Australian Leukodystrophy Clinical and Research Program

# Hypomyelination with Atrophy of the Basal Gandglia and Cerebellum (H-ABC)

## What is H-ABC?

**H-ABC 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.

H-ABC is characterized by abnormal levels of the components that make up the protective covering, or myelin sheath. As a result, the neuron's ability to transmit signals is limited. This is called hypomyelination. H-ABC also reduces the size and function of the basal ganglia and cerebellum.

## What are the symptoms of H-ABC?

**The symptoms and progression depend on when the disease first appears.**

If symptoms begin in the first few months of life, the disease tends to be severe and its progress more rapid. If symptoms begin in early childhood, the disease tends to be milder and its progress slower.

**Symptoms include:**

- Motor developmental delay or regression of motor skills.
- Progressive muscle stiffness (spasticity).
- Involuntary muscle contraction (dystonia).
- Uncontrolled muscle movement (choreoathetosis).
- Uncoordinated muscular movements (ataxia).
- Speech impairment (dysarthria) and weak voice (dysphonia).
- Swallowing problems (dysphagia).
- Progressive paralysis of lower limbs.
- Learning difficulty.
- Seizures.

## What causes H-ABC?

**H-ABC is caused by changes in the *TUBB4A* gene.**

Alpha-tubulin (α-tubulin) and beta-tubulin (β-tubulin) are two proteins that attach to form microtubules. Microtubules form the framework of the cytoskeleton, an important structure of all types of cells in the body. The *TUBB4A* gene provides instructions for β-tubulin that is found in the cells inside various parts of the brain.

Changes in the *TUBB4A* gene result in abnormal β-tubulin in the cells of the putamen, cerebellum, and white matter of the brain. Abnormalities in these parts of the brain lead to the issues with movement, speech, learning and the neurological symptoms seen in affected individuals.

## How is H-ABC diagnosed?

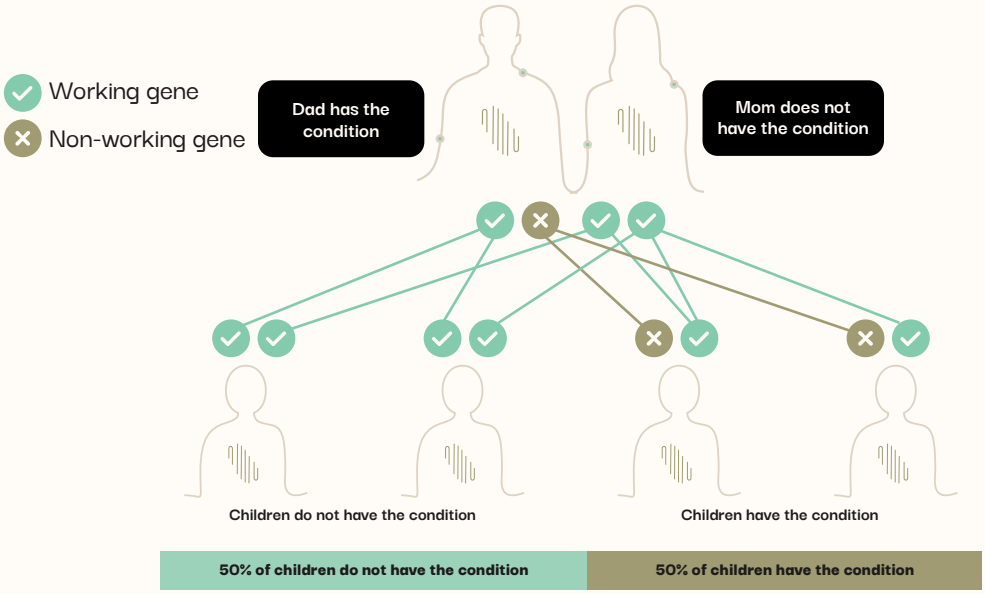
**Diagnosis is made based on physical symptoms, imaging of the brain and results of genetic testing.**

- Abnormal neuroimaging: Brain magnetic resonance imaging (MRI) shows hypomyelination, with or without abnormalities of the basal ganglia and cerebellum.
- Molecular testing of the *TUBB4A* gene.

## How is H-ABC inherited?

**H-ABC follows autosomal dominant inheritance.**

However most cases are due to de-novo mutations (arises in the affected person due to random chance). In these cases, neither parent is a carrier, and the chance of having another child with the disease is extremely low. There is a small chance that one parent does not have symptoms but may carry the gene change in some cells (mosaicism) and therefore may still be able to transmit the condition.




## Can H-ABC be treated?

There is no cure for H-ABC, but treatment is available to manage symptoms and improve the quality of life for individuals affected by the disease.

Use of L-dopa is recommended for individuals with certain MRI-brain findings.

## Support and resources:

- **H-ABC Foundation UK** h-abcfoundation.org
- **Foundation to fight H-ABC** h-abc.org
- **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: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