



CAH Support Group. Registered Charity

Congenital Adrenal Hyperplasia (CAH)

An information leaflet for
patients and families

The CAH Support Group is a registered charity – No. 1178951

What is CAH?

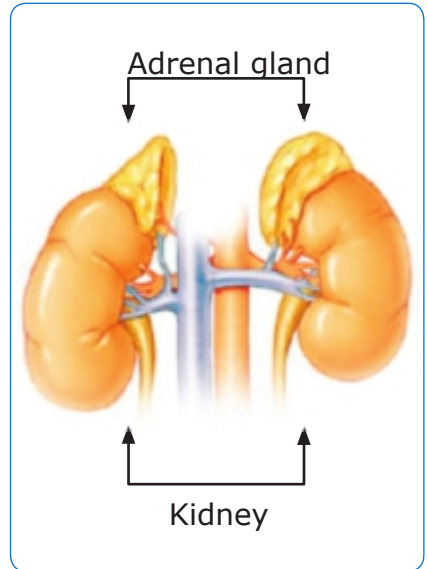
CAH is a disorder causing impaired hormone production from the adrenal glands. Hormones are chemical messengers released into the bloodstream that act on other cells. The faulty adrenal hormone production leads to different signs and symptoms depending on the severity of the fault.

What does CAH mean?

Congenital – this means the condition is present at the time of birth and the symptoms and features of the condition are usually apparent during the first few weeks of life.

Adrenal – two small glands sitting above each kidney which produce hormones.

Hyperplasia – this means the adrenal gland is larger than usual because it is working harder to regulate hormone production.



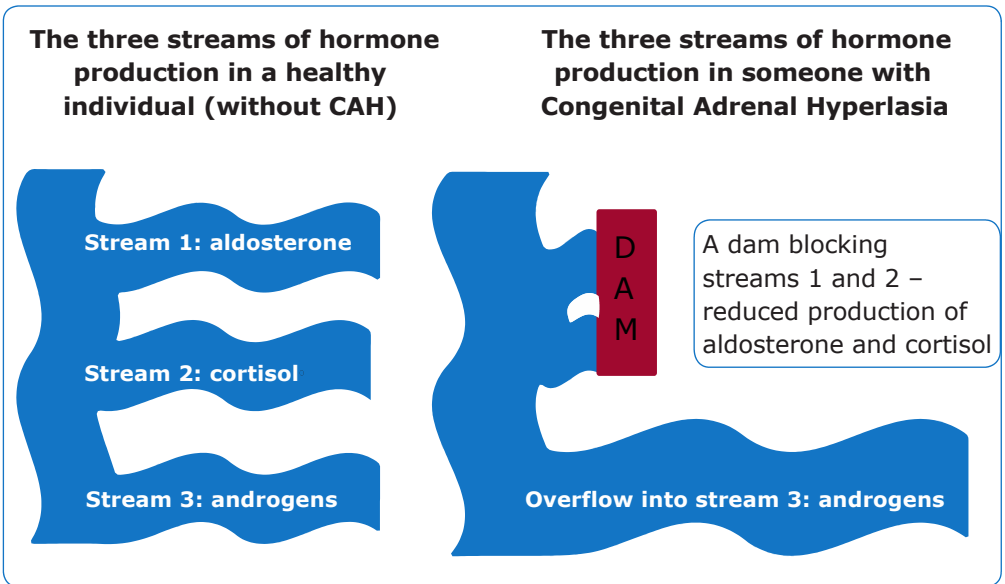
What hormones does the adrenal gland produce?

The outer layers of the adrenal gland produces 3 different hormones. (The inner part produces adrenalin, but this is not affected in CAH)

- 1) Cortisol – this hormone is produced at times of physical stress, for example during an infection or inflammation when your body is trying to protect you from illness.
- 2) Aldosterone – this hormone helps regulate salt levels in the body. Low levels cause salt and water to be lost in the urine leading to dehydration.
- 3) Androgens – these are sex related hormones which regulate body growth and pubertal development, they are usually produced in males with much lower levels in females.

Why are Cortisol and Aldosterone hormones not produced in CAH?

