ENZYMES OF CLINICAL IMPORTANCE II

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Advance Clinical Biochemistry II (MA 406)

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Lecture Seven

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Outlines

- Markers for Liver disease diagnosis
- Markers for Pancreatic disease diagnosis
- Markers for Muscles disease diagnosis
- Markers for Myocardial infraction
- Markers for Prostate disease diagnosis
- Markers for bone disease diagnosis

Objectives

- **At the end of this lesson, the students should be able to:**
- Understand the general concept of the clinical enzymology.
- Understand the enzymatic importance in clinical diagnosis.
- Understand how enzymes are used as markers in disease diagnosis.
- Understand the alternative marker enzymes for disease diagnosis.

Markers of cholestasis

- **Alkaline phosphatase (ALP)**
  - **The alkaline phosphatases** are a group of enzymes that hydrolyze organic phosphates at high pH.
  - They are present in most tissues but are in particularly high concentration in the **osteoblasts of bone and the cells of the hepatobiliary tract, intestinal wall, renal tubules, and placenta**.
  - Normal level: **0-45 IU/L**
  - In adults, plasma ALP is derived mainly from **bone and liver in approximately equal proportions.**
  - The proportion due to the bone fraction is increased when there is increased osteoblastic activity that may be physiological

❖ Causes of raised Plasma ALP activity

- **Physiological:**
  - **During pregnancy**: the plasma total ALP activity rises due to the contribution of the placental isoenzyme.
  - **In infants**: plasma total ALP activity is up to five times that in adults and consists predominantly of the bone isoenzyme.
  - **In children**: the total activity increases by about 2 to 5 times during the pubertal bone growth

- **Pathological**
  - **Liver disease**
    - Intrahepatic or extrahepatic cholestasis
    - Inflammatory bowel disease: the gut ALP isoenzyme can be increased in ulcerative colitis.
  - **Bone disease :**
    - Rickets (in child) and osteomalacia.
    - Paget's disease of bone (may be very high)
    - osteogenic sarcoma
    - hyperparathyroidism.
  - **Malignancy:** bone or liver involvement or direct tumor production

❖ Isozymes of Alkaline Phosphatase (ALP)

- **Hepatic Isoenzyme:** Its level rises in extrahepatic biliary obstruction.
- **Bone Isoenzyme:** Increases due to osteoblastic activity and is normally elevated in children during periods of active growth.
- **Placental Isoenzyme:** Rises during the last 6 weeks of pregnancy.
- **Intestinal Isoenzyme:** Rise occurs after a fatty meal. May increase during various GI disorders.

❑ Gamma-glutamyl-transferase (GGT)

- **Gamma-glutamyl-transferase** catalyzes the transfer of the γ–glutamyl group from peptides and compounds that contain it to an acceptor.
- It is involved in **amino acid transport** across the membranes.
- **Gamma-glutamyl-transferase** is found mainly in **biliary ducts of the liver**, **kidney,** and **pancreas.**
- Y-GGT increased in liver diseases, especially in obstructive jaundice.

➢ Clinical Significance

- Normal values for GGT
- Male: <55 U/L, Female: <38 U/L

➢ Causes of raised plasma GGT activity

- Induction of enzyme synthesis, without cell damage, by drugs or alcohol.
- Hepatocellular damage, such as that due to infectious hepatitis
- In Cholestatic liver disease, elevated GGT activity usually parallels those of ALP activity

❑ 5’ Nucleotidase

- It catalyzes the hydrolysis of the phosphoric ester bond of 5′-ribonucleotides to the corresponding ribonucleoside and phosphate.
- The enzyme hydrolyses 5’ nucleotides to 5’ nucleosides at an optimum pH of 7.5.
- Moderately increased in **hepatitis and highly elevated in biliary obstruction**.
- Unlike ALP the level is unrelated to osteoblastic activity and is thus **unaffected by bone disease.**

Enzymes for Diagnosis of Pancreatic Diseases

- **Amylase**

- It belongs to the hydrolase class that catalyzes the hydrolysis of 1,4- a-glycosidic linkages in polysaccharides.

- They are low molecular weight proteins (54 to 62 kDa) that can pass the glomeruli of the kidneys. It is the only plasma enzyme physiologically found in urine.

- **Plasma amylase** is derived from the **pancreas and salivary glands**. Thus, pancreatic juice and saliva contain high concentrations of amylase.

- Estimation of plasma amylase activity is mainly used for diagnosis of acute pancreatitis.

