Biochemical Markers

Lecture 15

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• What is Biomarker?

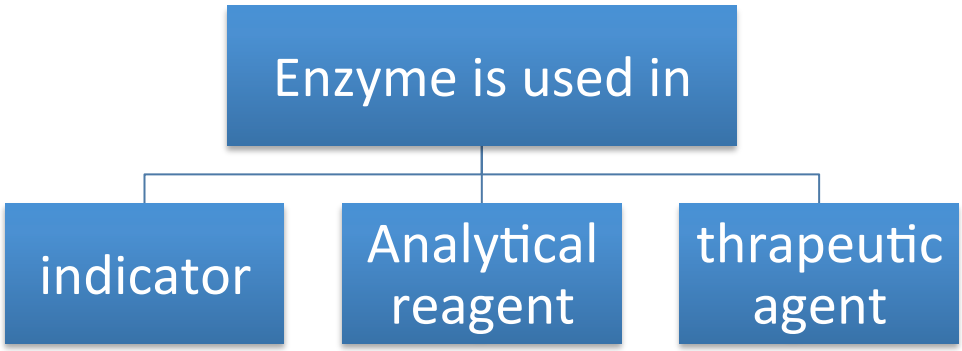
A biological molecule found in blood, other body fluids, or tissues that indicates a normal or abnormal process such as a disease or a condition. And it's measured to follow up a disease or treatment.

- e.g. Amylase, ALT, AST
- Plasma proteins as markers of disease: Albumin.
- Tumor markers: α-fetoprotein, PSA.
- A biomarker is measured to follow up the disease.

Diagnosis: Identification of a disease from its signs and symptoms

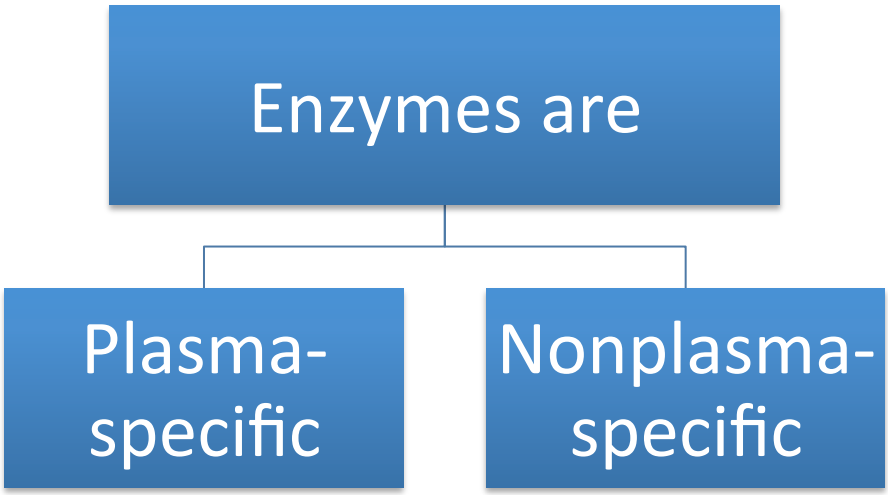
Prognosis: The future outcome of disease.

Enzymatic diagnosis and prognosis of disease:



1) As indicators of enzyme activity or conc. in body fluids (serum, urine) in the diagnosis/prognosis of a disease.
2) As analytical"تحليل" reagents in measuring activity of other enzymes or compounds in body fluids.
3) As therapeutic"علاجي " agents.

Most common body fluids: serum & plasma.



Plasma-specific enzymes:

- Normally present in plasma.
- Perform their functions in blood.
- High level of activity in plasma than in tissue cells.

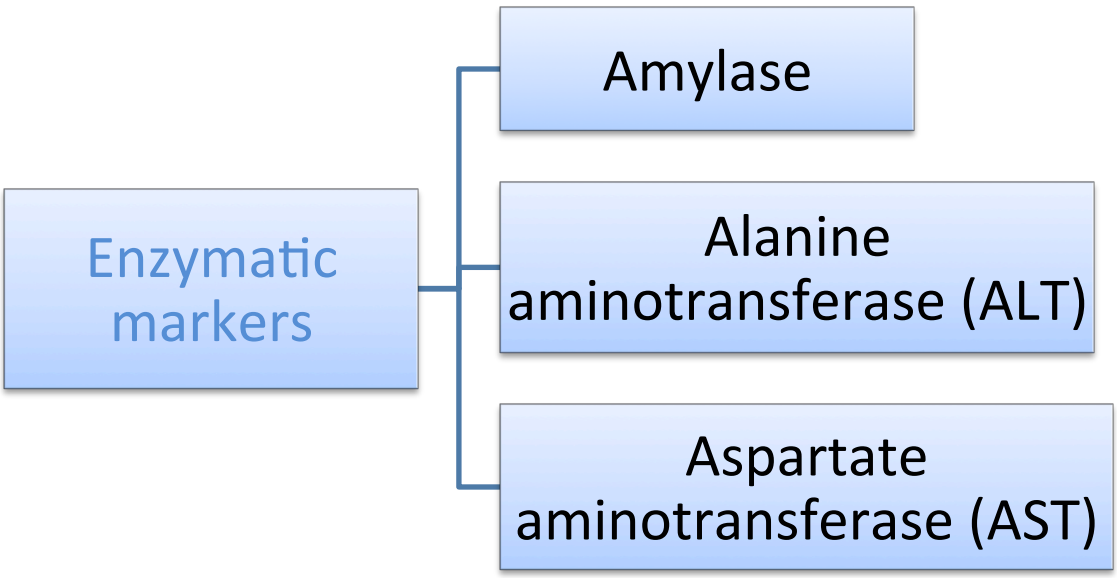
-e.g. blood clotting enzymes (thrombin), cholinesterase, etc.

