

Biochemical markers

- Color Index:
 - **Important.**
 - Extra Information.
 - **Doctors slides.**

436 Biochemistry team

Objectives :

- ❖ Comprehend the importance & diagnostic qualities of various biomarkers .
- ❖ Understand the importance of different biomarkers in the diagnosis, treatment, & follow up of a disease .
- ❖ Recognize the types of biomarkers & their use in specific diseases such as heart, cancer, liver, kidney, & pancreatic diseases .

What is biomarkers?

- A biological molecule found in blood ,and 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 & Prognosis

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

*هناك إختلافات بين سلايدز الطلاب والطالبات.

Most common body fluids (**Samples**) for measurement of biomarkers are :

1. Serum
2. Plasma
3. Urine



What is the difference between Serum and Plasma ?
They are the same , but plasma has coagulation factors and serum has no coagulation factors.



Biomarkers can be either :

Plasma specific

Tissue specific

Plasma-specific Biomarkers:

- Normally present in Plasma .
(can be present in tissues in low amount or totally absent).
- Perform their functions in blood.
- High level of activity in plasma than in tissue cells .
- **Examples :**
- Blood clotting enzymes (thrombin), cholinesterase, etc.

When Tissue-specific biomarkers are released to body fluids , it will help us diagnose which part of the body has the problem (for example: if the patient has a heart attack or kidney failure)

Tissue-specific biomarkers:*

- Present inside the cell .
- A low concentration can be detected in plasma due to cellular turnover.
- Released into body fluids in high conc. Due to :
 1. **Cell damage***.
 2. Defective cell membrane.

***Cell damage can be due to:**

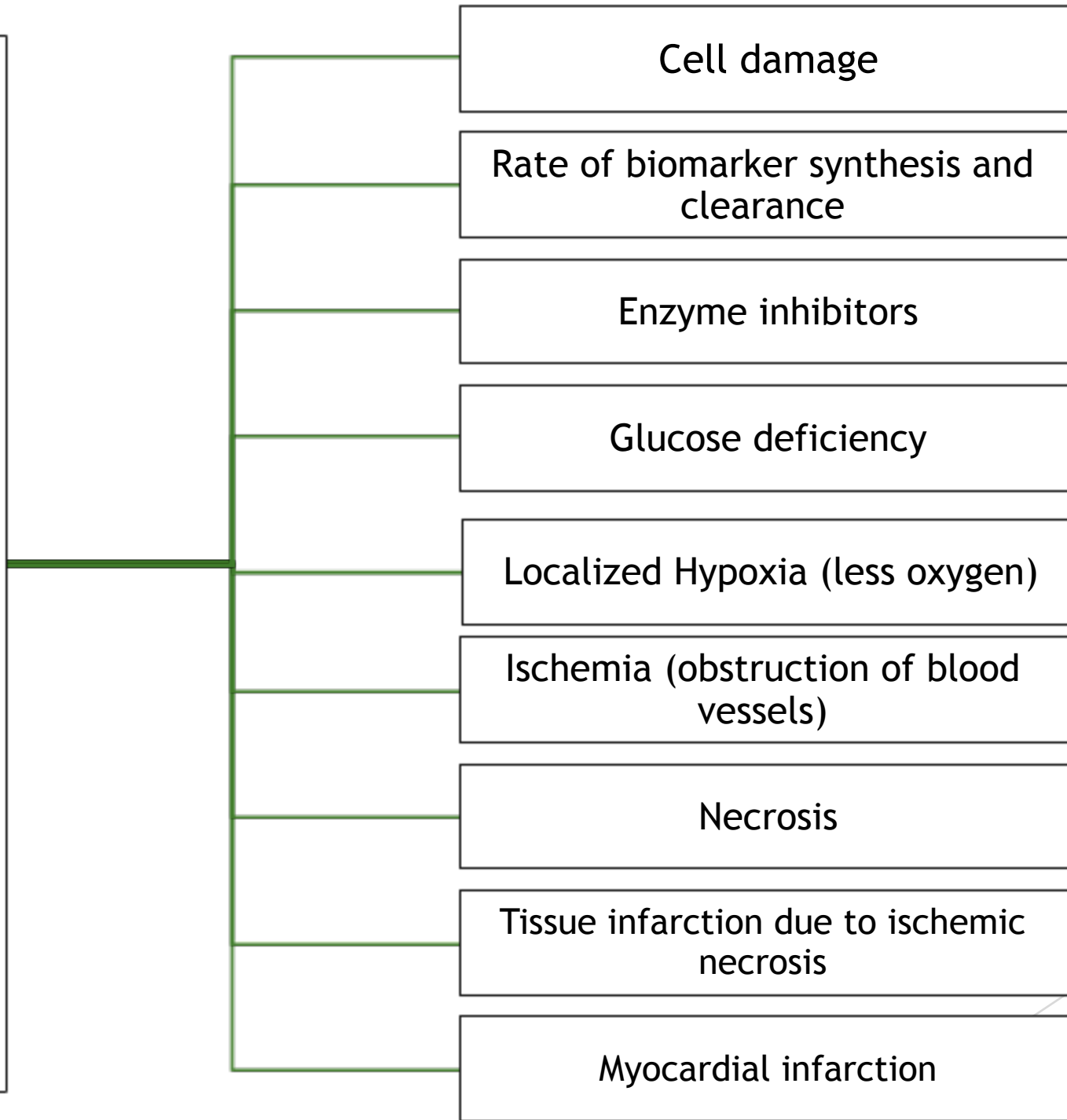
- 1- Tissue inflammation, **example:**
 - ALT* in liver disease (e.g. acute hepatitis)
 - Amylase in acute pancreatitis
- 2- Ischemia → hypoxia → infarction →
↑ plasma [Troponin] in myocardial Infarction