- **Clinical Significance**
- Normal values of amylase: 28-100 U/L

❖ Causes of Raised Plasma Amylase Activity

- **Marked increase (5 to 10 times the upper reference limit)**:
  - Acute pancreatitis
  - Severe glomerular impairment

- **Moderate increase (up to five times the upper reference limit)**

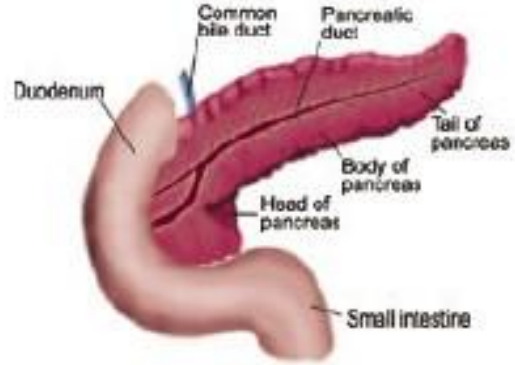
  - **Acute abdominal disorders**
    - Acute cholecystitis((inflammation of the gall bladder)
    - Perforated peptic ulcer
    - Intestinal obstruction
    - **Salivary gland disorders** like mumps, salivary calculi

Cont.

❑ Lipase

- **Lipase is** a single-chain glycoprotein with a molecular weight of 48 kDa.
- Lipase is derived from the pancreas but is more specific for pancreatic pathology than amylase.
- In addition, lipase has a longer half-life than amylase and, therefore may be more useful in the diagnosis of acute pancreatitis and carcinoma of the pancreas.
- serum amylase is increased in mumps, pancreatic disease, or due to some other cause, whereas lipase is increased only in pancreatitis.
- Therefore, the determination of both amylase and lipase together helps in the diagnosis of acute pancreatitis
- **Clinical Significance:** Normal values: 40-200 U/L

Pancreatic Enzymes



AMYLASE	LIPASE
N: 25-125 U/L	N: 10-150 U/L
↑acute pancreatitis	↑acute pancreatitis
↑ starts at 4-12 h	↑ starts at 12-18 h
maximum 12-24 h	
Returns N 48-72 h	Returns N 5-7 days

Cont.

❑ Trypsin

- **Trypsin** is a serine proteinase that hydrolyzes the peptide bonds formed by the carboxyl groups of lysine arginine with other amino acids.

- **Clinical Significance**
  - Normal values of trypsin: 25 ± 5.3 μ g/L

- Though it increased in pancreatic disease. However, as there is no distinct role of trypsin estimation in the routine management of patients with acute pancreatitis, this test is therefore considered of limited clinical value.

Markers for diagnosis of skeletal muscle disease

- **Creatine Kinase (CK)**

- **Creatine phosphokinase (CPK)** It is an enzyme found primarily in the heart and skeletal muscles, and to a lesser extent in the brain but not found at all in the liver and kidney.

- Catalyzes the transfer of phosphate between creatine and ATP/ADP Provides rapid regeneration of ATP when ATP is low.

- In tissues and cells that consume ATP rapidly, especially skeletal muscle **CPK** serves as an energy reservoir for the rapid buffering and regeneration of ATP *in situ.*

- Creatine + ATP ⟶ phosphocreatine + ADP

- **Clinical significance**

- Normal range for total CK:
  - **Male: 46-171 U/L, –Female: 34-145 U/L**

Cont.

❖ Causes of raised plasma CK activities

- Physiological: enzyme activity in serum is highest in infancy and childhood (7-10 years of age).

