Liver functions for AMS students

2/2558

Chalongchai Chalermwat, MD

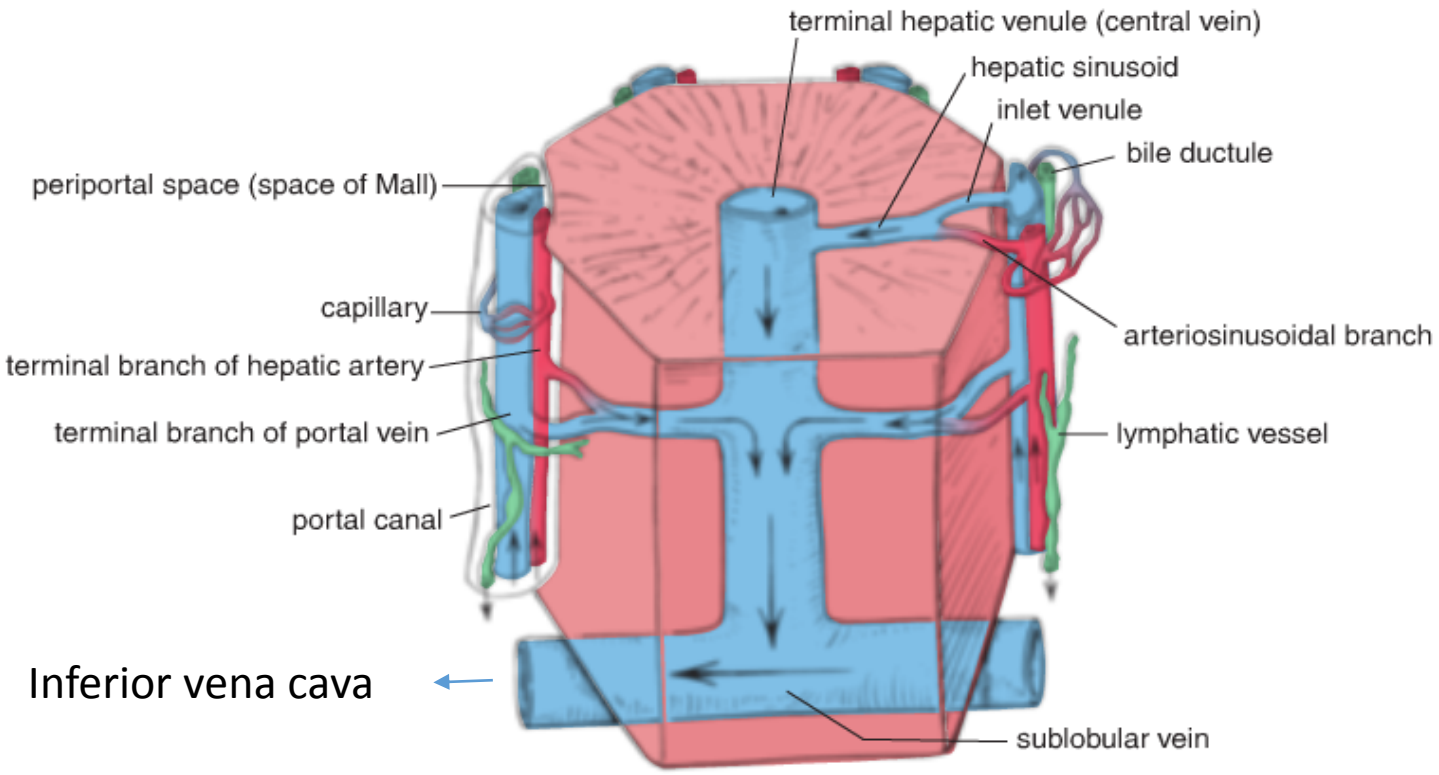
Department of Biochemistry, Faculty of Medicine

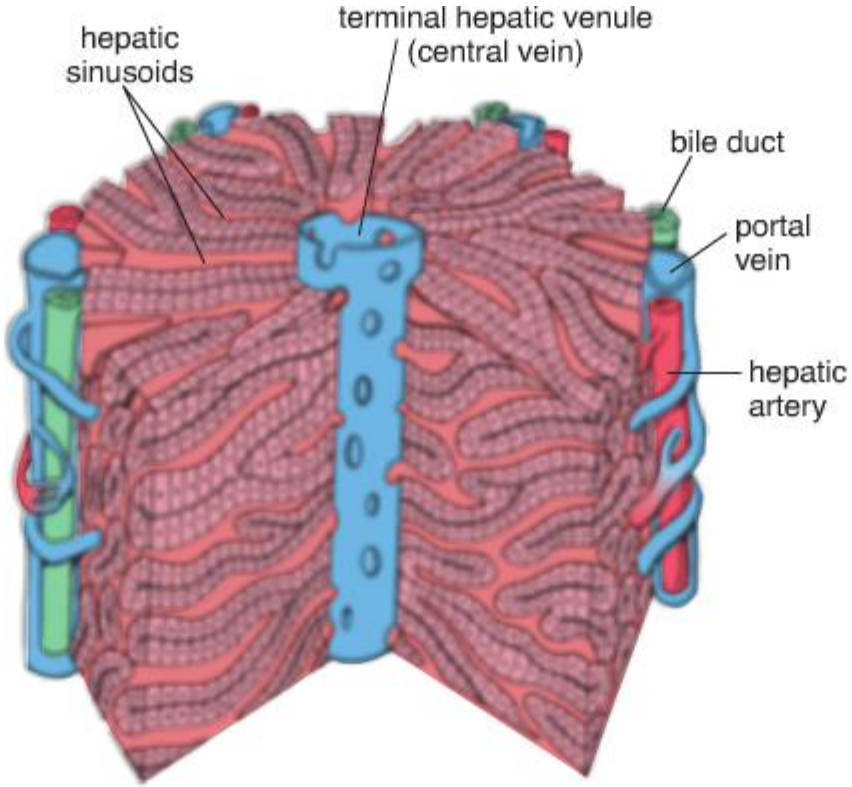
Khon Kaen University

Objectives

1. ทบทวนโครงสร้าง ของตับ
2. อธิบายการทำงาน ของตับ
3. อธิบายหลักการทดสอบ การทำงานของตับ
4. อธิบาย ความผิดปกติของตับ ที่พบบ่อยได้

