Leukodystrophies associated with Mitochondrial disease

Most cells of the human body have a nucleus, which contains the hereditary information known as the nuclear DNA (nDNA). The nucleus is separated from other components of the cell, and it controls vital functions of the cell such as replication and growth.

Mitochondria are cellular structures that produce most of the energy required for cellular function. There are multiple mitochondria scattered inside the cell. They each contain a small amount of their own hereditary material which is called the mitochondrial DNA (mtDNA). The mtDNA governs a small number of mitochondrial functions and the majority of functions are governed by the nuclear genetic material.

Mitochondrial disease:

mtDNA and specific nDNA genes code for proteins that play a role in the 'mitochondrial energy chain'; a process by which cellular energy requirements are met.

Mitochondrial diseases result from a reduced or absence amount of one of the proteins needed for mitochondrial function, caused by change in a gene encoding that protein. There are hundreds of different types of mitochondrial disease. Most of the implicated genes are in the nuclear DNA.

When the cause is a mtDNA mutation, there is usually a mix of normal and mutated mitochondria. This mix is referred to as 'heteroplasmy'. The proportion of mutated mitochondria in the affected body part determines how severe the symptoms are.

What are the symptoms seen in leukodystrophies associated with mitochondrial disease?

Leukodystrophies are a group of genetic conditions that mainly affect the white matter of the brain and spinal cord. The white matter is the wiring network of the brain that connects different brain regions and links the brain to the spinal cord and rest of the body.

Mitochondrial leukodystrophies are characterized by the loss of the protective covering, or myelin, on the neurons. This is called demyelination. Additionally, other body systems that rely on mitochondrial energy production can be affected, such as the heart.

Neurological symptoms associated with mitochondrial disorders include:

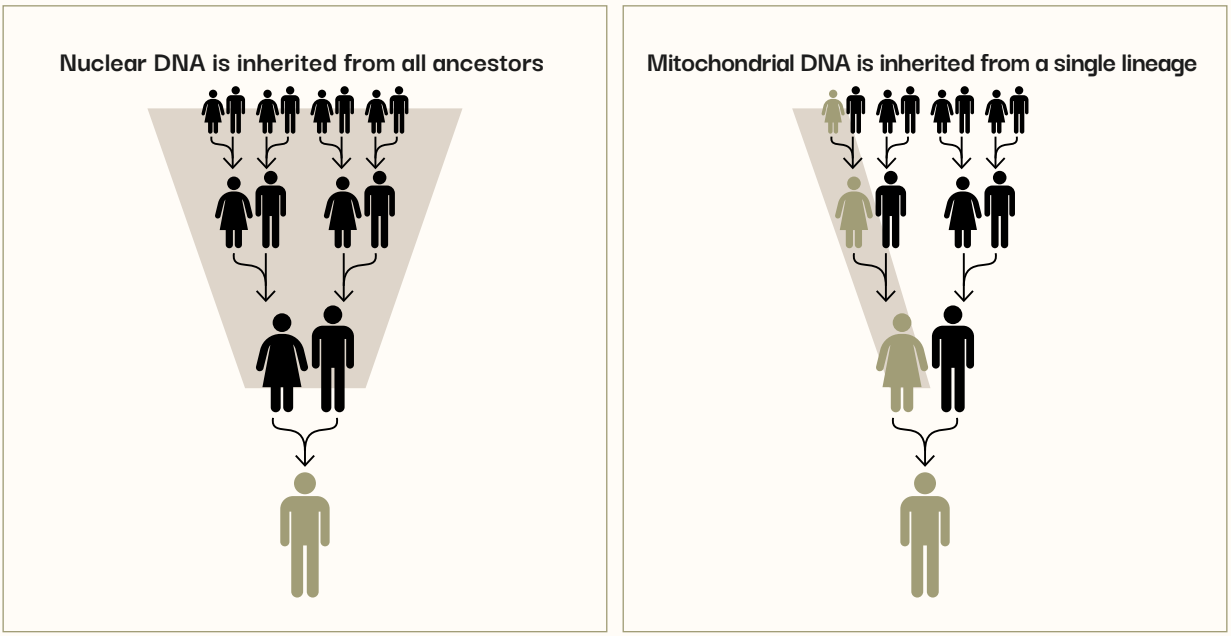
- Stiff posture (spasticity).
- Difficulty walking.
- Seizure like episodes.
- Movement disorders.
- Epilepsy.
- Dementia.
- Psychosis.

