

ALT (GPT) — Alanine Aminotransferase

Introduction

The purpose of this technical bulletin is to provide information about Alanine Aminotransferase (ALT), how and why it is measured, applications for use, its significance in human health and disease, and important notes about the procedure for testing ALT on the Cholestech LDX®.

ALT is found in many tissues in the body, including kidney, heart, skeletal muscle, pancreas, spleen, lung, and red blood cells, but the largest concentration resides in the liver. Large quantities of ALT are released into the bloodstream when the liver is damaged. Therefore, the measurement of ALT is useful in the diagnosis and monitoring of hepatobiliary disease states such as chronic alcohol ingestion, exposure to hepatotoxins, liver damage caused by certain medications, and following infections such as viral hepatitis. In viral hepatitis, and other forms of liver disease or damage, levels of serum ALT may be elevated even before clinical signs and symptoms of the disease, such as jaundice, appear.

ALT is also normally present in human plasma, bile, cerebrospinal fluid and saliva. ALT is not found in the urine unless a kidney lesion is present.

Waived Status Approved for the Cholestech ALT Test

Cholestech received approval for waived status for the ALT test on 4/13/01. The Cholestech ALT test is the first ALT test to receive waived status. The ALT test is only waived for the testing of capillary (fingerstick) or venous whole blood. If you use serum for ALT testing you will be classified as moderately complex.

Even though the Cholestech LDX is a CLIA "Waived" test system, each laboratory or testing site using the LDX must have a CLIA Certificate of Waiver. To obtain a Certificate of Waiver, call your state department of health or Cholestech Technical Service (800-733-0404) for an application.

The ALT test is waived under CLIA '88 regulations. If a laboratory modifies the test system instructions, then the test is considered high complexity and subject to all CLIA requirements.

What is ALT?

ALT, also known as alanine aminotransferase, belongs to a group of substances called enzymes. 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. The enzyme ALT is a member of the transaminase family of enzymes. Transaminases act in the transfer of amino groups in various reactions.

ALT, produced mainly in the liver, catalyzes the transfer of amino groups between L-Alanine and glutamate to meet physiological needs.

Why Measure ALT?

The measurement of ALT is used on a routine basis by physicians to diagnose and monitor liver disease. It is often part of a Chemistry Profile. ALT is also used by blood banks as a screen for liver damage in potential blood donors. 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.

Although it is present in skeletal muscle, heart and kidney tissue, it is primarily used to diagnose and monitor liver disease.

A side effect of some lipid-lowering drugs (the statin group), in about 1% of patients receiving this therapy, is a persistent increase in serum ALT 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 activity in patients on lipid-lowering drug therapy. It is recommended that liver function tests be performed prior to the initiation of therapy and on a regular basis thereafter. Serum ALT increases generally occur in the first 3 months of treatment with statins. Patients who develop increased ALT levels should be monitored until the abnormalities resolve. An increase in ALT to more than 3 times the upper limit of normal may be an indication for discontinuing drug therapy. ALT levels typically return to normal after drug therapy is discontinued.

The FDA has also recently recommended that patients on the glitazone class of diabetes drugs (i.e. Actos® and Avandia®) have their liver function monitored every month for at least eight months and every 2 months for the remainder of the first year.

ALT Reference Range:

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

10 - 40 U/L at 37°C

Values in men are slightly higher than in women.

ALT may be slightly elevated in apparently healthy individuals due to the following factors: obesity, male gender, Hispanic or American-Indian descent, persons aged 25 - 35 years, alcohol use and long-term acetaminophen use. The upper limit of the reference range may vary in different geographic areas of the country due to the same factors.

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.

ALT Testing on the Cholestech LDX

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

- Fingerstick samples must be applied *immediately* after collection. Do not let the blood sample sit in the capillary tube before dispensing it into the sample well. Place the cassette into the drawer of the analyzer immediately after dispensing the sample into the well.
- When running controls, serum, whole blood, proficiency testing or calibration verification material use the *tan colored 35 µL Mini-Pet* or a pipette which delivers 35 µL. Do not use the gray 50 µL Mini-Pet for ALT.
- There is a separate Cholestech ALT control available for use with the ALT test cassette. Refer to the ALT control assay sheet for information regarding the appropriate setting for the sample type when running ALT controls.

- Hematocrit levels between 30% - 50% do not affect results.
- Assays for ALT may be run at different temperatures, 30°C or 37°C. Enzyme levels are very dependent on temperature, with higher temperatures producing higher ALT results. The Cholestech LDX ALT is calibrated to provide results which are equivalent to results run at 37°. 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 test 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.

Choice of Materials

A high and a low control is preferred. Cholestech recommended controls work well with the Cholestech LDX System. If you use other controls, you will need to set ranges for the Cholestech LDX System.

Handling

- Follow the instructions that come with your controls.
- Check the expiration date before use. Do not use if expired.

External Quality Control

External controls must be used to demonstrate that the reagents and assay procedure perform properly. Liquid ALT Level 1 and Level 2 controls are available from Cholestech. Controls must be tested:

- 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.

Good Laboratory Practice principles suggest that external controls must be run whenever the laboratory director has any question about test system integrity or operator technique (e.g., when reagents may have been stored or handled in a way that can degrade their performance or when operators have not performed a particular test in recent weeks).

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 should be in range before testing patient samples. See the Cholestech LDX User Manual if they are not.

Moderate Complexity

If you will be running the Cholestech ALT Test under CLIA Moderately Complex status, there are a few important points to remember:

Sample Type

Any sample type may be used—fingerstick or venous whole blood, serum or plasma. Run fingerstick or venous whole blood in the "Whole B." mode. When running serum or plasma change the Sample Type in the Configuration Menu to "Serum".

Quality Control

When testing under CLIA Moderately Complex status, quality control material should be tested:

- On each new shipment of cassettes
- On each lot of cassettes received
- If you think cassettes may not have been stored properly
- Each day that patient samples are tested

Proficiency Testing

Proficiency testing is required when testing under CLIA Moderately Complex status. Cholestech recommends the following proficiency testing agencies for ALT:

CAP The College of American Pathologists
EXCEL Program
325 Waukegan Road
Northfield, Illinois
60093-2750
(800) 323-4040

WSLH Wisconsin State Laboratory of Hygiene
465 Henry Mall,
Room GCD
Madison, WI 53706
(800) 462-5261

API American Proficiency Institute
1159 Business Park Drive
Traverse City, MI 49686
(800) 333-0958

Calibration Verification

Call Cholestech Technical Service, 800-733-0404, for recommended Calibration Verification material.

The CPT code for waived ALT is 84460QW.

Cholestech ALT Catalog No.: 11-772

References

1. Sherman KE, Alanine Amino-transferase in Clinical Practice, A Review, Arch Intern Med, Vol 151, 260-265 (1991).
2. Burtis CA, Ashwood, ER (Ed), Tietz Textbook of Clinical Chemistry, Third Edition W.B. Saunders Co., Philadelphia, PA, (1999).

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

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