PLA2G6-Associated Neurodegeneration (PLAN)

What do I need to know about testing my child for PLAN?
PLAN is an inherited group of diseases caused by changes in a child's genes (instructions that tell the body how to work and grow). Children with the common form of PLAN, called infantile neuroaxonal dystrophy, have problems with developing skills like walking and talking. Later they have trouble moving and seeing well. A genetic test is now available to help decide whether a child has PLAN.

What is PLAN?
PLAN is a progressive genetic condition that mainly affects the nervous system and muscles. Progressive means that it becomes worse over time. Individuals with the most common form, infantile neuroaxonal dystrophy (INAD), are usually healthy at birth. By 2 years of age, most affected children will develop some signs or symptoms. The first signs are often delays in developing skills, like walking or talking. Later, children may begin to lose skills that they previously had. Children may be floppy or have low muscle tone (hypotonia) early on, but usually have stiff muscles (spasticity) as they get older, especially in their arms and legs. Eye disease (optic neuropathy) is also common and can cause poor vision and eventual blindness. At the end stages of the disease, children are usually blind and no longer have voluntary movements.

INAD can be difficult to diagnose and several tests may be done before a diagnosis is made. These tests often include magnetic resonance imaging (MRI) of the brain. In most cases, the MRI will show damage to part of the brain that helps control movement (cerebellar atrophy). In some cases, the MRI will show too much iron in another part of the brain called the basal ganglia. If the doctor thinks your child has INAD, he/she may do more studies of the nerves. Individuals with INAD have specific swellings (spheroid bodies) on the part of the nerve that helps transmit messages to other parts of the body. A biopsy must be done to find these.

A less common form of the disease, atypical neuroaxonal dystrophy (NAD), occurs later in childhood. The symptoms progress more slowly and may include a type of constant muscle cramping called dystonia. Individuals with atypical NAD can have behavior changes, such as being impulsive, not being able to pay attention for long periods of time, or becoming depressed, which may require treatment by a doctor.

Another form of the disease is called dystonia-parkinsonism, where symptoms commonly arise in late adolescence to early adulthood. Symptoms of this disease can include the rapid onset of parkinsonism, such as a tremor, slowed movement, or rigidity. Some other symptoms include dystonia and behavioral changes, such as depression. Treatments to assist with these symptoms include physical therapy and psychiatric support.

How is PLAN inherited?
PLAN is an inherited condition caused by changes in a gene called PLA2G6. Genes are instructions that tell the body how to build necessary proteins. Most of our genes come in pairs, one copy from our mother and the other from our father. PLAN is a recessive condition, which means that neither copy of the PLA2G6 gene is working right. This is because both copies have changes, called mutations. Individuals with one working copy and one mutation are called carriers. Having only one mutation is not enough to cause disease, so a carrier will have no symptoms of PLAN.

If both parents are carriers of PLA2G6 mutations, then there is a chance that each
parent will pass that mutation on to their child. With each pregnancy there is a:

- 25% (1 in 4) chance that the child will inherit two working copies of the gene
- 50% (2 in 4) chance that the child will inherit one working copy and one mutation and will be a carrier of PLAN
- 25% (1 in 4) chance that the child will inherit two mutations, one from each parent, and will develop PLAN

**How is testing for PLAN done?**
The genetic test is done by looking at an individual's two copies of the PLA2G6 gene. This process is similar to screening a book for typos. The test detects about 85% of all possible gene changes. This means that it will miss some mutations, even if they are there.

**What do the test results mean?**
- **2 mutations:** when two disease-causing mutations are found in an individual, the diagnosis of PLAN is confirmed.
- **1 mutation:** in some cases only one mutation is found in a person who has many symptoms of PLAN. This usually means that there is a second mutation, but the test cannot find it. In this case, the child usually has the diagnosis of PLAN.
- **No mutations:** if no mutations are found, then PLAN is unlikely to be the right diagnosis. In some rare cases, if the child has all the symptoms of PLAN, that diagnosis might be right and the test cannot find the mutations.

**When and how will I get the results?**
It takes 3-4 weeks to get the results and they will be sent to your doctor.

**Who else in the family should be tested?**
The test results may be important for you as well as other family members. If the genetic mutations causing PLAN can be found in a child, then it may be possible for the parents to do prenatal testing in future pregnancies to see if the developing fetus has PLAN. It may be possible to use newer technologies to start a pregnancy that is unaffected with PLAN.

Other family members, such as siblings, aunts, uncles and cousins of an affected child may benefit from knowing these genetic testing results. Your genetic counselor or doctor can help you decide how to share test results with other family members.

**How much does the testing cost and will my child’s health insurance pay for it?**
Testing costs approximately $2,000. If a family member with PLAN has already been tested, then it will cost much less for others in that family. Many insurance companies pay for testing. It may be helpful to give these CPT codes to your insurance company: 83891, 83898x17, 83904x17, 8391

**Where can I learn more?**
International PLAN Research Registry
Oregon Health & Science University
Portland, OR
503-494-4344

NBIA Disorders Association
El Cajon, CA
www.NBIAdisorders.org
(619) 588-2315

International Dystrophie Neuro Axonale Infantile
Association
Paris, France
http://asso.orpha.net/DNAI/

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