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Congenital Adrenal Hyperplasia is one of the worst managed conditions in paediatric endocrinology. Because this is a life long condition similar comments apply to adult endocrinology. Why, when it is fairly simple to understand the condition, are patients treated inappropriately?

There is no single way of treating CAH as many of the experts disagree with each other. Different centres have different ways of achieving the same aims. The management of a child should be undertaken by a Consultant/Endocrinlogist, who is experienced in treating this condition.

COUNSELLING

Initial psychological counselling for the parents is extremely important The emotions generated in individual parents having a girl with ambiguous genitalia is catastrophic. Unfortunately, there are few psychologists who have the training and experience to undertake such work.

SURGERY

Equally important are the surgical aspects. It is vital that the Consultant who does the surgery is experienced in the management of intersex problems. Whether the surgeon is a Urologist or Gynaecologist is immaterial. This does not necessarily have to take place in a Teaching Hospital, as long as the surgeon is experienced in this type of surgery. In that context one of the largest problems at a later age is dyspareunia (painful sexual intercourse) which contributes to difficulties with sexual relationships and fertility. Certainly, satisfactory vaginal surgery during childhood is essential.

The first operation usually takes place at between six months and a year of age. At around the age of 10-11 years, a gynaecologist should then make an examination of the internal/external genitalia. Usually this will mean a light anaesthetic to have an adequate examination and occasionally, another small operation is necessary. If there is any doubt, it is much better to operate in the pre-teenage years, than just to wait and see what happens. If the vaginal orifice is inappropriate, then this may lead to enormous distress when the girl is sexually active.

BASICS

There is a steroid, cholesterol, which is metabolised within the adrenal gland by a series of steps controlled by enzymes to glucocorticoids, mineralocorticoids and sex steroids.. Cortisol is important for general well-being and particularly during episodes of severe illness. The sex steroids that are produced are predominantly oestrogen in women and testosterone in men. The abnormality in the adrenal gland in congenital adrenal hyperplasia, is an enzyme blockage involving one of the metabolic steps from cholesterol. 90% of CAH is due to 21-hydroxylase deficiency. This interferes with the production of cortisol, and usually also mineralocorticoids. This leads to an excess of metabolites which are redirected to the production of excessive sex steroids. The latter results in either the virilisation in a girl or precocious pubertal development in a boy.

DIAGNOSIS / SALT LOSERS

Making the diagnosis is extremely important. In a salt losing baby, there will usually be a metabolic crisis at between 6-10 days of life. The baby becomes dehydrated and severely ill. The appropriate investigations will then reveal the diagnosis. In a girl, the increased sex steroid secretion in intrauterine life usually leads to virilisation and this should be identified at birth.

DIAGNOSIS / NON-SALT LOSERS

Girls with non-salt losing CAH can usually be identified by ambiguous genitalia (enlargement of the clitoris and fusion of the folds over the vaginal opening). In a boy, an excess of male hormones are not usually identifiable at birth and in a boy with non-salt losing CAH , he may not present until the middle childhood years with precocious puberty. The child will grow rapidly because of increased male hormones and will enter precocious puberty, but not a normal puberty because the hormones are secreted from the adrenal glands and not from the testes. The testes are small, but the penis is usually large and they may also have pubic hair development. The problems of making the diagnosis in this older age group are usually twofold:

1) Short adult stature is usually a problem because the increased male hormone secretion has continued for many years. The age of the bones will have advanced very rapidly with premature fusion of the growing plates at the ends of the bone. It is extremely difficult to do anything about this at a late stage, whereas the final height of children diagnosed with CAH in the first few weeks of life should, theoretically, be normal, although in practice they are slightly shorter than they would have been but within the normal height range.

2) When hydrocortisone treatment is commenced in boys with non-salt losing CAH, instead of pseudopuberty, when the male hormones come from the adrenal gland, they often change their sexual development into true precocious puberty with the male hormones coming from the testes. This problem tends to have an even further adverse effect on final height.

