Farber Disease Fact Sheet

Definition

Farber disease is a rare, progressive disease caused by a deficiency (reduced function) of an enzyme called acid ceramidase. Farber disease is also sometimes called Farber lipogranulomatosis, acid ceramidase deficiency, or an *ASAH1*-related disorder.

What are the symptoms of Farber disease?

The most common symptoms[1] of Farber disease are:

- Joint disease affecting multiple joints on both sides of the body (arthritis, contractures), generally leading to pain and difficulty moving the joints
- Bumps (nodules) under the skin, most common on the hands, feet, and head (also called granulomas or lipogranulomas)
- Hoarse or weak voice caused by nodules or swelling of the vocal cords

These symptoms may not all appear at the same time and may vary in severity. There are many other symptoms that some patients with Farber disease will have, and others will not. The symptoms also depend on the progression of the disease and age of the individual. These symptoms[2] include:

- Respiratory problems, such as chronic or progressive difficulty breathing
- Pain, especially in the joints
- Recurring or persisting fever
- Inflammation throughout the body which may register in blood tests such as sedimentation rate (ESR) or C-reactive protein (CRP)
- Failure to thrive, such as difficulty gaining weight or short stature
- Abnormal bones or resorption of bones (peripheral osteolysis)
- Developmental delay or loss of developmental milestones, like the ability to crawl or walk
- Muscle and brain disease, such as progressive muscle weakness, loss of coordination, neuropathy, seizures, or difficulty swallowing
- Liver and/or spleen enlargement that may be felt by a doctor or seen with ultrasound
- Changes in the eye seen by an eye doctor (such as “cherry-red spots”)

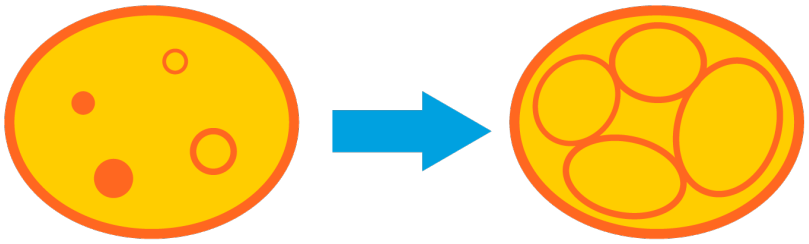
The progression and severity of Farber disease varies widely. In some cases, babies or infants with severe disease will develop symptoms quickly and may die at a very young age. Other patients living with Farber disease may not develop symptoms for many years and can live well into adulthood. Patients with Farber disease are often misdiagnosed as having juvenile idiopathic arthritis (JIA) or other types of arthritis.[3,4]

What causes Farber disease?

Variants of the *ASAH1* gene → **Enzyme (Acid Ceramidase) Deficiency** → **Farber disease**

Farber disease is an inherited (genetic) disease which is caused by variants or differences of the *ASAH1* gene. Genes are inherited from our parents and give instructions to our cells. If the genes have a variant or alteration, the instructions may be missing or not work correctly, which can cause a genetic disease. Variants in the *ASAH1* gene cause the body to not produce enough of the enzyme called acid ceramidase, a condition also called an acid ceramidase deficiency.[1]

Acid ceramidase is very important in the normal functioning of cells in our body because it controls the amount of a material called ceramide. When there is not enough acid ceramidase, ceramide builds up in the cells and causes inflammation, cell death, and tissue and organ damage. Without enough acid ceramidase enzyme, this inflammation and damage to cells and tissues goes on and on, leading to the symptoms of Farber disease. This ceramide builds up in the part of the cell called the lysosome, so Farber disease is considered part of a group of somewhat similar diseases called lysosomal storage disorders.



Typical Cell **Farber Disease Cell**

How is Farber disease diagnosed?

Farber disease can be diagnosed in two ways[1]:

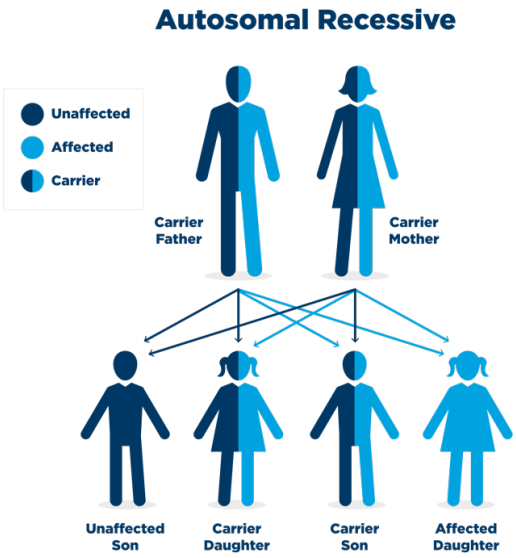
- Genetic testing (performed on blood, saliva, or a cheek swab) can confirm *ASAH1* gene variants
- Enzyme testing (performed on blood) can confirm low acid ceramidase activity (deficiency)

These tests are performed in specialized laboratories and can be coordinated by a healthcare provider.