ALT*: alanine aminotransferase

- ▶ Intracellular enzymes are present only in their cells of origin
- ▶ Some secretory enzymes 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

(عند تشخيص المرض يتم قياس الانزيمات في الانسجة)

Factors affecting serum biomarker levels



#Qualities of a good biomarker:

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

*This means it changes after treatment which allows us to evaluate the progress (weather the treatment working or not) and predict prognosis

#Qualities (Criteria) of a good biomarker assay:

*Assay means a test, So a biomarker assay is a test that measures a biomarker

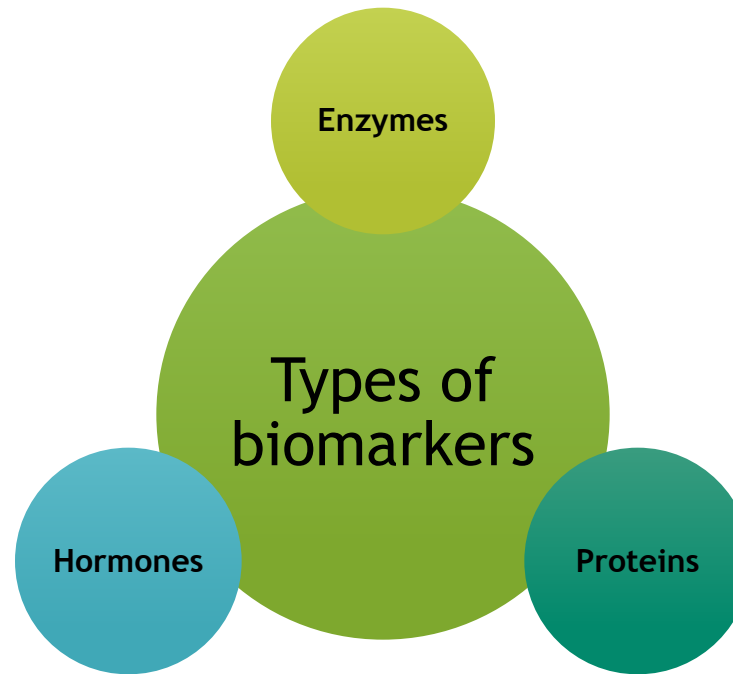
Rapid *Robust*
to deliver
results faster

