Enzyme Patterns In Different Diseases and More..

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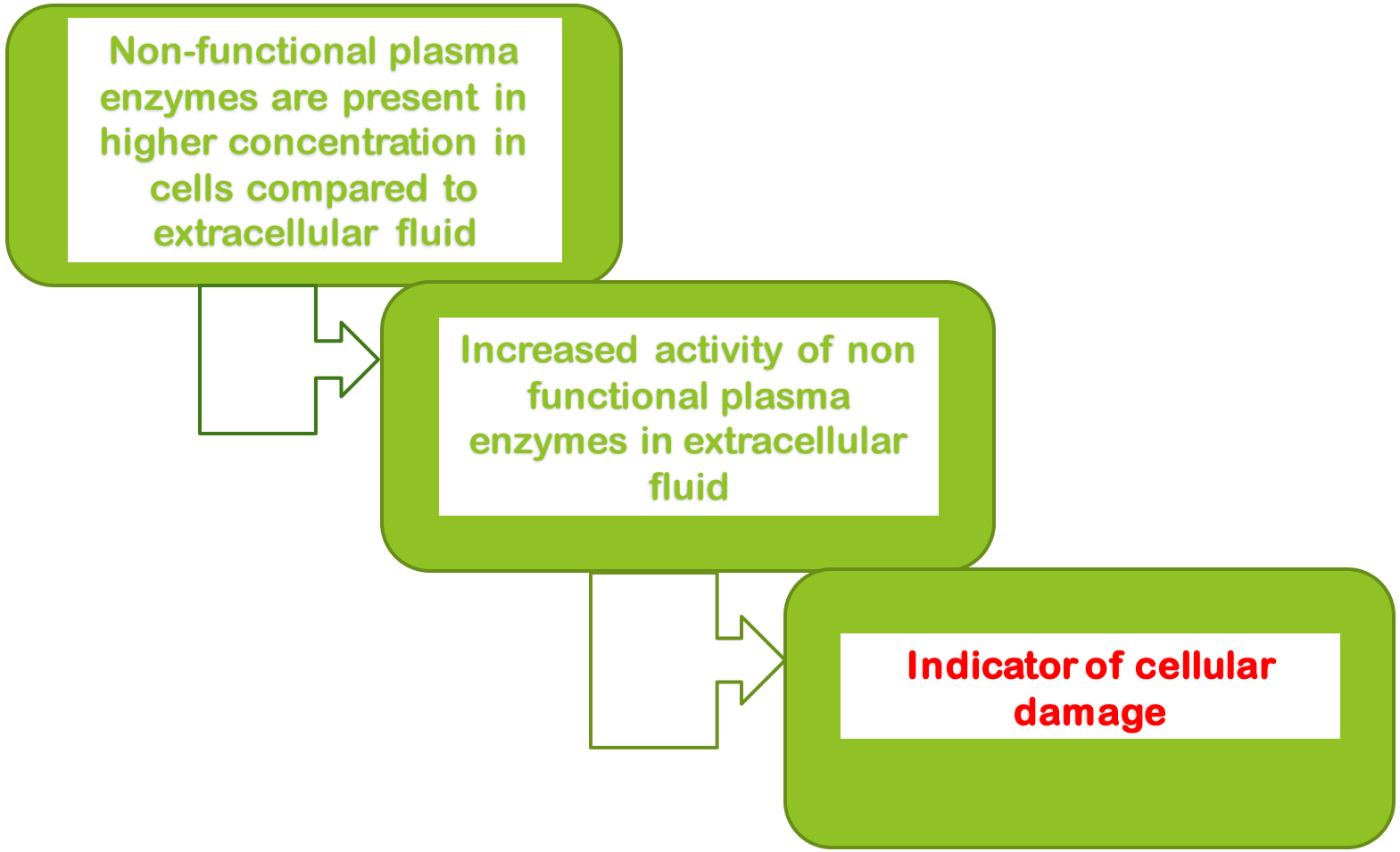
Introduction

- Enzymes are biocatalysts – the catalysts of life

- Enzyme in the circulatory system are divided into two groups:
  - Functional plasma enzymes
  - Non-functional plasma enzymes

Functional plasma enzymes	Non-functional plasma enzymes
Present in higher concentration in plasma than in most tissues	Present in very high concentration in tissues than in the plasma
Have known functions	No known functions
Their substrates are always present in the blood	Their substrates are absent from the blood
• Enzymes involved in blood coagulation • Ferroxidase • Pseudo cholinesterase • Lipoprotein lipase	▪ Aspertate Aminotransferase ▪ Alanine Aminotransferase ▪ Creatinine Kinase ▪ Lactate dehydrogenase ▪ Amylase