These hormones are made by a series of chemical reactions controlled by enzymes (proteins which speed up reactions). We have a series of genes which makes enzymes to allow these chemical reactions to take place, the most common gene affected in CAH is the 21 hydroxylase gene. If a gene is altered these enzymes are not produced, there is a block to the series of chemical reactions. This is like blocking a stream with a dam. Downstream of the dam no cortisol or aldosterone are produced. However this allows the hormones produced at the beginning of the series of reactions to build up in the same way a dam causes a lake to form behind it. With time the lake will overflow and other streams become larger. This is why one of the other hormones (testosterone a form of androgen) is produced at higher levels.



CAH signs and symptoms

CAH can present severely, shortly after birth, with severe vomiting, failure to thrive and dehydration. This is a life-threatening condition if untreated.

It can also present in a milder form, in childhood with early puberty or milder still, as an adult with fertility problems.

In the severe form, the excess of androgens in the womb throughout pregnancy causes virilization (development of masculine features) in girls meaning they can be born with ambiguous genitalia (more male appearance). Only the outside appearance is affected and internally the vagina, womb and ovaries form normally.

Congenital Adrenal Hyperplasia (CAH) is a genetic condition, which has a recessive pattern of inheritance.

So firstly, what are genes?

Genes are the unique set of instructions in every cell, which make each of us an individual. There are many thousands of genes each carrying a different instruction. If a gene is altered, it can cause a genetic condition or disease. This gene alteration is known as a mutation.

We have two copies of each gene. One copy is inherited from our mother and one copy from our father. When we have children, we pass on only one copy of each of our genes.

What does recessive inheritance mean?

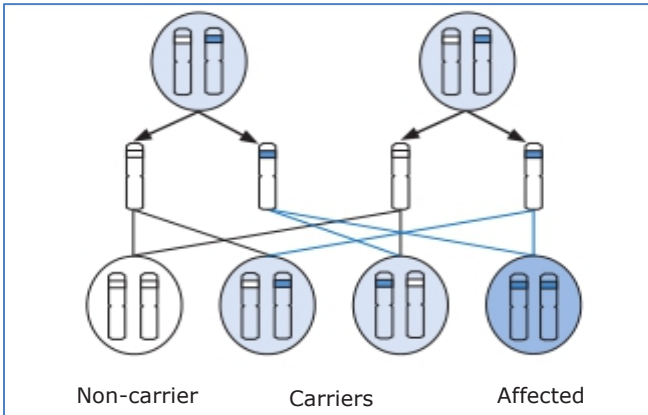
Some conditions are inherited in a way that is called autosomal recessive inheritance. Only individuals who have two altered copies of a gene are affected with the condition. Individuals who have one altered copy of a gene are usually completely healthy. They are known as carriers because they carry one altered copy of a gene and one normal copy. Their normal copy of the gene keeps them healthy and compensates for the altered copy.

Having children

If both parents carry the same altered recessive gene then there are four possible outcomes for each pregnancy they have regardless of the sex of the child they have.

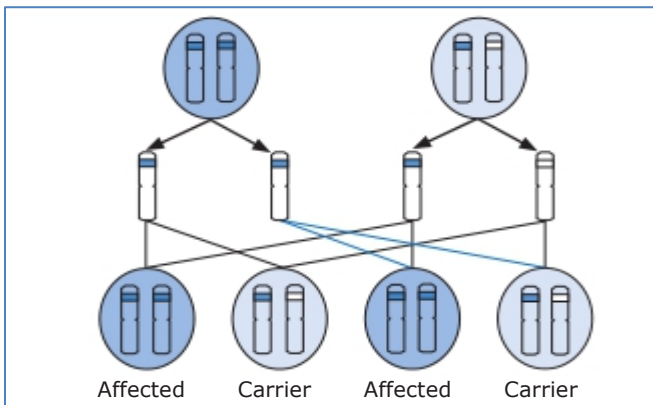
Recessive inheritance

If you and your partner are carriers your child will have:



- A 1 in 4 (25%) chance of inheriting the altered gene from both parents and being [affected](#)
- A 1 in 2 (50%) chance of inheriting the altered gene from one parent and therefore being [a healthy carrier](#)
- A 1 in 4 chance (25%) of inheriting the normal gene from both parents and being [neither a carrier nor affected](#)

If you are affected and your partner is a carrier, your child will either have CAH or be an unaffected carrier (50/50 either way).



What is the risk that my partner is a carrier?

In the UK about 1 in 50 people carry a CAH gene mutation. This would be the risk of your partner carrying an alteration unless they are related to you, or have a history of CAH in their own family, in which case the risk might be greater.