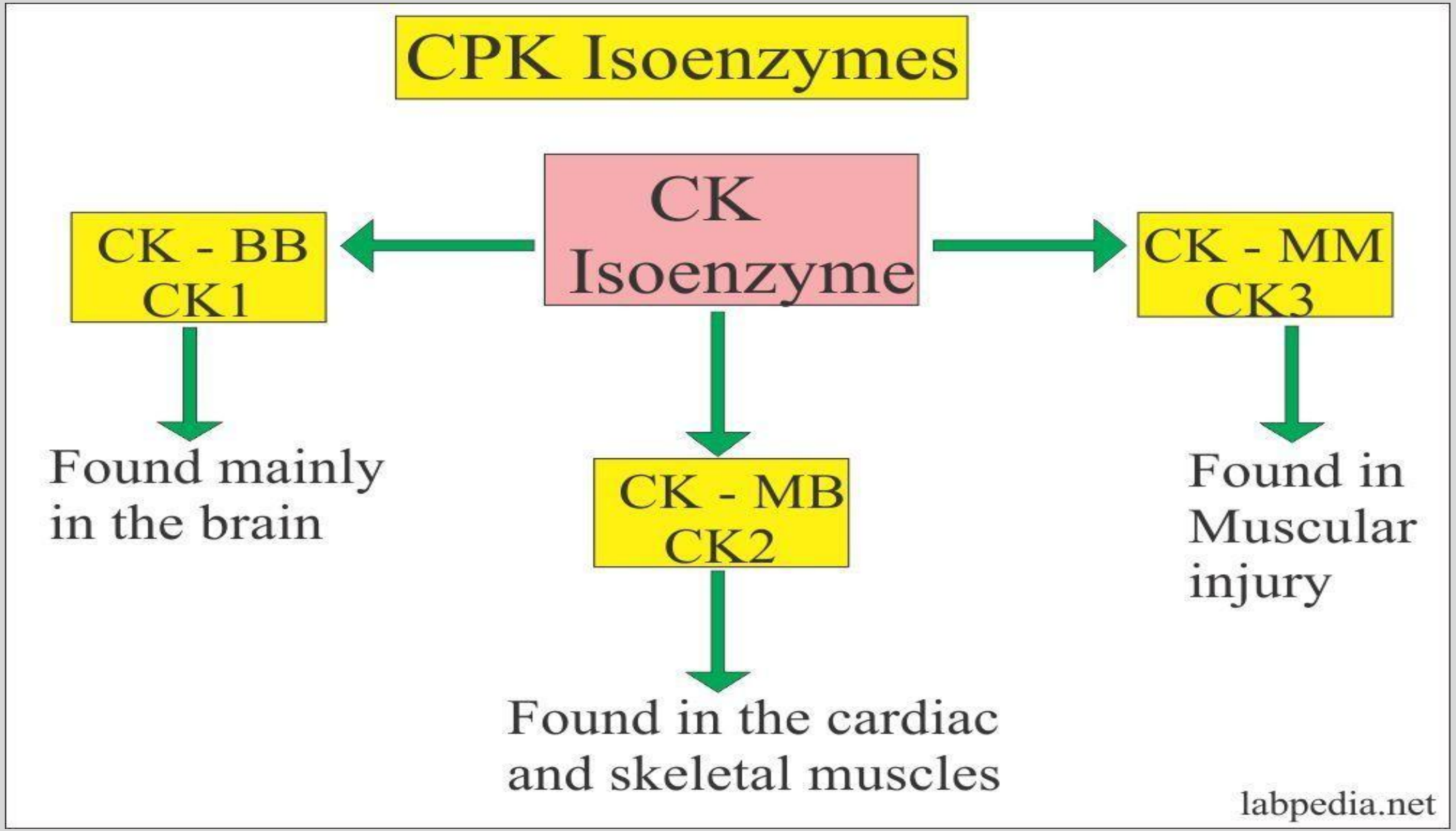
- Pathological:
  - Elevation of CK is an indication of muscle damage.
  - Clinically, CK is assayed in blood tests as a marker of damage to CK-rich tissue such as in
    - Myocardial infarction (heart attack)
    - Rhabdomyolysis (severe muscle breakdown)
    - Muscular dystrophy
    - Autoimmune myositides
    - Acute kidney injury

❖ Isoenzymes of CK

- CK activity is found largely in skeletal muscles, brain, and heart tissue.
- Isoenzymes of CK: CK consists of two protein subunits, M (for muscle) and B (for brain), which combine to form three isoenzymes.

- Three isoenzymes:
  - CK1 (CK-BB): in the brain
  - CK2 (CK-MB): mostly in the cardiac muscles
  - CK3(CK-MM): in both the skeletal and the cardiac muscles.

- CK-MB
  - is more specific for cardiac muscle, so it is a more sensitive marker of myocardial injury than total CK activity. its plasma activity is always high after myocardial infarction.
- CK-BB
  - high concentrations in the brain, after brain damage
  - CK-BB increased plasma activities may occur during parturition (childbirth).


CPK Isoenzymes
CK Isoenzyme
CK - BB CK1
CK - MB CK2
CK - MM CK3
Found mainly in the brain
Found in the cardiac and skeletal muscles
Found in Muscular injury
labpedia.net

❑ Lactate Dehydrogenase(LDH)

- **LDH** is an enzyme that produces energy and catalyzes the interconversion of lactate and pyruvate.
- It is found extensively in body tissues with high concentrations in cells of cardiac and skeletal muscle, liver, kidney, brain, and erythrocytes
- Measurement of plasma total LDH activity is therefore a non-specific marker of cell damage.
- LDH is released during tissue damage, a common marker of injuries and diseases such as heart failure.

