

Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)

Introduction

When certain types of cells are damaged, they may leak enzymes into the blood, where they can be measured as indicators of cell damage. Alanine aminotransferase (ALT) is one such enzyme. It is markedly elevated in hepatitis and from other acute liver damage. The enzyme, aspartate amino-transferase (AST), has a similar role, but found in other tissues, such as the heart (striated muscle), so it is not as specific to the liver. In viral hepatitis and other forms of liver disease associated with hepatic necrosis, blood levels of ALT and AST are elevated even before the clinical signs and symptoms of disease (such as jaundice) appear.¹ Therefore, ALT and AST levels are elevated in patients with cardiovascular disease, liver disease and muscle disease.

What are ALT and AST?

ALT and AST are members of the transaminase family of enzymes. ALT and AST are sometimes called glutamate pyruvate transaminase (GPT) and glutamate oxaloacetate transaminase (GOT), respectively. Transaminases, also referred to as *aminotransferases*, facilitate certain chemical reactions within cells. An enzyme is a protein produced by living organisms which functions as a biochemical catalyst. An enzyme initiates or accelerates a chemical reaction without itself being affected or consumed in the reaction.²

ALT, produced mainly in the liver, catalyzes the transfer of amino groups between L-alanine and glutamate to meet physiological needs. AST catalyzes the transfer of amino and keto groups between alpha-amino acids and alpha-keto acids thereby acquiring the term transferase.²

Why measure ALT and AST?

ALT is found in large amounts in the liver, and small amounts of this enzyme are also found in the heart, muscle, and kidney. When the liver is injured or inflamed, the levels of ALT in the blood usually rise; therefore, this test is performed to check for signs of liver disease.

AST is found in many body tissues including the heart, muscle, kidney, brain, and lung. It is also present in the liver. When body tissue or an organ such as the heart or liver is damaged, additional AST is released into the bloodstream. The amount of AST in the blood is directly related to the extent of the tissue damage.

A side effect of some lipid-lowering drugs (the statin group), in about 1% of patients receiving this therapy, is a persistent increase in blood levels of transaminases (ALT and AST) to more than 3 times the upper limit of normal. Patients who have experienced these increases usually have no symptoms. Therefore it is important to monitor liver enzyme activity in patients on lipid-lowering drug therapy. It is recommended that ALT and AST tests be performed prior to the initiation of therapy to establish a baseline enzyme level and on a regular basis thereafter. Increases in blood transaminase levels generally occur in the first 3 months of treatment with statins. Patients who develop increased transaminase levels should be monitored until the abnormalities resolve. An increase in ALT and/or AST to more than 3 times the upper limit of normal may be an indication for discontinuing drug therapy. ALT and AST levels typically return to normal after drug therapy is discontinued.

Physicians, on a routine basis, will include the measurement of ALT and AST, as part of a *chemistry profile*, to aid in the diagnosis of cardiac or liver disease. Serum ALT levels increase rapidly when the liver is damaged by any cause including: hepatitis, hepatic cirrhosis, liver tumor, obstructive jaundice, Reye's syndrome or hepatotoxicity of certain drugs.³ Serum levels of AST are elevated to some degree in almost all types of liver disease. Some non-hepatic causes of elevated AST are seen with myocardial infarction (MI), severe arrhythmias, severe angina, skeletal muscle necrosis and renal necrosis.

Although serum levels of both ALT and AST become elevated whenever disease processes affect liver cells, ALT is the more liver-specific enzyme. Elevations of ALT activity persist longer than do those of AST activity.⁴ Measurement of both ALT and AST has some value in distinguishing hepatitis from other parenchymal lesions.

Because of the high concentration of AST in heart muscle, patients with acute myocardial infarction (MI) usually develop elevated levels, 4 to 10 times normal, within 6-12 hours of the cardiac event. AST levels will peak in 24-36 hours and return to normal limits within 3-4 days provided another injury has not occurred.

