

UNDERSTANDING INFANTILE REFSUM'S DISEASE

What is Infantile Refsum's Disease?

Infantile Refsum's Disease (REF-SOOMZ) is an inherited metabolic disorder that is characterized by the abnormal accumulation of phytanic acid in blood plasma and tissues. Phytanic acid is not made in the human body; it comes from the diet - dairy products, beef, lamb, and some seafood. People with Infantile Refsum's are missing phytanoyl-CoA hydroxylase, the enzyme that breaks down phytanic acid.

Think of the food in our system as a person with a big delivery to make. As long as the person has all the keys, the load can be delivered and everyone gets their packages. When enzymes or keys are missing, the packages cannot be delivered and the delivery person is left with a big load, and no one gets the packages they need to do their job.

 Nerves are fibres that carry signals to and from the brain and spinal cord and parts of the body. Each nerve is covered in insulation, called the **myelin sheath**. Myelin is like the plastic coating around an electrical cord. Myelin is largely made up of fat. In Infantile Refsum's Disease, the phytanic acid builds up in the blood and tissues causing the myelin sheath around nerves gets eaten away, eventually causing the nerve to "short-circuit".

What are the symptoms of Refsum's Disease?

Infantile Refsum's Disease is an extremely rare and complex disorder that affects many parts of the body. Symptoms are varied from person to person. These may include:

- **Retinitis Pigmentosa (RP)** - harmful levels of phytanic acid collect beneath the retina in the eye. The first symptom of RP is night blindness followed by a gradual loss of peripheral (side) vision. Night blindness makes vision difficult in dark or dimly lit places. The loss of peripheral

vision is often referred to as tunnel vision. RP tends to progress slowly in patients with Infantile Refsum's Disease.

- **Nystagmus** - rapid, involuntary to-and-fro eye movements.
- **Peripheral Polyneuropathy** - 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** - balance disorder (ataxia is wobbliness). This refers to the fact that the defect is in a specific part of the brain (the cerebellum). 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. This stems from the demyelination (or short-circuiting) of the nerve cells in the brain.
- **Anosmia** - loss of the sense of smell.
- **Pupillary Abnormalities** - abnormality of the pupils of the eye.
- **Ichthyosis** - non-inflammatory 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 epiphysus is the growth area at the end of a bone, while dysplasia means abnormal formation. This means that patients with Refsum's often have shortened limbs.

How do people get Refsum's Disease?

Infantile Refsum's Disease is an inborn error of metabolism. It is genetic. This means that the person has the disorder from the time they are conceived. At conception, the baby receives two sets of genetic material, one from the mother, and one from the father. This genetic material, called **DNA**, acts as a recipe for the baby's development.



DNA includes information about the baby's eye and hair colour, and even whether the baby will be right or left-handed. DNA comes in units called **genes**. Each pair of genes gives directions to a certain part of the body.

In Infantile Refsum's Disease, there is a problem with the genes that give information on how the body breaks down phytanic acid. The disorder is caused by getting two copies of the faulty gene that gives the wrong instructions. One copy comes from the mother and one comes from the father. If the child inherits only one copy of the gene, they are a carrier for Infantile Refsum's Disease but are not affected. There is a 1 in 4, or 25% chance that two carriers of the gene will have a baby with Infantile Refsum's. Boys and girls are equally affected.

Children born to carriers have:

- a 25% chance of having Infantile Refsum's Disease,
- a 50% chance of being a carrier and
- a 25% chance of being unaffected.

With each pregnancy, there is the **same** 25% chance of having a child with Infantile Refsum's Disease. In some families, there may be only one child with Infantile Refsum's Disease, while in other families, multiple children may be affected.

How is Infantile Refsum's Disease treated?

The cornerstone of Infantile Refsum's Disease treatment is dietary therapy. Plasmapheresis may also be required in some cases.

1. Dietary therapy



The diet for Infantile Refsum's Disease includes restricting foods that contain phytanic acid. It has been shown that the phytanic acid, which accumulates in the body, is taken in from the diet. If this can be avoided, the condition of the patients can be substantially improved.

2. Plasmapheresis

Plasmapheresis is the removal and reinfusion of blood plasma. It is used rarely and the main indication is in patients with severe or rapidly worsening clinical condition.

How is Infantile Refsum's Disease monitored?

It is important to closely monitor any changes to the brain, eyes, skin and to nerve function that may result from the buildup of phytanic acid. The person with Infantile Refsum's should be followed by a metabolic physician and may have (yearly) MRI (or MRS scans if available), and blood tests.

Regular visits to the metabolic clinic are needed to consult with the team. Referrals can be made to other specialists to closely monitor the effects of Infantile Refsum's on the body.



How can family and friends help?

Recognize and accept that the person with Infantile Refsum's may have physical limitations and may tire easily. Become familiar with how they are affected by the disorder. Don't make assumptions about their level of physical or mental functioning. Learn as much about Infantile Refsum's as you can and help to explain it to others. This not only increases awareness of the disorder, it helps the person affected to have a break from explaining it over and over again.

Helpful Resources

The Adult Metabolic Diseases Clinic
Vancouver General Hospital
4th Floor - 2775 Laurel Street
Vancouver, BC V5Z 1M9
(604) 875-5965

National Organization for Rare Disorders (NORD)
P.O. Box 1968
(55 Kenosia Avenue)
Danbury, CT 06813-1968
Orphan@rarediseases.org
<http://www.rarediseases.org>