Nebraska Newborn Screening Program
Physician ACT sheet for REPEAT INCONCLUSIVE X-LINKED ADRENOLEUKODYSTROPHY (X-ALD) Result

You Should Do The Following:

☐ Consult with metabolic specialist on call. Please refer to the letter included within this packet.

☐ Notify baby's family of newborn screening results. Assess status of newborn and provide follow up information as discussed with the metabolic specialist.

☐ Arrange for follow up as specified by the metabolic specialist

Screening Test Results

Screening for X-ALD begins with measurement of a lipid (lysophosphatidyl-choline) containing the very long chain fatty acid, C26:0. If the C26:0 remains elevated on the requested repeat newborn screen, the lab reflexes to DNA sequencing of the *ABCD1* gene, which is causative for X-ALD.

Condition Information

X-ALD is a peroxisomal disorder that is inherited on the X chromosome. Therefore, males with an X-ALD mutation are affected. Females with the same X-ALD mutation are considered carriers. The mutation for X-ALD results in deficiency of a protein (ALDP), which transports very long chain fatty acids (VLCFAs) into peroxisomes for subsequent degradation. As a result of this deficiency, VLCFAs accumulate in the body. High levels of VLCFAs may be toxic to the adrenal cortex leading to insufficient adrenal function. Elevated VLCFAs can also be toxic to myelin resulting in demyelination and progressive neurologic symptoms.

There is wide variability in severity and age of onset, even among family members. Adrenal insufficiency can develop in males with any form of X-ALD and at any age.

In **males,** there are **three clinical types** of X-ALD and **newborn screening cannot distinguish between them.** The three types and symptoms <u>if untreated</u>, include:

Childhood cerebral ALD—learning and behavior problems begin before age 10 and progress to multiple neurologic symptoms leading to total disability and death within a few years of symptom onset.

Adrenomyeloneuropathy (AMN)—adults develop progressive spastic paraparesis, peripheral neuropathy, bladder problems, and adrenocortical insufficiency.

Addison disease only—adrenocortical insufficiency. Most will eventually develop features of AMN by mid-adult years.

Many **carrier females** develop symptoms of myelopathy in their later adult years. Cerebral or adrenal disease is very rare.

Treatment

Treatments will be determined in consultation with specialists. Close follow up is important for initiation of treatment at the appropriate time. Treatments can include adrenal hormone replacement and, for boys with cerebral disease, hematopoietic stem cell transplantation.

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