AST/ALT ratio

The ratio of AST to ALT (AST:ALT, calculated by dividing the AST value by the ALT value) can sometimes help determine whether the liver or another organ has been damaged. Both ALT and AST levels are reliable indicators of liver damage. The AST to ALT ratio may sometimes help determine if liver damage is related to alcohol dependence.^{3,5}

Reference Range

The reference range for ALT and AST on the Cholestech LDX System is:

ALT = 10 - 40 U/L at 37°C

AST = 10 - 30 U/L at 37°C

The highest elevations of ALT are found in cases of drug and viral hepatitis, acute heart failure and exposure to hepatotoxins such as carbon tetrachloride. Values may reach 20 to 100 times the upper limit of the reference range. Five- to 10-fold elevations of ALT occur in patients with primary or metastatic carcinoma of the liver. In infectious mononucleosis, with liver involvement, elevations may be up to 20 times the upper limit of the reference range.

Extremely high levels of AST (>1000) occur in severe liver necrosis, skeletal muscle damage and acute myocardial infarction. Minor elevations can be seen in congestive heart failure, pericarditis, cirrhosis, metastatic liver disease, skeletal muscle disease, and generalized infections such as infectious mononucleosis.

Note: Samples with ALT or AST enzyme activity greater than 1000 U/L may consume the substrate prior to the measurement of enzyme activity and could yield falsely low results.

Testing on the Cholestech LDX®

Instructions for running the ALT•AST test will be found in the package insert in each box of ALT•AST cassettes. Please read the ALT•AST package insert before running an ALT•AST test and note the following:

Fingerstick samples for the ALT•AST test cassette can sit for up to 5 minutes in the capillary tube. Place the cassette into the drawer of the analyzer immediately after dispensing the sample into the well. After

pressing RUN, ALT and AST results and the AST/ALT ratio will be displayed in 5 minutes.

Hematocrit levels between 30% and 50% do not affect results.

Assays for ALT and AST may be run at different temperatures: both 30°C and 37°C are common in clinical diagnostic laboratories. Enzyme levels are very dependent on temperature, with higher temperatures producing higher ALT and AST results. The Cholestech LDX ALT•AST cassette is calibrated to provide results which are equivalent to results run at 37°C. If you are going to compare the LDX results with another method make sure the comparison method is run at 37°C.

Blood samples from patients taking therapeutic doses of statin and glitazone drugs were tested and no interference with the Cholestech ALT and AST tests was found.

Quality Control

CLIA regulations require that customers follow manufacturer's recommendations.

Quality control must be run routinely to show that your system is giving accurate results. We recommend the following quality control procedures for the Cholestech LDX System:

- With each new shipment of cassettes (even if cassettes are from the same lot previously received).
- With each new lot of cassettes.
- As otherwise required by your laboratory's standard quality control procedures.
- If you are not running the Cholestech LDX under CLIA-waived status, or if your local or state regulations require more frequent testing of quality control material, then quality control must be

performed in compliance with those regulations.

If the controls do not perform as expected, repeat the test or contact Cholestech Technical Service (800 733.0404) before testing patient specimens.

The quality control results must be in range before testing patient specimens. See the Cholestech LDX User Manual if they are not.

CPT codes

Waived ALT 84460QW

Waived AST 84450QW

References

1. Dufour DR, Lott JA, Nolte FS, Gretch DR et al. Diagnosis and monitoring of hepatic injury. II. Recommendations for use of laboratory tests in screening, diagnosis, and monitoring. Clin Chem 2000; 46:2050-68.
2. Tolman KG, Rej R. Liver function. In: Burtis CA, Ashwood ER, editors. Tietz Textbook of Clinical Chemistry. Philadelphia, PA: W.B. Saunders Company, 1999: 1125-1177.
3. Pratt DS, Kaplan MM. Evaluation of abnormal liver-enzyme results in asymptomatic patients. N Engl J Med 2000; 342:1266-71.
4. Johnston DE. Special considerations in interpreting liver function tests. Am Fam Physician 1999; 59:2223-30.
5. Rochling FA. Evaluation of abnormal liver tests. Clin Cornerstone 2001; 3:1-12.

To assist you with any further questions, please call Technical Service: 800-733-0404

CHOLESTECH 

3347 Investment Blvd.
Hayward, CA 94545 U.S.A.
Tel 800 733.0404
Fax 510 732.7227
www.cholestech.com