Non-functional plasma enzymes are present in higher concentration in cells compared to extracellular fluid
Increased activity of non functional plasma enzymes in extracellular fluid
Indicator of cellular damage

Factors Affecting Results of Plasma Enzyme Assays

- **Analytical factors:**
- Substrate concentration
- Product concentration
- Enzyme Concentration
- Reaction temperature
- Presense of activators or inhibitors
- Reaction pH

- **Non-disease factors:**
- Age:
- ✓ AST - Neonate > Adult
- ✓ ALP - Children > Adult

- Sex:
- ✓ GGT & CK activity- Men > Women

- Race/ethnicity

- Physiological conditions:
- ✓ AST and CK rises immediately after labour or strenuous exercise

Clinical Case

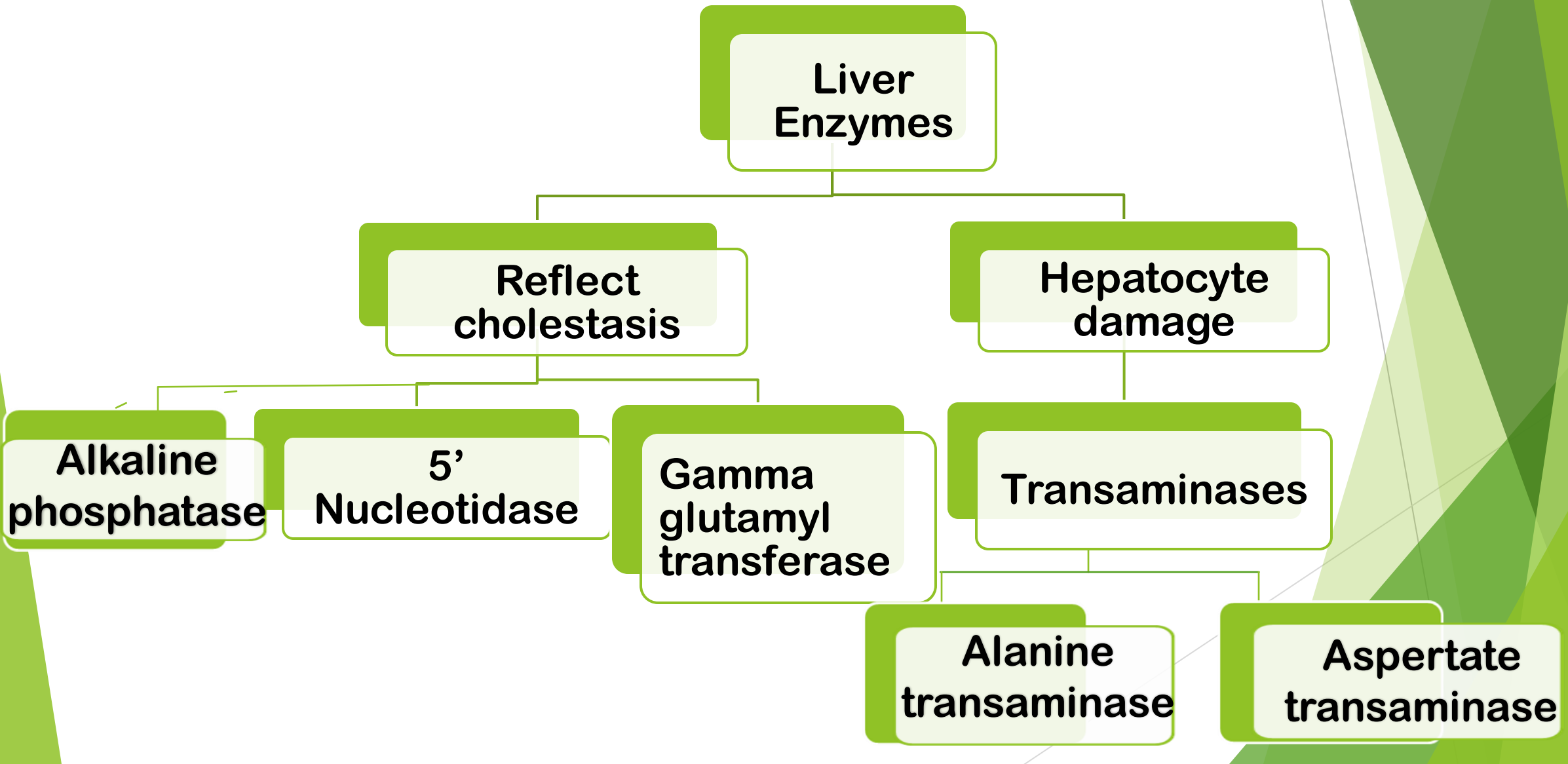
A 8 years old clinically icteric boy came to the department of Paediatrics with the complaints of nausea, loss of appetite, yellowish discoloration of urine and pale stool for 15 days. He also complained of abdominal pain in the periumbilical region for 20 days. Body temperature, pulse rate and resp. rate were normal.

