Refsum disease

Description

Refsum disease is an inherited condition that causes vision loss, absence of the sense of smell (anosmia), and a variety of other signs and symptoms.

The vision loss associated with Refsum disease is caused by an eye disorder called retinitis pigmentosa. This disorder affects the retina, the light-sensitive layer at the back of the eye. Vision loss occurs as the light-sensing cells of the retina gradually deteriorate. The first sign of retinitis pigmentosa is usually a loss of night vision, which often becomes apparent in childhood. Over a period of years, the disease disrupts side (peripheral) vision and may eventually lead to blindness.

Vision loss and anosmia are seen in almost everyone with Refsum disease, but other signs and symptoms vary. About one-third of affected individuals are born with bone abnormalities of the hands and feet. Features that appear later in life can include progressive muscle weakness and wasting; poor balance and coordination (ataxia); hearing loss; and dry, scaly skin (ichthyosis). Additionally, some people with Refsum disease develop an abnormal heart rhythm (arrhythmia) and related heart problems that can be life-threatening.

Frequency

The prevalence of Refsum disease is unknown, although the condition is thought to be uncommon.

Causes

More than 90 percent of all cases of Refsum disease result from mutations in the *PHYH* gene. The remaining cases are caused by mutations in a gene called *PEX7*.

The signs and symptoms of Refsum disease result from the abnormal buildup of a type of fatty acid called phytanic acid. This substance is obtained from the diet, particularly from beef and dairy products. It is normally broken down through a process called alpha-oxidation, which occurs in cell structures called peroxisomes. These sac-like compartments contain enzymes that process many different substances, such as fatty acids and certain toxic compounds.

Mutations in either the *PHYH* or *PEX7* gene disrupt the usual functions of peroxisomes,

including the breakdown of phytanic acid. As a result, this substance builds up in the body's tissues. The accumulation of phytanic acid is toxic to cells, although it is unclear how an excess of this substance affects vision and smell and causes the other specific features of Refsum disease.

Learn more about the genes associated with Refsum disease

- PEX7
- PHYH

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Adult Refsum disease
- ARD
- Classic Refsum disease
- CRD
- Hereditary motor and sensory neuropathy type IV
- Heredopathia atactica polyneuritiformis
- HMSN IV
- HMSN type IV
- Phytanic acid storage disease
- Refsum syndrome
- Refsum's disease

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Adult Refsum Disease (https://www.ncbi.nlm.nih.gov/gtr/conditions/C5781059/)
- Genetic Testing Registry: Refsum disease, classic (https://www.ncbi.nlm.nih.gov/gtr/conditions/C5780941/)

Genetic and Rare Diseases Information Center

- Refsum disease (https://rarediseases.info.nih.gov/diseases/5691/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Refsum disease%22)

Catalog of Genes and Diseases from OMIM

- PEROXISOME BIOGENESIS DISORDER 9B; PBD9B (https://omim.org/entry/614879)
- REFSUM DISEASE, CLASSIC (https://omim.org/entry/266500)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Refsum*+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

References

- Jansen GA, Waterham HR, Wanders RJ. Molecular basis of Refsum disease: sequence variations in phytanoyl-CoA hydroxylase (PHYH) and the PTS2 receptor(PEX7). Hum Mutat. 2004 Mar;23(3):209-18. doi: 10.1002/humu.10315. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/14974078)
- Ruether K, Baldwin E, Casteels M, Feher MD, Horn M, Kuranoff S, Leroy BP, Wanders RJ, Wierzbicki AS. Adult Refsum disease: a form of tapetoretinaldystrophy accessible to therapy. Surv Ophthalmol. 2010 Nov-Dec;55(6):531-8. doi:10.1016/j.survophthal.2010.03.007. Epub 2010 Sep 20. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20850855)
- Van den Brink DM, Brites P, Haasjes J, Wierzbicki AS, Mitchell J,Lambert-Hamill M, de Belleroche J, Jansen GA, Waterham HR, Wanders RJ.Identification of PEX7 as the second gene involved in Refsum disease. Adv Exp MedBiol. 2003;544:69-70. doi: 10.1007/978-1-4419-9072-3_9. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/14713215)
- van den Brink DM, Wanders RJ. Phytanic acid: production from phytol, itsbreakdown and role in human disease. Cell Mol Life Sci. 2006 Aug;63(15):1752-65.doi: 10.1007/s00018-005-5463-y. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16799769)

- Wanders RJ, Jansen GA, Skjeldal OH. Refsum disease, peroxisomes and phytanicacid oxidation: a review. J Neuropathol Exp Neurol. 2001 Nov;60(11):1021-31. doi:10.1093/jnen/60.11.1021. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11706932)
- Wanders RJ, Komen JC. Peroxisomes, Refsum's disease and the alpha-andomega-oxidation of phytanic acid. Biochem Soc Trans. 2007 Nov;35(Pt 5):865-9. doi: 10.1042/BST0350865. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17956234)
- Waterham HR, Wanders RJA, Leroy BP. Adult Refsum Disease. 2006 Mar 20 [updated2021 Sep 30]. In: Adam MP, Bick S, Mirzaa GM, Wallace SE, Amemiya A, editors.GeneReviews(R) [Internet]. Seattle (WA): University of Washington,Seattle; 1993-2026. Available from http://www.ncbi.nlm.nih.gov/books/NBK1353/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20301527)
- Wierzbicki AS, Lloyd MD, Schofield CJ, Feher MD, Gibberd FB. Refsum's disease:a peroxisomal disorder affecting phytanic acid alpha-oxidation. J Neurochem. 2002Mar;80(5):727-35. doi: 10.1046/j.0022-3042.2002.00766.x. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11948235)
- Wierzbicki AS. Peroxisomal disorders affecting phytanic acid alpha-oxidation:a review. Biochem Soc Trans. 2007 Nov;35(Pt 5):881-6. doi: 10.1042/BST0350881. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17956237)

Last updated November 1, 2016