Nonplasma-specific enzymes:

- Present inside the cell.
- Conc. is lower in plasma.
- Released into the body fluids in high conc. due to:
  - cell damage.
  - defective cell membrane.
- Intracellular enzymes are present only in their cells of origin.
- Some are secretory enzymes that are secreted by salivary glands, gastric mucosa and pancreas.
- In disease, plasma levels of secretory enzymes increase when their cells are damaged.
- The diagnosis of organ disease is done by measurement of enzymes of that tissue.

Factors affecting serum enzyme levels:

Cell damage	Rate of Enzyme synthiesis and clearance	Enzyme inhibitors
Glucose deficiency	Localized hypoxia (less Oxygen)	Ischemia (Obstruction of blood vessels)
Necrosis	Tissue infraction due to ischmic necrosis	Mycardial infraction



Amylase

- Elevated serum amylase level is a diagnostic indicator of acute pancreatitis
  - Amylase level greater than 10 times the upper limit indicates acute pancreatitis
- The test has low specificity because elevated serum amylase level is also present in other diseases
- Amylase appears in the serum within 2-12 hours after abdominal pain
- Free amylase (unbound form) is rapidly cleared by the kidneys.

Amylase in acute pancreatitis:

Acute pancreatitis is the inflammation of pancreas caused by:

- Obstruction of the pancreatic duct.
- Gallstones.
- Alcohol abuse.

What happens in pancreatitis?

- Abnormal release of pancreatic enzymes and their premature activation.
- The main pancreatic enzyme is trypsinogen.
- Trypsinogen is activated to trypsin.
- Trypsin converts other enzymes to active form such as kallikrein, phospholipase A2, elastase, etc.
- Effects of abnormal release of enzymes: autodigestion of pancreas, vasodilation, respiratory failure, etc.

Enzymatic diagnosis for pancreatitis:

- Amylase
- Lipase
- Trypsinogen

High ALT & AST in liver diseases

Alcohol abuse	Medication	Chronic hepatitis B & C
Steatosis and steatohepatitis	Autoimmune hepatitis	Wilson's disease
α1-antitrypsin deficiency	Malignancy	Poisons and infectious agents

Serum enzymes used in the assessment of liver function:

1) Markers used in hepatocellular necrosis
   - Alanine aminotransferases
   - Aspartate aminotransferases
2) Markers used in cholestasis
   - Alkaline phosphatase
   - 5'-nucleotidase
   - ɣ-glutamyl transferase

Alanine aminotransferase (ALT)

- Mostly present in liver
- Small amounts in heart
- More specific for liver disease than AST
- Major diagnosis: liver disease

Aspartate aminotransferase (AST)

