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THE MEDICAL HISTORY OF CONGENITAL ADRENAL HYPERPLASIA

IN THE 1950'S

We must never forget that before 1950, children with the salt losing type of CAH died. It was a lethal condition. In 1950 Cortisone Acetate (the first steroid made synthetically) was produced. At first this was given by injection 2,3 or 4 times a week to keep babies alive. It was of course experimental in the 1950's so the results of treatment then were far from perfect, usually resulting in undertreatment of the condition. This would allow excessive male hormone (androgen) production to continue leading to complications such as:

a) masculinisation of girls and disordered puberty

b) excessive growth in girls and boys

c) premature fusion of the growth plates of bones

d) short adult stature

e) poor adult fertility

IN THE 1960'S

Other steroids were synthesised - oral CORTISONE, HYDROCORTISONE and PREDNISOLONE. During this time Endocrinologists began to understand how to balance these hormone treatments more successfully and also surgical techniques for genital surgery were becoming more sophisticated.

IN THE 1970'S AND 1980'S

DEXAMETHASONE and CYPROTERONE ACETATE were produced and better laboratory measurements of steroids such as androgens, 17-OH-Progesterone were discovered. During this time therefore the careful balance between overtreatment and undertreatment was worked out so that the complications described above could be avoided. In the UK, specialist paediatric centres developed.

IN THE 1990'S

Dexamethasone has been used in pregnancies affected by a CAH girl in utero. The results are still being analysed because so few have been carried through. Watch this space!

FERTILITY

Fertility in CAH adults should be excellent but...

	MALES	FEMALES
Good CAH hormone control	Fertility Good	Fertility Good
Poor CAH hormone control	Fertility Variable	Fertility Poor

ADOLESCENCE

In many medical conditions where doctors and parents expect adolescents to take medication regularly every day, there are often phases when medication is forgotten, missed out or even rejected. Poor hormone control in CAH in adolescence may be because a young person in puberty is not always taking the treatment properly. This is sometimes difficult to detect and difficult to understand.

PUBERTY AND CAH

IN BOYS puberty starts when the testicles begin to grow, producing more male hormone (testosterone). Testosterone causes an acceleration of height growth, more muscle bulk and eventually a beard. Acne is another unwanted effect. Growth in CAH boys is usually not a problem.

IN GIRLS however growth in puberty can be a problem. In the 1950's and 1960's, excess male hormone accelerated and later stunted growth and disturbed puberty. Nowadays better CAH control enables girls to start normally in puberty (breast development average age 11 years) and have periods (average age 13 years) at an almost normal time. Nevertheless growth in puberty might not be quite as great as normal in some CAH girls.

Fertility in girls depends on good control so that ovulation occurs normally between the periods. Many endocrinologists therefore continue CAH treatment in early puberty with the natural steroid HYDROCORTISONE and then when periods are well established and growth is slowing down, will switch to other stronger synthetic steroids such as PREDNISOLONE or DEXAMETHASONE. These seem to suppress the male hormone even more and allow the ovary to ovulate successfully.

PREGNANCY

(1) Prior to conception in a family already affected by one child with CAH the risks (1:4) should be carefully discussed with a GENETICS EXPERT.

(2) The options of:

a) taking the 1:4 risk without treatment

b) treating an affected female foetus (with DEXAMETHASONE - DXM)

c) termination of an affected foetus

should be discussed carefully and sensitively before conception. Genetic tests are available to identify a particular family's genetic CAH background.

(3) Planned pregnancy:

a) inform CAH consultant/geneticist immediately

b) at 5 weeks; Dexamethasone started

c) at about 9-12 weeks; Chorionic Villus Biopsy to show sex of foetus and whether affected by CAH
- male foetus stop DXM
- female foetus continue DXM throughout pregnancy to avoid her becoming severely masculinised.

IN SUMMARY

In the last 45 years severe salt-losing CAH has become treatable, the precision of treatment both medical and surgical has improved greatly and with good, consistent expert control young people with CAH should remain very healthy, grow well, have virtually normal puberty and be fertile in adulthood. However all these good results can be made more difficult if medication is not taken regularly and this is the important message.

Notes taken at CAH Conference – High Wycombe 1997