



# Hepatic Clearance and Elimination

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# Liver function test

- Liver function tests (LFT) are a helpful screening tool to detect hepatic dysfunction. Thereby hepatic clearance of the drugs can be estimated with the results of liver functions test.



# Classification of Liver Function Tests

A. Tests of the liver's capacity to transport organic anions and to metabolize drugs:

Serum bilirubin

Urine bilirubin

Urobilinogen etc.

B. Tests that detect injury to hepatocytes (serum enzyme tests):

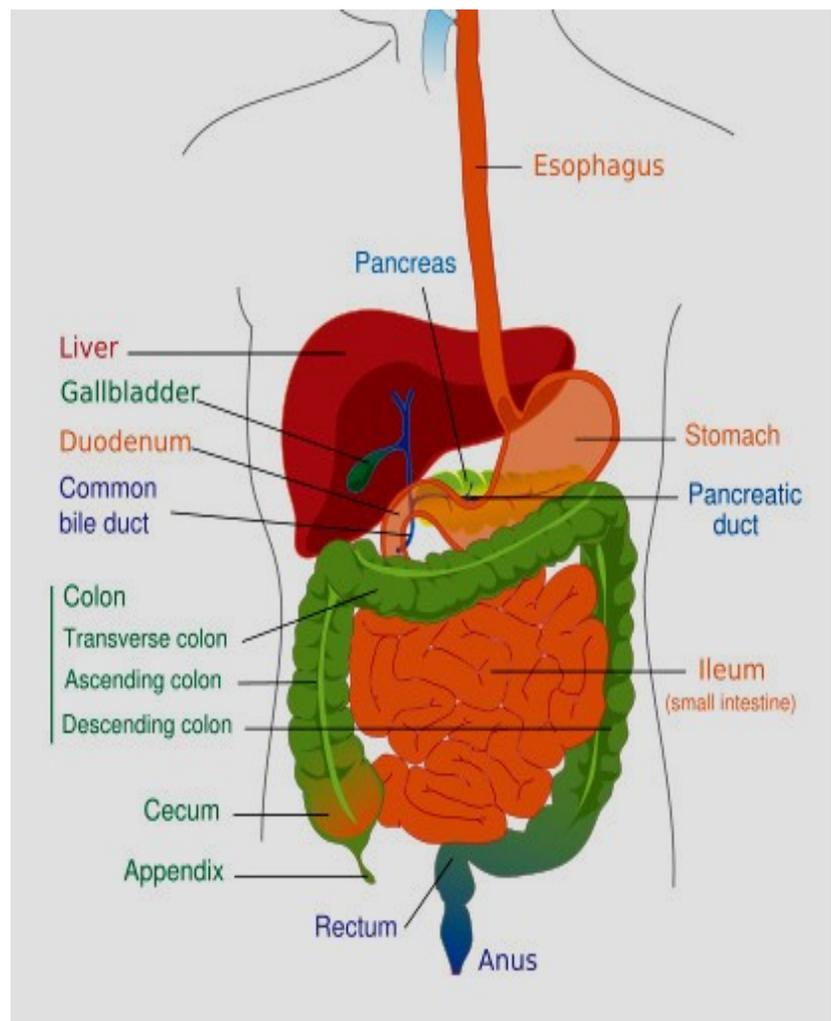
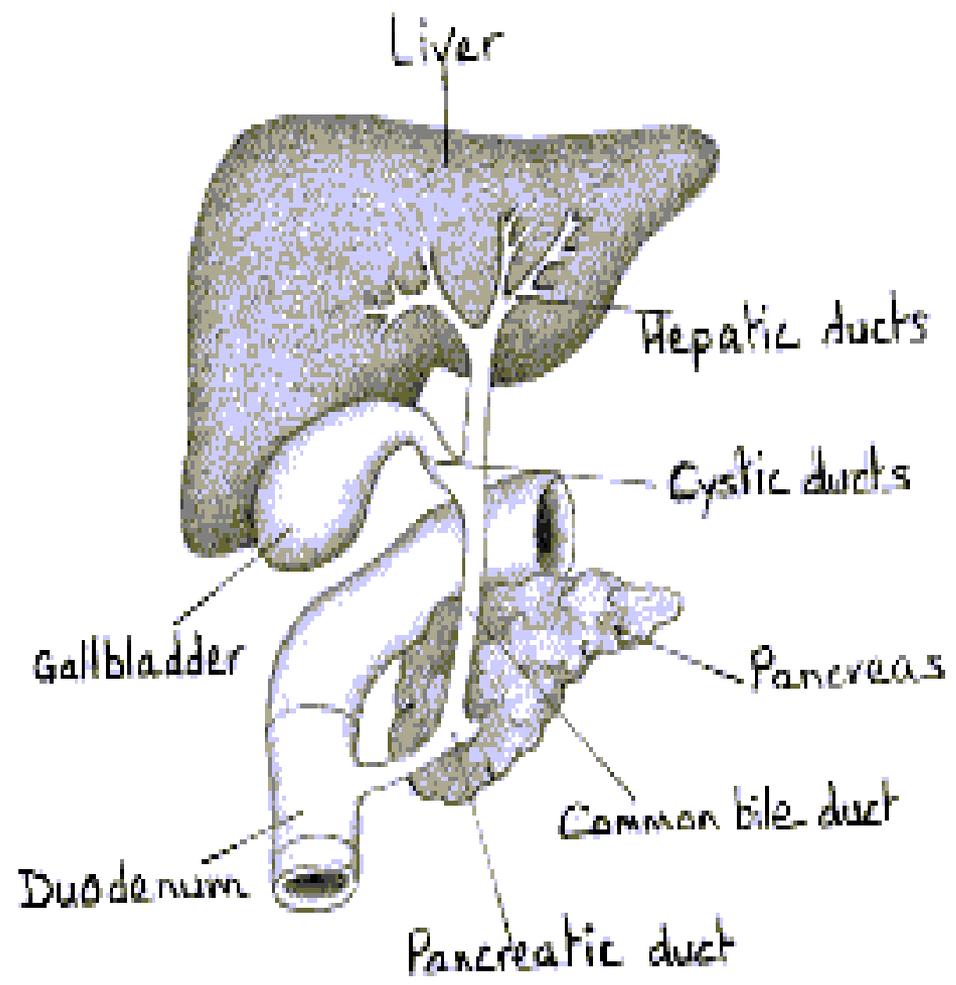
Aminotransferases, alkaline phosphatase, etc.