Sensitive:
able to detect
small quantities
of a marker

Specific:
Able to detect
only the marker
of interest

Enzymes as biomarkers

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



Enzymes include

Amylase

Lipase

Alanine aminotransferase (ALT)

Aspartate aminotransferase (AST)

Proteins include

Cystatin C

BNP*

PSA**

α -Fetoprotein***

Hormones include

AMH

*B-type natriuretic peptide (BNP)

**Prostate Specific Antigen (PSA) (tumor marker)

*** α -Fetoprotein is also (tumor marker)

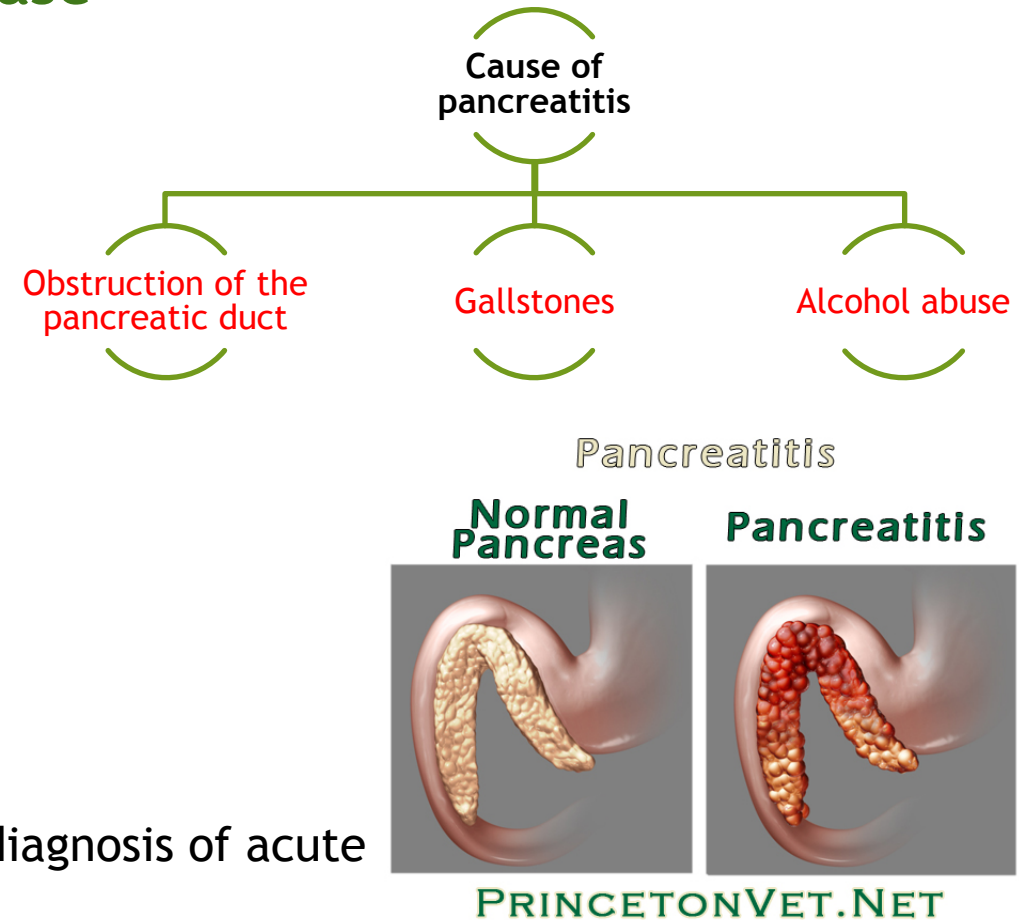
Enzymes: Amylase and Lipase

- ❖ **Acute pancreatitis:** the inflammation of pancreas
- ❖ There is abnormal release and premature activation of pancreatic enzymes (for example amylase, lipase)
- ❖ **Diagnosis conducted by measuring pancreatic enzymes**

