#### Lecture 7

# Alkaline phosphatase

## **Test description**

Alkaline phosphatase (ALP) is an enzyme found in the liver, bone, placenta, intestine, and kidneys but primarily in the cells lining the biliary tract and in the osteoblasts involved in the formation of new bone. The ALP is normally excreted from the liver in the bile. Increased ALP levels are found most commonly during periods of bone growth (as in children), in various types of liver disease, and in biliary obstruction. The ALP is also considered a tumor marker that increases in the case of osteogenic sarcoma and in breast or prostate cancer that has metastasized to the bone.

# **Specimen**

- Serum or plasma from a blood sample taken from a vein.
- Fasting for 10 to 12 hours is usually required before the test.

### **Normal values**

Female: 30-100 U/L, Male: 45-115 U/L

Elderly: Slightly higher norms

Children: One to three times adult norms

Puberty: Five to six times adult norms

### Conditions that increase or decrease ALP level

Increased in biliary obstruction, cancer of head of pancreas, bone metastasis, hyperparathyroidism, pregnancy and Paget's disease.

Decreased in lack of normal formation of bone, malnutrition, placental insufficiency, pernicious anemia and scurvy.

### **Contributing factors to abnormal values**

- (1) Hemolysis of the blood sample may alter test results.
- (2) Drugs that may increase ALP levels are numerous and include: ACE inhibitors, acetaminophen, anticonvulsants, heparin, antipsychotics, benzodiazepines, lipid lowering agents and NSAIDs.
- (3) Drugs that may decrease ALP levels: nitrofurantoin, propranolol and cyanides.

## Techniques for the determination of ALP

The method currently used to measure ALP activity is the AMP (2-amino-2-methyl-1-propanol) method. The current clinical method of quantifying ALP is the spectrophotometric method.

# Acid phosphatase

## **Test description**

Acid phosphatase, also known as prostatic acid phosphatase (PAP), is an enzyme found primarily in the prostate gland, with high concentrations found in the seminal fluid. It is found in smaller concentrations in the kidneys, liver, spleen, bone marrow, erythrocytes and platelets. Acid phosphatase is used to diagnose advanced metastatic cancer of the prostate. However with the advent of the prostate-specific antigen (PSA) test, monitoring of the acid phosphatase is decreasing in popularity. An additional use of acid phosphatase testing is testing for its presence in vaginal secretions during the investigation of cases alleged rape.

### **Specimen**

Serum or plasma. No fasting is required before the test.

#### **Normal values**

2.2-10.5 U/L

#### Conditions that increase PAP level

Increased in prostate cancer, sexual abuse, acute renal impairment, cirrhosis, hepatitis, hemolytic anemia, multiple myeloma.

## **Contributing factors to abnormal values**

- (1) Hemolysis of the blood sample may alter test results.
- (2) Any manipulation of the prostate gland, including rectal examination or cystoscopy, should be avoided for 2 days before the test.
- (3) Acid phosphatase levels vary during the day. Multiple tests of acid phosphatase should be drawn at the same time each day.
- (4) Drugs that may increase acid phosphatase: anabolic steroids, androgens, clofibrate.
- (5) Drugs that may decrease acid phosphatase: alcohol, fluorides, oxalates, and phosphates.

### **Techniques for the determination of PAP**

The spectrophotometric method is currently used.

### Alanine aminotransferase

# **Test description**

Alanine aminotransferase (ALT) or glutamic-pyruvic transaminase (GPT) is an enzyme found in the kidneys, heart, and skeletal muscle tissue, but primarily in liver tissue. Its functions as a catalyst in the reaction needed for amino acid production. The test is used mainly in the diagnosis of liver disease and to monitor the effects of hepatotoxic drugs.

The ALT is assessed along with aspartate aminotransferase (AST) in monitoring liver damage. These two values normally exist in an approximately 1:1 ratio. The AST is greater than ALT in alcohol – induced hepatitis, cirrhosis, and metastatic cancer of the liver. The ALT is greater than AST in the case of viral or drug induced hepatitis and hepatic obstruction due to causes other than malignancy.

The degree of increase in these enzyme levels provide information as to the possible source of the problem. A two fold increase is suggestive of an obstructive problem, often requiring surgical intervention. A 10 fold increase of ALT and AST indicates a probable medical problem such as hepatitis.

## **Specimen**

Serum or plasma. No fasting is required before the test

#### Normal values

Female: 7-30 U/L, Male 10-55 U/L

### Conditions that increase ALT level

Increased in hepatic diseases, congestive heart failure, muscle inflammation, shock, eclampsia and trauma.

# **Contributing factors to abnormal values**

- (1) Hemolysis of the blood sample may alter test results.
- 2) Drugs that may increase ALT levels are numerous and include: ACE inhibitors, acetaminophen, anticonvulsants, heparin, antipsychotics, benzodiazepines, lipid lowering agents and NSAIDs.

#### Clinical alerts

Liver enzymes, including ALT and AST, are routinely monitored in patients who take HMG-CoEnzyme A reductase inhibitors (statin medications), because one major side effect of statins use is liver toxicity.

### **Techniques for the determination of ALT**

Spectrophotometric detection is the widely used method.

## Aspartate aminotransferase

## **Test description**

Aspartate aminotransferase (AST) or glutamic oxaloacetic transaminase (GOT) is an enzyme found primarily in the heart, liver, and muscle. It is released into the circulation after injury or death of cells. The AST levels usually increase within 12 hours of the injury and remain elevated for 5 days. Thus, this test is one of several tests that are performed when there has been damage to the heart muscle, as in myocardial infarction (MI), and in assessing liver damage. Other cardiac enzymes also assessed are the creatine kinase (CK) isoenzymes, lactic dehydrogenase (LDH), and troponin.

