BIOCHEMICAL MARKERS FOR DIAGNOSIS OF DISEASES AND FOLLOW UP

"KEEP CALM AND NEVER GIVE UP"

435 Biochemistry Team

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.

BIOMARKERS [المؤشرات الحيوية]

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

Biomarkers are either:

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.

*Most common body fluids for the measurement of biomarkers are:

▪ Blood   ▪ Urine   ▪ Plasma   ▪ Serum

Tissue-specific biomarkers

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

- Factors affecting serum biomarker level
    - Cell damage
    - Rate of biomarker synthesis and clearance
    - Enzyme inhibitors
    - Glucose deficiency
    - Localized hypoxia (less oxygen)
    - Ischemia (obstruction of blood vessels)
    - Necrosis
    - Tissue infarction due to ischemic necrosis
    - Myocardial infarction

Cell damage

Can be due to:

A) Tissue inflammation
e.g. Acute hepatitis (↑ALT)
Acute pancreatitis (↑amylase)

B) Hypoxia
Ischemia → hypoxia → infarction
e.g. myocardia infarction (↑troponin)

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 <u>small quantities</u> of a marker

- ✓ **Specific:** Specificity is the ability of an assay to detect <u>only the marker of interest</u>

- ✓ **Robust** to produce fast results

Examples of biomarkers

Enzymes

Biomarkers

Proteins

Hormones
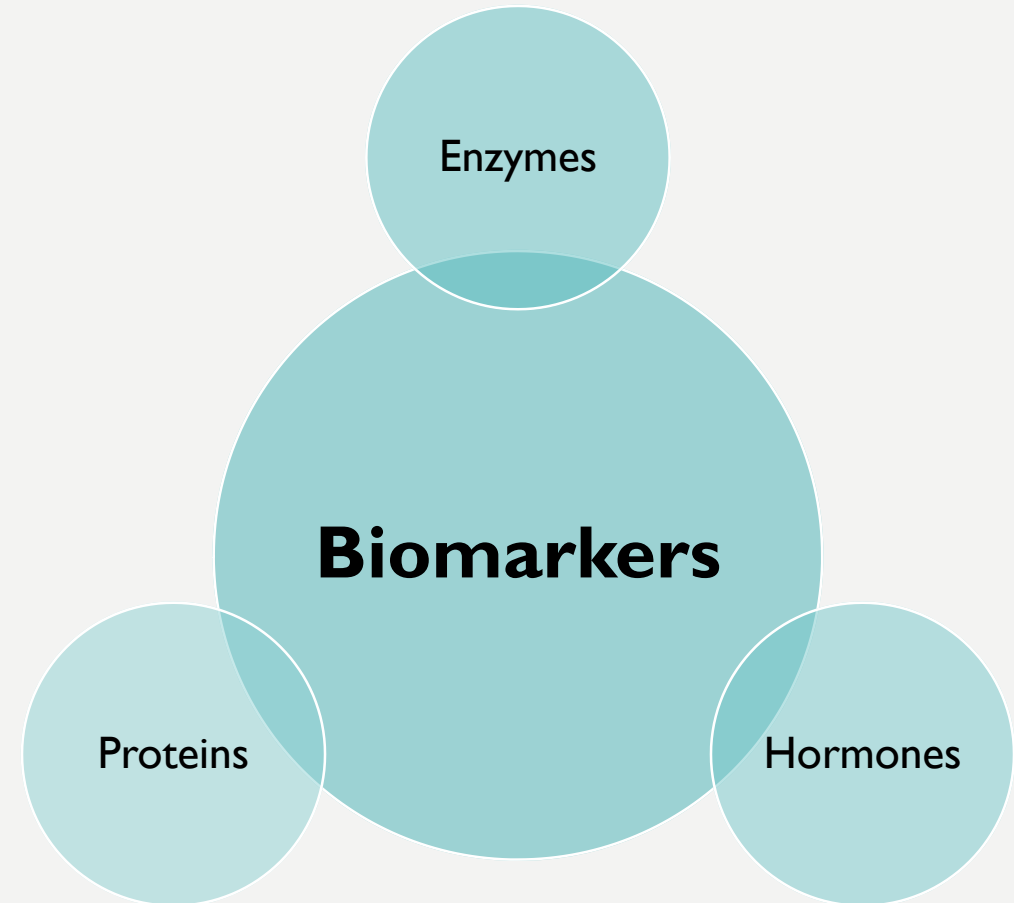
Enzymes as biomarkers

Examples:

Aspartate aminotransferase (AST)

Alanine aminotransferase (ALT)

