# 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

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:
- <u>Sensitive:</u> Sensitivity is the Ability of an assay to detect small quantities of a marker
- <u>Specific:</u> 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



•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:**

- a-Fetoprotein
- Prostate Specific Antigen (PSA)
- Cystatin C
- B-type Natriuretic Peptide (BNP)



- It is produced by the fetal liver, and falls until term in newborn babies **a**-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

<u>B-type natriuretic peptide</u> (<u>BNP</u>)

- 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:

### <u>Anti-Mullerian hormone</u> (<u>AMH):</u>

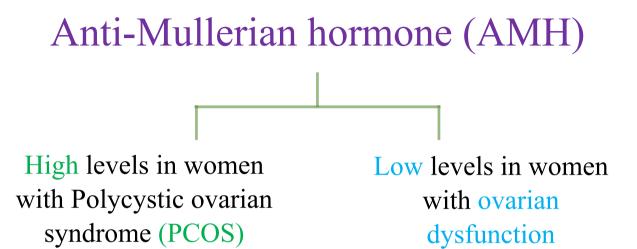
•In females it is produced by ovaries

•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

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#### 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