Australian Leukodystrophy Clinical and Research Program

Hypomyelination with brainstem and spinal cord involvement and leg spasticity (HBSL)

What is HBSL?

HBSL is a type of leukodystrophy.

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.

HBSL affects the brain and certain regions of spinal cord that are pathways (tracts) for motor and sensory stimuli and the region of the spinal cord that attaches to the brain (brainstem).

What symptoms are associated with HBSL?

Despite normal early development, symptoms appear between 6 to 18 months of age, with varying age of onset. Symptoms include:

- Muscle stiffness (spasticity) only in the legs that worsens over time, resulting in loss of ability to walk independently.
- Abnormal jerky side-to-side movements of the eyes (nystagmus).
- Weak muscle tone (hypotonia) in the trunk.
- Speech difficulties (dysarthria).
- Mild intellectual disability and impaired learning function.

What causes HBSL?

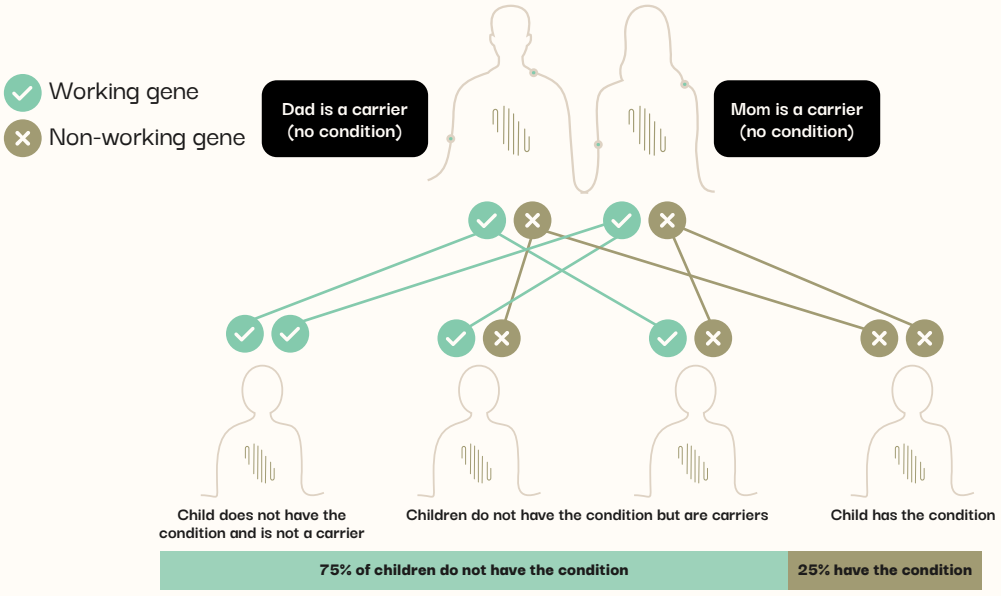
HBSL is caused by changes in the *DARS1* gene. Changes in the *DARS1* gene result in impaired aspartyl-tRNA production and abnormal protein chains. There is no clear understanding on how this causes the symptoms seen in individuals with HBSL.

How is HBSL diagnosed?

- MRI brain: shows characteristic white matter changes in the brain, spinal cord and brainstem.
- Genetic testing that shows disease-causing changes (pathogenic variants) in the *DARS1* gene.

How is HBSL inherited?

HBSL is inherited in an autosomal recessive pattern. This is where altered two copies of the *DARS1* gene causes HBSL. Each parent passes on one copy of the altered gene change. This means that in each of the subsequent pregnancies the couple has a 1 in 4 chance of having an affected child. This also means that siblings of the parents and the affected child can also be carriers.



Can HBSL be treated?

There is no specific treatment or cure for HBSL. Treatment is based on management of symptoms. Researchers are trying to understand what the *DARS1* gene does in order to develop better treatments.

Support and resources:

- **Mission Massimo Foundation** missionmassimo.com
- **Yasho's Leukodystrophy Foundation** yashofoundation.nl
- **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
- **Global Leukodystrophy Initiative** theglia.org

References:

- ncbi.nlm.nih.gov/gtr/conditions/C3809008/?_ga=2.10908468.1638322331.1621818712-644392159.1618927469.
- medlineplus.gov/genetics/condition/hypomyelination-with-brainstem-and-spinal-cord-involvement-and-leg-spasticity/#resources
- missionmassimo.com