biochemical markers for diagnosis and follow up of diseases



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Objectives:



Define biomarkers and its criteria.



Recognize different types of biochemical markers.



Demonstrate the clinical applications of biomarkers in diagnosis of various diseases.



Comprehend the importance and diagnostic qualities of various biomarkers.



Understand the importance of different biomarkers in the diagnosis, treatment and follow up of a disease.



Recognize the types of biomarkers and their use in specific diseases such as heart, cancer, liver, kidney and pancreatic 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.
- A biomarker is measured to follow up a disease or treatment.

Diagnosis and Prognosis

	Diagnosis	Prognosis
Definition	 Identification of a disease from its signs and symptoms 	- The future outcome of a disease

Most common body fluids for measurements of biomarkers are:

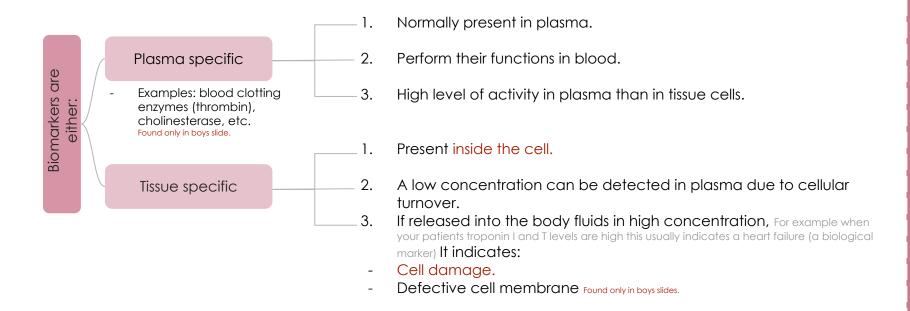






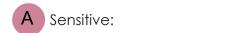


Types of biomarkers



- Cell damage can be due to:
- 1. Tissue inflammation, example:
- ALT (alanine aminotransferase) in liver disease (e.g. acute hepatitis).
- Amylase in acute pancreatitis.
- 2. Ischemia \rightarrow hypoxia \rightarrow infarction \rightarrow plasma (Troponins) in myocardial infarction.

Criteria of A Good Biomarker Assay



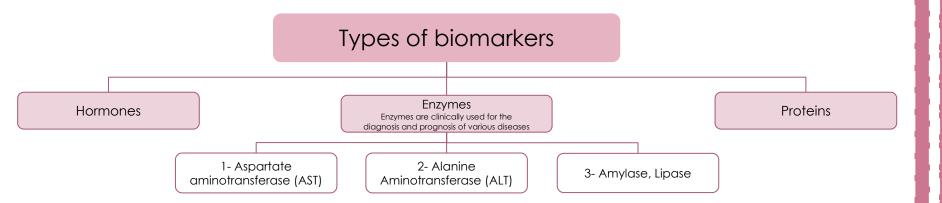
 Sensitivity ability of an assay to detect small quantities of a marker.

You have to know what is specific, what is sensitive and what is not.

B Specific:

 Specificity ability of an assay to detect only the marker of interest Robust to produce fast results

- Found only in boys slides.



A Good biomarker should be:

- Able to accurately diagnose a disease
- Able to accurately predict prognosis of a disease
- Compliant with treatment follow up
- Easily obtainable from blood, urine, etc.

Enzymes As Biomarkers: Amylase vs Lipase

Amylase (not specific)	Lipase
 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 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.

Enzymes As Biomarkers: AST and ALT

- 1. Alanine Aminotransferase (ALT):
- Produced by: liver.
- Elevated in: liver diseases (More specific for liver disease than AST)
- Mostly present in: liver and small amounts in heart.
- Major diagnosis: liver disease.

2. Aspartate aminotransferase (AST):

- Produced by: heart, liver, skeletal muscle, kidney and erythrocytes.
- Elevated in: Liver disease, heart disease, skeletal muscle disease and hemolysis (so it's not specific).
- Widely distributed in: heart, liver, skeletal muscle, kidney and small amounts in erythrocytes.
- Major diagnosis: liver and muscle disease.

Case

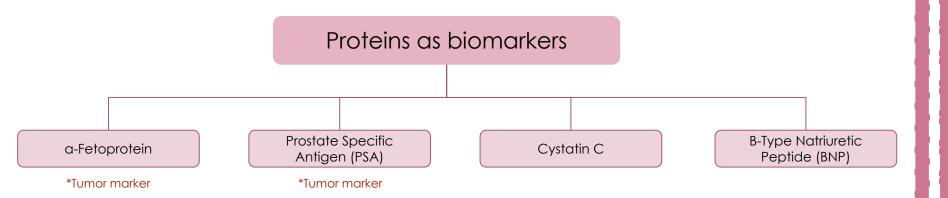
A GP was called to see a 21-year-old female student who had been complaining a flu-like illness for two days, with symptoms of fever, vomiting and abdominal tenderness in the right upper quadrant. On examination she was jaundiced, moreover; the liver was enlarged and tender. A blood was taken for liver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

What is the most likely diagnosis?