How is Farber disease inherited?

DNA is the genetic information in our body that gives instructions for how the body grows and functions. This information is packaged into genes. In every cell in the body, there are two copies of the *ASAH1* gene, one copy passed down from the mother and one copy passed down from the father. If BOTH copies of a person's *ASAH1* gene have a variant causing Farber disease, he or she will have Farber disease. If ONLY ONE copy has a variant, he or she is a carrier of Farber disease. Carriers do not have any symptoms but can pass the disease onto their children.

If both parents are carriers of Farber disease, each of their children will have a 25% (1 in 4) chance of having Farber disease, a 50% (1 in 2) chance of being a carrier like their parents, and a 25% (1 in 4) chance of not having Farber disease or being a carrier. Farber disease affects both males and females.



How is Farber disease treated?

There are currently no treatments specific to Farber disease. Anti-inflammatory medication, specifically tocilizumab (an interleukin-6 receptor inhibitor), has shown benefits in some individuals by reducing joint swelling and pain.[5]

Other supportive therapies may be provided as needed such as feeding tubes, breathing/respiratory support, physical and/or occupational therapy, mobility aids such as a walker or wheelchair, and medications for symptoms such as seizures.

Some patients with Farber disease have undergone hematopoietic stem cell transplant or bone marrow transplant (HSCT or BMT). HSCT has been able to resolve symptoms such as inflammation (swelling) and nodules (bumps) in some patients, however, reports indicate that it does not appear to prevent or improve neurologic (brain or central nervous system) disease.[6,7]

When a patient is diagnosed with Farber disease, they may be recommended to see multiple specialists. These may include a:

- rheumatologist (specialist who treats swelling, pain, and stiffness in joints)
- geneticist/genetic counselor (specialist who diagnoses and manages individuals with genetic conditions)
- orthopedist (specialist who treats bone and joint disease)
- pulmonologist (specialist who treats lung diseases)
- otolaryngologist (also called an ENT, a specialist who treats conditions of the ears, nose, and throat)
- ophthalmologist (specialist who treats eye diseases)
- gastroenterologist (specialist who treats problems of the stomach, liver, and digestive tract)
- neurologist (specialist who treats conditions of the brain and nervous system such as seizures)
- dermatologist (specialist who diagnoses and treats skin disorders)

What research is being done?

More information about clinical research in Farber disease can be found by visiting clinicaltrials.gov or clinicaltrialsregister.eu or by talking with a healthcare provider.

Where can I find more information?

National Organization for Rare Disorders
Search for: *ASAH1*-Related Disorders
rarediseases.org

Genetic and Rare Diseases Information Center (GARD)
Search for: Farber disease
rarediseases.info.nih.gov

Orphanet
Search for: Farber disease
www.orpha.net

GeneReviews
Search for: *ASAH1*-Related Disorders
www.ncbi.nlm.nih.gov/books/NBK488189/

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References

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4. Moghadam SH, Tavasoli AR, Modaresi M, Ziaee V. Farber disease: report of three cases with joint involvement mimicking juvenile idiopathic arthritis. J Musculoskelet Neuronal Interact. 2019 Dec 1;19(4):521-525.

5. Mitchell J, Solyom A, Makaya B, Arslan N, Batu ED, Ozen S, Hugle B, Schuchman E, Magnusson B. "Farber disease: Implications of anti-inflammatory treatment". Molecular Genetics and Metabolism. 2016 Feb 117 (2):S81-82.

6. Ehlert K, Levade T, Di Rocco M, et al. Allogeneic hematopoietic cell transplantation in Farber disease. J Inherit Metab Dis. 2019 Mar;42(2):286-294.

7. Goudie C, Alayoubi AM, Tibout P, Duval M, Maranda B, Michell D, Mitchell JJ. Hematopoietic stem cell transplant does not prevent neurological deterioration in infants with Farber disease: Case report and literature review. JIMD Rep. 2019 Mar 14;46(1):46-51.