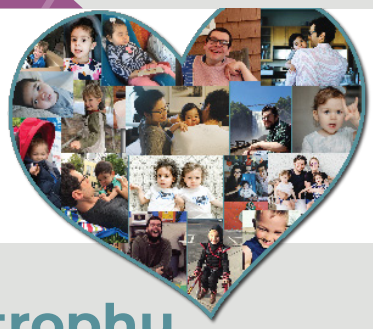
Learn about 4H Leukodystrophy

YAYA FOUNDATION for 4H LEUKODYSTROPHY

Overview

4H Leukodsytrophy is a rare disease of the central nervous system. The name 4H stands for hypomyelination, hypogonadotropic hypogonadism and hypodontia.



Leukodystrophies

A group of conditions that affect the white matter of the brain. These diseases damage the **myelin sheath**, which surrounds and protects the nerve cells in the brain and spinal cord and assists with transmission of messages between cells.

4H Leukodystrophy

a rare genetic disorder that affects the nervous system.

- short for hypomyelination with hypogonadotropic hypogonadism and hypodontia.
- **also known as:** 4H syndrome, POLR3-related leukodystrophy, POLR3-related disorder

Myelination

Why is it important?

The process of the body forming protective myelin sheath is called **myelination**. Typically, myelination develops in the first few years of life. Hypomyelination means that the body is unable to produce myelin at normal levels. This prevents the body from completing normal myelination of the brain.

hypomyelination
myelin deficiency

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hypogonadotropic hypogonadism
a condition that results in absent/delayed or arrested puberty

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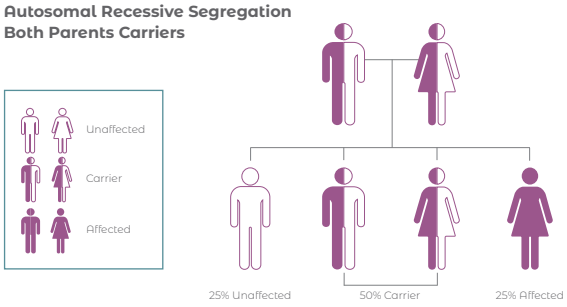
hypodontia
having fewer teeth than normal or an abnormal development of those teeth

= **4H Leukodystrophy**

Causes

mutations in **1 of 4 genes**
POL3RA, POL3RB, POLR1C, POLR3K

Autosomal Recessive Segregation
Both Parents Carriers



Genes are instructions that allow our bodies to function properly. We all have two copies of each gene; one is inherited from each parent. If there is a spelling mistake (mutation) in a gene, it can prevent it from doing its job, leading to symptoms of a genetic condition.

4H leukodystrophy is inherited in an autosomal recessive pattern, which means an individual has the condition if both copies of a gene are not working. Parents are "carriers" because they have just one mutated copy—the other functions as expected. When two carriers have children together, there is a 25% (1 in 4) chance each child will have 4H leukodystrophy. Unless this random event occurs, most have no way of knowing they are carriers because they are not affected and have no symptoms.

Varying Disease Severity

The disease severity for a patient with 4H Leukodystrophy, including the time of onset, presenting symptoms, and speed and nature of disease progression can vary significantly depending on the particular genetic difference, or mutation, of the child. It can be confusing to read scientific articles or connect with other parents that describe cases that are different from your child's. Because so few cases have been reported, and no two cases are exactly the same, it is most important that you seek specialized care from a physician recognized as an expert on 4H Leukodystrophy or at a center with experience treating patients affected by Leukodystrophies.

Possible Symptoms

Children with 4H Leukodystrophy typically start to show symptoms in early infancy or as toddlers, though some don't show signs of the disease until they are teenagers or adults.

People with 4H Leukodystrophy have different combinations of symptoms, such as:

Motor Problems
stiffness of the limbs and problems with walking, balance and coordination

Movement Disorders
tremor or abnormal postures of the limbs, or other involuntary movements

Learning Disabilities
ranges from mild to severe and varies based on progression and severity of the disease

Stature
may be small for their age, and may not go through typical puberty

Fine Motor Skills
trouble holding and controlling small items like pens and cups

Vision Problems
trouble focusing on things far away (myopia)

Speech Problems
slurred speech, impacting the ability to communicate

Feeding Difficulty
difficulty chewing and swallowing

Teeth
may have delayed eruption of the teeth, abnormal pattern of tooth eruption, abnormal shape of the teeth, etc

Explore other symptom information here

Areas of Specialty Care

Children with 4H Leukodystrophy may need regular monitoring and support from a range of medical specialists and therapists in order to adapt treatment to changing needs. The care is currently geared to providing the highest possible quality of life and to address any symptoms that cause discomfort.

Specialists can include, but may not be limited to:

Neurologist
Can help families understand disease progression and make recommendations regarding care required.

Endocrinologist
Can help identify and treat effects on the body's endocrine system, such as the delayed puberty/ hypogonadotropic hypogonadism-related effects of 4H.

Feeding Team
Team may include pediatrician/family doctor, gastroenterologist, ENT, occupational therapist, speech therapist, etc.
Children affected by 4H often develop problems with swallowing, which can lead to challenges with eating and drinking. Creating safe and nutritious feeding strategies and also identify appropriate therapies to help with eating and drinking, if necessary.

Physiatrist & Other Rehabilitation Specialists
Team may include physiotherapy, occupational therapy, speech therapy, etc.
Can help identify therapies and medication to help with the motor-related symptoms of 4H, including stiffness, and problems with mobility.

Ophthalmologist
Can help identify and treat vision-related symptoms of the disease.

Pulmonologist
Can help address respiratory challenges that may result from problems with swallowing that can develop.

Otolaryngologist
Can help address the drooling and help the management of difficulties swallowing.

Psychologist and/or Social Worker
Can provide support to the patients and his or her loved ones, including psychological support, but also support in obtaining services or allocations.

Support

4H Leukodystrophy does not have a cure yet and efforts are underway to better understand the disease and to develop therapies to help families. Leading clinicians and researchers have committed to care and support for families diagnosed with 4H. The Yaya Foundation for 4H Leukodystrophy is committed to accelerating therapy discovery and connected families with additional resources.

Leukodystrophy Care Network
Hunter's Hope

Locate centers of excellence and specific providers who are knowledgeable on various Leukodystrophies.

Leading 4H Clinicians

Geneviève Bernard, MD, MSc, FRCPc
Pediatric Neurologist
Montreal Children's Hospital
McGill University Health Centre
MyelinNeuroGene Lab

Nicole Wolf, MD, PhD
Pediatric Neurologist
Amsterdam University
Medical Center & Lab

Adeline Vanderver, MD
Pediatric Neurologist
Children's Hospital of Philadelphia
Vanderver Lab

The Yaya Foundation for 4H Leukodystrophy

YAYA FOUNDATION for 4H LEUKODYSTROPHY

The Yaya Foundation for 4H Leukodystrophy is the only organization fighting for children and families affected by 4H Leukodystrophy. We have built an ecosystem of patients, families, researchers, clinicians and supporters to accelerate research that will better define 4H Leukodystrophy, develop therapies that will help patients live longer and better lives, and find a cure.

To provide educational and emotional support to patients and families affected by 4H Leukodystrophy, The Yaya Foundation can be available for a call with you, help connect you to care and to other families impacted by 4H Leukodystrophy. The Foundation also hosts regular family Zoom calls and provides fundraising tools and support.

We understand the emotional whirlwind of receiving this diagnosis and are here to support you in any way we can. Please do not hesitate to Contact Us.

info@yayafoundation4hl.org
yayafoundation4hl.org
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