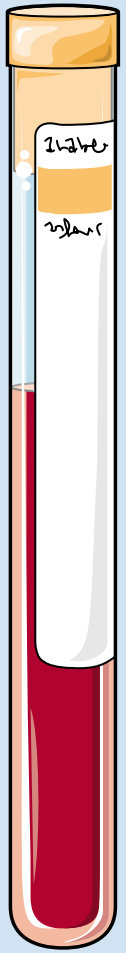


Biochemical Markers for Diagnosis & Follow up of Diseases

MED441
KING SAUD UNIVERSITY

Revised & Reviewed by:
Abdulaziz & Bahammam
Faye Wael Sendi

15
V1

Foundation Block - KSU

Color Index:
- Main text
- Important
- Notes
- Boys slides'
- Girls slides'
- Extra

Editing File

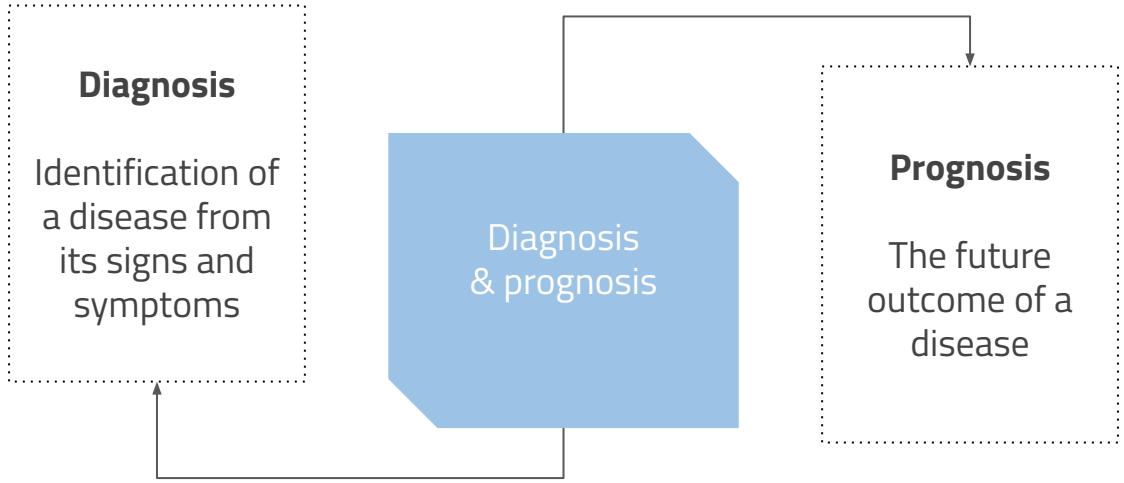
Objectives

- 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?

1. 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.

2. A biomarker is measured to follow up a disease or treatment.



Most common body fluids for measurement of biomarkers are :

- Serum
- Blood (Plasma)
- Urine

Biomarkers Classifications

Biomarkers can either be:

Plasma-specific biomarkers

- 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 biomarkers

- Present inside the cell
- Concentration is lower in plasma due to cellular turnover
- Released into the body fluids in high conc. due to: cell damage or defective cell membrane

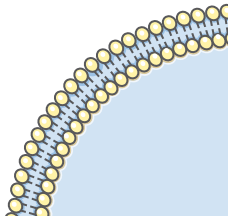
Cell damage can be due to:

1. **Tissue inflammation**

   Examples: Alanine aminotransferase (ALT) in liver disease (e.g. acute hepatitis)
   Amylase in acute pancreatitis

2. **Ischemia**

   Ischemia → hypoxia → infarction → ↑ plasma [Troponins] in myocardial infarction



Qualities of a good biomarker

A good biomarker should be able to:

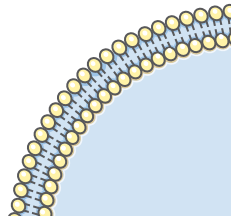
- Able to accurately diagnose a disease
- Able to accurately predict prognosis of a disease
- Compliant with treatment follow up (sensitive)
- Easily obtainable from blood, urine, etc.

Qualities of a good biomarker assay

A good biomarker assay should be able to:

- Able to be rapid + robust 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

Assay is an analytical test by which we can measure biochemical markers in the lab.