Hepatic lobule

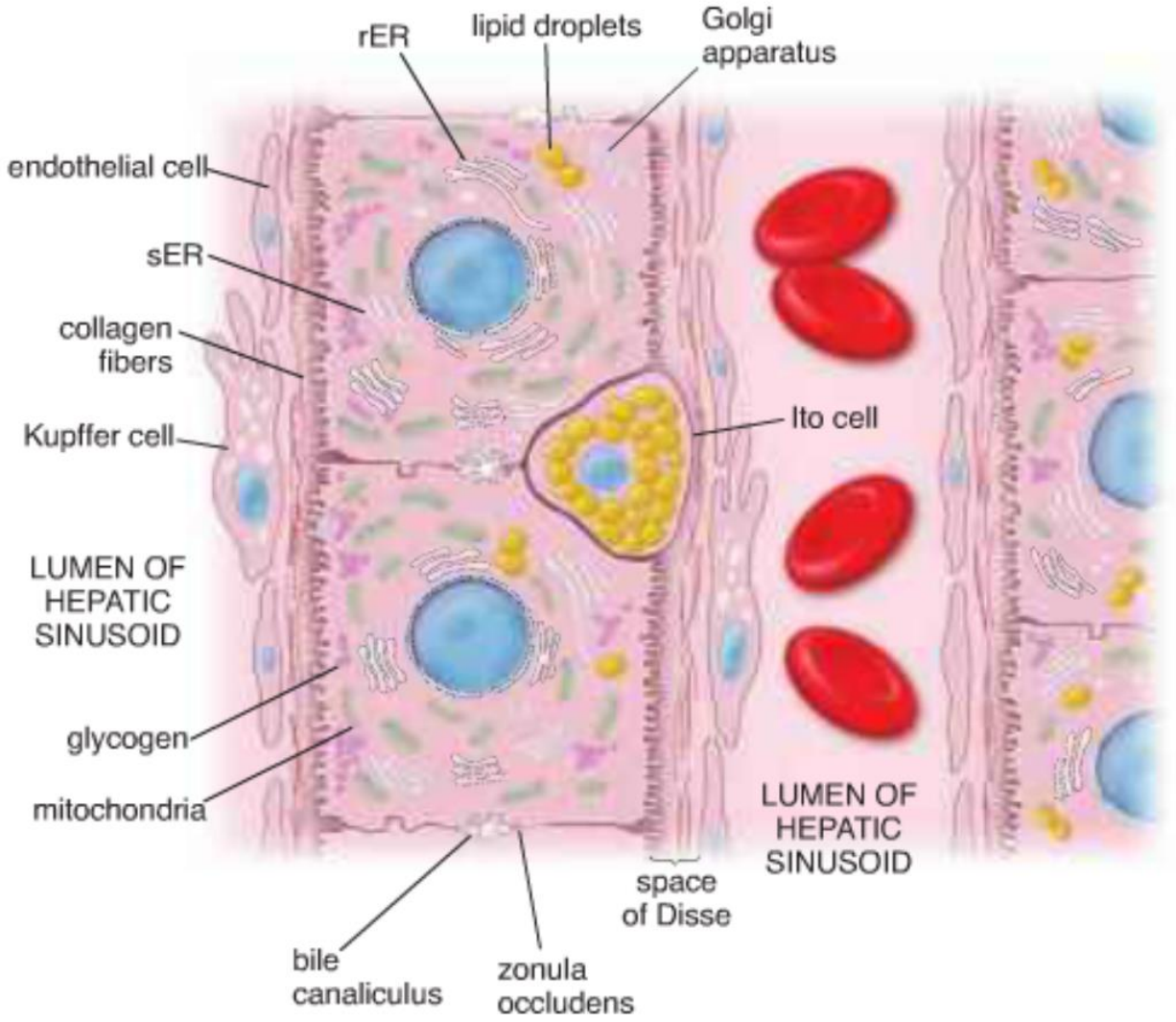




Histology a text and atlas, 6th edition

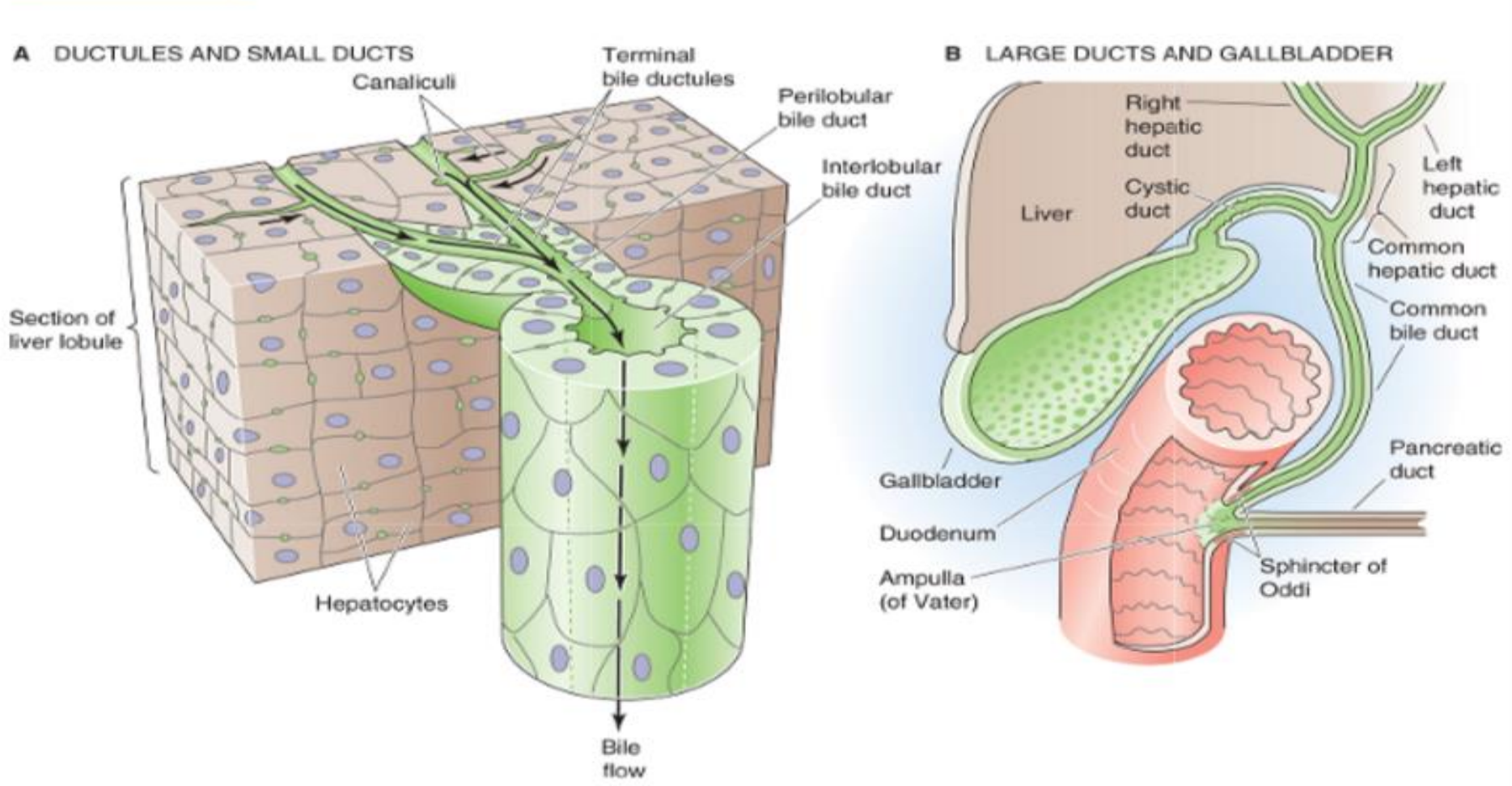
Liver parenchyma cells

- Hepatocytes (80%)
- Kuffer cells
- Hepatic stellate cell (Ito cell)
- Hepatic progenitor cells