Amylase, Lipase

Acute pancreatitis is the inflammation of pancreas caused by:
- Obstruction of the pancreatic duct
- Gallstones
- Alcohol abuse

	(AST)	(ALT)
Produced by:	Heart, liver, skeletal muscle, kidney, erythrocytes.	Liver.
Elevated in:	Liver disease, heart disease, skeletal muscle disease, haemolysis.	Liver disease

- Serum lipase has higher specificity than serum amylase (elevated only in acute pancreatitis)

- Appears in plasma: within 4-8 hr. and remains: for 8-14 days
- Measurement of amylase and lipase give 90-95% accuracy in the diagnosis of acute pancreatitis and abdominal pain

- Diagnostic indicator of acute pancreatitis: Elevated serum amylase level.

- Indicator of acute pancreatitis: Amylase level greater than 10 times the upper limit.

- The reason the test has low specificity: because elevated amylase level is also present in other diseases.

- It appears in the serum: within 2-12 hr. after abdominal pain, and returns to normal: in 2-3 days.
- Free amylase (unbound form) is rapidly cleared by the kidneys

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HIGH SERUM ALT AND AST LEVELS IN LIVER DISEASES ARE DUE TO:

- Alcohol abuse

- Medication

- Chronic hepatitis B and C

- Steatosis and steatohepatitis

- Autoimmune hepatitis

- Wilson's disease

- a_1-antitrypsin deficiency

- Malignancy

- Poisons and infectious agents

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

Proteins as biomarkers

Proteins as biomarkers

B-type natriuretic peptide (BNP)

- A peptide secreted mainly in the cardiac ventricles in response to cardiac expansion and pressure overload
- High serum (abnormal) levels are observed in congestive heart failure

Note :
It can be used to differentiate patients whose symptoms are due to heart failure (if it high) from those whose symptoms are due to other causes such as pulmonary disease (if it low).

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 (abnormal) cystatin C indicates early renal disease
• Clinically used as a marker for:
  o detecting early kidney disease
  o monitoring kidney transplantation
  o acute kidney injury

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 (abnormal) are also observed in:
  o Benign prostatic hyperplasia (BPH)
  o Prostatic inflammation/infection

Alpha-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 (abnormal) conc. are observed in:
  o hepatocellular carcinomas (hepatoma)
  o testicular carcinomas
  o GI tract carcinomas
- It is a non-specific marker.

Proteins as biomarkers

	Alpha-Fetoprotein	B-type natriuretic peptide (BNP)	Cystatin C	Prostate Specific Antigen (PSA)
Normal	Low	-----	Low	Low
Abnormal	high	High	High	Very high
Disease	- hepatoma. - Testiclar carcinomas. - GI tract carcinomas.	Congestive heart failure.	Renal disease.	(BPH). Prostatic inflammation \ infection.
Produce by	Fetal liver.	Secreted mainly in the cardiac ventricles in response to cardiac expansion and pressure overload.	All nucleated cells	Prostate gland.

Hormones as biomarkers :

Anti-Mullerian hormone (AMH):

Where?

- In female it is produced by ovaries.

- Only growing follicles produce AMH.

What does it do?

- Appears to be a best marker for estimating egg cell reserve in the ovaries.