Laboratory investigation revealed-

- Hb- 11.5g/dl
- ALT- 210U/L (Elevated)
- AST- 195U/L (Elevated)
- ALP- 150U/L (Normal)
- Total bilirubin- 4.5mg/dl (Elevated)
- Direct bilirubin- 2.5mg/dl (Elevated)
- Hepatitis A IgM- positive

Diagnosis: Acute Viral Hepatitis (Hepatitis A virus)

Liver Enzymes



Alanine Transaminase

- Found in liver (mainly), kidney, skeletal muscle and heart
- Normal range: 5-40 IU/L
- More specific for hepatic disease than AST
- Markedly increased (>5-10times URL) in shock, acute viral or toxic hepatitis
- Moderate to slightly increased(<5 times URL) in-
- ✓ Cirrhosis, Infectious mononucleosis, Cholestatic jaundice

- ALT may be found low in alcoholic liver disease due to alcohol induced pyridoxal phosphate deficiency

Aspertate Transaminase

- Found in liver, cardiac and skeletal muscle, kidney and erythrocytes
- Normal range: 5-40 IU/L
- AST is not specific for hepatic disease
- Causes of raised AST:
- ✓ Markedly increased in shock, acute viral hepatitis, MI
- ✓ Moderately or slightly increased in cirrhosis, infectious mononucleosis,cholestatic jaundice

Diagnostic Significance of Transaminases

- ↑ALT ≥ AST in ⟶ most acute hepatocellular disorders
- ↑↑ AST and ALT (>500IU/L) ⟶ hepatocellular jaundice
- ↑ AST and ALT (>200IU/L) ⟶ cholestatic jaundice
- **Persistence of elevated** ALT and AST for ≥6 months in a case of hepatitis ⟶ chronic hepatitis
- **Falsely low** transaminase level ⟶ long term haemodialysis and uremia

AST/ALT Ratio

- ✓ **Normal: 0.8**
- ✓ **<1: acute viral hepatitis, nonalcoholic steatohepatitis**
- ✓ **>1: acute fulminant hepatic failure**
- ✓ **>2 : alcoholic hepatitis, Wilson's disease**

Alkaline Phosphatase

- Found in most tissues but high in osteoblasts of bone, hepatobiliary tract, intestine, renal tubules, placenta
- Normal range: 39-117 IU/L

- Causes of raised ALP:
- ✓ Physiological: Pregnancy, preterm infants, children
- ✓ Bone disease: Rickets, osteomalacia, Paget's disease of bone
- ✓ Liver disease: Cholestasis, tumours
- ✓ Malignancy

- ALP increases **>10 times of normal** in obstruction of biliary tract by stone in duct, SOL, ascending cholangitis
- A low plasma ALP may be found in hypothyroidism, achondroplasia, treatment of hyperlipidemia with fibrate drug, OCP, blood transfusion
- EDTA falsely lowers the ALP activity

Gamma Glutamyl transferase

- Found in liver, kidney,pancreas and prostate
- Normal range: 10-47 IU/L (Male > Female)

- Serum GGT increases **> 10 times of normal** in-
- ✓ Alcoholic hepatitis, Anticonvulsant drugs, Cholestatic liver disease

- **Clinically used to differentiate the increased level of ALP in biliary tract disease from bone disease**

5’ Nucleotidase

- Widely distributed in the body, predominantly liver
- Normal range: 2-17 IU/L
- Clinical significance:
- ✓ Determine whether the source of elevated ALP is liver or bone.

Ceruloplasmin

- Copper containing protein bound in blood
- Synthesized by the hepatic parenchymal cells and lymphocytes
- Normal level: 20-35 mg/dl
- Lower level < 10mg/dl may found in **Wilsons disease**
- **Higher level is usually found in pregnancy, cancer and several neurological conditions such as Alzheimer's disease**

Plasma Cholinesterase and Suxamethonium sensitivity

- Suxamethonium and mivacurium are usually broken down by plasma cholinesterase which limit the duration of their action

- Patients with low cholinesterase activity may develop prolonged period of apnoea if suxamethonium was given