LABupdate

New ALT Reference Intervals for Children and Adults

Background

Serum liver chemistry tests provide a useful and cost-effective evaluation of liver function. They are ordered regularly for individuals who are asymptomatic—for routine screening, blood banking, and physical examinations to obtain life insurance—as well as for inpatients with medical or surgical issues unrelated to liver fuction.[1] The most commonly used serum liver chemistry tests are alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, alkaline phosphatase, prothrombin time, serum albumin, γ-glutamyltransferase (GGT), bile acids, 5′-nucleotidase, and lactate dehydrogenase.[1]

One of the major markers of hepatocellular damage is ALT.[1] ALT activity occurs predominantly in the liver; however, significant activity also occurs in the kidneys, heart, skeletal muscle, pancreas, spleen, and lung tissue. Consequently, elevated levels of ALT may indicate myocardial infarction, hepatic disease, muscular dystrophy, and organ damage.[1,2] Parenchymal liver disease is the most common reason for elevated ALT, since ALT is more liver-specific than elevated AST.[1,2]

Evaluation of Elevated ALT Levels

The American Gastroenterology Association categorizes elevations in ALT levels depending on the magnitude of elevation (see below) in order to narrow the differential diagnosis for the possible cause of liver damage.[1]

Mild elevation (less than five times the upper limit of the reference interval). Common etiology may be[1]:

- Chronic hepatitis B or C
- Acute viral hepatitis (A–E, EBV, CMV)
- Steatosis/steatohepatitis
- Hemochromatosis
- Medications/toxins
- Autoimmune hepatitis
- α_1-Antitrypsin deficiency
- Wilson's disease
- Celiac disease
- Alcohol-related liver injury
- Cirrhosis

(Nonhepatic reasons: hemolysis, myopathy, thyroid disease, strenuous exercise.)

Severe elevation (greater than 15 times the upper limit of the reference interval). Common etiology may be[1]:

- Acute viral hepatitis (A–E, herpes)
- Medications/toxins
- Ischemic hepatitis
- Autoimmune hepatitis
- Wilson's disease
- Acute bile duct obstruction
- Acute Budd-Chiari syndrome
- Hepatic artery ligation

Rationale for Changing ALT Reference Intervals

The high specificity of ALT for liver damage makes accurate population-based reference intervals critical for medical decisionmaking; however, reference intervals for serum ALT vary widely among laboratories. Often the reference subjects used for reference interval studies were not well defined and may have included subjects with subclinical liver disease.

One study (that included more than 6000 total subjects) carefully selected certain subjects with low risk for subclinical liver disease and found the upper limits for normal ALT to be as low as 30 U/L for males and 19 U/L for females.[3] In addition, ALT activity in patients with viral hepatitis, who achieved sustained virologic response, was often below 30 U/L. This suggests that necroinflammatory activity was present before treatment at ALT levels above 30 U/L.[3] A recent review of new developments in the evaluation of patients with chronic hepatitis B reported that ALT levels of 45 U/L or lower were associated with higher HBV antigen seroclearance.[4] Guidelines from the National Academy of Clinical Biochemistry indicated that a value of 45 U/L in men is a clinically useful upper limit of reference intervals for ALT.[5]

In 2010, included in the American Gastroenterology Association publication, *Clinical Gastroenterology and Hepatology,* was an important study on the proper cut-off values for the reliable detection of chronic pediatric liver disease. The authors found that the upper limits of ALT used in children's hospitals is usually set too high and does not reliably detect chronic liver disease in children and suggested the upper limits for children 12 to 17 years old be 26 U/L for boys and 22 U/L for girls.[6]

New Reference Intervals

Recently, LabCorp conducted an internal study of ALT reference intervals that included more than 260,000 male and female subjects. The results demonstrated a close correlation to other investigations. The new ALT reference intervals are calculated as below.[7]

Gender	Age Range (Years)	ALT (U/L)
Female	0–11	<29
	12–17	<25
	≥18	<33
Male	0–11	<30
	12–17	<31
	≥18	<45