Histology a text and atlas, 6th edition

Biliary system



Walter F. Boron et al. Medical physiology, 2nd edition

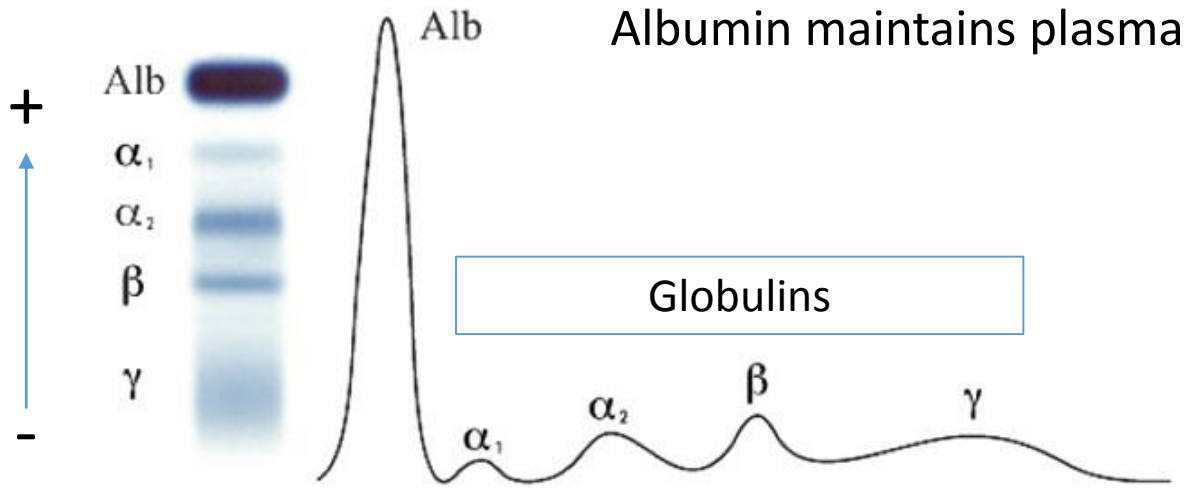
Liver functions

- Synthetic function
- Metabolic function
- Excretory function
- Storage function

Synthetic functions

- **Plasma proteins**
- Lipoprotein
- Glucose
- Glycogen
- **Heme**

Plasma proteins



Albumin is the most abundant protein in plasma.
Albumin maintains plasma oncotic pressure and intravascular volume.

Y-globulins is secreted from B-lymphocytes.

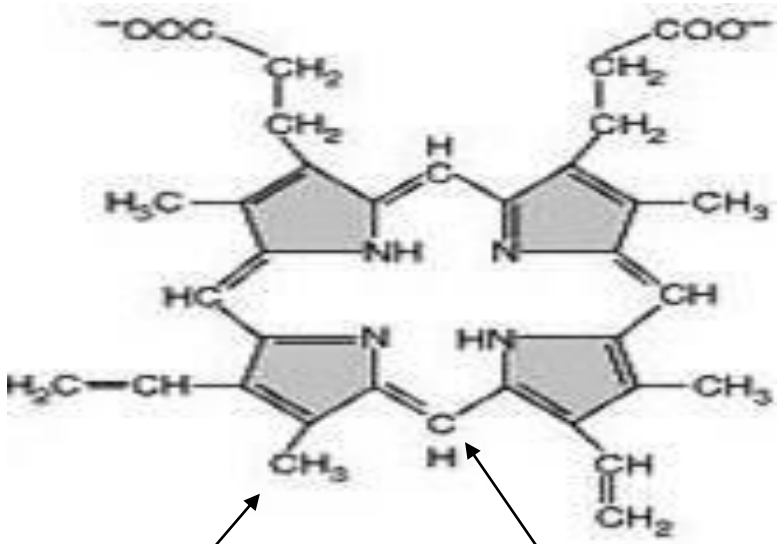
Globulins are clotting factors,
transport proteins, protease inhibitors, etc.

Representative of serum proteins detected by electrophoresis

Heme

Porphyrin:

