USEFUL FOR
Second-tier newborn screen for X-linked adrenoleukodystrophy (X-ALD)

GENETICS TEST INFORMATION
This test is used as a second-tier newborn screen for X-linked adrenoleukodystrophy (X-ALD).

CLINICAL INFORMATION
This assay measures C20, C22, C24, and C26 lysophosphatidylcholine (LPC) species in dried blood spots by liquid chromatography-tandem mass spectrometry.

Peroxisomes are organelles present in all human cells except mature erythrocytes. They carry out essential metabolic functions including beta-oxidation of very long-chain fatty acids (VLCFA), alpha-oxidation of phytic acid, and biosynthesis of plasmalogens and bile acids. Peroxisomal disorders include 2 major subgroups: disorders of peroxisomal biogenesis and single peroxisomal enzyme/transporter defects. Peroxisome biogenesis defects such as Zellweger spectrum syndrome are characterized by defective assembly of the entire organelle, whereas in single enzyme/transporter defects such as X-linked adrenoleukodystrophy, the organelle is intact, but a specific function is disrupted. These disorders are clinically diverse and range in severity from neonatal lethal to later onset milder variants.

X-linked adrenoleukodystrophy (X-ALD) is a disorder affecting the nervous system, adrenal cortex, and testis. It is the most common of the peroxisomal disorders, affecting 1 in 17,000 to 1 in 21,000 males. At least 50% of all females who are heterozygotes for X-ALD are symptomatic. A defect in the ABCD1 gene is responsible for the disease. X-ALD shows a wide range of phenotypic expressions. The clinical phenotypes occurring in males can be subdivided in 4 main categories: cerebral inflammatory, adrenomyeloneuropathy (AMN), Addison only, and asymptomatic. The first 2 phenotypes account for almost 80% of the patients, while the frequency of the asymptomatic category diminishes with age and it is very rare after age 40. It is estimated that approximately 50% of heterozygotes develop an AMN-like syndrome. Treatment options are hormone replacement therapy, dietary intervention, or hematopoietic stem cell transplantation.

Elevations of C24 lysophosphatidylcholine (LPC) and C26 LPC may be indicative of X-ALD. In 2016, X-ALD was added to the US Recommended Uniform Screening Panel (RUSP), a list of conditions that are nationally recommended for newborn screening by the Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children. Therefore, measurement of LPCs is a useful second-tier test for newborn screening for X-ALD.

TEST ID: LPCBS
LYSOPHOSPHATIDYLCHOLINES BY LC MS/MS, BLOOD SPOT

REFERENCE VALUES

<table>
<thead>
<tr>
<th>ANALYTE</th>
<th>NORMAL RANGE (MCG/ML)</th>
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<tbody>
<tr>
<td>C20 Lysophosphatidylcholine</td>
<td>Not applicable</td>
</tr>
<tr>
<td>C22 Lysophosphatidylcholine</td>
<td>Not applicable</td>
</tr>
<tr>
<td>C24 Lysophosphatidylcholine</td>
<td>≤0.25</td>
</tr>
<tr>
<td>C26 Lysophosphatidylcholine</td>
<td>≤0.20</td>
</tr>
</tbody>
</table>

ANALYTIC TIME
2 days

06/2017

CONTENT AND VALUES SUBJECT TO CHANGE. SEE THE MAYO MEDICAL LABORATORIES TEST CATALOG FOR CURRENT INFORMATION.
Zellweger syndrome spectrum (ZSS) is a continuum of severe disorders affecting the nervous system, vision, hearing, and liver function. Most individuals present in infancy, but adult patients have been identified. The prevalence of ZSS is 1 in 50,000. ZSS follows autosomal recessive inheritance. At least 12 different genes have been implicated in ZSS, with approximately 60% to 70% of mutations occurring in \textit{PEX1}. The clinical phenotypes include Zellweger syndrome, neonatal adrenoleukodystrophy (NALD), and infantile Refsum disease (IRD).

Individuals with Zellweger syndrome typically die within the first year of life without making any developmental progress. Individuals with NALD or IRD typically present in childhood with developmental delays, vision loss, hearing loss, and have a much slower disease progression. There is no specific treatment for ZSS. Although ZSS disorders are not a primary disease target for testing, this test will detect infants with these disorders.

**INTERPRETATION**

An interpretive report is provided.

In females: Elevations of C24 LPC or C26 LPC may be indicative of heterozygosity for X-linked adrenoleukodystrophy (X-ALD), or other forms of peroxisomal disorders.

In males: Elevations of C24 LPC or C26 LPC may be indicative of X-ALD or other forms of peroxisomal disorders.

Abnormal results are not sufficient to conclusively establish a diagnosis of a particular disease. To verify a preliminary diagnosis based on the analysis, independent biochemical (eg, in vitro enzyme assay) or molecular genetic analyses are required.

**CLINICAL REFERENCE**

