

## FACT SHEET: ADRENO MYELONEUROPATHY (AMN)

### What is AMN?

Adrenomyeloneuropathy (AMN) is a form of X-linked adrenoleukodystrophy (X-ALD; see the general fact sheet on X-ALD). AMN patients generally have spinal cord dysfunction, which leads to the initial symptoms that include difficulties in walking or a change in the walking pattern. The average age at which symptoms first appear is 28, but onset can occur anywhere from the second to the fifth decades of life.

AMN can be broken down into two general clinical forms: AMN with cerebral involvement (the spinal cord and brain are both affected), and AMN without cerebral involvement (only the spinal cord is affected). Of patients with AMN, approximately 54% have normal brain function, while 46% have brain involvement of varying degrees. Whether or not the brain is involved in AMN can be assessed by a Magnetic Resonance Image scan (MRI). This is a method of imaging that can be used to produce detailed images of the brain. Please see our fact sheet on the MRI for more information.

#### **AMN without cerebral involvement**

“Cerebral involvement” means that the disease has affected the brain. AMN occurs without any cerebral involvement in approximately half of all AMN patients. These patients have a significantly better prognosis than those with cerebral involvement. In general, neuropsychological function is normal except for mild deficits in motor speed and visual memory. Physical therapy, management of the problems with urinary control, and counseling are recommended for men with AMN. If there is no cerebral involvement, it is possible for men with AMN to maintain successful personal and professional lives.

#### **AMN with cerebral involvement**

Those AMN patients with cerebral involvement have a poorer prognosis than those without cerebral involvement. In approximately 20% of patients with AMN, brain involvement is severely progressive and leads to serious cognitive and behavioral disturbances that eventually may progress to total disability and death.

### How is AMN diagnosed?

AMN can be diagnosed by a simple blood test that analyzes the amount of very long chain fatty acids; the levels of these molecules are elevated in X-ALD (see our general fact sheet on X-ALD). A DNA-based blood test is also available.

If the blood test suggests X-ALD, then generally an MRI will be performed in order to assess cerebral involvement. Additionally, the patient will be evaluated for adrenal insufficiency (by another blood test), as this is a common symptom of the disease that can be corrected.

### What are the symptoms of AMN?

- Like all of the categories of X-ALD, the symptoms of AMN can be quite variable. Below we have listed some of the symptoms that could be present, along with definitions as necessary.
- Difficulty in walking/change in walking pattern: this is the most common initial symptom of patients with AMN
- Spastic paraparesis: gradual, progressive weakness and stiffness of the legs; in AMN this is often specific to the lower limbs
- Ataxia: loss of the ability to coordinate muscle movement
- Hypertonia: excessive muscle tone
- Visual defects
- Dysarthria: Difficulty in articulating words, caused by impairment of the muscles used in speech
- Seizures: sudden convulsions/attacks/spasms
- Adrenal insufficiency: The adrenal glands are located above the kidneys, and are responsible for releasing certain hormones such as adrenaline and cortisol. These hormones are important in the control of blood pressure, heart rate, and sexual development and reproduction. In adrenal insufficiency, these hormones are not

produced at the appropriate levels and so these processes are not properly controlled. Adrenal insufficiency occurs in approximately 70% of men with AMN.

- Sexual dysfunction/impotence – This may be related either to involvement of the spinal cord or the testes themselves. The latter is relatively uncommon. It can be diagnosed by measuring testosterone levels in plasma.
- Behavioral changes
- Bladder dysfunction
- Mild peripheral neuropathy
- Weight loss
- Nausea

### **What are the treatments for AMN?**

One of the possible symptoms of patients with AMN is adrenal insufficiency. The adrenal glands are located above the kidneys, and are responsible for releasing certain hormones such as adrenaline and cortisol. These hormones are important in the control of blood pressure, heart rate, and sexual development and reproduction. In adrenal insufficiency, these hormones are not produced at the appropriate levels and so these processes are not properly controlled. Adrenal insufficiency can be corrected by steroid replacement therapy, which generally will improve the quality of life of the patient. Failure to test for and treat adrenal insufficiency can lead to a fatal outcome. Only replacement dosage of steroids, which do not cause the side effects of “pharmacologic” doses, are required.

Another potential treatment for AMN is Lorenzo's oil, which is a mixture of two oils (glyceryl trierucate, or GTE, and glyceryl trioleate, or GTO). It is thought to aid in the normalization of the fatty acid levels. However, this oil does not seem to alter the progression of the disease once the brain is involved. It is not yet clear if Lorenzo's oil could prevent progression prior to onset of brain involvement.

### **If a man is diagnosed with AMN, should his children and other blood relatives be tested for the disease?**

This is a personal decision that can be made with the assistance of a genetic counselor. It is important to recognize that even if a man has a mild form of AMN without cerebral involvement, he could have relatives that develop severe X-ALD either in childhood or as adults, as the type of defect in the gene does not correlate directly to the clinical course of the disease. Because of this, he may want to have his family members tested for the presence of the defective gene, so that they can make informed decisions regarding whether or not to have children or whether to have prenatal testing for the disease. It should be noted that due to the pattern of inheritance (see fact sheet on pattern of inheritance) all of his daughters will be carriers, but none of his sons will be affected.