Protoporphyrin IX

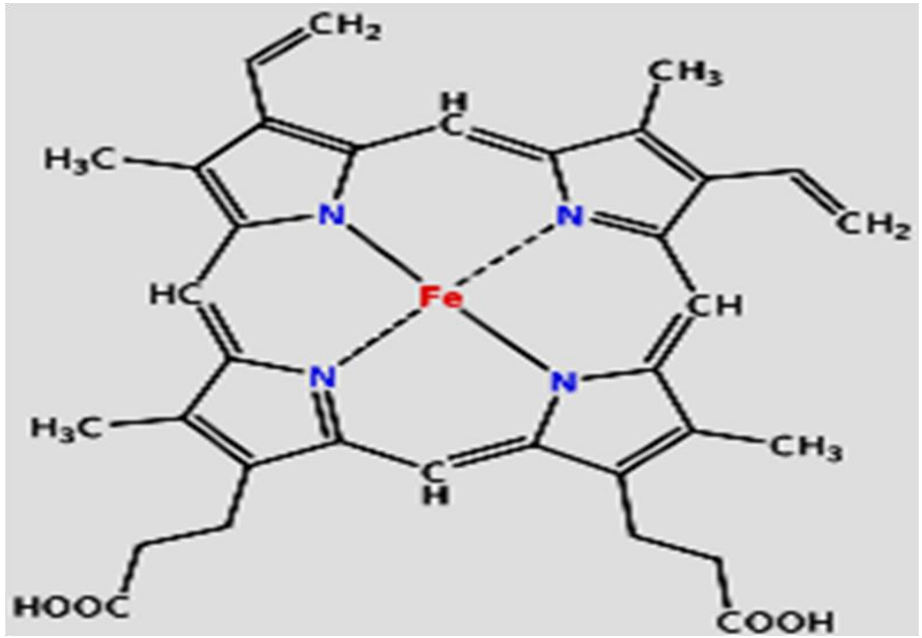


Pyrrole ring

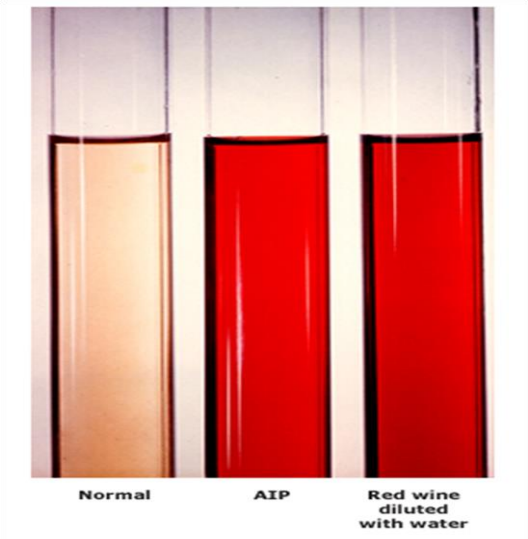
Methene bridge

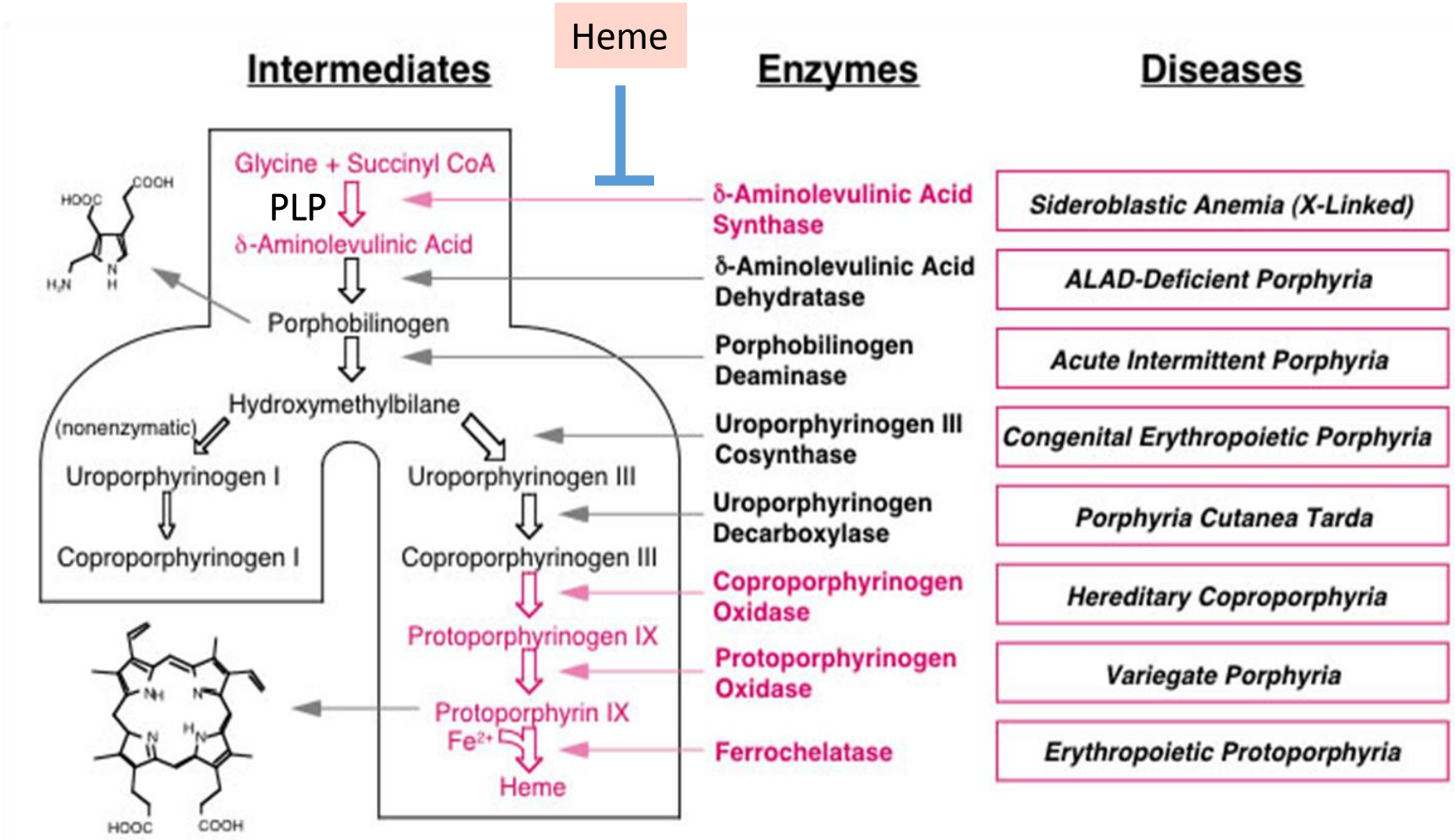
Heme:

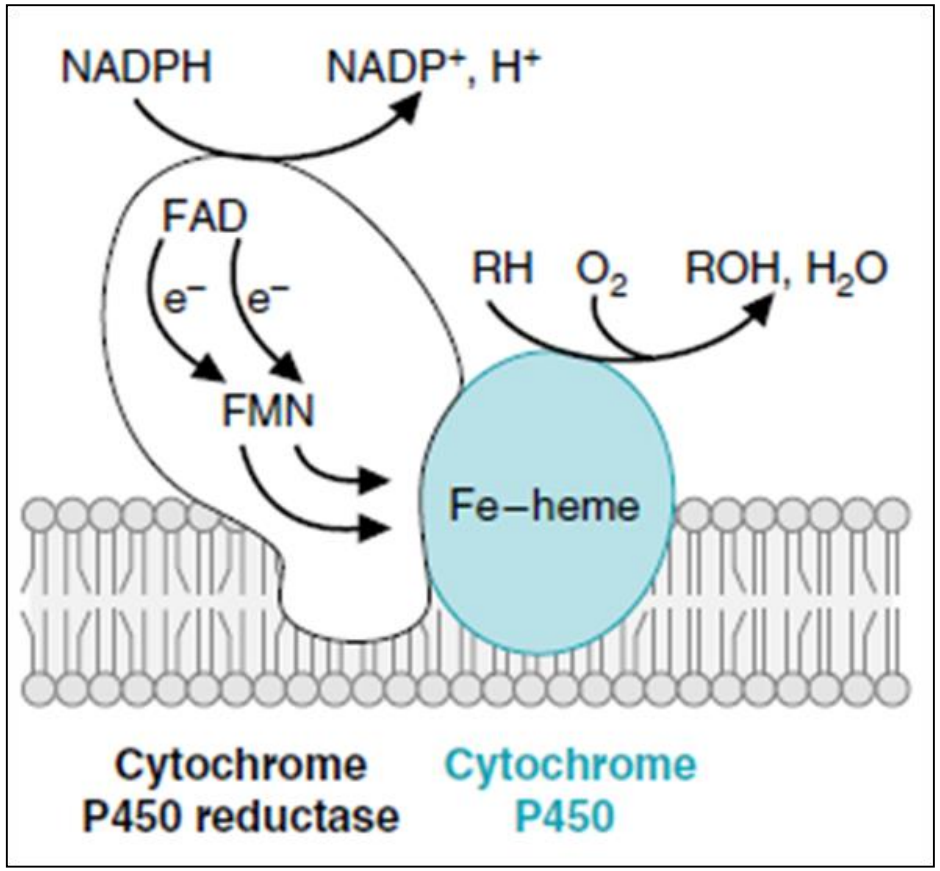
Protoporphyrin IX + Fe



Heme biosynthesis and disease (porphyrias)







Microsomal P450 system

Heme is required for drug metabolism in hepatocytes.