During pancreatitis	Amylase	Lipase
Level in plasma compared to normal	10 times	2 times
Required time to appear in serum	2-12 hour after abdominal pain (onset symptom) and returns to normal in 2-3 days	4-8 hours and remain for 8-14 days
Specificity	low	high

- ❖ Measurement of amylase and lipase give **90-95% accuracy** in the diagnosis of acute pancreatitis and abdominal pain.
- ❖ Amylase test has low specificity because elevated serum amylase level ↑ is present in other diseases. Lipase elevated **ONLY** in **Acute pancreatitis**.
- ❖ Free amylase (unbound form) is rapidly cleared by the kidneys.

Gallstones are a common cause of pancreatitis. Gallstones, produced in the gallbladder, can block the bile duct, stopping pancreatic enzymes from traveling to the small intestine and forcing them back into the pancreas. The enzymes then begin to irritate the cells of the pancreas, causing the inflammation associated with pancreatitis.



Enzymes: ALT and AST

ALT (Alanine amino-transferase) and AST (Aspartate amino-transferase) are tissue-specific biomarkers. Which means they are normally found in the serum in LOW levels, when there is a condition or a disease in the liver (cell damage) “or any other tissues have those biomarkers“ there will be HIGH serum levels of ALT & AST.

High serum ALT and AST levels in liver diseases are due to:

- Alcohol abuse
- Medication
- Chronic hepatitis B and C
- Wilson’s disease
 - accumulation of copper in the liver.
- Autoimmune hepatitis
- Steatosis and steatohepatitis
 - Steatosis is ‘Fatty liver’ a condition in which Fatty acid accumulates in the liver
- α 1-antitrypsin deficiency
 - Protease inhibitor
- Malignancy
- Poisons and infectious agents

Markers used in hepatocellular necrosis	
ALT	AST
HIGH SPECIFIC	LOW SPECIFIC
Produced by: Mostly in liver, small amounts in heart.	Produced by: Heart, liver, skeletal muscle, kidney and small amount in RBC *erythrocytes*.
Major diagnosis *elevated in*: liver diseases.	Major diagnosis *elevated in*: (High serum activity) liver, skeletal muscle, heart diseases and hemolysis.

Hemolysis means the RBC’s lysis. As AST can be found in small amounts in RBC’S that means when RBC’S are lysed AST will be found in the serum

Proteins as biomarkers

Cystatin C	B-type natriuretic** peptide (BNP)	Prostate Specific Antigen (PSA) (Tumor marker)	α-Fetoprotein: (Tumor marker)
<ul style="list-style-type: none"> • 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 kidney (renal) failure • Clinically used as a marker for: <ol style="list-style-type: none"> 1- detecting early kidney disease. 2- monitoring kidney transplantation & acute kidney injury 	<ul style="list-style-type: none"> • A peptide secreted mainly in the cardiac ventricles in response to cardiac-expansion and pressure overload. • High serum levels (abnormal) are observed in congestive heartfailure. (فشل القلب الاحتقاني) • It can be used to differentiate patients whose symptoms are due to heart failure (very high) from those whose symptoms are due to other causes such as pulmonary disease (slightly high). 	<ul style="list-style-type: none"> • A serine protease*** enzyme also called kallikrein III, seminin. • Produced by prostate gland • PSA level is used as a tumor marker to aid diagnosis and for monitoring in patients with prostatic cancer. • Liquefies ejaculate. • Less specific in diagnosis • High serum levels (abnormal) are also observed in: <ul style="list-style-type: none"> ❖ Benign prostatic hyperplasia (BPH) ❖ Prostatic inflammation /infection 	<ul style="list-style-type: none"> • It is produced by the fetal liver, plasma levels decrease rapidly after birth→ in newborn babies α-fetoprotein levels are very low. • It remains low under normal conditions. • High conc. (abnormal) are observed in: <ul style="list-style-type: none"> ➢ hepatocellular carcinomas (hepatoma) ➢ testicular carcinomas. ➢ GI tract carcinomas. • high conc. Are also found in benign (non-cancerous) conditions e.g. hepatitis, So it is non-specific marker.