Types of biomarkers

1. Enzymes
2. Hormones
3. Proteins

1-Enzymes as biomarkers :

Enzymes are clinically used for the diagnosis and prognosis of various diseases

Examples include:	Amylase and Lipase	Alanine aminotransferase (ALT)	Aspartate aminotransferase (AST)

Amylase

1	- Elevated serum amylase level is a diagnostic indicator of acute pancreatitis. - Amylase level greater than 10 times the upper limit indicates acute pancreatitis.
2	The test has low specificity because elevated serum amylase level is also present in other diseases
2	Amylase appears in the serum within **2-12 hours** (long) after abdominal pain and returns to normal within **3-5 days** (disappear fast)

Lipase

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

Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT)

AST		ALT
Heart,liver,skeletal muscle,kidney,erythrocytes	<—Produced by—>	Liver
Liver disease, heart disease,skeletal muscle disease, hemolysis	<—ELevated in—>	Liver disease

ALT is more specific than AST because it elevates only in liver diseases

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

Summary for enzyme biomarkers:

Acute Pancreatitis Biomarkers	Acute Hepatitis Biomarkers
1. **Lipase**: More specificity / within 4-8hrs up to 8-14 days. 2. **Amylase**: Low specificity (present in other diseases) / within 2-12hrs up to 3-5 days / x10 the upper limit	1. **ALT**: More specific to liver diseases 2.**AST**: Low specificity (elevated in other diseases)

2- Proteins as biomarkers

1- Cystatin C
2- B-type natriuretic peptide (BNP)
3- a-Fetoprotein
4- Prostate Specific Antigen (PSA)

3 and 4 are
Tumor markers

1- Cystatin C

- A cystatin 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, serum conc. is independent of gender, age or muscle mass.

- Abnormally high serum levels of cystatin C indicates early renal disease "kidney failure"

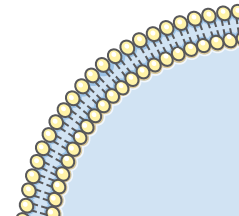
- Clinically useful marker for detecting:
1- early kidney disease
2- monitoring kidney transplantation

2- B-type natriuretic peptide (BNP):

- BNP is 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



cont: Tumor markers

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

3- a-fetoprotein: (Nonspecific tumor marker)

- 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 serum levels are also found in benign (non-cancerous) conditions. Eg; Hepatitis.

- High conc. are not always suggestive of a tumor..

- High conc. are observed in:
➢ hepatocellular carcinomas (hepatoma)
➢ testicular carcinomas
➢ GI tract carcinomas

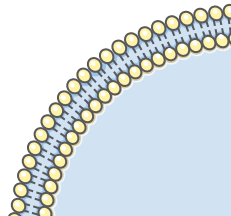
4- *Prostate Specific Antigen (PSA):*

- Produced by prostate gland

▪ PSA level is used as a tumor marker to aid diagnosis and for monitoring in patients with prostatic cancer.

- Less specific in diagnosis.

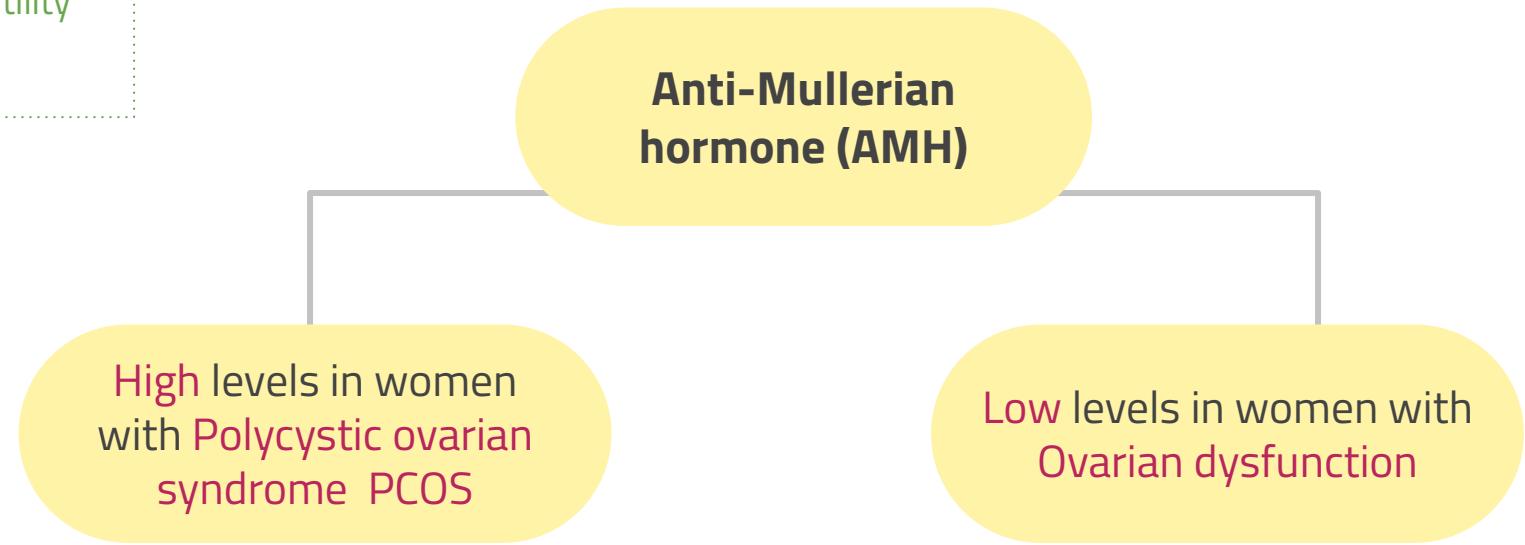
▪ High serum levels are also observed in:
➢ Benign prostatic hyperplasia (BPH)
➢ Prostatic inflammation/infection