Marks' Basic Clinical Biochemistry, 2nd edition

Metabolic function

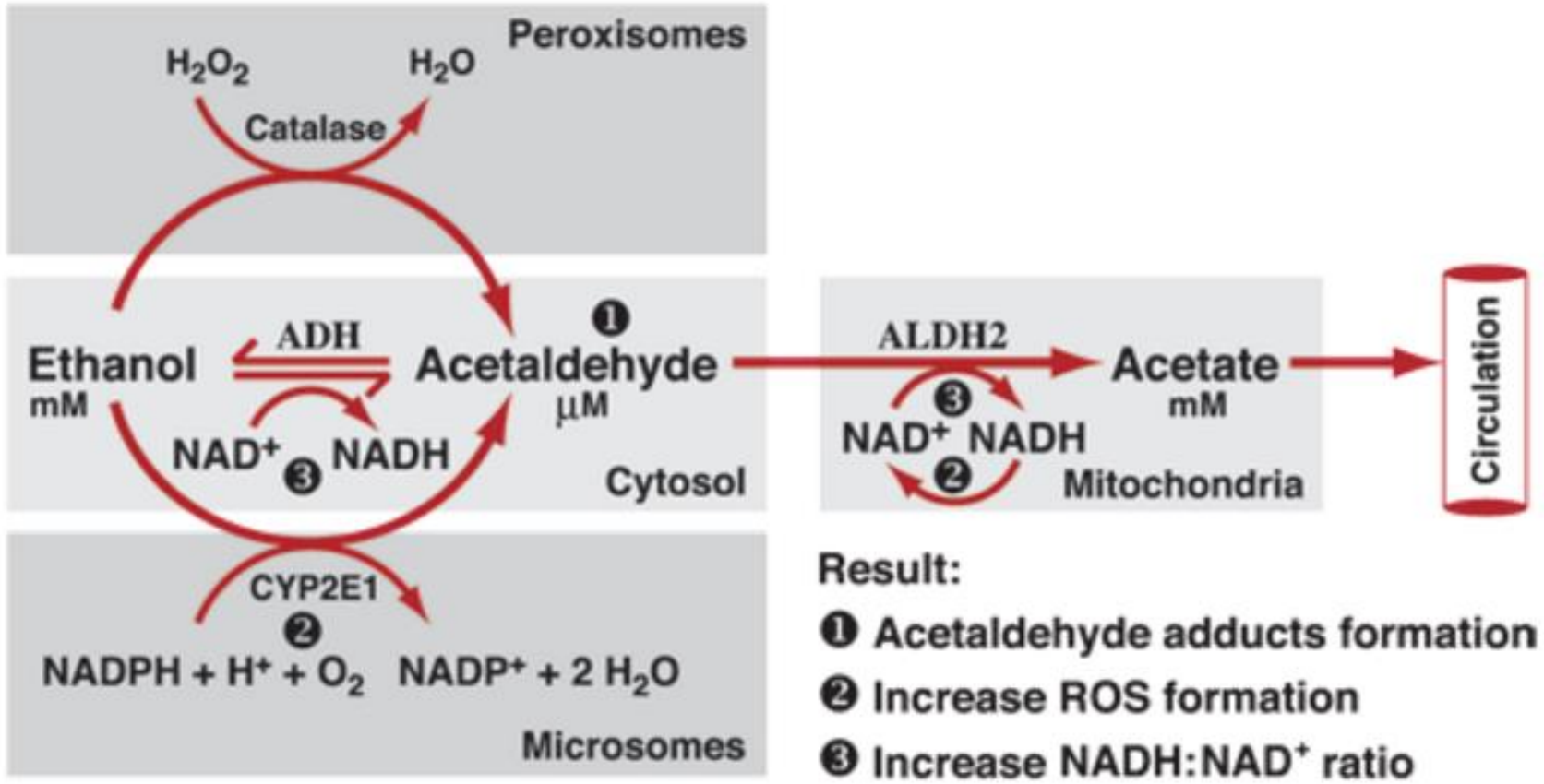
Endogenous substrate

- Ammonia
- **Cholesterol**
- **Bilirubin**
- Steroid hormones

Exogenous substrate

- **Ethanol**
- Drugs
- Chemical substances

Ethanol metabolism



http://www.niaaa.nih.gov/alcohol-health

Excretory function

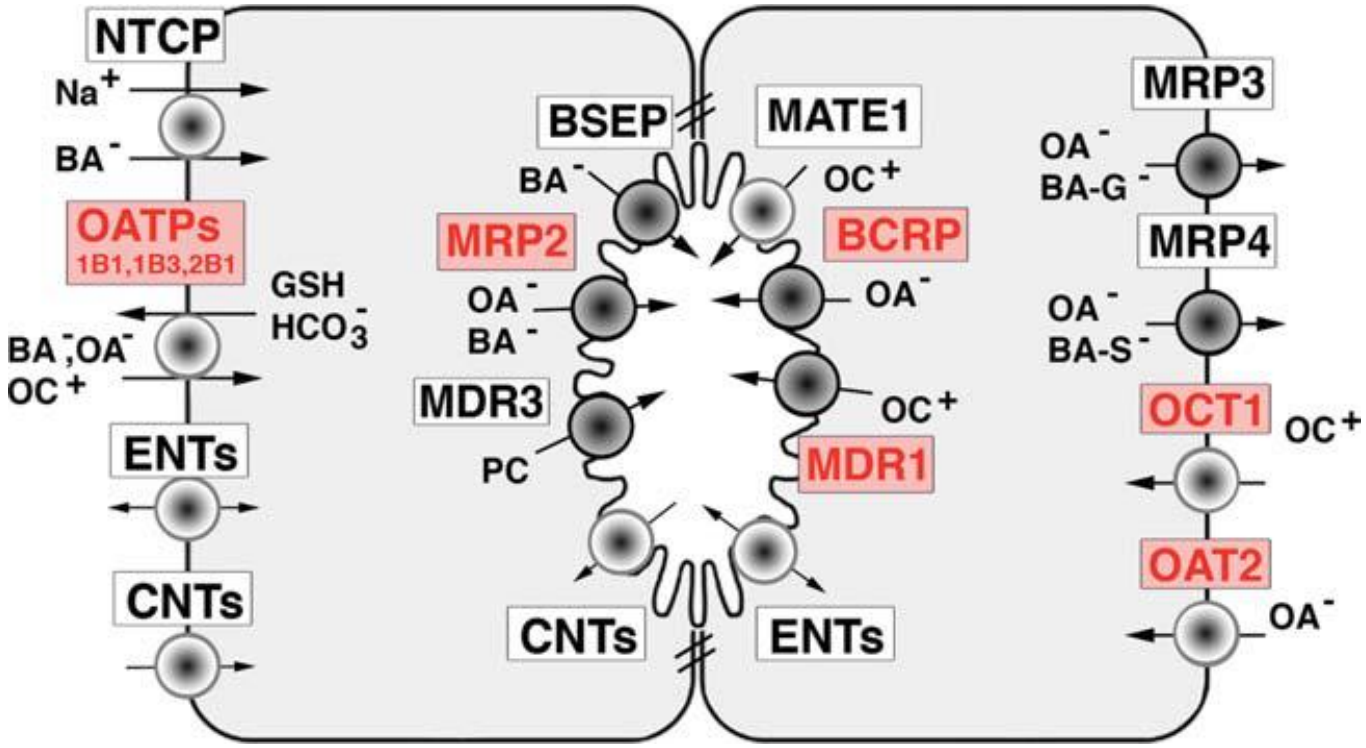
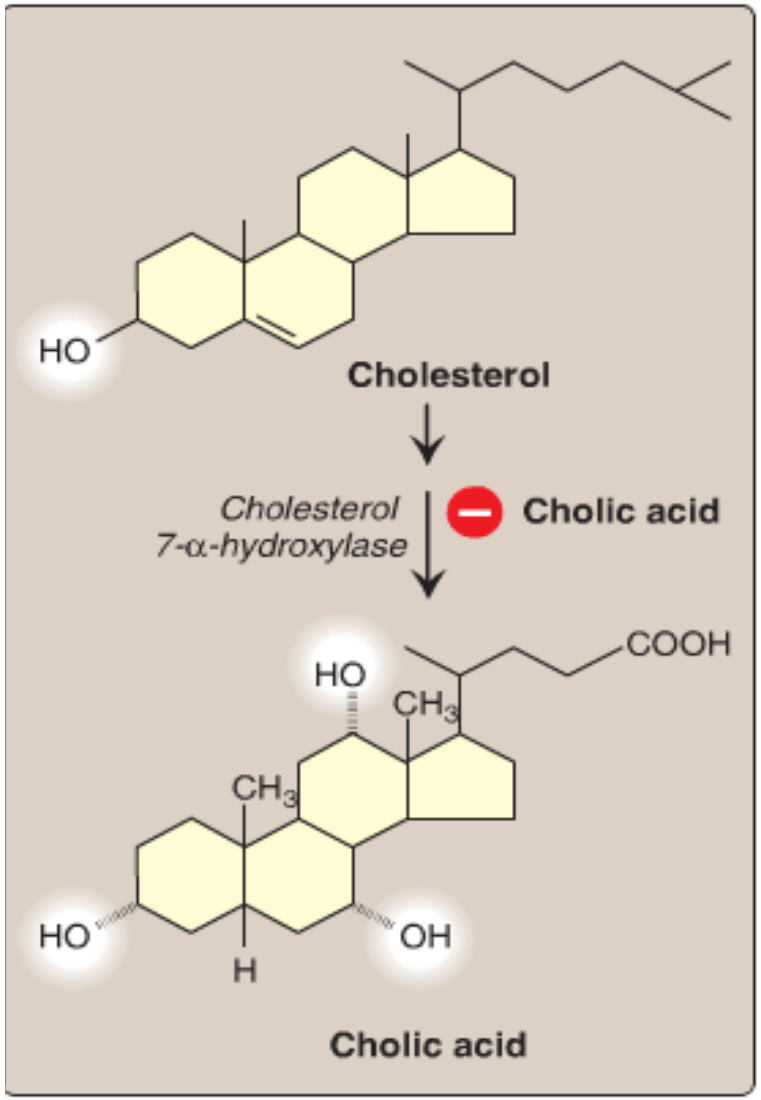


