Arkansas Department of Health
Newborn Screening Result: Elevated C26:0 LCD
Infant may have X-linked Adrenoleukodystrophy (X-ALD)
Interpretation Sheet for Health Professionals

X-ALD is a rare genetic disorder found primarily in males. If occurs when the body cannot break down very long chain fatty acids known as VLCFA which are found in foods. The ABCD1 gene is either missing or not working properly causing the VLCFA's to build up in the body. The ABCD1 gene is located on the X chromosome. A mutation in the ABCD1 gene will cause X-ALD.

X-ALD is primarily found in males. Females that have the same gene mutation are carriers. There are three forms of X-ALD: a) childhood cerebral form (which is primarily found in males) b) adult onset (adrenomyeloneuropathy – referred to as AMN) c) Addison disease.

Not all infants who screen positive for elevated C26:0 LCD will have a confirmed diagnosis of X-ALD. However, timely confirmation of diagnosis will allow the early start of treatment and help reduce the risk of complications.

Screening result	Elevated C26:0 LCD
Interpretation	Infant may have X-ALD. This occurs most often in males.
Differential diagnosis	Other peroxisomal disorders including Zellweger spectrum disorders
Deficient enzyme	ALDP, a protein involved in the transmembrane transport of very long-chain fatty acids (VLCFA)
Symptom onset	Childhood in males, adulthood in females
Symptoms	No clinical signs are expected in newborns. In infancy: poor feeding, bony abnormalities, abnormal liver function testing, hypotonia, renal cysts, sphincter paraparesis and increased skin pigmentation. Males develop adrenocortical insufficiency in childhood, with later development of progressive myelopathy and peripheral neuropathy. Some males can develop a fatal cerebral demyelinating disease instead. Female patients can develop progressive myelopathy and peripheral neuropathy decades later.
Natural history without treatment	Ranges from isolated adrenocortical insufficiency and slowly progressing myelopathy over decades, to devastating cerebral demyelination in childhood
Diagnostic evaluation	No confirmatory labs requested. Contact metabolic genetic specialist for assistance with interpretation of results: Call the Arkansas Children's Newborn Screening Coordinator for assistance with clinical evaluation and testing. You can call Arkansas Children's at 501-364-1100 and ask to page the UAMS Newborn Screening Coordinator
Treatment	Adrenal steroid replacement for adrenal insufficiency. Hematopoietic stem cell transplantation may be helpful
Inheritance	X linked mutation in the ABCD1 gene
Population incidence	1:17,000 for males and females (estimated)

Communicating Results to Parents

Reassure the parents. Not all cases that are screened positive will have a diagnosis. Further testing is required to confirm or rule out the diagnosis. If the infant is doing well, reassure the parents and ensure that the parents understand the importance of following recommendations for any subsequent testing and/or referrals to a specialist. Once diagnosis is confirmed, parents should realize that metabolic intervention is available, but treatment is not curative. The infant will be followed up by the metabolic specialists for long-term management, monitoring and compliance with treatment recommendations that are essential to the child's well-being. Genetic counseling services are indicated to understand risk of recurrence and reproductive options.

For more information visit:

Arkansas Department of Health Newborn Screening Program website at http://www.arnewbornscreening.com.
https://www.huntershope.org/family-care/leukodystrophies/adrenoleukodystrophy/
https://rarediseases.org/rare-diseases/adrenoleukodystrophy/
https://www.babysfirsttest.org/newborn-screening/conditions/adrenoleukodystrophy