C. Tests of the Liver's biosynthetic capacity:

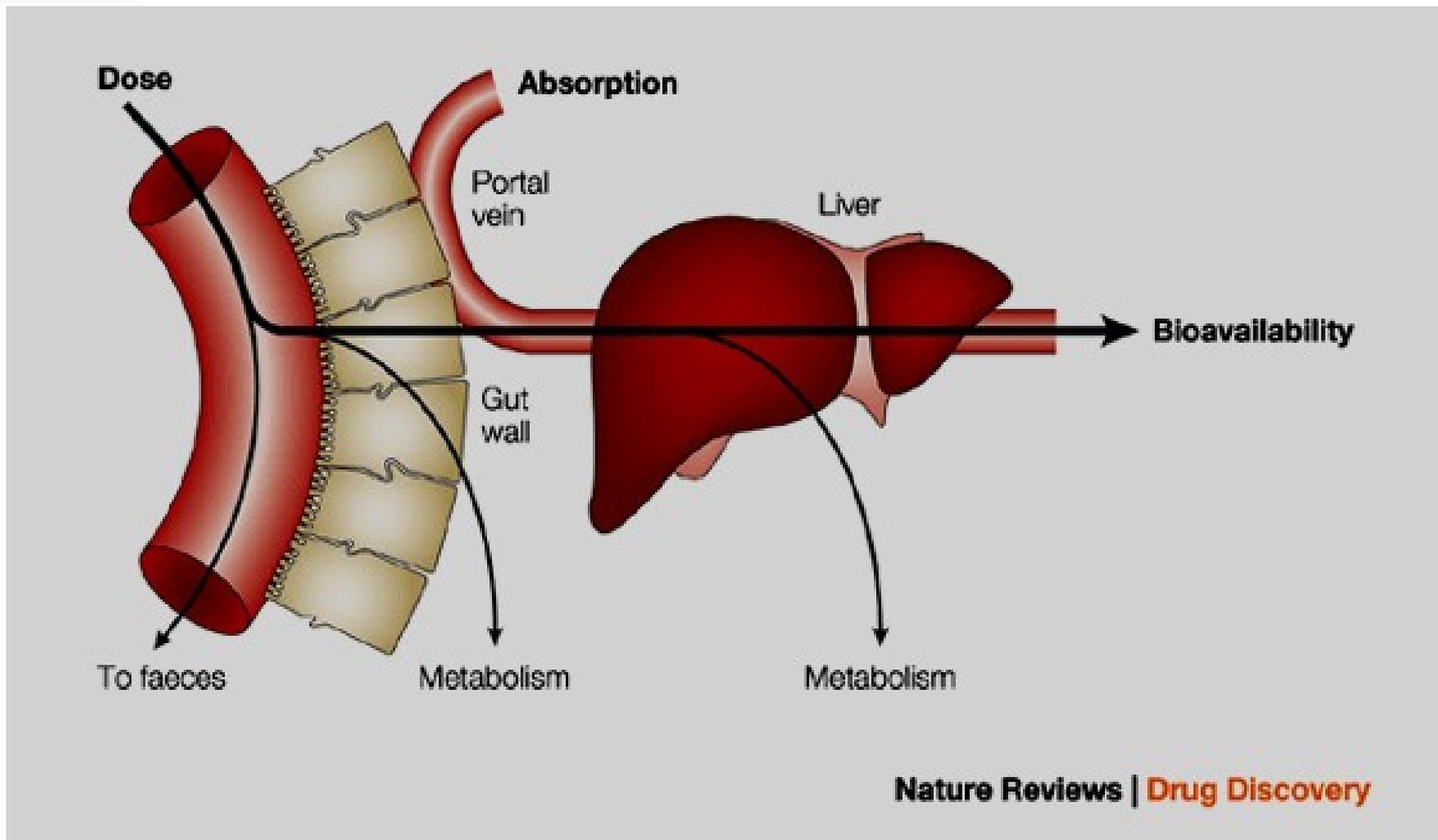
Serum proteins, albumin, etc.



# Liver function test



# Presystemic metabolism





# Liver function test

- Largest gland, weight 1 and 2.3 kg, situated upper part of the abdominal cavity
- Functions:
  - Carbohydrate metabolism-blood glucose level
  - Fat metabolism
  - Protein metabolism
  - Breakdown of erythrocytes and defense against microbes
  - Detoxification of drugs and noxious substances
  - Metabolism of ethanol
  - Inactivation of hormones
  - Synthesis of vitamin A from carotene
  - Production of heat
  - Secretion of bile



# Biochemical tests useful for



- Detection of disease
- Diagnostic work-up
- Estimate severity
- Assess prognosis
- Evaluate therapy



# Uses of Liver function tests

- They are helpful to recognize the pattern of liver disease.
- Like being helpful in differentiating between
  - Acute viral hepatitis
  - Various cholestatic disorders
  - Chronic liver disease
- They are helpful to assess the severity and predict the outcome of certain diseases like primary biliary cirrhosis.