Fig. 1. Hepatocyte couplet illustrating location of major transporters that determine bile production and hepatic drug transport. The major drug transporters are indicated in red. ATP-dependent transporters are the dark circles. See Table 4 for their definition and function. BA^-, bile acid; BA-G, bile acid glucuronides; BA-S, bile acid sulfates; CNT, concentrative nucleoside transporter; ENT, equilibrative nucleoside transporter; GSH, glutathione; Na^+, sodium; OA^-, organic anion; OC^+, organic cation; PC, phosphatidylcholine.

Hepatology. 2011 Apr; 53(4): 1377–1387.

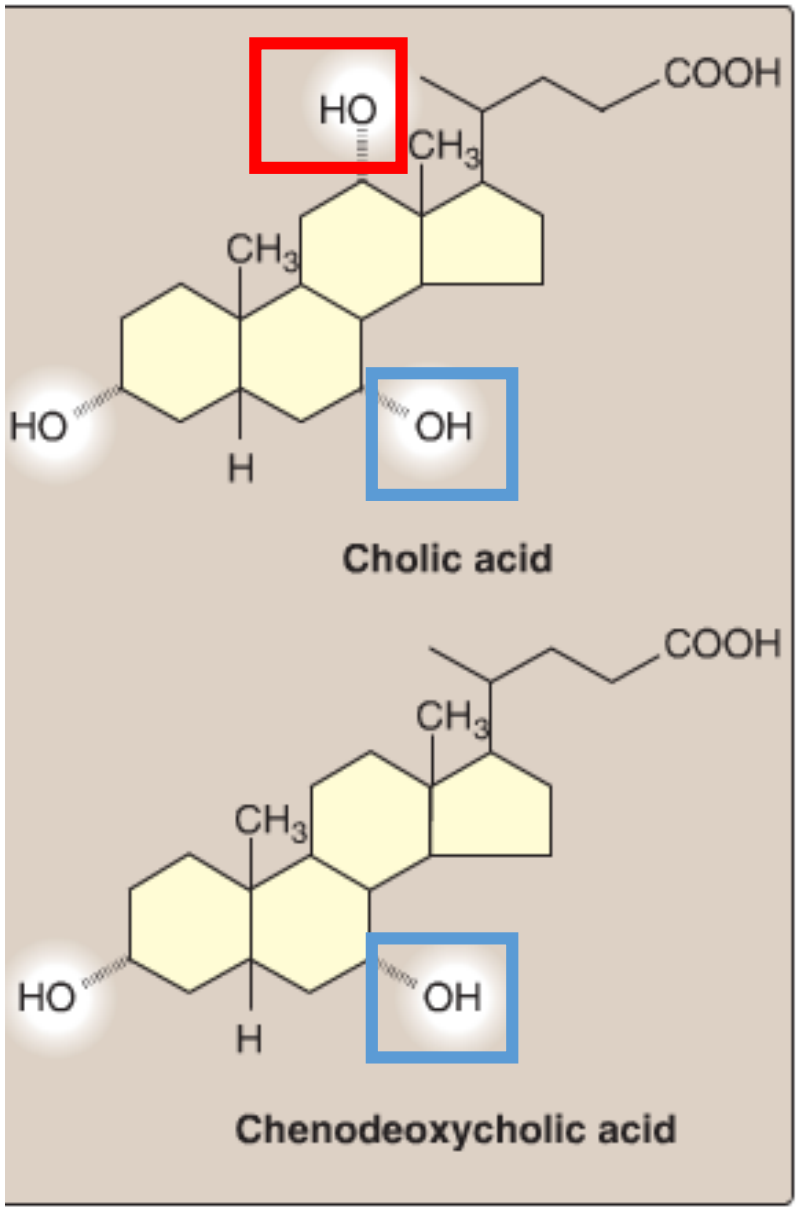
Cholesterol

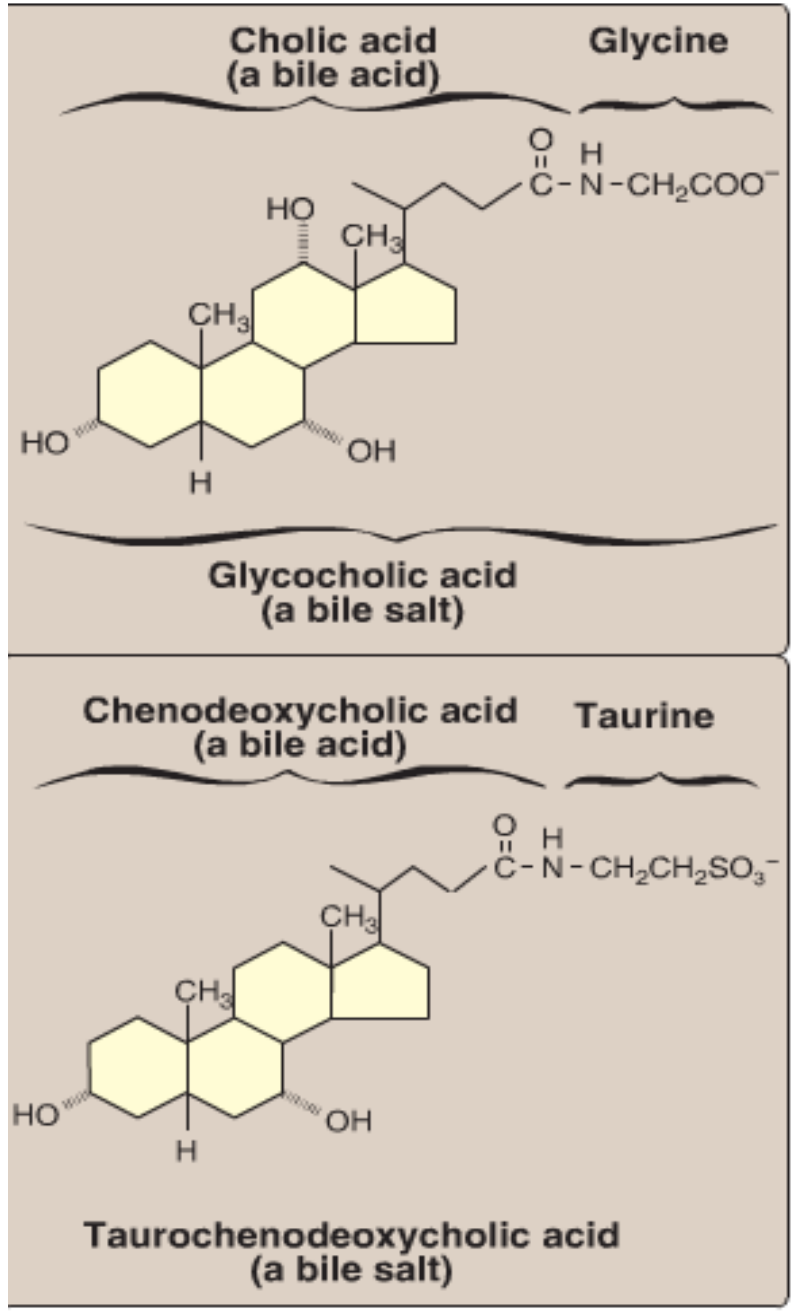
- Primary bile acids
  - Cholic acid
  - Chenodeoxycholic acid
- Secondary bile acids
  - Deoxycholic acid
  - Lithocholic acid