- **Clinical significance:**
  - **Normal Values Of LDH: 140u/l to 280 u/l**
  - **It is increased in plasma in Myocardial injury, acute leukemias, generalized carcinomatosis, and in acute hepatitis.**
  - **Estimation of its isoenzymes is more useful in clinching diagnosis between hepatic disease and Myocardial injury.**

❖ Causes of Raised Plasma Total LDH Activity

- **Artefactual***:* In vitro haemolysis or delayed separation of plasma from whole blood.

- **Marked increase (may be greater than 5–10 times)**:
  - Circulatory failure with ‘shock’ and hypoxia
  - Myocardial infarction.
  - In some haematological disorders: megaloblastic anaemia, acute leukaemias and lymphomas.

- **Moderate increase**. (usually less than five times)
  - Viral hepatitis
  - Malignancy of any tissue
  - Skeletal muscle disease
  - Pulmonary embolism: **Pulmonary embolism** is the sudden blockage of a major blood vessel (artery) in the **lung**

Markers for Diagnosis of Myocardial Infraction

- Enzyme assays for the diagnosis of Acute Myocardial Infarction are:

1. **Creatine kinase (CK).**
2. **Creatine kinase-MB (CK-MB) isoenzyme**
3. **Lactate dehydrogenase (LD).**
4. **Aspartate aminotransferase (AST).**

Markers for Diagnosis of Prostate Disease

- **Acid Phosphatase(ACP):** Include all phosphatases that hydrolyze phosphate esters with an optimum **pH of less than 7.0.**

- It is produced Primarily in prostate gland. It is also found in erythrocytes, platelets, leukocytes, bone marrow, bone, liver, spleen, kidney, and intestine.

- **Normal range of ACP: 1.5-4.5 U/L**

- **Clinical Implications:**

- Primarily used to diagnose prostate cancer and to monitor its treatment.
- ACP is replaced by the measurement of plasma **prostate-specific antigen (PSA)** a protein derived from the prostate. This test is more specific and sensitive for diagnosis and monitoring treatment
- In other non prostatic conditions e.g.
    - Hemolysis
    - Paget disease
    - Hyperparathyroidism with skeletal involvement
    - Presence of malignant invasion of bones by cancers

Markers for Diagnosis of Bone Disease

- **Alkaline Phosphatase(ALP):-**
  - Rises in Rickets, osteomalacia, hyperparathyroidism and in Paget's disease.
  - Also rises in primary and secondary malignancies of bones.
- **Acid Phosphatase(ACP):-**
  - Highly increased in bony metastasis of carcinoma prostate

Enzymes	Tissues	Clinical applications
Alanineamino transferase	Liver	Hepato parenchymal diseases
Alkaline phosphatase	Liver, bone, intestinal mucosa, Placenta	Liver and bone diseases
Amylase	Salivary glands, Pancreas	Pancreatic diseases
Aspartate amino transferase	Liver, Skeletal muscle, Heart, Erythrocytes	Hepatic parenchymal disease, Muscle disease
Cholinesterase	Liver	Organophosphorus insecticide poisoning, Hepatic parenchymal diseases
Creatine kinase	Skeletal muscle,Heart	Muscle diseases
Gamma glutamyl transferase	Liver	Hepatobiliary diseases, Marker of alcohol abuse
Lipase	Pancreas	Pancreatic diseases
Lactate dehydrogenase	Heart, liver, skeletal muscle erythrocytes, lymph nodes, Platelets	Hepatic parenchymal diseases, muscle diseases Hemolysis, tumor marker
5'nucleotidase	Liver	Hepatobiliary diseases
Trypsin	Pancreas	Pancreatic diseases


Questions
Comments
Feedback

References

- Kramer, J.W. and Hoffmann, W.E., 1997. Clinical enzymology. In *Clinical biochemistry of domestic animals* (pp. 303-325). Academic Press.

- Srivastava, T. and Chosdol, K., 2007. Clinical enzymology and its applications. *Clinical Bio-chem*, *4*, pp.3-4.

- Nelson, D.L. and Cox, M.M., Lehninger Principles of Biochemistry 6th Edition (2013).

- Champe, P.C., Harvey, R.A. and Ferrier, D.R., 2005. *Biochemistry*. Lippincott Williams & Wilkins.

- Murray, K., Rodwell, V., Bender, D., Botham, K.M., Weil, P.A. and Kennelly, P.J., 2009. Harper's illustrated biochemistry. 28. *Citeseer, New York, United States*.

- Marshall, W.J. and Bangert, S.K. eds., 2008. *Clinical biochemistry: metabolic and clinical aspects*. Elsevier Health Sciences.