3- Hormones as biomarkers:

- **Anti-Mullerian Hormone (AMH)**
- produced in female 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.

It tells you about the fertility status of a woman



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
- Recent development in medicine provides new biomarkers

Quiz

Q1: A biological molecule that can be measured to follow up a disease or treatment.

A	Diagnosis	B	Biomarker	C	Prognosis	D	Serum

Q2: A biomarker that is released in myocardial infarction :

A	a-fetoprotein	B	Troponins	C	AMH	D	PSA

Q3: Which of these biomarkers can be considered as tumor markers?

A	a-fetoprotein	B	Amylase	C	PSA	D	A and C

Q4:Which of these biomarkers that elevates only in acute pancreatitis?

A	Amylase	B	AST	C	ALT	D	Lipase

Q5:Which biomarker can be used to differentiate between heart failure and pulmonary diseases?

A	Cystatin C	B	AMH	C	PSA	D	BNP

Answer Key: 1) B 2) B 3) D 4) D 5) D

Q6: Define the term "diagnosis" :

Q7: define a tumor marker

Q8:mention the places that produced the following biomarkers (ALT,BNB,PSA,AMH)

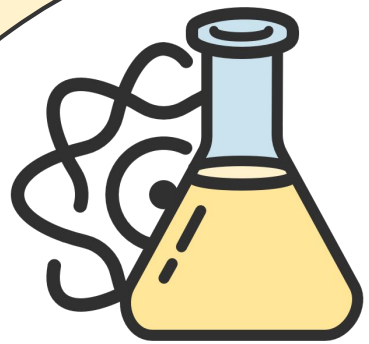
Q9:Mention the qualities of a good biomarker

Q6: Identification of a disease from its signs and symptoms

Q7: A molecule secreted by a tumor that is measured for diagnosis and management of a tumor

Q8:
ALT: Liver
BNB: cardiac ventricles
PSA: prostate gland
AMH: female ovaries

Q9: Slide 5



Biochemistry 441

Girls

Boys

Ghadah Alarify - Leader

Yara Almufleh
Reema Alrashedi
Wareef Almousa
Joud Alangari
Fay Alluhaidan
Sarah Alhamlan
Arwa Almobeirek
Jumana AL-qahtani
Latifa Alkhdiri
Alanoud Alhaider
Futoon Almotairi
Manal Aldhirgham
Raaoum Jabor
Norah alawlah
Shahad Helmi
Rand Aldajani

Khalid Alhamdi - Leader

Ahmed Alayban
Sultan Alosaimi
Abdullah Alomran
Bassam Alghizzi
Ibrahim Aljurayyan
Mohammed Almutairi
Turki Alkhalifa
Malik Alshaya
Faisal Alhmoud
Abdulrahman Alnoshan
Ahmed Alqahtani
Hamad Alshaalan
Anas Alharbi
Mohammed Alwahibi
Saad Alghadir

BiochemistryTeam441@gmail.com