Vanishing White Matter Disease (VWM)

Other names:

Childhood Ataxia with Central Nervous System Hypomyelination (CACH)

What is VWM disease?

Vanishing White Matter Disease 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.

VWM disease causes abnormal production of myelin and loss over time. Myelin forms the part of the brain and spine that provides support for the wiring networks (nerves). It enables rapid transmission of signals between the nerves in the brain and spine and the rest of the body.

In the absence of myelin, the structure and functionality of nerves are lost over time. This results in neurological symptoms such as muscle stiffness (spasticity), uncontrolled movements (ataxia) and visual impairment (optic atrophy).

What are symptoms seen in VWM?

Symptoms vary depending on the age of onset, which can range from birth to adulthood. Early onset is associated with a more severe form of the disease and later onset with a milder form.

An episode of stress such as fever or head trauma can cause a worsening of symptoms and neurological decline.

Symptoms include:

- Progressive muscle stiffness (spasticity)
- Progressive difficulty in coordinating movements (ataxia)
- Visual impairment (optic atrophy)
- Decline in intellectual abilities or behavior
- Ovarian failure
- Seizures

What causes VWM disease?

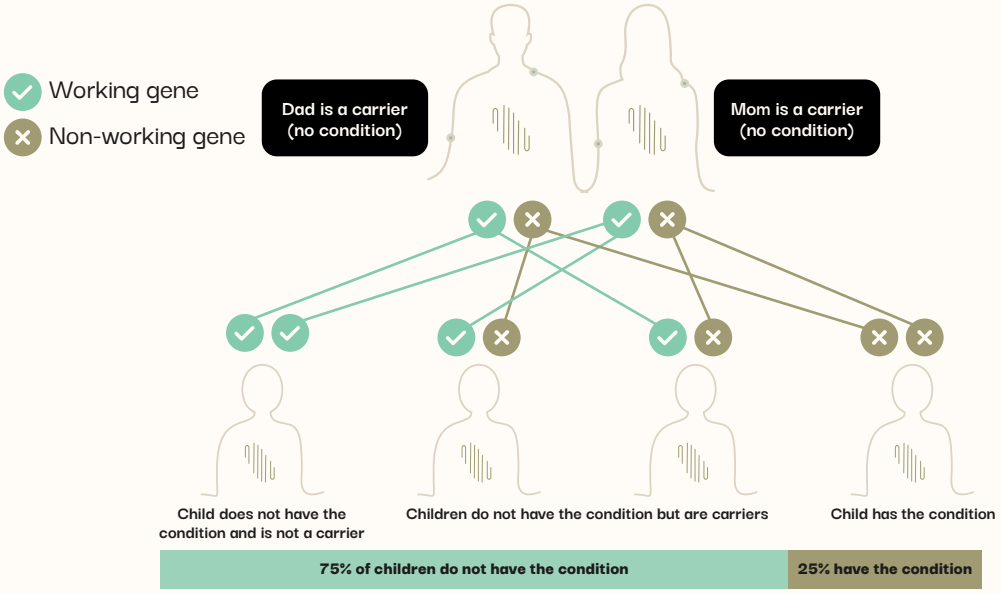
VWM is caused by changes in the *EIF2B1, EIF2B2, EIF2B3, EIF2B4* and *EIF2B5* genes. These genes code for the eIFB2 protein, which plays a major role in regulating protein production in the cell and helps adapt to changes during episodes of stress. Changes in these genes result in abnormal eIF2B protein function which is why episodes of stress can trigger a progression of disease and decline in brain function.

How is VWM disease diagnosed?

- MRI brain abnormalities: the pattern of abnormal signal in the white matter may be recognized as VWM disease.
- Genetic testing: identification of disease-causing changes ("pathogenic variants") in any of the above-mentioned genes confirms the clinical diagnosis.

How is VWM inherited?

VWM disease is inherited in an autosomal recessive pattern. This is where both copies of the relevant gene are altered. Each parent is a carrier and passes on one altered copy of the gene. When both parents are carriers, they have a 1 in 4 chance, in each pregnancy, of having an affected child. Siblings of the affected individual and the parents may also be carriers.



Can VWM be treated?

- There is currently no cure or specific treatments for VWM disease.
- Treatment is aimed at management of symptoms.
- Researchers are trialing a drug called Guanabenz in some patients with VWM disease.

Support and resources:

- **Saving Chloe Saxby** chloesaxby.com.au
- **Vanishing White Matter Consortium** vwmconsortium.org
- **Vanishing White Matter Foundation** vwmfoundation.com
- **VWM Families Foundation** vwmff.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
- **Clinical trials** https://clinicaltrials.gov/ct2/results?cond=vanishing+white+matter&term=&cntry=&state=&city=&dist=