# Pharmacists role



- Take accurate medication history
- Report ADR's, documented publish
- Be aware of liver toxins and monitor
- Avoid I. M. injections
- Be suspicious of drug induced liver disease
- Consider implications of hepatic dysfunction
- Understand Liver Function Test's and treatment of liver disease



# Hepatic clearance

- Hepatic clearance may be defined as volume of the blood that perfuses the liver that is cleared of drug per unit.

$$Cl_h = Q_h E_h$$

Where,

$Cl_h$  = Hepatic clearance

$Q_h$  = Blood flow to the liver

$E_h$  = Extraction ratio of the liver



# Hepatic clearance

- Hepatic clearance may also be expressed as the rate of drug removal divided by the plasma drug concentration in the artery.

Rate of drug removal by the liver

$$CL_h = \frac{\text{Rate of drug removal by the liver}}{\text{Plasma concentration of the drug}}$$

Plasma concentration of the drug

- It should be noted that only free drug in blood is available for hepatic extraction. Therefore, protein binding of drugs has to be considered in calculating the hepatic clearance.

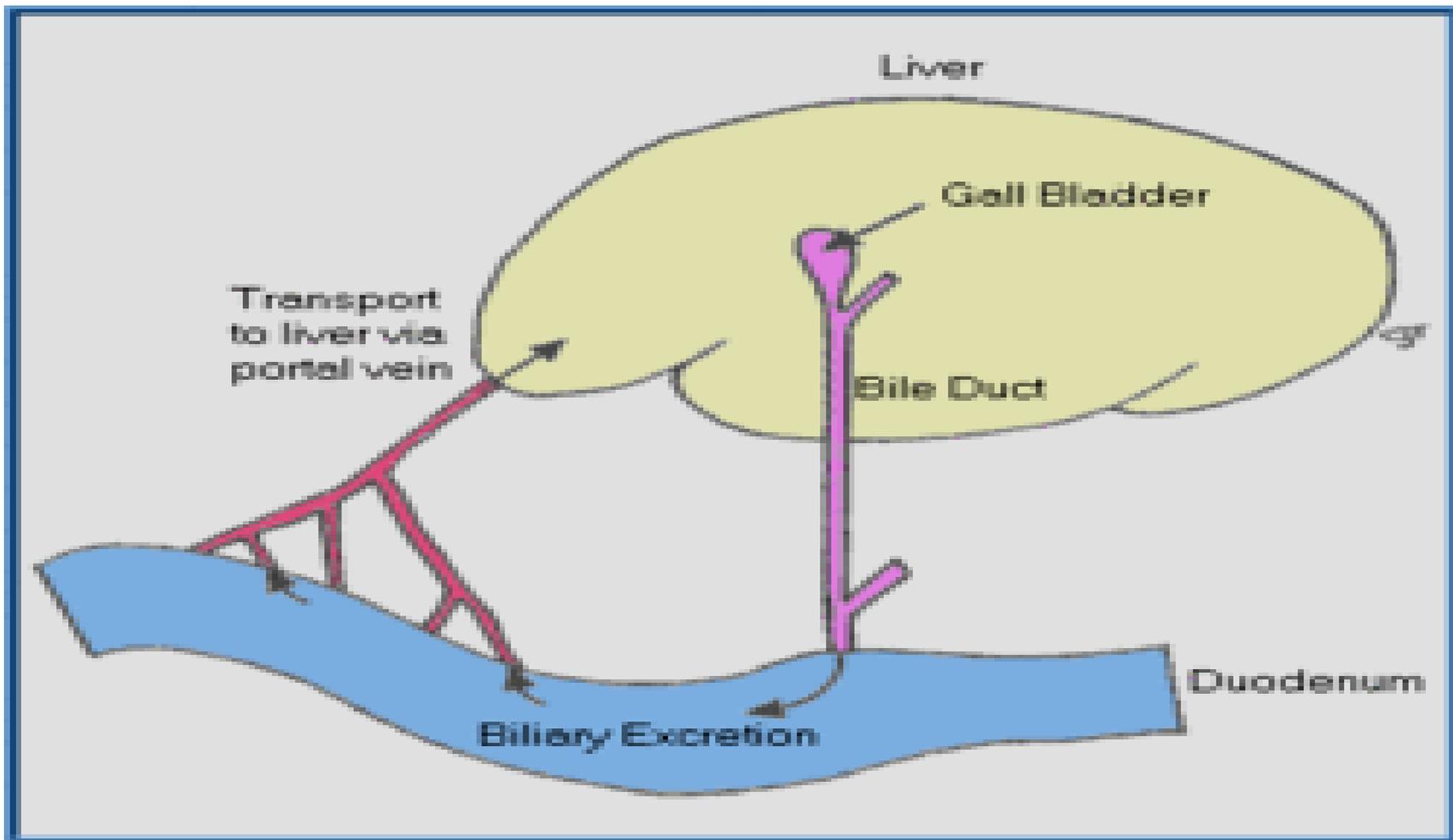


# Biliary excretion of drug

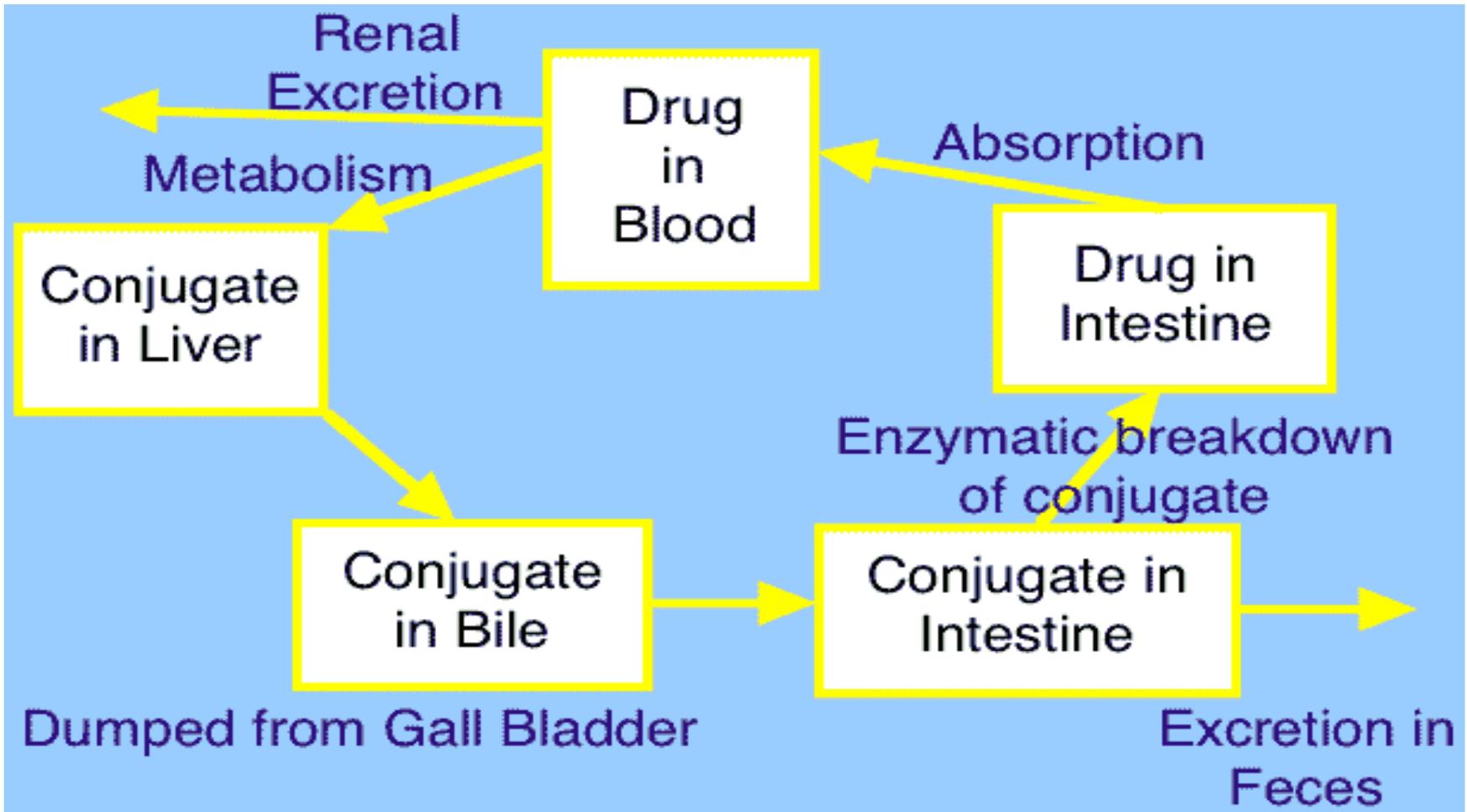


Bile juice is secreted by hepatic cells of the liver. The flow is steady-0.5 to 1ml /min. Its important in the digestion and absorption of fats. 90% of bile acid is reabsorbed from