ENZYMES OF THE BILIARY SYSTEM (ALP AND GGT)
Objectives:

1. To define and describe the bile ducts
2. To define Cholestasis and list its causes and sites of effects
3. To Identify the corresponding clinical and laboratory features
4. To diagram serum patterns in different liver diseases
Bile Ducts
Cholestatic disorders may consequently affect:

1. hepatocytes,
2. bile canaliculi or ductules,
3. intrahepatic or extrahepatic bile ducts, or
4. ampullary region.
Although these diverse cholestatic disorders can be classified into three broad categories:

1. Large bile ducts conditions
2. Small bile ducts conditions
3. Hepatocellular conditions

intrahepatic cholestasis. E.g. primary biliary cirrhosis.

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Jaundice indicates hyperbilirubinemia and, in particular, signals a serum bilirubin above about 43 μmol/l (2.5 mg/dl).
Additional clinical problems arise with prolonged cholestasis:

Steatorrhea results from impaired bile acid secretion and gives rise to fat-soluble vitamin deficiencies.

- **Vitamin D malabsorption** contributes to hepatic osteodystrophy,
- **Vitamin K deficiency** - bleeding abnormalities
- **Vitamin E deficiency in children** may produce a degenerative neurologic syndrome with ataxia, peripheral neuropathy, and ophthalmoplegia
Markers of cholestasis
1. Alkaline phosphatase (EC 3.1.3.1; orthophosphoric-monoester phosphohydrolase [alkaline optimum]; ALP). Half-life = 10 days
Causes of raised Plasma ALP activity

- **Physiological**: There is a gradual increase in the proportion of liver ALP with age: in the elderly the plasma bone isoenzyme activity may increase slightly.

- **Pathological**
  - Bone disease
    - rickets and osteomalacia
  - secondary hyperparathyroidism
  - Liver disease
  - Malignancy- bone or liver involvement or direct tumor production.
POSSIBLE CAUSES OF LOW PLASMA ALP ACTIVITY

- Arrested bone growth

- Hypophosphatasia: an autosomal recessive disorder, associated with rickets or osteomalacia.
ISOENZYMES OF ALKALINE PHOSPHATASE

Assays for ALP isoenzymes are needed when:

- The source of an elevated ALP in serum is not obvious and should be clarified.
- The main clinical question is concerned with detecting the presence of liver or bone involvement.
- In the case of metabolic bone disorders, to ascertain any modifications in the activity of osteoblasts to monitor the disease activity and the effect of appropriate therapies.
2. Gamma-glutamyl-transferase (EC 2.3.2.21; γ-glutamyl-peptide: amino acid γ-glutamyletransferase; GGT): catalyzes the transfer of the γ – glutamyl group from peptides and compounds that contain it to an acceptor

Gamma-glutamyltransferase occurs mainly in the cells of liver, kidneys, pancreas and prostate. Plasma GGT activity is higher in men than in women.
Causes of raised plasma GGT activity

1. Induction of enzyme synthesis, without cell damage, by drugs or alcohol.

2. Hepatocellular damage, such as that due to infectious hepatitis:

A patient should never be labeled an alcoholic because of a high plasma GGT activity alone.
↑ Alk Phos

GGT / 5'-nucleotidase

High |
     |
Liver source

Low |
     |
Bone source

Right upper quadrant ultrasound | Bone scan (Paget disease)
Serum Patterns in obstructive jaundice

Fig. Course of serum enzyme activities in obstructive jaundice
Serum Patterns in alcoholic hepatitis

Fig 3: Course of serum enzyme activities in acute alcoholic hepatitis
Conclusions:

1. Bile ducts are any of the ducts by which bile is carried from the liver, first to the gall bladder and then to the duodenum (the first section of the small intestine).

   The bile duct system:

   - Canaliculi
   - Hepatic ducts.
   - Common hepatic duct.
   - Cystic duct,
   - Common bile duct.
2. Cholestasis denotes a disruption in the normal process of bile secretion. Cholestatic disorders may consequently affect:
   1. hepatocytes,
   2. bile canaliculi or ductules,
   3. intrahepatic or extrahepatic bile ducts, or
   4. ampullary region.

3. Clinical features
   1. Jaundice
   2. Pruritus
   3. Steatorrhea

4. Laboratory features and markers for cholestasis
   1. serum alkaline phosphatase
   2. gamma-glutamyl transferase
Any questions