertainment through APSU for the same time period
- To characterise selected clinical and management characteristics of patients with classical and non-classical CAH

Case definition

Any new case of CAH in a child less than 16 years, confirmed biochemically by elevations in adrenal steroid precursors,*

with or without

clinical evidence of salt-losing or simple-virilizing CAH (clinical features may include: ambiguous genitalia, salt-wasting, adrenal crisis, virilization, hypertension)

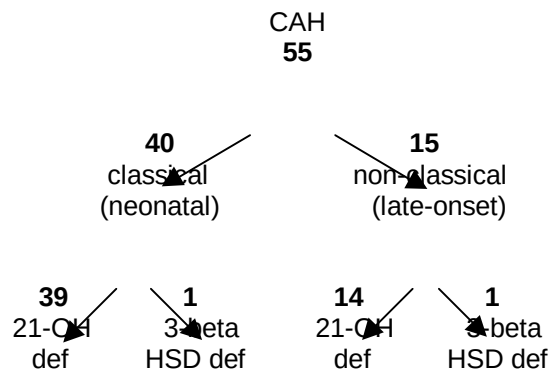
**elevated basal levels or synacthen test stimulated levels of 17-hydroxyprogesterone and/or other steroid precursors according to individual laboratory reference standards*

Note: *where there is borderline elevation of 17-OHP in sick or preterm neonates, a measurement repeated at a later time to confirm the diagnosis should be sought. Cases identified by newborn screening will always require confirmation of diagnosis by standard biochemical methods.*

Results and discussion

Between May 1995 and December 1997, 130 notifications of CAH were received by the APSU. One hundred and twelve (86%) questionnaires have been returned. From these, 55 cases of CAH were identified (Figure 13).

Figure 13 **Number of cases of different types of CAH**



Neonatal (classical) CAH

Forty of the 55 confirmed cases were classical neonatal CAH (Figure 13), giving an incidence of 5.9/100,000 live births. Thirty-nine were due to 21-hydroxylase deficiency (21-OH def) and one to 3-beta hydroxysteroid dehydrogenase deficiency (3-beta HSD def). Eighteen were males. Table 17 shows the state of origin and sex distribution of these cases.

Table 17 **State of origin and sex of classical CAH, May 1995 - Dec 1997**

State	Males	Females
NSW and ACT	7	8
Victoria	4	5
Queensland	2	2
Western Australia	0	6
Northern Territory	1	0
Tasmania	1	0
South Australia	3	1
Totals	**18**	**22**

Late onset (non-classical) CAH

Fifteen cases of non-classical, late-onset CAH were identified (Figure 13). Five (33%) were males. Fourteen were due to 21-hydroxylase deficiency and one to 3-beta hydroxysteroid dehydrogenase deficiency. Mean (SD) age at diagnosis was 7.3 (4.1) years. The bone age was advanced by a mean (SD) of 2.5 years (2.1) years. Cases of non-classical (late onset) CAH will be missed by APSU surveillance if they present to adult specialists.

Results of newborn screening

Between October 1995 and September 1997, newborn screening in NSW/ACT and APSU surveillance of CAH occurred simultaneously. During this period, 12 cases were confirmed from NSW/ACT, of which six (50%) were initially detected on newborn screening (Table 18). These included one female, who had no genital abnormalities and a relatively mild enzyme block and five males. Five other females with genital abnormalities, who were diagnosed clinically at birth, were subsequently found to be abnormal on newborn screening. One

male, who was normal on neonatal screening, was diagnosed with CAH at day 16. He had a mild 21-hydroxylase deficiency (non salt-wasting) and was tested because there was a family history of CAH. This is the only known case of CAH that was missed by newborn screening in NSW/ACT. Cases identified by newborn screening were notified to clinicians between seven and 10 days of age. During the screening period, no child in NSW/ACT presented clinically with salt-wasting or adrenal crisis.

During the period of screening in NSW/ACT, 17 cases from other states with no screening program were identified through the APSU. As shown in Table 18, 10 females and one male presented with genital abnormalities. Six other males presented with a salt-wasting or adrenal crisis. At least five of these would have been detected by newborn screening before salt-wasting or adrenal crisis occurred. One presented on day seven when results of neonatal screening may not have been available. Information is not yet available on a number of cases from outside NSW/ACT.

Table 18 **Initial method of detection of CAH, Oct 1995 - Sep 1997**

State	Males	Females
NSW and ACT		
Genital abnormalities	0	5*
Salt-wasting or adrenal crisis	0	0
Prenatal diagnosis	0	0
Newborn screening	5	1^
Family history	1#	0
Other states		
Genital abnormalities	1	10
Salt wasting / adrenal crisis	6	0
Prenatal diagnosis	0	0
Newborn screening	0	0
TOTAL	**13**	**16**

* all positive on newborn screening
^ no genital abnormalities, relatively mild enzyme block
\# mild enzyme block, normal neonatal screening, detected by testing at day 16 because of family history of CAH

Conclusion

The incidence of classical (neonatal) CAH in Australia was estimated at 5.9/100,000. The pilot newborn screening program in NSW/ACT suggested that, by enabling early diagnosis, screening may reduce the severe morbidity and potential mortality associated with salt-wasting adrenal crises. It also allowed comparison of the two methods and demonstrated the method used by the APSU to have a high sensitivity for case ascertainment. National newborn screening will not be introduced until cheaper technology, which is currently under development, is available.

Data analysis from this study is incomplete and a final report will be included in the 1998 annual report.

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