TREATMENT

Theoretically, treatment is simple with the replacement of both hydrocortisone and, if necessary, mineralocorticoids. Unfortunately, receiving tablets from a bottle is very different from a person controlling their hormone secretion on a minute-to-minute basis. Hydrocortisone will be necessary to replace what the adrenal gland cannot produce and this, in turn, suppresses the pituitary drive and reduces the sex steroid secretion from the adrenal gland. Hydrocortisone has a short half-life and will need to be given usually three times per day. There is now a considerable amount of evidence, mainly in adults, but also in children, that optimum hydrocortisone replacement requires at least three times daily administration. Obtaining an optimum control may be extremely important for the prevention of longer-term side-effects, such as obesity, hypertension (high blood pressure) and osteoporosis (brittle bones). Other glucocorticoids, such as cortisone acetate or prednisolone, may be used and your specialist would advise on the indications for this.

As well as hydrocortisone administration (a glucocorticoid), a mineralocorticoid will be needed if the patient is a salt loser. This is usually given as fludrocortisone on a once daily administration. It is important to achieve the correct dosage of fludrocortisone and this may well need an occasional blood test, as well as monitoring blood pressure. It is important to achieve the correct balance between glucocorticoid and mineralocorticoid treatment as both of these hormones do have a crossover effect. Once appropriate hormone replacement has been achieved, the stimulation of the adrenal gland to produce abnormal sex steroids will decrease and the virilisation suppressed. Although surgery will be required to correct virilisation that has occurred in a female, controlling the secretion of sex steroids into the normal range will prevent further virilisation occurring in the future.

If a child is growing and developing normally, it is probable that the hormone replacement is correct. Some endocrinologists will monitor the biochemical control by regular blood or saliva tests of hormones. However, careful monitoring of either growth or hormones achieves the same ends, both to produce the correct amount of glucocorticoid hormones and to suppress abnormal sex hormone secretion. If under-treatmentment occurs (the dose of hydrocortisone is too low), then there will be an excess of sex steroid secretion and the child will grow faster than normal, as well as advancing their bone age. An excess of hydrocortisone administration will suppress growth. However, if a child is salt losing, there will be no way of avoiding the occasional blood test in order to monitor mineralocorticoid therapy. Providing the child is progressing satisfactorily, then it may not be necessary to have any other blood tests. However, if the patient's control is inadequate, then it may be necessary to obtain a series of blood tests throughout the day to measure the exact hormone concentrations in the blood. The result of this would then help the specialist adjust the drug dosages.

ADRENALECTOMY

This is a surgical operation to remove both adrenal glands. Although this cures the problem of congenital adrenal hyperplasia (the problem no longer exists), there is an accompanying risk of being completely cortisol deficient. Most patients with CAH do produce some cortisol, but if the adrenal glands are removed, no cortisol is produced. In this case, there is a high risk of severe illness with an intercurrent infection and an emergency cortisol regimen will be extremely important. This subject will be addressed by Dr Donaldson in his later talk. In very severe cases of girls with CAH where concern is expressed over the effect of high male hormone levels on the development of the ovary and compromised fertility, adrenalectomy may be considered.

ADULTHOOD

In men who stop taking glucocorticoid treatment in adult life, there are often few problems, other than the management of acute illness and relative infertility. However, if they revert back to regular medication, fertility should be restored.

With women, the problem of gonadal function and fertility is more difficult. The ovaries are very sensitive to the amount of male hormones that are produced by the adrenal gland and, if there are too high levels, then the ovaries may become damaged and have an appearance which is described as polycystic ovaries. With such ovaries, there is often a compromise in their function and fertility may be more difficult. Once the ovaries have become damaged by the exposure to high male hormone levels, then a return to normal hormone levels may not restore the ovaries' function. The management of infertility in such women will require specialist advice from a reproductive endocrinologist.

The latest studies from the Cardiff group have suggested that with good control of CAH with appropriate early vaginal surgery, the chances of fertility are good.

Notes taken at CAH Conference – High Wycombe 1997