

COULD IT BE LAL-D? THESE SIGNS, SYMPTOMS, AND LAB VALUES SHOULD RAISE SUSPICION FOR LAL-D¹⁻⁶

Any of the following should increase suspicion of LAL-D:

- ✓ Unexplained hepatomegaly¹
- ✓ Cryptogenic cirrhosis¹
- ✓ Microvesicular or mixed steatosis¹
- ✓ Persistently elevated ALT with^{1,2,a,b}
 - LDL-c (mmol/L): ≥ 3.4 ^{2,3,a,c} or
 - HDL-c (mmol/L): ≤ 1.2 ^{2,3,a,d}
- ✓ Suspected NAFLD/NASH with any of the following:
 - Persistently elevated ALT^{1,2,a,b} and
 - LDL-c (mmol/L): ≥ 3.4 ^{2,3,a,c} or
 - HDL-c (mmol/L): ≤ 1.2 ^{2,3,a,d}
 - BMI \leq 95th percentile^{1,4,e}
 - Elevated ALT despite weight loss^{1,2,4,b}
 - Rapidly progressive fibrosis/cirrhosis⁵

TEST FOR LAL-D IF YOU RECOGNIZE ANY OF THESE SIGNS, SYMPTOMS, OR LAB VALUES IN YOUR PATIENTS¹⁻⁶

^aAt baseline, patients in a clinical trial evaluating a potential treatment for LAL-D had a mean LDL-c of 5.4 mmol/L and a mean HDL-c of 0.8 mmol/L; 73% (48/66) of patients had ALT ≥ 1.5 x ULN and < 3 x ULN, and 27% (18/66) of patients had ALT ≥ 3 x ULN. An ALT ≥ 1.5 x ULN according to specified gender-specific normal ranges was one of the eligibility criteria for enrollment.^{2,4}

^bAbove age- and gender-specific ULN.¹

^cIn adult patients (mmol/L): LDL-c ≥ 4.1 (≈ 3.4 in patients on LLMs).^{1,2,6}

^dIn adult patients (mmol/L): HDL-c ≤ 1.0 (males)/ ≤ 1.3 (females).^{1,2,6}

^eBMI \leq 95th percentile for age and gender.^{1,4}

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; HDL-c, high-density lipoprotein cholesterol; LAL-D, Lysosomal Acid Lipase Deficiency; LDL-c, low-density lipoprotein cholesterol; LLM, lipid-lowering medication; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; ULN, upper limit of normal.

AN ENZYMATIC DBS TEST CAN HELP DIAGNOSE LAL-D^{1,7}

The DBS test is highly accurate and easy to prepare, transport, and interpret for testing in high-risk populations^{7,8}

PREPARATION



A blood sample is spotted onto the DBS card; once completely dry, LAL activity is measured using a specific LAL inhibitor⁷

STORAGE



DBS can be stored at room temperature for short periods or at -20°C for longer periods⁷

TRANSPORT



DBS can be easily shipped via regular mail⁸

INTERPRETATION OF LAL ENZYME DBS RESULTS⁴

RESULTS	CLINICAL INTERPRETATIONS
Affected	LAL-D confirmed by reduced LAL activity
Indeterminate ^a	Repeat with fresh sample
Not affected	Rules out LAL-D

^aLAL above cutoff for affected, but below the normal reference range.

- Measurement of LAL activity in leukocyte and fibroblast samples can also be used to test for LAL-D³
- Testing for LAL-D may be simplified through the use of an EMR system
 - » If the LAL-D DBS test is available through your EMR system, create a preference list that includes LAL-D among the tests that you typically order for a liver or lipid diagnostic workup
- Family screening of identified patients is also critical³

TEST FOR LAL-D WITH AN ENZYMATIC DBS TEST^{1,7}

Abbreviations: DBS, dried blood spot; EMR, electronic medical record; LAL, lysosomal acid lipase.

References: 1. Reiner Z, et al. *Atherosclerosis*. 2014;235:21-30. doi:10.1016/j.atherosclerosis.2014.04.003. 2. Burton BK, et al. *N Engl J Med*. 2015;373:1010-20. doi:10.1056/NEJMoa1501365. 3. Bernstein DL, et al. *J Hepatol*. 2013;58:1230-43. doi:10.1016/j.jhep.2013.02.014. 4. Data on file, Alexion Pharmaceuticals. 5. Burton BK, et al. *J Pediatr Gastroenterol Nutr*. 2015;61:619-25. doi:10.1097/MPG.0000000000000935. 6. Daniels SR, et al. *Pediatrics*. 2008;122:198-208. doi:10.1542/peds.2008-1349. 7. Hamilton J, et al. *Clin Chim Acta*. 2012;413:1207-10. doi:10.1016/j.cca.2012.03.019. 8. Grüner N, et al. *J Vis Exp*. 2015;97:e52619. doi:10.3791/52619.

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