Can we check my partner's carrier risk?

Yes, you can check a partner's carrier risk with a blood test known as short synacthen test, and by looking at the CAH gene. A Synacthen test will test the adrenal glands function following an injection to stimulate the gland. Together these will tell us if your partner is a carrier or has a very low risk of being a carrier. If they do not appear to be a carrier the risk will be approximately 1 in 500. If we prove your partner is a carrier the risk will be 1 in 2 for any pregnancy if you have CAH or 1 in 4 if you are a carrier.

If it is not possible to check your partner's carrier risk, the risk for your children having CAH without any further tests would be 1 in 50 X 1 in 2 (i.e. chance of your partner being a carrier times by the risk of passing on the altered copy of the gene). This means the risk would be 1/100. This risk would be 1 in 200 if you are a carrier and not affected.

My partner is a carrier, what happens next?

If your partner is a carrier and you are a carrier or affected then there are a number of options you may wish to pursue in the pregnancy.

During pregnancy

Can we tell if my baby is a boy or girl?

Yes we can take a blood sample from mothers between 7-9 weeks and detect DNA from the baby in mothers' circulation (known as free fetal DNA). Using this DNA we can identify genetic material that is only present in males. If we prove the baby is a boy we do not need to give treatment to prevent virilisation.

Can CAH be diagnosed during pregnancy?

Yes, if we show that your partner is a carrier of CAH gene alteration then we could offer to do a test known as Chorionic Villus Sampling (CVS) where a small piece of placenta is removed via a needle passed through the tummy wall. This is usually taken around 11 weeks. The risk of CVS is an increased risk of miscarriage, 1% of pregnancies would miscarry because of CVS. It is important to recognise that this is in addition to the 2% risk of any pregnancy miscarrying at around 11-12 weeks because of natural causes independent to the rest.

See Flow diagram for couple requesting Dexamethasone treatment in a pregnancy.

Can it be treated during pregnancy?

Yes, but these would only be necessary if we prove your partner is a carrier and the baby is an affected girl. You also have an option to not have the treatment if you decide not to have any intervention.