## **Specimen**

Serum or plasma. No fasting is required before the test.

#### **Normal values**

Female: 9-25 U/L, Male: 10-40 U/L

Elderly: slightly higher norms.

Newborn: norms two to three higher.

#### Conditions that increase or decrease AST level

Increased in liver diseases, malignant hyperthermia, muscle inflammation, MI, shock, trauma, and severe burn.

Decreased in hemodialysis.

# **Contributing factors to abnormal values**

Drugs that may increase AST levels: acetaminophen, allopurinol, HMG CoA reductase inhibitors, isoniazid, oral contraceptives and methyldopa.

Drugs that may decrease AST levels: metronidazole, trifluoperazine.

#### Clinical alerts

When assessing for MI, this test is often performed on 3 consecutive days, and again in 1 week, necessitating multiple venipunctures.

### **Techniques for the determination of AST**

A spectrophotometric procedure is recommended.

## Lactate dehydrogenase

## **Test description**

Lactate dehydrogenase (LDH) or (LD) is an intracellular enzyme found primarily in the heart, liver, skeletal muscles, and the erythrocytes. It is present in smaller amounts in the brain, kidneys, lungs, pancreas, and spleen. It is released after damage to these tissues.

The LDH can be measured as the total enzyme in the serum, or each of its five isoenzymes may be measured. Measuring the isoenzymes can help to differentiate the source of the elevated total LDH. The isoenzymes and their primary sources include:

LDH<sub>1</sub>: Heart muscle and erythrocytes

LDH<sub>2</sub>: Reticuloendothelial system

LDH<sub>3</sub>: Lungs

LDH<sub>4</sub>: Kidneys, pancreas, and placenta

LDH<sub>5</sub>: Liver and skeletal muscle

The LDH along with AST and CK, have traditionally been assessed in the case of suspected MI. However, the availability of testing for troponin has decreased the use of LDH for diagnosing MI. The LDH typically appears in the bloodstream within 12 hours of the tissue injury, with peak values occurring 24 to 28 hours post injury. The peak value may reach 300 to 800 IU/L following MI. The LDH levels are usually elevated for approximately 10 days. Thus, LDH becomes elevated after CK following MI. In diagnosis a suspected MI, the total LDH, along with LDH<sub>1</sub> and LDH<sub>2</sub> are usually elevated, with LDH<sub>1</sub> being greater than LDH<sub>2</sub>.

### **Specimen**

Serum or plasma. No fasting is required before the test.

#### **Normal values**

Total LDH 110-210 IU/L.

#### Conditions that increase LDH level

Congestive heart failure, MI, hemolytic anemia, liver diseases, pneumonia, pulmonary infarction, acute pancreatitis, abruptio placenta, hyperthermia and skeletal muscle disease.

### **Contributing factors to abnormal values**

(1) Hemolysis of the blood sample and strenuous exercise prior to the test will alter test results.

- (2) Drugs which may increase LDH levels: alcohol, anabolic steroids, anesthetics, clofibrate, NSAIDs, sulfasalazine and verapamil.
- (3) Drugs which may decrease LDH levels: ascorbic acid and oxalates.

## Techniques for the determination of LDH

A spectrophotometric procedure.

## Creatine phosphokinase

## **Test description**

Creatine phosphokinase (CPK) or creatine kinase (CK) is an enzyme found primarily in the heart and skeletal muscles, and in smaller amounts in the brain. When the total CK level is substantially elevated, it usually indicates injury or stress to one or more of these areas. When a muscle is damaged, CK leaks into the bloodstream. Determining which isoenzyme (specific form of CK) is elevated will help determine which tissue has been damaged.

The CK can be measured as the total enzyme in the serum, or each of its three isoenzymes may be measured. The isoenzymes include:

CK<sub>1</sub> (CPK-BB): produced primarily by brain tissue and smooth muscle of the lungs

CK<sub>2</sub> (CPK-MB): produced primarily by heart tissue

CK<sub>3</sub> (CPK-MM): produced primarily by skeletal muscle

The CK, along with AST and troponin, is assessed in the case of suspected MI. It typically appears in the bloodstream within 3 to 6 hours of the tissue injury, with peak values occurring 18 to 24 hours post injury. The CK levels are usually elevated for approximately 2 to 3 days. Thus, CK is one of the first cardiac enzymes to become elevated following MI.

#### Specimen

Serum or plasma. No fasting is required prior to the test.

#### Normal values of total CK

Female: 40-150 U/L, Male: 38-174 U/L

### Conditions that increase or decrease total CK level

Increased in rhabdomyolysis, muscle inflammation, cardiac surgery, MI, alcoholism, IM injections, brain trauma and brain tumors.

Decreased in low muscle mass and anterior pituitary hyposecretion.

## **Contributing factors to abnormal values**

- 1- Hemolysis of the blood sample or strenuous exercise prior to the test will alter test results.
- 2- Factors that may affect test results include cardiac catheterization, intramuscular injections, trauma, trauma to muscles, recent surgery, and prolonged exercise.
- 3- Drugs which may increase total CK: amphotericin B, anticoagulants, aspirin, ethanol, dexamethasone, furosemide and some anesthetics.

#### Clinical alerts

- (1) Do not administer any intramuscular injections for 1 hour prior to the test.
- (2) It is recommended that baseline CK levels be checked upon initiating statin therapy. Determining the patient's pretreatment CK levels will prevent inappropriately attributing CK elevation to statin therapy in the event of muscle complaints later and assuming the presence of rhabdomyolysis.

### Techniques for the determination of CK

Several colorimeteric and spectophotometric methods are available