

# Biochemical markers for diagnosis of diseases and follow up

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## Lecture objectives:

Upon completion of this lecture, the students should be able to:

- Define biomarkers and its criteria
- Recognize different types of biochemical markers
- Demonstrate the clinical applications of biomarkers in diagnosis of various diseases

# What is a 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

Most common body fluids for the measurement of biomarkers are:

- Blood
- Urine
- Biomarkers are either:
  - Plasma-specific
  - Tissue-specific

# Plasma-specific biomarkers:

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

# Tissue-specific biomarkers:

- Present **inside the cell**
- A low concentration can be detected in plasma due to cellular turnover
- If higher concentration is detected in plasma, it indicates **cell damage**.

- Cell damage can be due to:

- 1- Tissue inflammation, example:

- ALT\* in liver disease (e.g. acute hepatitis)

- Amylase in acute pancreatitis

- 2- Ischemia → hypoxia → infarction →

- ↑ plasma [Troponin] in myocardial infarction

ALT\*: alanine aminotransferase

# diagnosis and prognosis:

Diagnosis: Identification of a disease from its signs and symptoms

Prognosis: The future outcome of a disease



# Criteria of a good biomarker assay:

A good biomarker assay should be:

- Sensitive: Sensitivity is the Ability of an assay to detect small quantities of a marker
- Specific: Specificity is the ability of an assay to detect only the marker of interest
- Robust to produce fast results

# Examples of biomarkers:

- Enzymes
- Hormones
- Proteins

# Enzymes as biomarkers:

Examples include:

- Amylase, Lipase
- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)

# 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 amylase level is also present in other diseases
- Amylase appears in the serum within 2-12 hours after abdominal pain, and returns to normal in 3-5 days

# Lipase:

- Serum lipase has higher specificity than serum amylase (elevated only in acute pancreatitis)
- It appears in plasma within 4-8 hours and remains for 8-14 days

# Case:

A GP was called to see a 21-year-old female student who had been complaining a flu-like illness for two days, with symptoms of fever, vomiting and abdominal tenderness in the right upper quadrant. On examination she was jaundiced, moreover; the liver was enlarged and tender. A blood was taken for liver function tests which **showed elevated ALT** (alanine aminotransferase) **and AST** (aspartate aminotransferase)

What is the most likely diagnosis?

**Acute Hepatitis**

# Aspartate aminotransferase (AST) Alanine aminotransferase (ALT):

	AST	ALT
Produced by:	heart, liver, skeletal muscle, kidney, erythrocytes	liver
Elevated in:	Liver disease, heart disease, skeletal muscle disease, hemolysis	Liver disease

# Proteins as biomarkers:

- $\alpha$ -Fetoprotein
- Prostate Specific Antigen (PSA)
- Cystatin C
- B-type Natriuretic Peptide (BNP)



# a-Fetoprotein:

- It is produced by the fetal liver, and falls until term  
→ in newborn babies  $\alpha$ -fetoprotein levels are very low
- It remains low under normal conditions.
- High conc. are observed in:
  - hepatocellular carcinomas (hepatoma)
  - testicular carcinomas
  - GI tract carcinomas
- It is a non specific marker

# Prostate Specific Antigen (PSA):

- Produced by prostate gland
- PSA level is used as a tumor marker to aid diagnosis and for monitoring in patients with **prostatic cancer**.
- High serum levels are also observed in:
  - Benign prostatic hyperplasia (BPH)
  - Prostatic inflammation/infection

# Cystatin C:

- A cysteine protease inhibitor mainly produced by all nucleated cells of the body
- Useful biomarker for measuring glomerular filtration rate (GFR) in assessing kidney function
- Unlike creatinine, its serum conc. is independent of gender, age or muscle mass
- High levels of serum cystatin C indicates early renal disease
- Clinically used as a marker for:
  - detecting early kidney disease
  - monitoring kidney transplantation

# B-type natriuretic peptide (BNP)

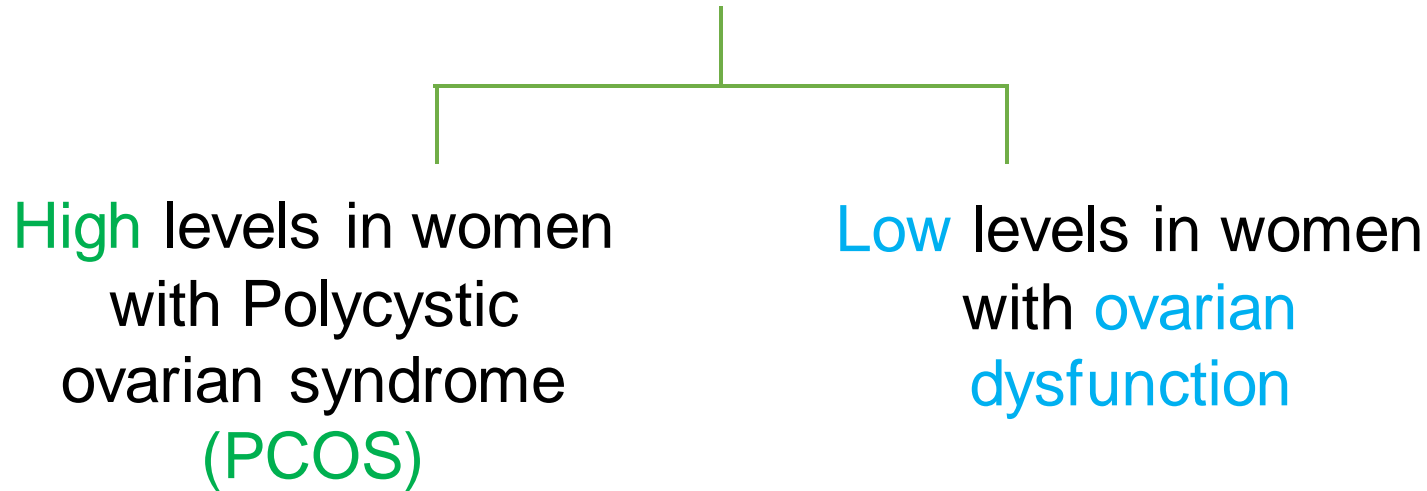
- A peptide secreted mainly in the cardiac ventricles in response to cardiac expansion and pressure overload
- High serum levels are observed in congestive heart failure
- It can be used to differentiate patients whose symptoms are due to heart failure from those whose symptoms are due to other causes such as pulmonary disease.

# Hormones as biomarkers:

## Anti-Mullerian hormone (AMH):

- In females it is produced by ovaries
- Appears to be a best marker for estimating egg cell reserve in the ovaries(ovarian reserve testing)
- only growing follicles produce AMH
- Plasma AMH levels strongly correlate with number of growing follicles

# Anti-Mullerian hormone (AMH)



# Take home message:

- Biochemical markers are essential accurate and non-invasive laboratory tools offering the treating physicians fast means for better management.
- They could be proteins, enzymes, or hormones.
- Recent development in medicine provides new biomarkers