

Lactate dehydrogenase

Human lactate dehydrogenase isoenzymes are primarily used by cells in specific tissue. Human LDH Isoenzymes, also known as lactic dehydrogenase, are responsible for converting muscle lactic acid into pyruvic acid, an essential step in producing cellular energy.

When injury occurs, cells containing specific LDH isoenzymes are released in the bloodstream. Analyzing specific LDH isoenzyme ratios helps identify certain patterns in order to aid in the diagnosis of disease such as heart attack, lung injury, lung disease, liver or muscle disease, advanced cancers and autoimmune diseases.

Human lactate dehydrogenase LD(LDH) isoenzyme elevation associations:

Human LD1 isoenzyme : germ cell tumors

Human LD1 > LD2 isoenzyme : renal or myocardial infarction, megaloblastic anemia, hemolysis

Human LD3 isoenzyme : platelet destruction, reactive, lymphadenopathy, lymphoma, lymphocytosis, pulmonary infarction, pneumonia, advanced cancer, acute pancreatitis

Human LD4 isoenzyme various solid tumors

Human LD5 isoenzyme : primary liver disease, liver anoxia, muscle injury or dystrophy; All forms: renal disease, carcinomatosis, collagen vascular disease, overwhelming sepsis, DIC

Used in General Chemistry Controls by IVD Clinical diagnostic Manufactures such as Lee Bio-solutions also offers animal source lactate dehydrogenase. Lactate Dehydrogenase is available as Rabbit LDH Lactate dehydrogenase, chicken LDH lactate dehydrogenase, porcine LDH lactate dehydrogenase and bovine LDH lactate dehydrogenase.

Lactate dehydrogenase test

Definition

Lactate dehydrogenase, also called lactic dehydrogenase, or LDH, is an enzyme found in the cells of many body tissues, including the heart, liver, kidneys, skeletal muscle, brain, red blood cells, and lungs. It is responsible for converting muscle lactic acid into pyruvic acid, an essential step in producing cellular energy.

Purpose

Lactic dehydrogenase is present in almost all body tissues, so the LDH test is used to detect tissue alterations and as an aid in the diagnosis of heart attack, anemia, and liver disease. Newer injury markers are becoming more useful than LDH for heart attack diagnosis.

Precautions

Because the LDH enzyme is so widely distributed throughout the body, cellular damage causes an elevation of the total serum LDH. As a result, the diagnostic usefulness of this enzyme by itself is not as valuable as determination of the five fractions that comprise the LDH. These fractions are called isoenzymes and are better indicators of disease than is the total LDH. The fractions are LDH-1, LDH-2, LDH-3, LDH-4, and LDH-5. A normal total LDH level does not mean that individual isoenzyme levels should not be measured. Individual isoenzyme ranges can help differentiate a diagnosis.

Description

When disease or injury affects tissues containing LDH, the cells release LDH into the bloodstream, where it is identified in higher than normal levels. For example, when a person has a heart attack, the LDH level begins to rise about 12 hours after the attack and usually returns to normal within 5-10 days. The LDH is also elevated in diseases of the liver, in certain types of anemia, and in cases of excessive destruction of cells, as in fractures, trauma, muscle damage, and shock.

Cancers can also elevate LDH level. Additionally, some patients have chronically elevated LDH with no identifiable cause and no apparent consequence.

Preparation

This test requires a blood sample. It is not necessary for the patient to fast (nothing to eat or drink) before the test unless the physician requests it.

Normal results

Reference ranges for total LDH vary from laboratory to laboratory. Normal values are also higher in childhood. For adults, in most laboratories, the range can be up to approximately 200 units/L, but is usually found within 45-90 U/L.

Abnormal results

Due to the fact that many common disease processes cause elevations in the total LDH level, a breakdown of the five different isoenzymes that make up the total LDH is often helpful for diagnosis. In certain disorders, the total LDH may be within normal limits, but individual isoenzyme elevations can indicate specific organ or tissue damage. For example, the LDH-2 fraction is normally greater than LDH-1 in the blood. After an acute heart attack, however, the LDH-1 rises over the LDH-2 in what is known as a "flipped LDH."

Certain diagnoses can be assisted by determination of the total LDH. One example is infectious mononucleosis, in which the LDH is usually more elevated than a liver enzyme called AST. Conversely, in cases of viral hepatitis, the liver enzymes AST and ALT are greatly increased over the LDH.

Enzyme

A protein that regulates the rate of a chemical reaction in the body, increasing the speed at which the change occurs.

Isoenzyme

One of a group of enzymes that catalyze the same reaction but are differentiated by variations in physical properties.

Isolated elevated LD is a non-specific indicator of disease due to its ubiquitous tissue distribution. Increased levels can be found in:

- Liver diseases
- Myocardial infarction
- Haemolysis and ineffective erythropoiesis, e.g. megaloblastic anaemia
- Renal diseases, including tubular necrosis, pyelonephritis and renal infarction
- Skeletal muscle diseases
- Malignancies, particularly if bulky or if associated with metastases
- Numerous other disease processes involving tissue damage
- Macro-LD (LD-immunoglobulin complexes) is a rare cause of a raised LD level with a prevalence of about 0.03% in the general population.