Lippincott's illustrated reviews, 5th edition

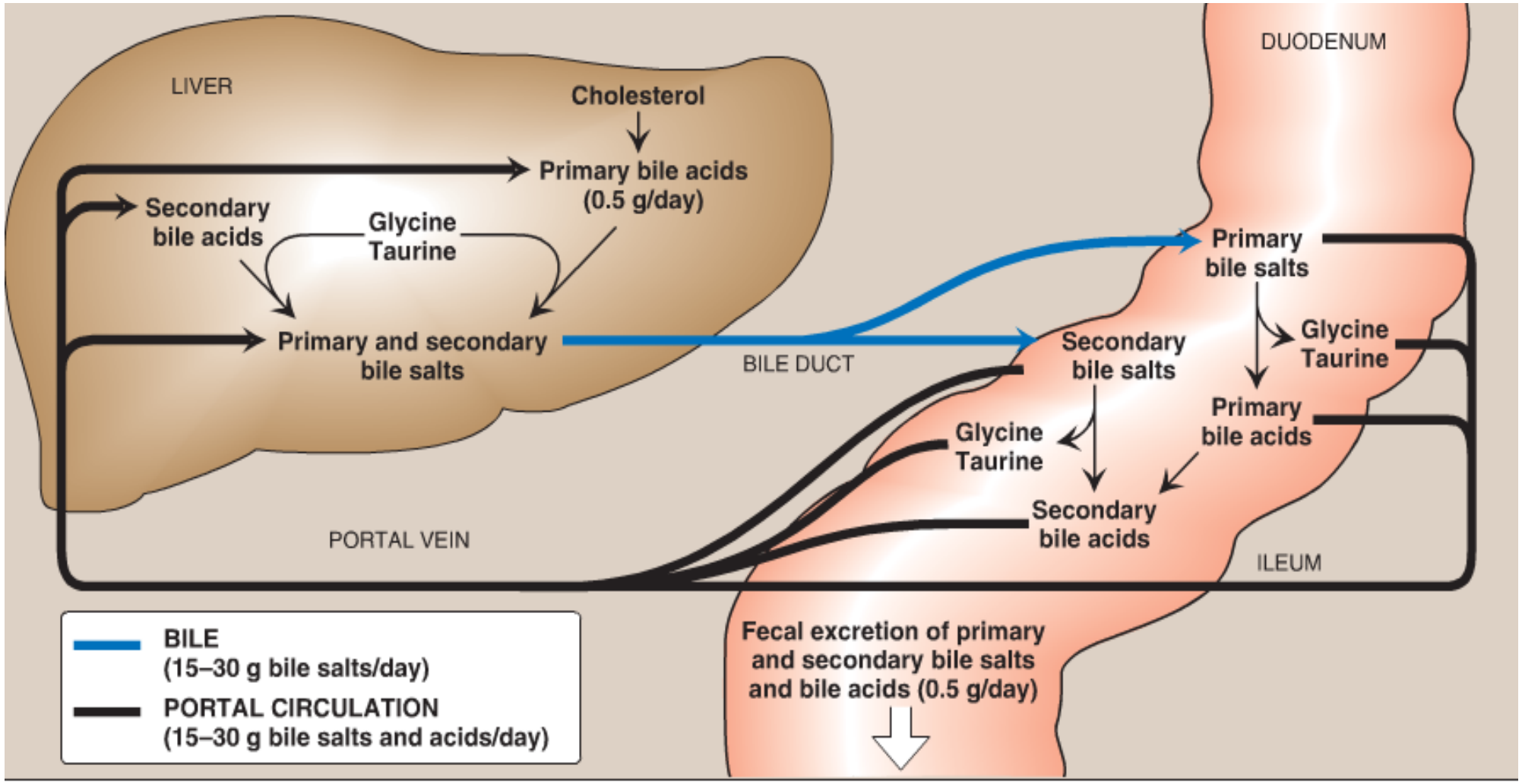
= can remove by microbial enzymes





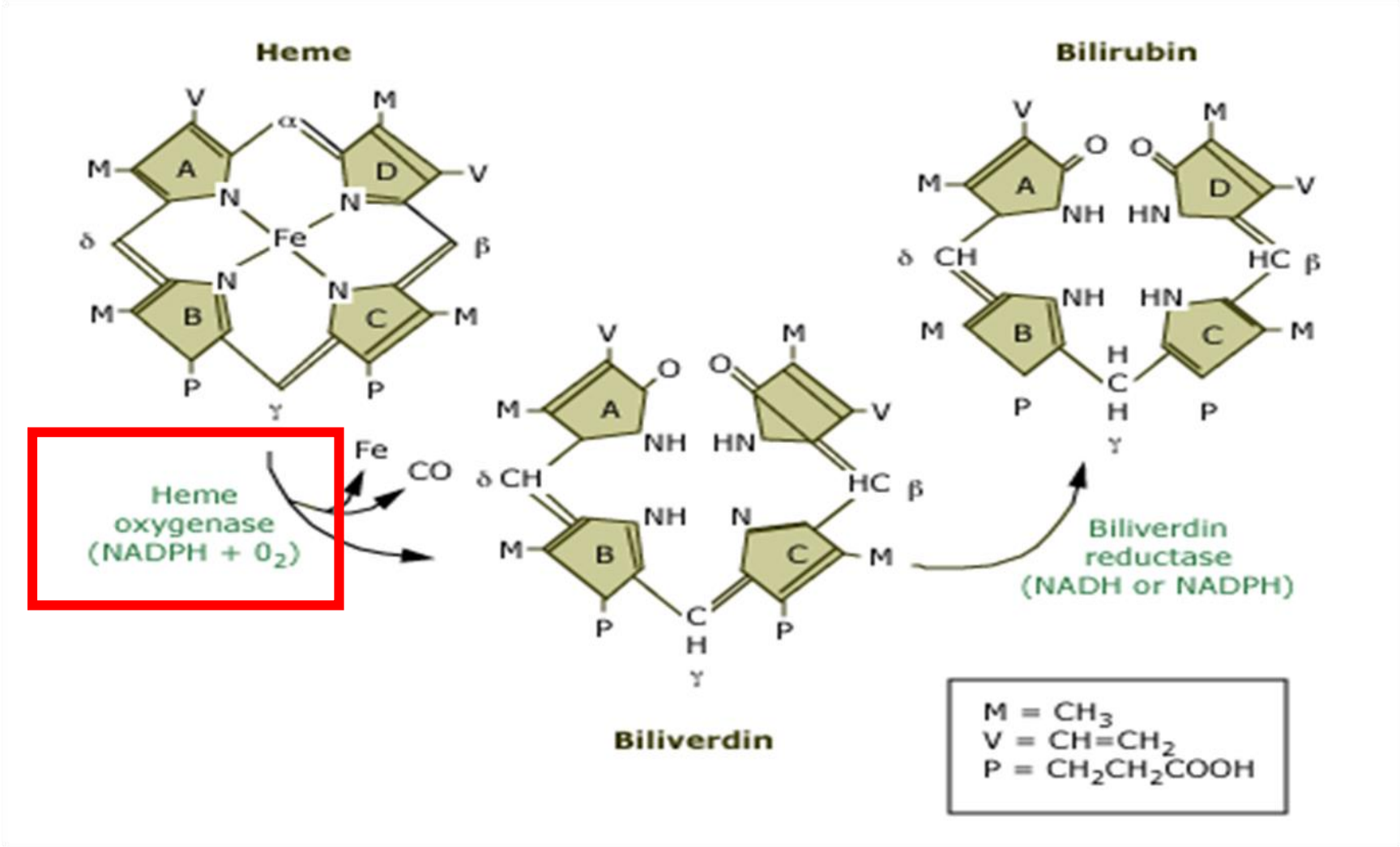
