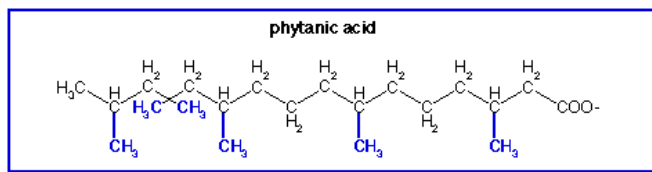


FACT SHEET: REFSUM DISEASE

What causes Refsum disease?

The peroxisome is responsible for the breakdown of certain branched chain fatty acids. A common branched chain fatty acid, phytanic acid, is shown below. It is different from the straight chain fatty acid shown above in that it has "branches" of carbon groups off the main carbon chain (**branches are colored in blue**).



Phytanic acid is a component of our diet, and therefore needs to be digested properly. The peroxisome is responsible for the breakdown of phytanic acid, and impairment of this specific function results in Refsum disease.

What are the clinical symptoms of Refsum disease?

Patients with Refsum disease do not generally show any obvious defects at birth, and growth and development appears normal. Initial symptoms will generally appear by age 20, although patients have been known who do not display symptoms until around age 50. The initial complaints usually involve vision problems, and/or weakness in the arms and legs. The disease is progressive, although there can be periods of unexplained remission. Below is a list of the most common symptoms of Refsum disease. We have included the clinical terms as well as a description of their meaning.

- **Retinitis pigmentosa:** Retinitis pigmentosa is a disease of the eye, resulting from degeneration of a part of the eye called the retina. It

affects night vision and peripheral vision, and eventually can lead to blindness.

- **Peripheral polyneuropathy:** Peripheral polyneuropathy is the term for dysfunction of the nerves outside of the spinal cord. Symptoms may include numbness, weakness, burning pain, and loss of reflexes.
- **Deafness:** loss of hearing
- **Cerebellar ataxia:** Ataxia is wobbliness. Cerebellar ataxia refers to the fact that the defect is in a specific part of the brain (the cerebellum), and the incoordination and unsteadiness is due to the brain's failure to regulate the body's posture, as well as the strength and direction of the body's movements.
- **Anosmia:** loss of the sense of smell
- **Papillary abnormalities:** abnormality of the pupils of the eye
- **Nystagmus:** rapid, involuntary, rhythmic eye movements
- **Ichthyosis:** Ichthyosis is a noninflammatory scalliness of the skin. These symptoms can range anywhere from scalliness of the palms and soles of the feet to scalliness on the trunk of the body.
- **Epiphyseal dysplasia:** The epiphysis is the growth area at the end of a bone, while dysplasia means abnormal formation. This means that patients with Refsum disease often have shortened limbs.

How is Refsum disease diagnosed?

As we mentioned above, Refsum disease results from an inability to break down a particular molecule known as phytanic acid. Therefore, Refsum disease can be confirmed by a simple blood test that measures the levels of phytanic acid.

In addition, most known cases of Refsum disease result from defects in a protein known as phytanoyl-

CoA hydroxylase, or PAHX. There are some common mutations which have been identified, which can allow family members to be screened in order to determine if they are carriers of the gene responsible for the disease. This can allow them to make informed decisions about having children.

What is the prognosis of Refsum disease?

Prognosis of Refsum disease varies dramatically. Strict adherence to a dietary regimen (see treatment, below) can cause the neurological symptoms to arrest, and nerve response can improve. Weakness, problems with walking, and scaliness of the skin can also improve. Prior to the initiation of dietary therapy, more than half of patients died before age 30. However, since the introduction of dietary therapy, very few patients have died so young.

What are the possible treatments for Refsum disease?

Nearly all phytanic acid is obtained from the diet, which means that dietary control is an option for Refsum disease. Patients are advised to keep consumption of phytanic acid below 10 mg/day (the normal intake is approximately 100 mg/day). Sources of high levels of phytanic acid include beef, lamb, full cream, milk, butter, and cheese. It is important to be careful to maintain weight, because loss of weight can cause release of stored phytanic acid from fat tissues. This results in an increase in plasma phytanic acid levels, and can lead to a worsening of symptoms. If there is difficulty reducing levels of phytanic acid in the plasma, sometimes plasmapheresis (replacement of the plasma) can help.