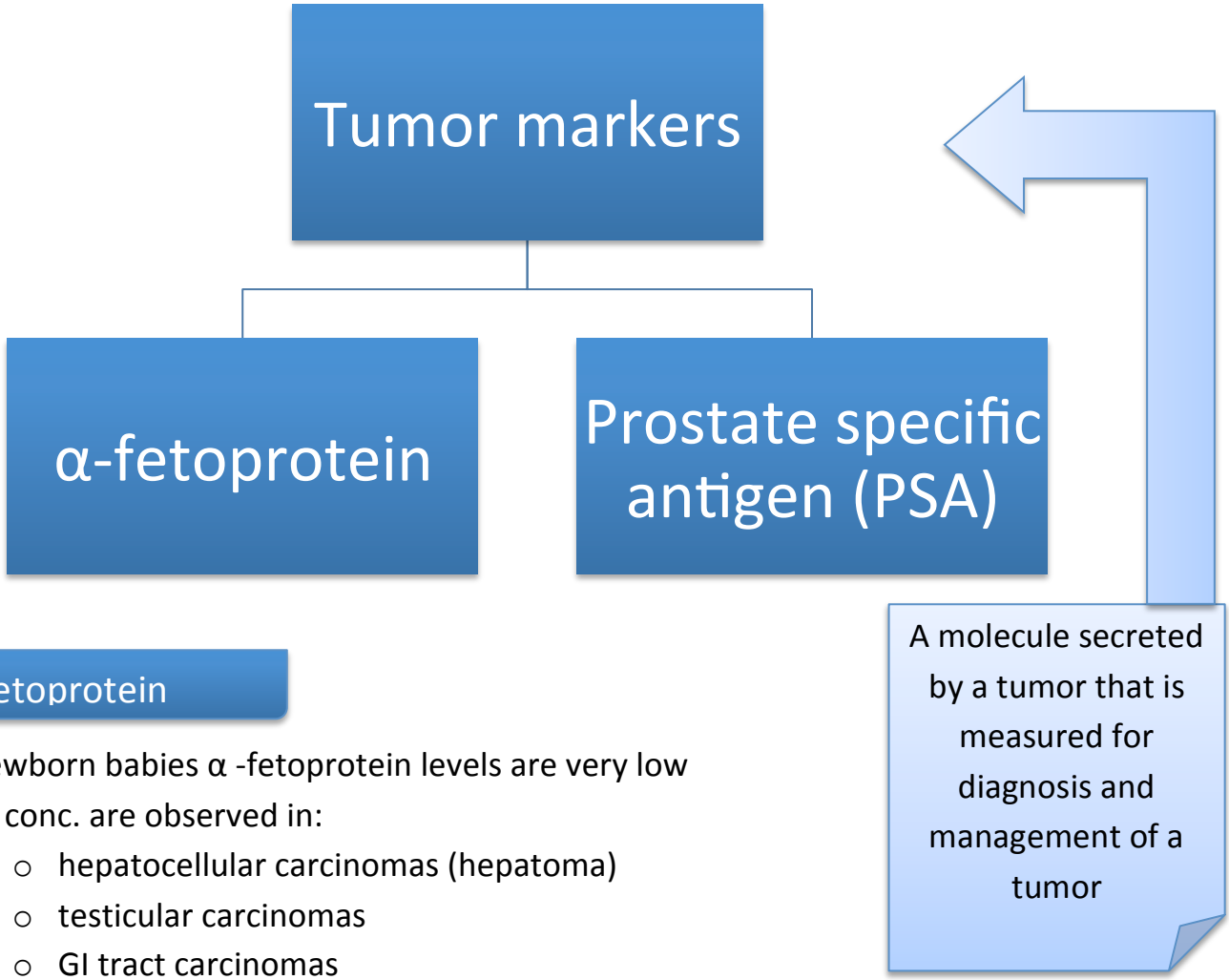
- Widely distributed in heart, liver, skeletal muscle, kidney
- Small amounts in erythrocytes
- High serum activity of AST found in:
  - Liver disease, heart disease, skeletal muscle disease, hemolysis
- Major diagnosis: myocardial infarction, liver and muscle diseases.

Plasma proteins as markers (albumin)

- **Functions:**
  - Oncotic pressure (pressure exerted by plasma proteins that pulls water into the circulatory system)– 80% of plasma oncotic pressure is maintained by albumin
    - Fluid distribution in and outside cell, maintains plasma volume
  - Buffering – some buffering function
  - Transport – lipid-soluble molecules, hormones, calcium, drugs, etc. in blood

- **Hypoalbuminemia:**
  - Causes
    1) Decreased albumin synthesis – failure of synthesis due to genetic reasons and malnutrition
    2) Increased volume of albumin distribution – in liver disease
    3) Increased losses of albumin – increased catabolism in infections, nephrotic syndrome, hemorrhage, severe burns, etc.
  - Effects
    1) Edema due to low oncotic pressure
       a. Albumin level drops in liver disease causing low oncotic pressure
       b. Fluid moves into the interstitial spaces causing edema
    2) Reduced transport of
       a. Substances in plasma
       b. Drugs (free form – more active)

- **Hyperalbuminemia**
  - Causes: Dehydration is a major cause of hyperalbuminemia.



α-fetoprotein

- In newborn babies α -fetoprotein levels are very low
- High conc. are observed in:
  - hepatocellular carcinomas (hepatoma)
  - testicular carcinomas
  - GI tract carcinomas
- However, high serum levels are also found in benign (non-cancerous) conditions e.g. hepatitis
- High conc. are not always suggestive of a tumor.

Prostate specific antigen (PSA)

- A serine protease enzyme also called kallikrein III, seminin
- Produced by prostate gland
- Liquefies ejaculate
- High serum PSA levels are observed in prostate cancer
- Less specific in diagnosis
  - High serum levels are also observed in benign prostatic hypertrophy (enlarged prostate gland).