Biochemical markers in diagnosis and follow up of disease

Foundation block..

Objectives:

- **What is a biomarker?**
- **Enzymatic diagnosis and prognosis of a disease**
- **Enzymes as markers of disease: Amylase, ALT, AST**
- **Plasma proteins as markers of disease: Albumin**
- **Tumor markers: a-fetoprotein, PSA**

- **what is a biomarker?**

A biological molecule found in blood, other body fluids(urine or serum), or tissues that indicates a normal or abnormal process such as a disease or a condition. Also, it is measured to diagnose and prognosis a disease, follow up a disease or treatment.

Diagnosis:
Identification of a disease from its signs and symptoms.
Prognosis:
The future outcome of a disease.

We took it in enzymesII lecture.

Enzymatic diagnosis and prognosis of diseases :

Enzyme are used clinically in three ways:

- **As indicators of enzyme activity or conc. In the body fluids(serum, urine)in the diagnosis/prognosis of diseases.**
- **As analytical reagents in measuring activity of other enzymes or compounds in the body fluids .**
- **As therapeutic agents.**

The most commonly used body fluids for measuring enzyme activity are :

- **serum**
  - **Serum markers in the diagnosis of disease:**
    - **Pancreatic disease**
    - **Heart disease**
    - **Liver disease**

Discussed in the next slides

- **Plasma**
  - **There are**
    - **Plasma-specific enzymes:**
      - Normally present in plasma
      - • Perform their functions in blood
      - • High level of activity in plasma than in tissue cells
      - • Examples: blood clotting enzymes (thrombin), cholinesterase, etc.
    - **Tissue-specific enzymes**
      - Present inside the cell
      - • Concentration is lower in plasma
      - • Released into the body fluids in high concentration due to:
      - cell damage and 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 synthesis and clearance
  - Enzyme inhibitors
  - Glucose deficiency
  - Localized hypoxia (less oxygen)
  - Ischemia (obstruction of blood vessels)
  - Necrosis
  - Tissue infarction due to ischemic necrosis
  (e.g. Myocardial infarction)

- Qualities of a Good Biomarker Assay:

  - Ability to accurately diagnose a disease
  - Ability to accurately predict prognosis of a disease
  - Complies with treatment follow up
  - Sample should be easily obtained (blood, urine, etc.)
  - Rapid test to deliver results faster
  - Sensitive
  – Ability of an assay to detect small quantities of a marker
  - Specific
  – Ability of an assay to detect only the marker of interest

❖ Some examples of enzymatic markers:

Amylase, Alanine amino transferase , Aspartate amino transferase

*Will be discussed one by one

❖ Amylase

- Amylase is a diagnostic indicator of acute pancreatitis, when The level of amylase elevated in serum Indicate acute pancreatitis .
  - Amylase in serum should be greater 10 times from upper limit to indicate acute pancreatitis .
- However , Amylase is a low specificity because elevated amylase level in serum is also present in other diseases.
- Amylase is appear in serum within 2-12 hours after abdominal pain.
- Free amylase " un bound form " is rapidly cleared by the kidney.

➢ Amylase in acute pancreatitis:

What is acute pancreatitis?

It is the inflammation of pancreas caused by:
– Obstruction of the pancreatic duct
– Gallstones
– Alcohol abuse

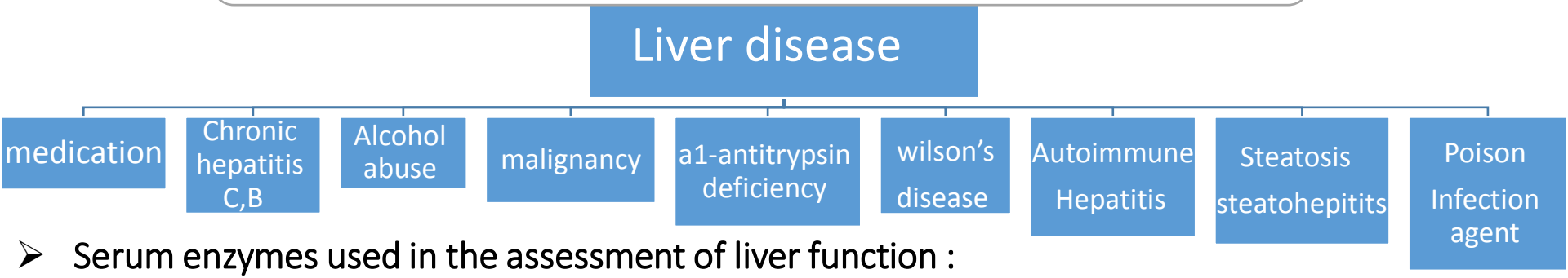
Enzymatic diagnosis of pancreatic diseases:

- Amylase
- Lipase
- Trypsinogen

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.