How are leukodystrophies associated with mitochondrial disease diagnosed?

Genetic testing to confirm the mutation is vital in the management of mitochondrial leukodystrophies.

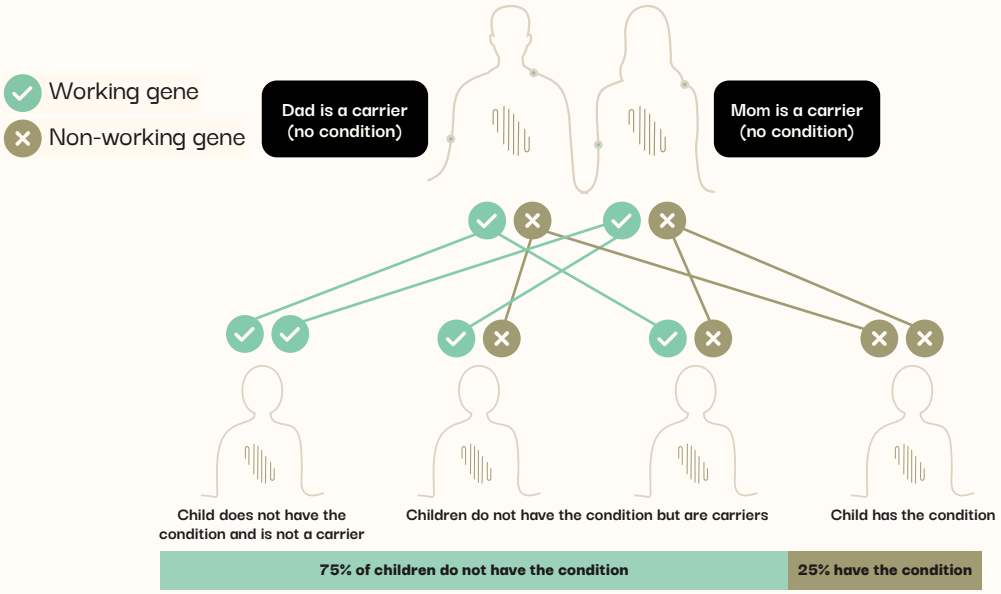
How is mtDNA-related mitochondrial disease inherited?

The mtDNA is derived from the egg cell, making it maternally inherited. Carrier screening in the mother may be followed by carrier screening in the maternal grandmother. If carrier status of the maternal grandmother is proven, screening is extended to all female members of the family. The risk in subsequent pregnancies can be discussed with a genetic counsellor, who can help with risk prediction in future pregnancies and can discuss various assisted pregnancy options with you.



How is nDNA-related mitochondrial disease inherited?

nDNA-related mitochondrial disease is inherited in an autosomal recessive pattern. This is where both copies of the affected gene are altered. Each parent passes on one copy of the altered gene change. This means that, in each of the subsequent pregnancy, the couple has a 1 in 4 chance of having an affected child. Healthy siblings may also be carriers.



Support and resources:

- **Leukodystrophy Australia** leuko.org.au
- **Mission Massimo Foundation** missionmassimo.com
- **United Leukodystrophy Foundation** ulf.org/leukodystrophies/adrenoleukodystrophy
- **Hunter's Hope** huntershope.org/familycare/leukodystrophies/adrenoleukodystrophy

Research:

- **Australian Leukodystrophy Clinical and Research Program** leukonet.org.au
- **Clinical trials** clinicaltrials.gov
- **Global Leukodystrophy Initiative** theglia.org

References:

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