- Plasma AMH levels strongly correlate with number of growing follicles

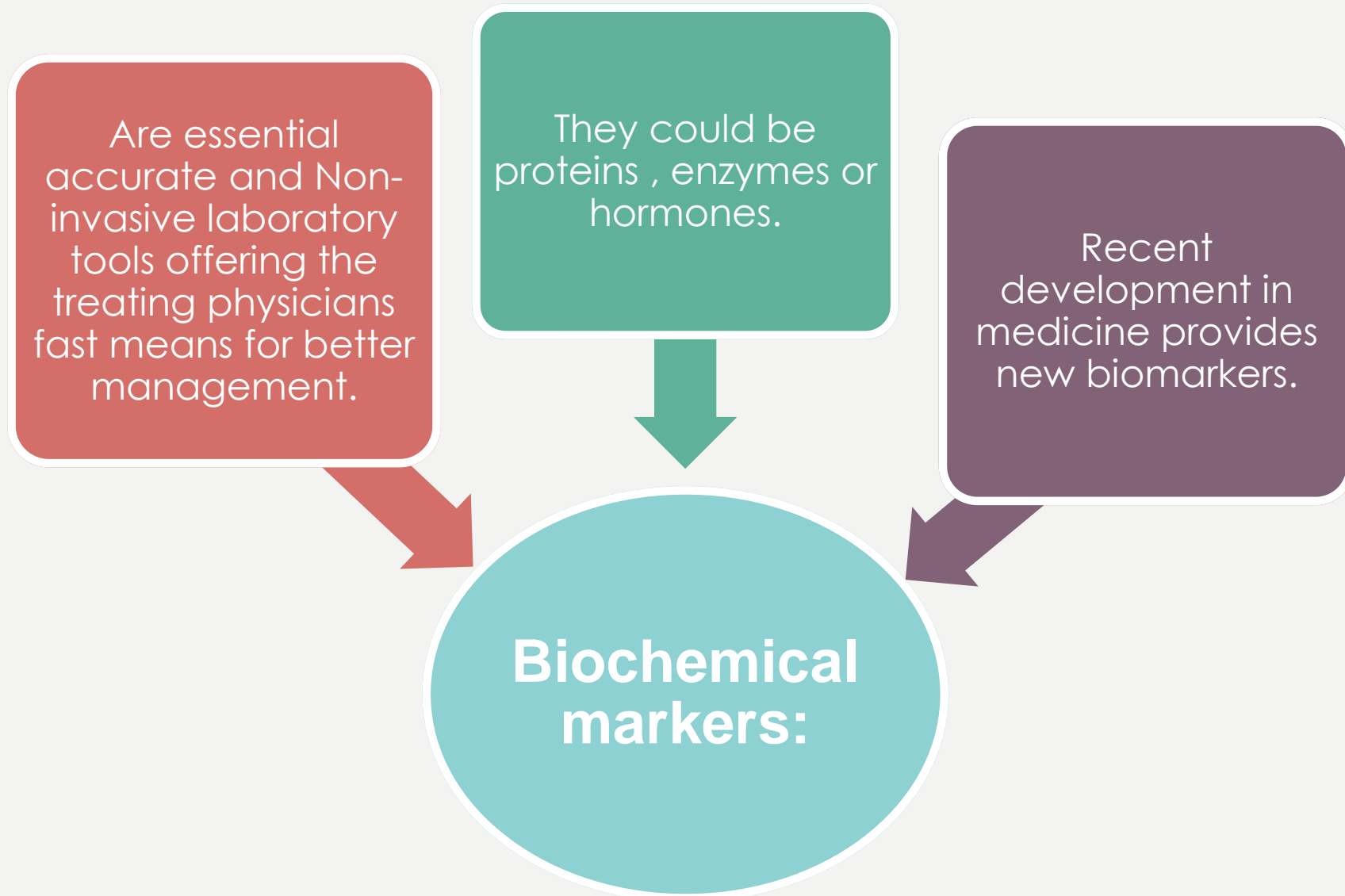A polypeptide hormone involved in sexual differentiation of male embryo.

HIGH LEVELS: in women with syndrome (PCOS).

عنددها بويضات كثيرة لكنها غير ناضجة

LOW LEVELS: in women with ovarian dysfunction

Take home message :

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.

Biochemical markers:

Summary

❖ <u>Biomarker</u> biological molecule found in body fluids (blood, urine) , or tissues that indicates a normal or abnormal process such as a disease or a condition.

❖ Diagnosis: Identification of a disease.

❖ Prognosis: The outcome.

<u>Criteria of a good biomarker assay:</u>
*<u>Sensitive:</u> small quantities   *<u>Specific:</u> only one marker