Acute Hepatitis

because high levels of ALT and AST are both indicators of liver diseases, but what made us sure is ALT (more specific than AST)

Proteins As Biomarkers



• Tumor Markers: A molecule secreted by a tumor that is measured for diagnosis and management of a tumor.

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Proteins As Biomarkers: a-Fetoprotein And PSA

- a-Fetoprotein:
- It is produced by: the fetal liver, and falls until term \rightarrow In newborn babies, a-Fetoprotein levels are very low.
- It remains low under normal conditions.
- High conc. are <u>NOT</u> always suggestive of a tumor.
- High conc. are observed in: Found only in boys slides.
 - Hepatocellular carcinomas (hepatoma). Testicular carcinomas.

 - GI tract carcinomas.
- It is a non-specific marker.
- However, high serum levels are also found in benign (non-cancerous) conditions e.g. hepatitis.

- 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: (less specific).
 - Benign prostatic hypertrophy (BPH) "enlarged prostate gland".
 - Prostatic inflammation/infection.

Proteins As Biomarkers: Cystatin C And BNP

• 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 and failure.
- Unlike creatinine, its serum conc. is independent of gender, age or muscle mass.
- Abnormally high serum levels of cystatin C indicates early renal disease "kidney failure".
- Clinically useful marker for detecting:
 - Early kidney disease.
 - Mońitoring kidney transplantation.

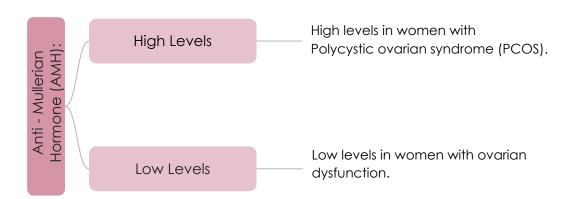
• B-Type Natriuretic Peptide (BNP):

- 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.

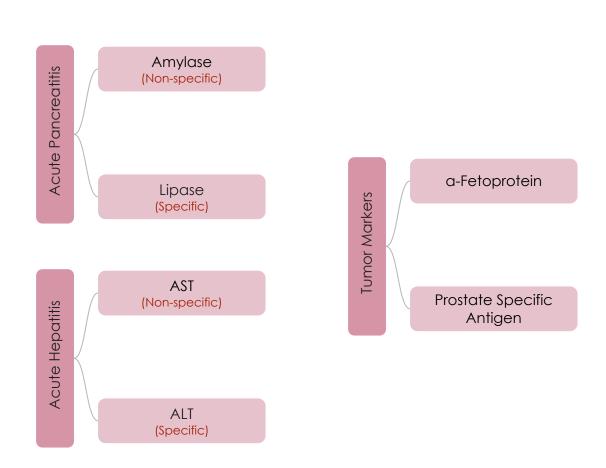


Hormones As Biomarkers: Anti-Mullerian Hormone (AMH)

- 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.



Summary



Take home messages



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.



Biomarkers are used for diagnosis, prognosis and follow up of diseases.



A biomarker should exhibit good diagnostic and prognostic values.



Examples of biomarkers used in different disease will help understand their qualities and limitations.



Q1 : Amylase and lipase are biomarkers of:						
A) Congestive heart failure	B) Pregnancy	C) Pancreatitis	D) Polycystic ovarian syndrome			
Q2 : Which one is the specific test for liver?						
A) AST	B) ALT	C) a-Fetoprotein	D) AMH			
Q3 : A non-specific biomarker seen in hepatoma and produced in high levels:						
A) Amylase	B) a-Fetoprotein	C) Lipase	D) AST			
Q4 : Identification of a disease from its signs and symptoms is the definition of:						
A) Prognosis	B) Diagnosis	C) Biomarker	D) None			
Q5 : The ability of a biomarker assay to detect small quantities of the marker is the definition of:						
A) Sensitivity	B) Specificity	C) Prognosis	D) Diagnosis			
Q6 : What's the best team ever?						
A) Biochemistry team 439	B) A	C) A&B	D) C			

SAQs:

Q1: Define a Biomarker

Q2: What can cause liver enzyme to be elevated?

- MCQs Answer key:
 - 1) C 2) B 3) B 4) B 5) A 6) A
- ★ SAQs Answer key:
- 1) Slide 3
- 2) Slide 8







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" Believe you can and you're halfway there"

Shatha Aldhohair

