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## Leukodystrophy

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### Summary

- Leukodystrophy refers to a group of genetic conditions that affect the white matter of the brain.
  - Leukodystrophy causes loss of normal brain functions.
  - Symptoms of leukodystrophy can vary.
  - Most leukodystrophies do not have a cure, but therapies are being developed that can help stop the condition from getting worse.
  - Supportive treatment can help manage some of the symptoms.
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Leukodystrophy refers to a group of conditions that mainly affect the white matter of the brain and the spinal cord. The white matter is the wiring network of the brain. It links the brain to the spinal cord and rest of the body.

Leukodystrophies affect myelin production or breakdown. Myelin is the substance that surrounds and insulates the nerve fibres in the nervous system. Damage to myelin slows down or blocks messages between the brain and the rest of the body.

Most leukodystrophies are progressive conditions. This means they can get worse over time. Leukodystrophies cause loss of normal brain functions. Life expectancy depends on the type of leukodystrophy you have and whether specific treatments are available to stop its progression.

### Symptoms of leukodystrophy

The symptoms of leukodystrophy can vary, depending on:

- how quickly damage to the white matter occurs
- which parts of the brain (or spinal cord) are affected
- how much the peripheral nerves are affected.

The white matter has a large role in motor function (movement), so damage usually leads to problems in this area.

The onset of symptoms varies. Symptoms can include subtle or gradual changes to:

- muscle tone
- body movements
- walking style
- speech
- ability to chew and swallow food
- eye sight
- hearing
- mental ability
- behaviour.

### Types of leukodystrophy

Some of the different types of leukodystrophy include:

- **adrenoleukodystrophy (ALD)** – this is a common leukodystrophy that usually only affects males. This is because the gene change is on the X chromosome.

The childhood form (childhood cerebral ALD) usually begins before 10 years of age and may progress rapidly. The adrenal glands may also be affected.

The adult form (adrenomyeloneuropathy) affects the spinal cord and the adrenal glands. Female usually have much milder symptoms because they have two X chromosomes.

In some people with the same genetic change, only the adrenal gland is affected (leading to Addison's disease)

- **metachromatic leukodystrophy (MLD)** – a common leukodystrophy that has a range of subtypes relating to the age when symptoms appear. For example, in the infantile form (late infantile MLD) a loss of motor (movement) and verbal skills may be the first signs. Symptoms typically become progressively worse. In addition to the brain, the peripheral nerves in the arms and legs are usually affected
- **Canavan's disease (spongy degeneration)** – this form of leukodystrophy affects myelin growth. It is most commonly seen in babies aged around three to five months.

Canavan's disease is typically characterised by poor head control, decreased muscle tone, regression and a markedly enlarged head. Eventually, the decreased muscle tone changes to stiffness.

Life expectancy is limited for babies with neonatal Canavan's disease. There is also a less-common mild form of Canavan's disease

- **Krabbe disease (globoid leukodystrophy)** – this affects the myelin of the central and peripheral nervous systems. About 90 per cent of people affected are babies, and symptoms usually show up before they are six months old. There is also a rare adult form of Krabbe disease
- **mitochondrial diseases** – this is a broad group of conditions due to mitochondria (the energy producers in our cells) not producing enough energy. Many of these conditions can also affect the white matter
- **hypomyelinating leukodystrophies** – are characterised by abnormal myelin production. This usually begins in childhood and causes problems with muscle tone, movement and eye movement.

## Causes of leukodystrophy

Genes come in paired sets, with one set inherited from each parent. The leukodystrophies are inherited in one of three ways:

- **X-linked inheritance** – the affected gene is carried on the X chromosome, a chromosome which is involved in determining the baby's sex. Males usually have an X and a Y chromosome and females usually have two X chromosomes. Because males only have a single copy of the genes on the X chromosome, if there is an altered gene, they do not have a second copy of the gene to compensate. Males and females are therefore affected differently
- **autosomal recessive inheritance** – the child can only inherit the condition if both parents are carriers of the genetic change. A carrier for an autosomal recessive condition has inherited one copy of the altered gene and normally shows little to no symptoms. The condition only becomes apparent when an individual inherits two copies of the altered gene. Boys and girls are equally affected. The parents won't have any symptoms, but each of their children will have a one in four chance of developing leukodystrophy and a one in two chance of being a carrier themselves
- **autosomal dominant inheritance** – one copy of the gene change is enough to cause the condition. Males and females are equally affected. The gene change may be inherited from a parent or may have occurred randomly in the affected individual.

Not every disease that affects white matter is a leukodystrophy. The white matter can be affected as a result of many genetic and non-genetic conditions. Non-genetic causes of white matter disease include ischaemia, infection and multiple sclerosis.

## Diagnosis of leukodystrophy

The diagnosis of a specific leukodystrophy is often not easy and may involve the input of a number of specialists, including neurologists, geneticists and metabolic physicians. In around one-third of cases, a named diagnosis may not be possible.

Depending on the type of leukodystrophy, diagnostic methods can include:

- physical examination
- blood tests
- urine tests
- MRI scans
- nerve conduction tests
- neurocognitive tests
- genetic tests.

### **Treatment for leukodystrophy**

Currently, most leukodystrophies cannot be cured. Stem cell therapy and bone marrow transplantation have been tried in some cases. However, the benefits depend on the timing, age of onset and severity of symptoms. When successful, these therapies may stop the disease from getting worse, but rarely reverse existing damage.

Therapies such as gene therapy and enzyme replacement therapy are under investigation. Improved understanding of leukodystrophies is leading to increased research to develop specific treatments.

Currently, treatment is mainly supportive and may include:

- physical therapy
- occupational therapy
- psychological counselling
- family counselling (including genetic counselling)
- medications (for example, medications for seizures and muscle spasticity).

### **Genetic counselling for leukodystrophy**

If your child or another family member has been diagnosed with leukodystrophy, or if leukodystrophy runs in your family, it can be helpful to speak to a genetic counsellor.

Genetic counsellors are health professionals qualified in both counselling and genetics. As well as providing emotional support, they can help you to understand a condition and what causes it, how it is inherited, and what a diagnosis means for your health, lifestyle, and plans for the future. Genetic counsellors are trained provide information and support that is sensitive to your family circumstances, culture and beliefs.

If a leukodystrophy runs in your family, a genetic counsellor can explain what genetic testing options are available to you and other family members. You may choose to visit a genetic counsellor if you are planning a family, to find out your risk of passing the condition on to your child, or to arrange for prenatal tests.

**Victorian Clinical Genetics Services (VCGS)** provides genetic consultation, counselling, testing and diagnostic services for children, adults, families, and prospective parents.

The **Genetic Support Network of Victoria (GSNV)** is connected with a wide range of support groups throughout Victoria and Australia and can connect you with other individuals and families affected by leukodystrophy.

### **Where to get help**

- Your **GP (doctor)**
- **Leukodystrophy Australia** Tel. **1800 141 400**
- **Victorian Clinical Genetics Services (VCGS)** Tel. **1300 118 247**
- **Genetic Support Network of Victoria (GSNV)** Tel. **(03) 8341 6315**

**This page has been produced in consultation with and approved by:**

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