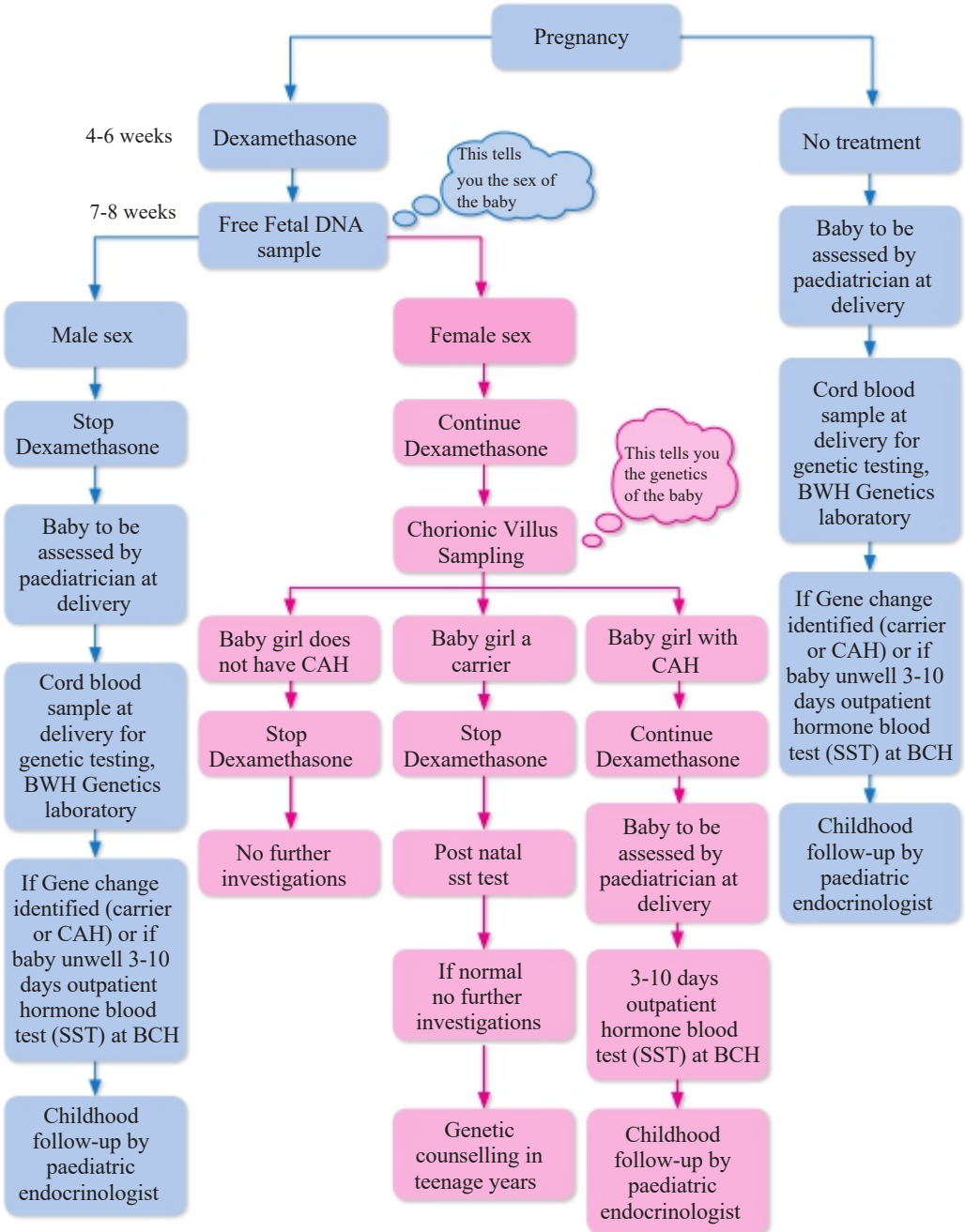
The treatment

There are studies which show that providing mothers with hormone treatment from around 6 weeks will reduce the risk of virilisation in girls (baby girls being born with ambiguous genitalia). It will not necessarily completely remove the risk of virilisation and further interventions, such as surgery, may still be necessary in childhood or adulthood. If you are already on hormone replacement for CAH it may be more difficult to predict whether we can achieve the same benefit and still maintain optimal treatment for your CAH. You should discuss the option of changing your steroid treatment with your endocrinologist before trying to conceive, especially if stopping the oral contraceptive pill.

How do I arrange treatment?

Start as early as possible, before the 7th week of pregnancy. In some cases your doctors might suggest changing you to dexamethasone if you are trying to become pregnant. Therefore it is very important to let either ourselves or the obstetric team know as soon as you are pregnant.

Flow diagram for couple requesting Dexamethasone treatment in a pregnancy



What are the risks to mothers from taking dexamethasone?

This is controversial for a number of reasons. If both parents are carriers, only 1 in 8 pregnancies need dexamethasone i.e. only an affected female baby. Therefore 7 out of 8 pregnancies would not need dexamethasone, including all male pregnancies, as there is no need to suppress testosterone production in males. The risk would be double this i.e. 1 in 4 if one partner has CAH themselves. Dexamethasone could increase a mother's risk of high blood pressure, diabetes and weight gain during pregnancy. Treatment needs to be carefully monitored by a hormone specialist (endocrinologist) to keep risk factors to a minimum. We believe that these effects can be reversed by modifying maintenance treatment in most cases.

What are the risks to the baby from dexamethasone?

This is controversial as only 1 in 8 pregnancies of carrier couples could benefit from dexamethasone. Again, 1 in 4 would benefit if one person has CAH themselves. There are theoretical reasons to believe that there would be some increased risk in later life of complications such as diabetes, hypertension and potentially an effect on the developing brain. However, these potential disadvantages need to be weighed against the potential advantages of reducing virilisation and exposure to androgens in the womb.

Why do only girls need dexamethasone?

The commonest form of CAH results in failure of the adrenal to produce cortisol and aldosterone. It does not however stop the production of androgens, which relies on some slightly different chemical reactions in the adrenal gland. The body senses that it is short of cortisol and aldosterone and tries to make the adrenal gland work harder. The effect of this is to drive the adrenal gland to produce more androgens. The androgens may result in a more male appearance to external genitals in females (for example an enlarged clitoris and partial closure of the vaginal opening). Since boys are normally masculinised by the testosterone they show no differences in their genital development.

After pregnancy

What happens after the baby is born?

If the diagnosis of CAH has definitely been excluded no further action is necessary.