intestine and transported back to the liver for resecretion. Compounds excreted by this route are sodium, potassium, glucose, bilirubin, Glucuronide, sucrose, Inulin, mucoproteins e.t.c. Greater the polarity better the excretion. The metabolites are more excreted in bile than parent drugs due to increased polarity.

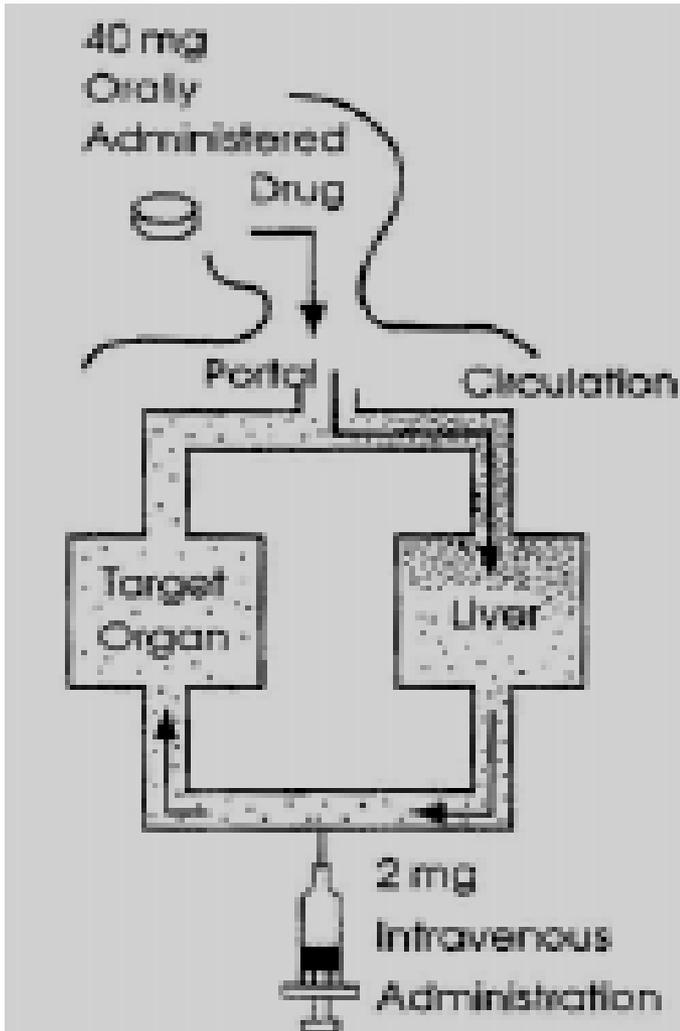
# Biliary excretion of drug



# Biliary excretion of drug- Enterohepatic Cycling



# Enterohepatic circulation



Because of hepatic metabolism, a portion of an orally administered drug dose is inactivated by the liver before reaching the systemic circulation (and  $\therefore$  the target organ)  $\rightarrow$  need to adjust dosage