*Muscle mass affects serum and urinary creatinine but not cystatin C; therefore, the use of cystatin may represent a more adequate alternative to assess renal function in healthy individuals.

**Natriuretic is release Na through urine.

• All markers are low in normal condition and become high with disease *abnormal condition*

***Protease: enzyme that performs protein catabolism by hydrolysis of the peptide bonds

****glomerular filtration rate(GFR): the volume of fluid filtered from the renal (kidney) glomerular capillaries into the Bowman's capsule per unit time

Hormones as biomarkers: Anti-Mullerian hormone (AMH)

A polypeptide hormone involved in **sexual differentiation of male embryo**

Appears to be a **best marker** for estimating egg cell reserve in the ovaries (ovarian reserve testing)

In females it is produced by ovaries

Only growing follicles produce AMH

Prevents premature depletion of ovarian follicles

Plasma AMH levels strongly correlate with number of growing follicles

Helps assess female fertility

Women are born with their lifetime supply of eggs, and these gradually decrease in both quality and quantity with age. **Anti-Mullerian Hormone (AMH)** is a hormone secreted by cells in developing egg sacs (follicles). The level of **AMH** in a woman's blood is generally a good indicator of her ovarian reserve

Anti-Mullerian hormone (AMH)

High levels in women with Polycystic ovarian syndrome (PCOS)

Low levels in women with ovarian dysfunction

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

Biomarkers	Type	Specificity	Abnormal levels	Disease	Produce by	
Amylase	Enzyme	Low	Very high	Acute pancreatitis & other diseases	Due to acute pancreatitis	
Lipase		High	High	Acute pancreatitis		
ALT		High		Liver diseases	Liver	
AST		Low		Liver & muscle diseases		
Cystatin C	Protein	-----		High	Renal diseases	All nucleated cells
BNP		-----	Congestive heart failure		Cardiac expansion and pressure overload	
PSA		Low	Very high		-BPH -Prostatic inflammation or infection	Prostate gland
α-Fetoprotein		Low	High		-hepatoma -Testicular carcinomas -GI tract carcinomas	Fetal liver
AMH	Hormone	-----	-----	-Estimating egg cell reserve -Assessing female fertility	Ovaries (growing follicles)	

Quiz:

1-Which one of these is biomarker indicate renal disease?

- A- BNP B- Cystatin C C- α -Fetoprotein

C-3

2-What is the major diagnose of highserum levels of ALT?

- A- Muscle diseases B- Liver diseases C- Both are possible

B-2

B-1

3-Which one of these is low specificity biomarkers?

- A- Lipase B- ALT C- α -Fetoprotein

4- What are the roles of AMH?

Slide (13) 1st& 5thpoints

5-What are the Causes of pancreatitis?

Slide (10)

نتمنى لكم التوفيق والنجاح!

436 Biochemistry team

► girls team members:

1- نوره الشيب.

-Contact us:

Biochemistryteam436@gmail.com

twitter.com/436biochemteam

► Boys team members:

1- محمد المهوس

2- حمد الحسون

3- محمد حكمي

4- محمد حبيب

5- فهد العتيبي

6- هشام القوسي

7- عبدالعزيز الصومالي

8- محمد العسيري

9- خالد القحطاني

10- طلال الطخيم

-Team leaders:

نوره السهلي.
عبدالله المانع.