ALT , AST are enzymatic marker indicate liver disease:



- Serum enzymes used in the assessment of liver function :

1- marker used in hepatocellular necrosis

- Alanine amino transferase
- Aspartate amino transferase.

2- marker used in cholestasis

- Alkaline phosphatase
- 5'-nucleotidase
- g-glutamyl transferase

❖ Alanine amino transferase(ALT)

- Present in liver

-small amount in heart

- More specific to liver function more than AST

Major diagnosis : Liver diseases

❖ Aspartate amino transferase(AST)

-Present in heart , liver , skeletal muscle , kidney,

-Small amount 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)

- **function :**

1- oncotic pressure:Is pressure exerted by plasma proteins that pulls water into the circulatory system, 80% plasma oncotic pressure is maintained by albumin , Fluid distribution in and outside cell, maintains plasma volume.
2- buffering: some buffering functions.

3-transport: Lipid soluble molecules , hormones , calcium , drugs , in blood.

- **Hypoalbuminemia**

Causes :
1- Decreased albumin synthesis due to genetic reasons and malnutrition.
2- Increased volume of albumin distribution – liver disease
3- Increased losses of albumin – increased catabolism in infections ,nephortic syndrome , Hemorrhage , severe burns.

Effects

1- Edema due to low oncotic pressure
Albumin level drops in liver disease due to low oncotic pressure.
- Fluid move into the interstitial spaces causing edema
2- Reduce transport of plasma substance , drug

- **Hyperalbuminemia:**

The major causes of Hyperalbuminemia is dehydration.

❖tumor markers:

A molecule that is secreted by a tumor that is for diagnosis and management of a tumor.

Types of tumor markers :

1- a-fetoprotein

In newborn babies a-fetoprotein level are very low.

-High conc. Are Observed in :

- Hepatocellular carcinomas (hepatoma)
- testicular carcinomas
- Gastro Intestinal tract carcinomas

high serum levels are also found in benign (non-cancerous) conditions e.g.

Hepatitis

High concentration are not always suggestive of a tumor.

2- 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 because

–High serum levels are also observed benign prostatic hypertrophy (enlarged prostate gland)

SUMMARY

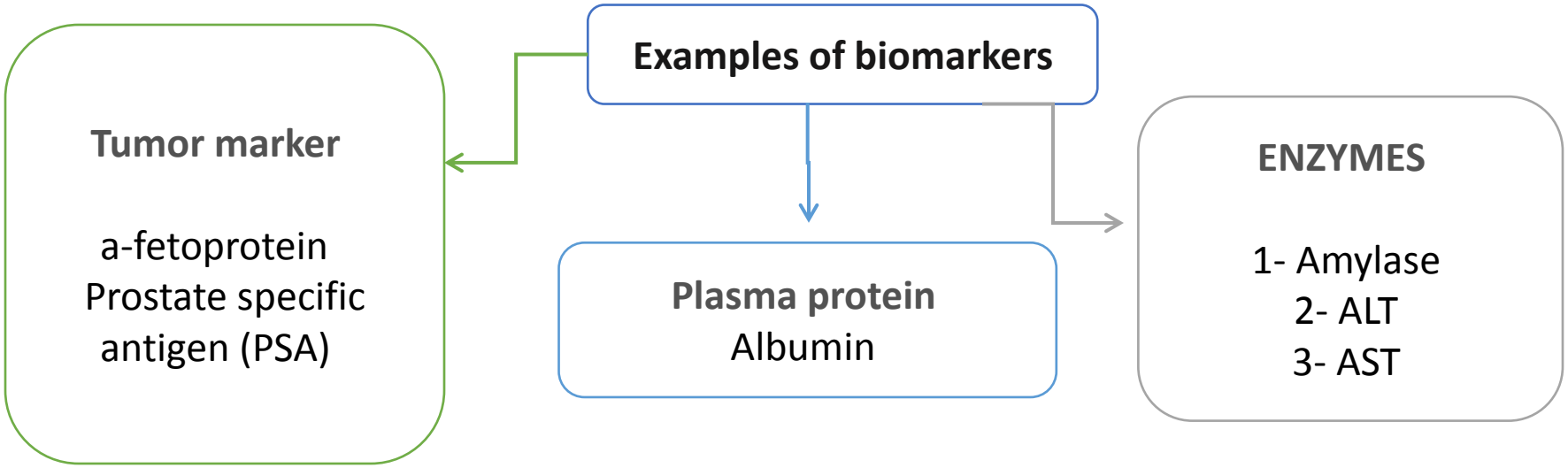
Biomarker is biological molecule that is found in tissue or in body fluid such as blood indicate normal or abnormal condition , diseases.

A biomarker is measured to diagnose, follow up or monitor a diseases or treatment.

Assays to measure biomarkers should be :

sensitive, specific, fast, and using samples that

are easy-to-obtain Such as urine & blood.



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