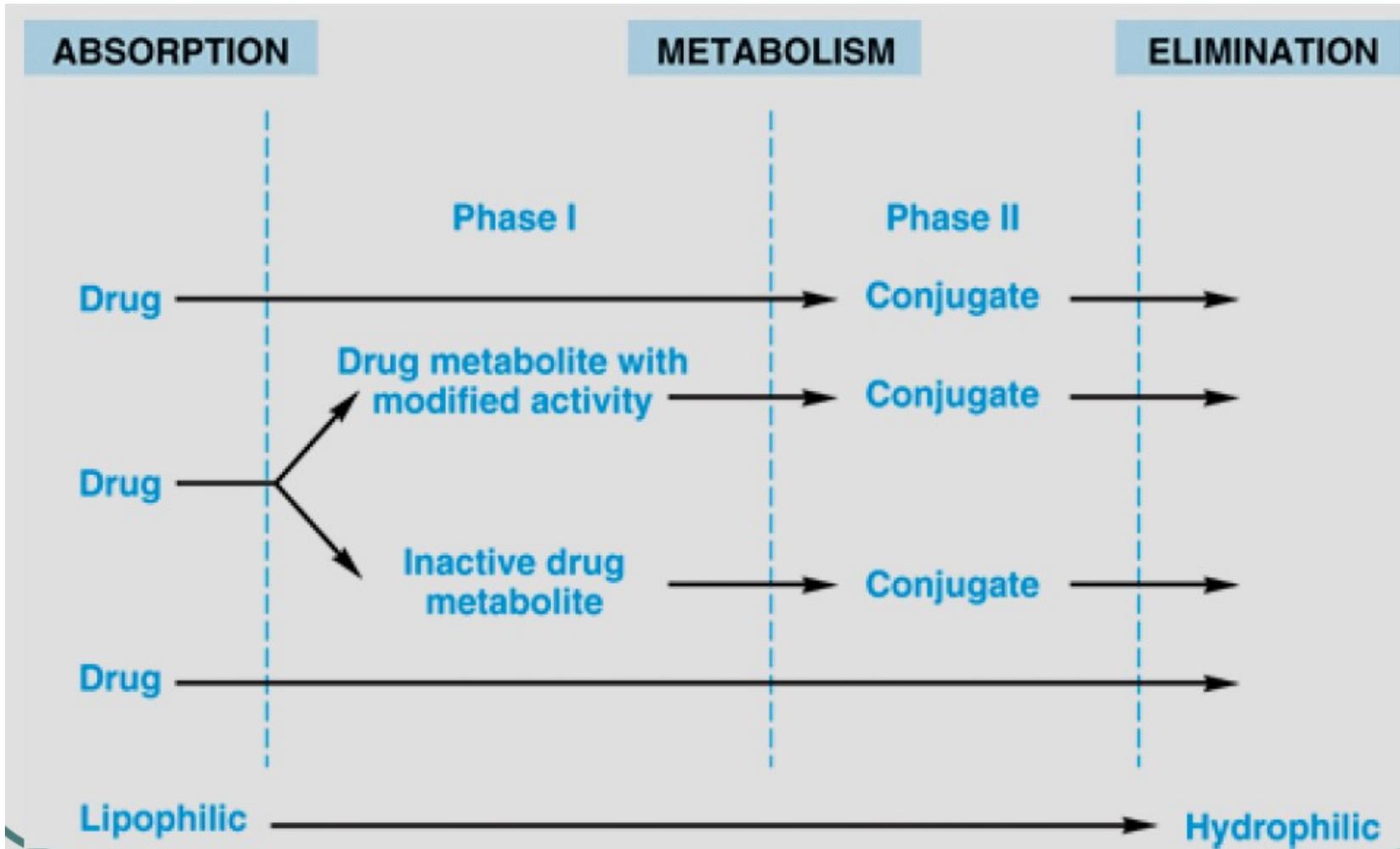


# Hepatic elimination

- *Elimination is defined as the process that tends to remove the drug from the body and terminate its action.*



# Hepatic elimination





**THANK YOU**

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