



Adrenoleukodystrophy

Adrenoleukodystrophy (ALD) is a rare inherited disorder affecting the adrenal glands and 'white matter' of the brain, causing a progressive loss of physical and mental skills.

What is the cause?

ALD is one of a group of disorders caused by a defect of peroxisomes which are essential for the breakdown of fatty acids in cells. In ALD the gene responsible for activating the normal chemical processes is faulty, which results in damaging effects on the adrenal glands, the brain cells and myelin (the substance around nerve fibres that is essential for transmission of messages between brain cells and the rest of the body).

How is it diagnosed?

When high levels of Very Long Chain Fatty Acids (VLCFAs) are found on a blood test, additional tests on blood may be done to confirm the ABCD1 gene mutation.

Does it have any alternative name?

The condition used to be called Addison-Schilder's Disease, after the doctor who first recognised it in 1923.

Is it inherited?

ALD is an X-linked recessive disorder, which means that only boys are affected and the mother may be a carrier of the disease. Human beings have about 30,000 to 40,000 different genes, each of which has a function in making an individual person. The genes are arranged in pairs (one of the pair from each parent) on 23 chromosomes; inevitably some of these genes are faulty. The chromosome

that determines the gender of the child will either contain 'XX' (female) or 'XY' (male).

The faulty gene in ALD is on the 'X' chromosome; as females have two 'X' chromosomes, the fault can be completely or partially overcome by the other healthy 'X' in the pair but in males, who only have one 'X', there is not another 'X' to provide a functioning gene. Unless there have been other affected boys in the family there may be no way of knowing who is a carrier, as most carriers remain healthy; a proportion of female carriers may develop much milder neurological symptoms in adulthood.

Each pregnancy carries a:

25 per cent chance of the child being an **unaffected non-carrier** girl

25 per cent chance of the child being an **unaffected carrier** girl

25 per cent chance of the child being an **unaffected** boy

25 per cent chance of the child being an **affected** boy.

Is prenatal testing available?

Prenatal testing is possible by chorionic villus sampling early in pregnancy.

How common is it?

It affects approximately 1 in every 20,000 males.

How does the disease progress?

The child will probably have been well for at least the first few years of life. Between the ages



of four years and early teens hyperactivity may develop with disruptive behaviour, and memory and learning skills may cause concern. Sometimes a minor infection can make him very ill due to the problem with the adrenal glands. Over the course of several months or a few years he will become increasingly unsteady, lose skills and, eventually, become totally dependent. Vision will deteriorate and epilepsy will develop. The condition is not a painful one and he will be unaware of what is happening in the later stages of the disease.

The brain's control of the muscles responsible for chewing, coughing and swallowing and so on eventually becomes affected so that assistance with a feeding tube may be needed. Chestiness will develop and may lead to infections and increasing physical weakness. Eventually the combination of the diseased brain and physical weakness becomes too great to sustain life and death will be inevitable. Parents and carers will be aware of the young person's increasing frailty, and palliative care treatments can help to reduce pain and suffering in those dying from the disease.

The age of onset of problems, the rate of the disease progression, and the life expectancy can vary very considerably even between affected brothers but, sadly, although some boys or young men may live into mid-late teens and beyond, many are likely to be in a state of unresponsiveness within a few years, or even months, of the onset of symptoms. Those who onset of symptoms occurs between the ages of three and ten years tend to have a more rapid decline than those whose onset is later.

Is there any treatment?

Although much is known about the disease, no effective treatment is yet available to reverse the damaging process. The adrenal insufficiency can be treated by giving replacement hormones (which are essential for life) but they do not affect the underlying condition.

Dietary changes (including Lorenzo's oil) correct

the VLCFA levels and probably slow down (but, sadly, not halt) the progression of symptoms if used from before or soon after symptoms develop. Every effort is made to treat the symptoms as they occur, using drugs or therapy to treat infections and epilepsy, relax muscles, and ensure a comfortable quality of life. Specialist schooling can provide a stimulating environment and routine, which is important for the child and allows his family to have some time for themselves. Though not scientifically proven, many boys gain some symptomatic relief from some of the complementary therapies such as cranial osteopathy or massage in the later stages.

In boys who are known to have the condition but in whom symptoms have not yet appeared, experimental treatment may be offered in the form of stem cell transplant. The results of this are, as yet, uncertain and the process itself is a very high-risk procedure. If performed in boys whose demyelination has progressed (as seen on a brain scan), it can increase the rate of decline.

Is any research being done?

Much research is being done into ALD and related disorders. In the future gene therapy is likely to provide the best hope of treatment or cure but sadly this is unlikely to be soon enough to help boys who are already symptomatic. Your neurologist and support group can keep you informed of research progress.

Is there a support group?

The **ALD Life charity** offers support and advice for anyone affected by ALD. Call their advice line on 020 7701 4833 Monday to Friday from 9am to Friday or visit their website at www.aldlife.org

The umbrella organisation **Contact a Family** may be able to put you in touch with another family affected by adrenoleukodystrophy. Call their helpline on 0808 808 3555 or visit their website at www.cafamily.org.uk