If a baby is known to be at a 1 in 2 (or 1 in 4) risk of CAH, further testing will depend on the available information on genetic changes. Gene tracking studies (known as linkage studies) provide the most rapid result (less than 5 days) from a cord blood sample. To enable this rapid test, parental blood will need to be collected and examined several weeks before delivery. This test can also detect non paternity as a coincidental finding.

Babies known to have CAH should be referred urgently to a paediatric endocrinologist. Symptoms of CAH are not common in the first 5 days following birth but if your child is vomiting, not taking feeds or drowsy you should seek urgent medical advice.

If one parent is a known carrier but the carrier status of the second parent is uncertain, the same linkage studies should be done to confirm or exclude the identified alteration. All babies who are known to be at least a carrier should be referred to a paediatric endocrinologist for a hormone test, known as a short synacthen test. This tests the adrenal glands function following an injection to stimulate the gland.

Children with CAH will need life-long hormone treatment.

At the end of pregnancy Mothers will need endocrinological advice concerning their change back to other steroids for individuals with CAH or discontinuation for carriers. Dexamethasone will not be stopped suddenly.

Will my daughter need surgery?

Whether surgery is required and the nature of that surgery depends on the degree of virilisation. This will be discussed by surgeons after birth. Some surgery may be recommended within the first year of life.

Frequently asked questions

Can CAH occur again in the family?

Yes. This is an inherited disorder and is due to genes which we inherit from our parents.

Will my daughter be 'a normal female' in other respects?

Yes, the extra androgen affects only the external female genitalia (the clitoris, external labia and opening of the vagina), this means the internal parts (the remaining vagina, womb and ovaries) form normally and females with CAH can produce eggs and are usually able to have children normally.

Are there different types of CAH?

Yes, there are different grades of severity of CAH depending on the impairment of production of cortisol and aldosterone.

1. Classic CAH (with virilisation in girls)

- **Salt wasting:** a severe deficiency in the enzyme block meaning both cortisol and aldosterone are reduced and androgens are increased. Lifelong replacement treatment of the stress and salt hormones will be needed. Dose should be doubled or trebled during illness, extreme stress or surgery. A steroid card should always be carried.
- **Simple virilising:** a moderate deficiency in the enzyme block in which cortisol production is reduced but aldosterone deficiency is not as severe. There is still an excess of sex hormones. Children may present with very early puberty or an early growth spurt (but usually end up short as their bones finish growing too soon) Stress hormone (+/- salt hormone) replacement will be needed. A steroid card should always be carried.

You should wear or carry medical alert identification so that any health professional treating you in an emergency will know you have CAH.

2. Non classic CAH (no virilisation)

Mild deficiency in the enzyme block. Minor or little stress/salt hormone disturbance. Hormone replacement may not be needed. Some patients may have very little symptoms, particularly males. However girls may present in early adulthood with irregular periods,

excess body hair, acne and infertility.

All of the types of CAH above are deficiencies of the enzyme 21 hydroxylase, which account for over 90% of people with CAH. The next most common deficiency is of the enzyme 11-beta hydroxylase. Treatment of this type of CAH is more complicated because high blood pressure can be severe if treatment inadequate. The balance of treatment in 11-beta hydroxylase deficiency is very difficult and an experienced specialist is essential. Deficiencies of other enzymes are exceedingly rare.

Is it ever 'too late' to start antenatal treatment?

Yes, after 8 weeks of pregnancy it is too late to start treatment because the body's development of the external genitalia will have already begun and dexamethasone will be much less effective in reducing virilisation in affected females.

What if I require further information about CAH?

The CAH Support Group is happy to provide further leaflets on CAH for information and educational purposes but for specific questions regarding care, please contact your own endocrine consultant.

Website: www.livingwithcah.com

E-mail: sue@cah.org.uk

This leaflet was written and produced for advice purposes only by:

**The Clinical Genetics Unit,
Birmingham Women's NHS Foundation Trust,
Edgbaston, Birmingham, B15 2TG**

Authors: Tamsin Ellis, Dr Trevor Cole, Susan Stewart

and has been reproduced by the CAH Support Group with their kind permission.

Birmingham Women's NHS Foundation Trust is not responsible for any third party information and does not endorse any product, view or process or opinion from any such sources. General information and specific enquiries and actions should be discussed with your own doctors.