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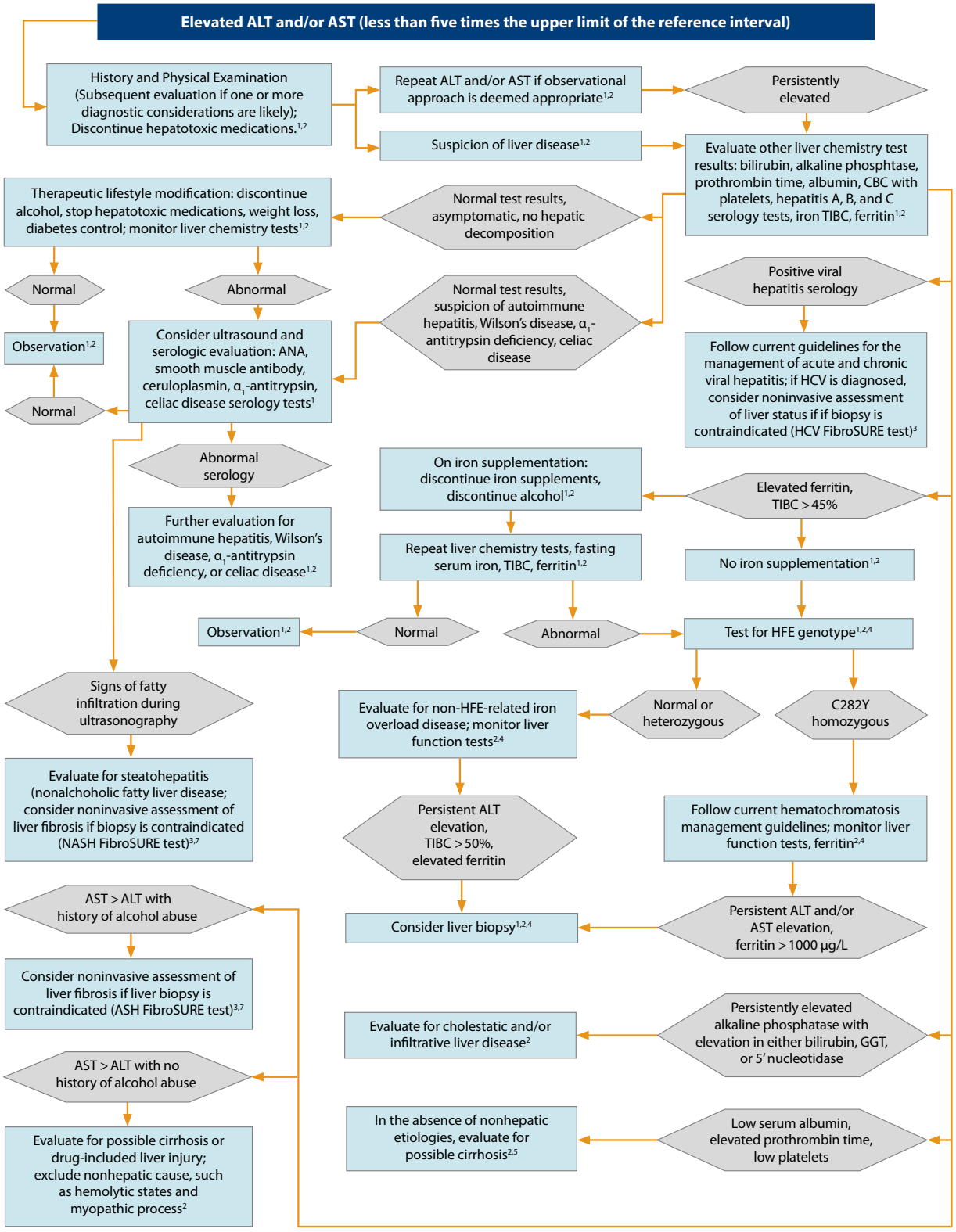
Clinical and Laboratory Evaluation of Mild Elevations of Serum ALT and/or AST



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