Biomarkers

Plasma-specific

- present in <u>plasma</u>
- Perform their functions in blood

Tissue-specific

- Present <u>inside the cell</u>
- low conc. in plasma = cellular turnover
- high conc. In plasma = cell damage
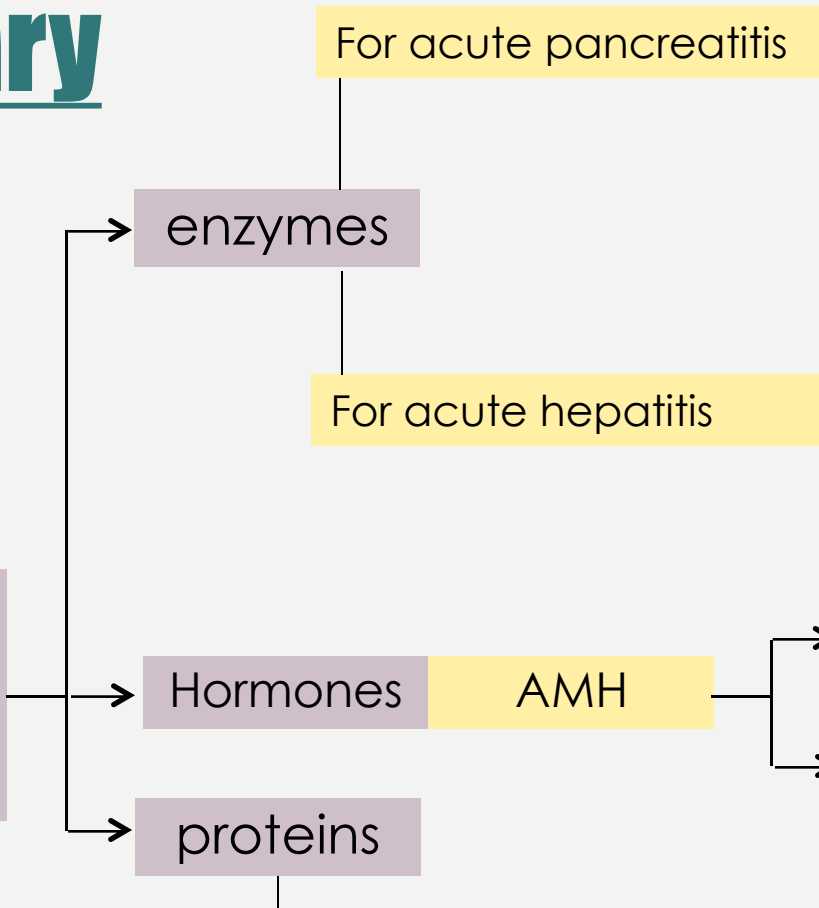
Cell damage

Tissue inflammation   ALT = acute hepatitis   Amylase = acute pancreatitis

Ischemia → hypoxia → infarction → ↑ plasma [Troponin] in MI

Summary

Examples of biomarkers

→ **enzymes**

For acute pancreatitis

Amylase	Lipase
* greater than 10 times the upper limit. * low specificity. * appears within 2-12 hours after abdominal pain. * returns to normal in 2-3 days.	* higher specificity. * appears within 4-8 hours * remains for 8-14 days

For acute hepatitis

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

→ **Hormones** — **AMH**

→ Low levels in women with ovarian dysfunction

→ High levels in women with Polycystic ovarian syndrome (PCOS)

→ **proteins**

α-Fetoprotein
* Produced by the fetal liver
* High conc. are observed in: (hepatocellular carcinomas (hepatoma), testicular carcinomas, GIT carcinomas)

Cystatin C
* Produced by all nucleated cells of the body.
* Used as a marker for: (detecting early kidney disease, monitoring kidney transplantation)

PSA
* Produced by prostate gland.
* High conc. are observed in: (prostatic cancer, Benign prostatic hyperplasia, Prostatic inflammation/infection)

BNP
* Secreted in the cardiac ventricles in response to cardiac expansion and pressure overload.
* High conc. are observed in congestive heart failure.

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Videos

✓ [Biomarker overview](#)

✓ [Serum AST and ALT](#)

MCQs

1-In the case of myocardial infarction, which of the following is elevated:
A. BNP
B. AST
C. Troponin
D. All of the following

2-……….is a type of proteins as biomarkers:
A. PSA
B. AST
C. ALT
D. Lipase

3-high concentration of PSA can causes …….disease:
A. BPH
B. Hepatoma
C. Renal disease.
D. Heart failure.

4-Biomarkers could be all these except:
A. proteins.   B. enzymes.   C. vitamins.   D. hormones.

5-Women with syndrome (PCOS) her (AMH) levels will be :
A. High B. low C. normal

5-A
4-C
3-A
2-A
1-D

6- Which of the following in the best marker for the diagnosis of acute pancreatitis?

a) Lactase.
b) Amylase.
c) Cholesteryl esterase.
d) Y- Glutamyl trans peptidase.
e) Sucrase.

7-Both ALT and AST levels can test for:

a) Liver damage.
b) Heart problems.
c) Damage in the pancreas.
d) Infections.
e) Sarcoidosis.

8-All are true about plasma-specific biomarkers except:
a) Perform their functions in blood.
b) If higher concentration is detected in plasma, it indicates cell damage.
c) High level of activity in plasma than in tissue cells.
d) Normally present in plasma.

8-B
7-A
6-B

MCQs

9-A low concentration can be detected in plasma due to cellular turnover" describes:

A. Tissue-specific biomarkers
B. Plasma-specific biomarkers

10-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. Transporters
B. RNA
C. Biomarkers
D. Cells

10-C
9-A

Boys Team:

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- مهند الزهراني.

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- محمد الصهيل .

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- ساره العنزي.
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- نوره القحطاني.
- بدور جليدان.
- علا النهير.
- أفنان المالكي.
- فاطمه الدين.
- جوهره المالكي.
- خوله العريني.
- لجين السواط.
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