Consideration should also be given to a high LD being due to difficulty experienced during collection or handling of the sample.

Although haemolysis is generally readily detected and reported by the laboratory, other effects including prolonged refrigeration of uncentrifuged blood or centrifuge overheating may lead to an artificial increase in the level. A repeat test clarifies the nature of the finding.

In the absence of other abnormal laboratory findings or clinical indicators, LD isoenzymes will often provide useful direction if the test is available.

A significant consideration in this patient is silent myocardial infarction several days prior to the sample collection. AST and CK fall earlier than LD (CK is only performed if specifically requested). A request for LD isoenzymes (LD1 approximately twice LD2 is characteristic) or preferably troponin will clarify the diagnosis.

Another possibility is unrecognised malignancy. Although this presentation is often accompanied by elevation of urate and if liver involvement, ALP and GGT, this is not always the case. LD

isoenzymes reveal elevation of LD2, 3 and 4.

Requesting a plethora of tumour markers is generally of limited value. Perhaps the most useful approach is further clinical examination and possibly addition of tests for multiple myeloma.

A common, less significant cause, particularly in the elderly, is the presence of heart valve pathology causing erythrocyte damage. This is usually accompanied by a reduced haptoglobin (mopping up freed haemoglobin) and frequently reticulocytosis and an elevation of the unconjugated bilirubin.

The clinical history generally clarifies the diagnosis. The LD isoenzymes show a mature red cell pattern (LD1 and 2). This finding is common to all causes of increased erythrocyte turnover including haemoglobinopathies, compensated ineffectual erythropoiesis, haematoma resorption, etc.

An unusual aetiology is low-grade skeletal myopathy or myositis. Although the CK is frequently elevated, this is occasionally not the case. Symptoms such as weakness or tiredness may have been dismissed in the history.

LD isoenzymes reveal an elevation of LD5 with a lesser elevation of LD4, a pattern that is essentially indistinguishable from a liver source, although a normal ALT argues strongly against the latter. To further clarify this possibility, autoantibody testing and thyroid function tests are useful.

Serum lactate dehydrogenase activity as a biomarker in children with sickle cell disease

Serum lactate dehydrogenase (LDH) levels were studied in children with HbSS and HbSC in a single institution, and their relationship to cerebral vasculopathy as assessed by transcranial Doppler scanning (TCD). All children with HbSS (n = 97) and HbSC (n = 18) who underwent a TCD scan should be studied. Lactate dehydrogenase

LDH levels were higher in HbSS patients than HbSC (581 IU/l vs. 305 IU/l, $P < 0.001$). In children with HbSS, LDH correlated significantly with haemoglobin, reticulocytes, aspartate transaminase and creatinine. Lactate dehydrogenase LDH also correlated positively and significantly with TCD measurements in the middle and anterior cerebral artery circulations in the children with HbSS.

Serum lactate dehydrogenase levels and glycolysis significantly correlate with tumor VEGFA

Objectives: In an attempt to elucidate the relationship between biomarkers of tumor hypoxia, glycolysis and angiogenesis, we tested the hypothesis that intratumoral gene expression of the hypoxia response (hypoxia inducible factor [HIF1alpha and 2alpha]), glycolysis (lactate dehydrogenase A [LDHA]), glucose metabolism (glucose transporter-1 [Glut-1]) and genes involved in angiogenesis (i.e., VEGFA , VEGFR1-3 , and neuropilin [NRP]1) are upregulated in metastatic colorectal cancer (mCRC) patients with high serum lactate dehydrogenase (LDH).

Patients and methods: 78 formalin-fixed, paraffin-embedded (FFPE) tumor samples were collected from 36 patients with mCRC. Tumor gene expression was correlated with serum Lactate Dehydrogenase LDH levels from the same group of patients. FFPE tissues were dissected using laser-captured micro-dissection and analyzed for gene expression using a quantitative real-time RT-PCR method.

Results: Intratumoral gene expression of VEGFA and VEGFR1 showed a statistically significant correlation with serum Lactate dehydrogenase LDH levels ($p = 0.006$, $r = 0.45$ and $p = 0.004$, $r = 0.50$, respectively). Intratumoral expression of LDHA gene showed a significant correlation with Glut-1, VEGF, HIF1alpha, HIF2alpha and VEGFR1 ($p = 0.007$, $r = 0.44$; $p < 0.001$, $r = 0.57$; $p = 0.013$, $r = 0.41$; $p = 0.044$, $r = 0.34$; $p = 0.026$, $r = 0.40$). Serum LDH levels also correlated with micro vessel density analyzed by immuno-histo-

chemical analysis.

Conclusion: The results demonstrated a significant correlation between the intratumoral gene expression of LDHA, HIF1alpha, HIF2alpha, Glut-1, NRP1, VEGFA and VEGFR1. Patients with high serum Lactate dehydrogenase LDH have increased intratumoral gene expression of VEGFA and VEGFR1. The results also support the hypothesis that serum LDH levels may serve as a surrogate marker for activation of the HIF-related genes in the tumor.