

FACT SHEET: LEUKODYSTROPHIES

The leukodystrophies are a group of rare genetic disorders that affect the central nervous system by disrupting the growth or maintenance of the myelin sheath that insulates nerve cells. These disorders are progressive, meaning that they tend to get worse throughout the life of the patient. Below we describe the source of the disorders in more detail. Fact sheets on the individual leukodystrophies are also available from the United Leukodystrophy Foundation.

What is the nervous system?

In order to understand the leukodystrophies, we need to discuss some basic facts about the nervous system. The nervous system is made up of two main components: the central nervous system (CNS) and the peripheral nervous system (PNS). Together, these two systems interact to carry and receive signals that are responsible for nearly everything we do, including involuntary functions such as our heartbeat, and voluntary functions such as walking.

The CNS consists of the brain and the spinal cord, and contains billions of specialized cells known as neurons. Neurons have specialized projections called dendrites and axons that contribute to their unique function of transmitting signals throughout the body. Dendrites carry electrical signals to the neuron, while axons carry them away from the neuron.

The PNS consists of the rest of the neurons in the body. These include the sensory neurons, which detect any sensory stimuli and alert the CNS of their presence, and motor neurons, which connect the CNS to the muscles and carry out instructions from the CNS for movement.

What is Myelin?

Myelin, sometimes referred to as "white matter" because of its white, fatty appearance, protects and insulates the axons. It consists of a protective sheath of many different molecules that include both lipids (fatty molecules) and proteins. This protective sheath acts in a manner very similar to that of the protective insulation that surrounds an electric wire; that is, it is necessary for the rapid transmission of electrical signals between neurons. It does this primarily by containing the electrical molecules within the axon so that they are all properly transmitted to the next neuron. With the protective myelin coat, neurons can transmit signals at speeds up to 60 meters per second. When the coat is damaged, the maximum speed can decrease by ten-fold or more, since some of the signal is lost during transmission. This decrease in speed of signal transmission leads to significant disruption in the proper functioning of the nervous system.

What is a leukodystrophy?

The word leukodystrophy comes from the Greek words leuko (meaning white), trophy (meaning growth), and dys (meaning ill). If you put these words together, the word leukodystrophy describes a set of diseases that affect the growth or maintenance of the white matter (myelin).

How are the leukodystrophies different from one another?

All leukodystrophies are a result of problems with the growth or maintenance of the myelin sheath. However, there are many genes that are important in this process. For example, some genes are involved with

the synthesis of the proteins needed for the myelin, while others are required for the proper transport of these proteins to their final location in the myelin sheath that covers the axons. Defects in any of the genes (called a mutation) may lead to a leukodystrophy. However, the symptoms of the individual leukodystrophies may vary because of the differences in their genetic cause.

How do you get leukodystrophy?

Leukodystrophies are mostly inherited disorders, meaning that it is passed on from parent to child. They may be inherited in a recessive, dominant, or X-linked manner, depending on the type of leukodystrophy. The individual pages on each leukodystrophy will describe the particular pattern of inheritance for that disease. There is also a separate fact sheet describing the different genetic inheritance patterns available from the United Leukodystrophy Foundation.

There are some leukodystrophies that do not appear to be inherited, but rather arise spontaneously. They are still caused by a mutation in a particular gene, but it just means that the mutation was not inherited. In this case, the birth of one child with the disease does not necessarily increase the likelihood of a second child having the disease.

Are the leukodystrophies related to multiple sclerosis?

The leukodystrophies do share some common features with multiple sclerosis (MS). Like the leukodystrophies, MS is caused by the loss of myelin from the axons. However, the cause is different; whereas leukodystrophies are generally caused by a defect in one of the genes involved with the growth or maintenance of the myelin, MS is thought to be caused by an attack on the myelin by the body's own immune system.

How many different leukodystrophies are there?

New leukodystrophies are always being identified. We try to keep our information as up-to-date as possible, and so the 34 leukodystrophies we have listed here comprise the defined leukodystrophies to the best of our knowledge. Not all of these meet the

strict criteria for the definition of a leukodystrophy. These have been marked with an asterisk. They are included here because they have features that resemble the leukodystrophies. Please let us know if you are aware of any other types so that we can add them to our list. A fact sheet on each of these diseases is available from the United Leukodystrophy Foundation.

- 18q Syndrome with deficiency of myelin basic protein
- Acute disseminated encephalomyelitis (ADEM)*
- Acute Disseminated Leukoencephalitis*
- Acute Hemorrhagic Leukoencephalopathy*
- Adrenoleukodystrophy (ALD)
- Adrenomyeloneuropathy (AMN)
- Aicardi-Goutieres Syndrome*
- Alexander Disease
- Autosomal Dominant Diffuse Leukoencephalopathy with neuroaxonal spheroids
- Autosomal Dominant late-onset leukoencephalopathy
- Canavan Disease
- Cerebral Autosomal Dominant Arteropathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL)*
- Cerebrotendinous Xanthomatosis (CTX)
- Craniometaphysical dysplasia with leukoencephalopathy
- Extensive Cerebral White Matter abnormality without clinical symptoms*
- Familial adult-onset leukodystrophy manifesting as cerebellar ataxia and dementia
- Familial leukodystrophy with adult onset dementia and abnormal glycolipid storage
- Globoid Cell Leukodystrophy (Krabbe Disease)
- Hereditary adult onset leukodystrophy simulating chronic progressive multiple sclerosis
- Lipomembranous osteodysplasia with leukodystrophy (Nasu Disease)
- Metachromatic Leukodystrophy (MLD)
- Neonatal Adrenoleukodystrophy (NALD)
- Neuroaxonal leukoencephalopathy with axonal spheroids
- Oculodeltatodigital Dysplasia with cerebral white matter abnormalities
- Orthochromatic leukodystrophy with pigmented glia
- Ovarioleukodystrophy Syndrome
- Pelizaeus Merzbacher Disease (X-linked spastic paraplegia)
- Refsum Disease* (affects peripheral nerve myelin)

- Sjogren-Larssen Syndrome
- Sudanophilic Leukodystrophy
- Vacuolating megalencephaly with subcortical cysts
- van der Knaap Syndrome (Vacuolating Leukodystrophy with Subcortical Cysts)
- Vanishing White Matter Disease (Childhood ataxia with diffuse central nervous system hypomyelination, or CACH)
- Zellweger Syndrome (ZS)*