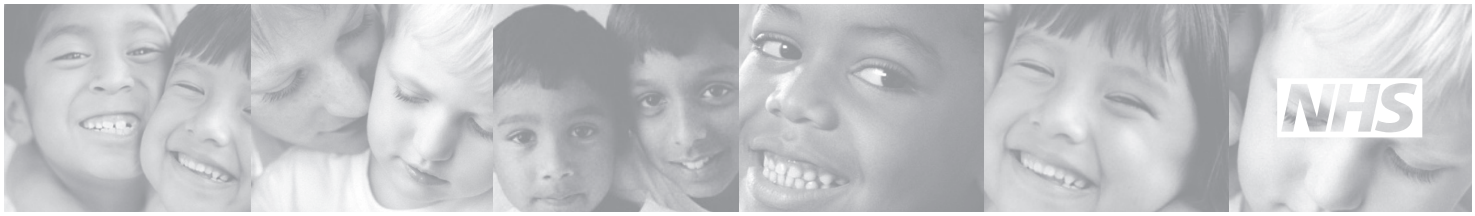

Great Ormond Street Hospital for Children NHS Foundation Trust: Information for Families

Metachromatic leukodystrophy (late infantile form)

Metachromatic leukodystrophy is a rare inherited disorder affecting mainly the 'white matter' of the brain, causing a progressive loss of physical and, later, mental skills.

What is the cause?

Metachromatic leukodystrophy (MLD) is one of a group of leukodystrophies caused by an abnormal build-up of substances (metachromatic material called sulphatides) in the nerve cells, particularly in the white matter of the brain, which take the place of myelin, the insulating material which is essential for normal transmission of messages between nerves. These substances are normally broken down and removed from the body by an enzyme (arylsulphatase A) but in MLD, the gene responsible for producing the enzyme is faulty so the normal process cannot occur. As the brain is the control centre of the whole body, blockages in the messages to other parts of the body will prevent those parts working efficiently, even though the parts themselves seem quite healthy.

How is it diagnosed?

An MRI brain scan may suggest the diagnosis which can be confirmed on a urine test that shows the metachromatic material (sulphatides) and on a blood test that shows an absence of the enzyme (arylsulphatase A).

Does it have any alternative name?

MLD is sometimes known by its medical description: Sulphatide Lipidosis or Sulphatidosis and the late infantile form may also be called Greenfield's Disease.

Is it inherited?

MLD is an autosomal recessive disorder; this means that both parents are carriers 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; a normal gene can overcome a faulty one, but if both genes in the pair are faulty, the genetic instructions cannot work. Most people carry different faulty genes but in MLD (and other recessive conditions) parents, though healthy themselves, carry the same faulty genes, and risk passing them on to their children. Each pregnancy carries

- a **25 per cent** chance of the child being **affected**
- a **75 per cent** chance of the child **not** being **affected**.

Is prenatal testing available?

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

How common is it?

It is estimated that the incidence in the UK is approximately 1:40,000.

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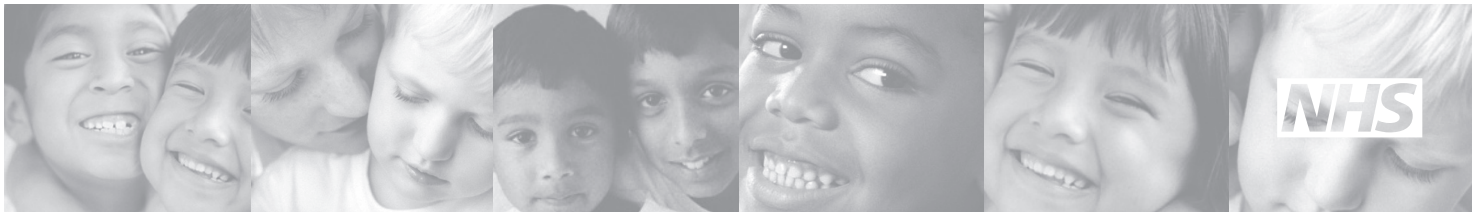

How does the disease progress?

In the late infantile form of MLD the infant's development starts to slow down between the ages of six months and two years. He or she may become rather unsettled and appear physically floppy (hypotonic). Over the following months, motor skills will not progress as expected and, indeed, skills that have been learnt will be lost.

Over the course of the next few years the child becomes totally dependent again, usually developing stiffness of the legs (spasticity) and eventually losing all understanding or real awareness of his or her surroundings. Vision will be very reduced and sometimes epileptic seizures may develop. The condition is not a painful one and the child 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 eventually becomes affected so that assistance with a feeding tube may be needed, and 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 usually occurs between the ages of five to eight years. Parents and carers will be aware of the child's increasing frailty, and death is usually relatively peaceful and expected when the time comes.

Is there any treatment?

Although there is no treatment yet available that can stop the disease, every effort is made to treat the symptoms as they occur. Drugs can be given to relieve muscle spasms, treat infections and try to control seizures (should they occur); pain relief and sedative drugs can be given if required, and feeding can be assisted. Physiotherapists and others can advise parents on positioning, seating and exercising the limbs to maintain comfort. Specialist schooling will be required and it is important for the child to have this stimulating environment and social contact and, indeed, for the parents to have some time for themselves and other family members and friends. Though not scientifically proven, many children gain some symptomatic relief from some of the complementary therapies such as cranial osteopathy and massage.

In affected siblings who have as yet shown few or no signs of problems and whose MRI brain scans do not show demyelination experimental treatment may be offered in the form of bone marrow, umbilical cord blood or stem cell transplantation. The results of these are very uncertain and the processes themselves are very high risk procedures.

Is any research being done?

Research is progressing in various areas concerning leukodystrophies and other progressive neurological disorders, particularly 'mapping' genes and understanding which gene is responsible for what process with a view to gene therapy in the future. Work is also being done into how the missing enzyme could be replaced in the brain cells. Sadly, any treatment that could reverse the disease process is unlikely to be discovered quickly enough to help children who already have symptoms. Your neurologist and information available from the support group can keep you informed of research progress.

Is there a support group?

The National Information Centre for Metabolic Diseases (previously known as Children Living with Inherited Metabolic Diseases – CLIMB) can provide written information, telephone advice, support and contact (if wanted) with other families. Call their helpline on 0800 652 3181 or visit their website at www.climb.org.uk.

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