Lippincott's illustrated reviews, 5th edition

Enterohepatic circulation of bile acids

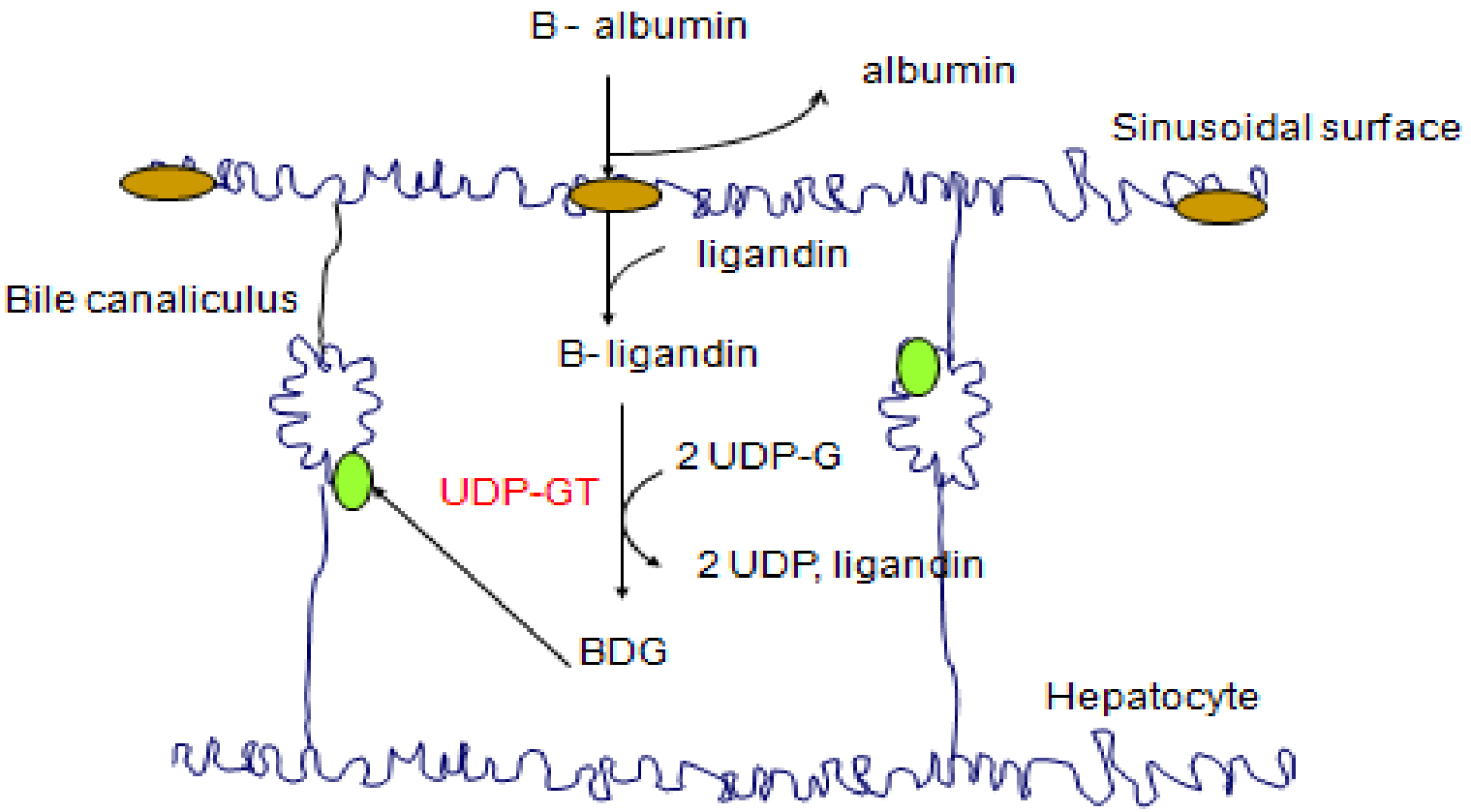


Lippincott's illustrated reviews, 5th edition

Bilirubin

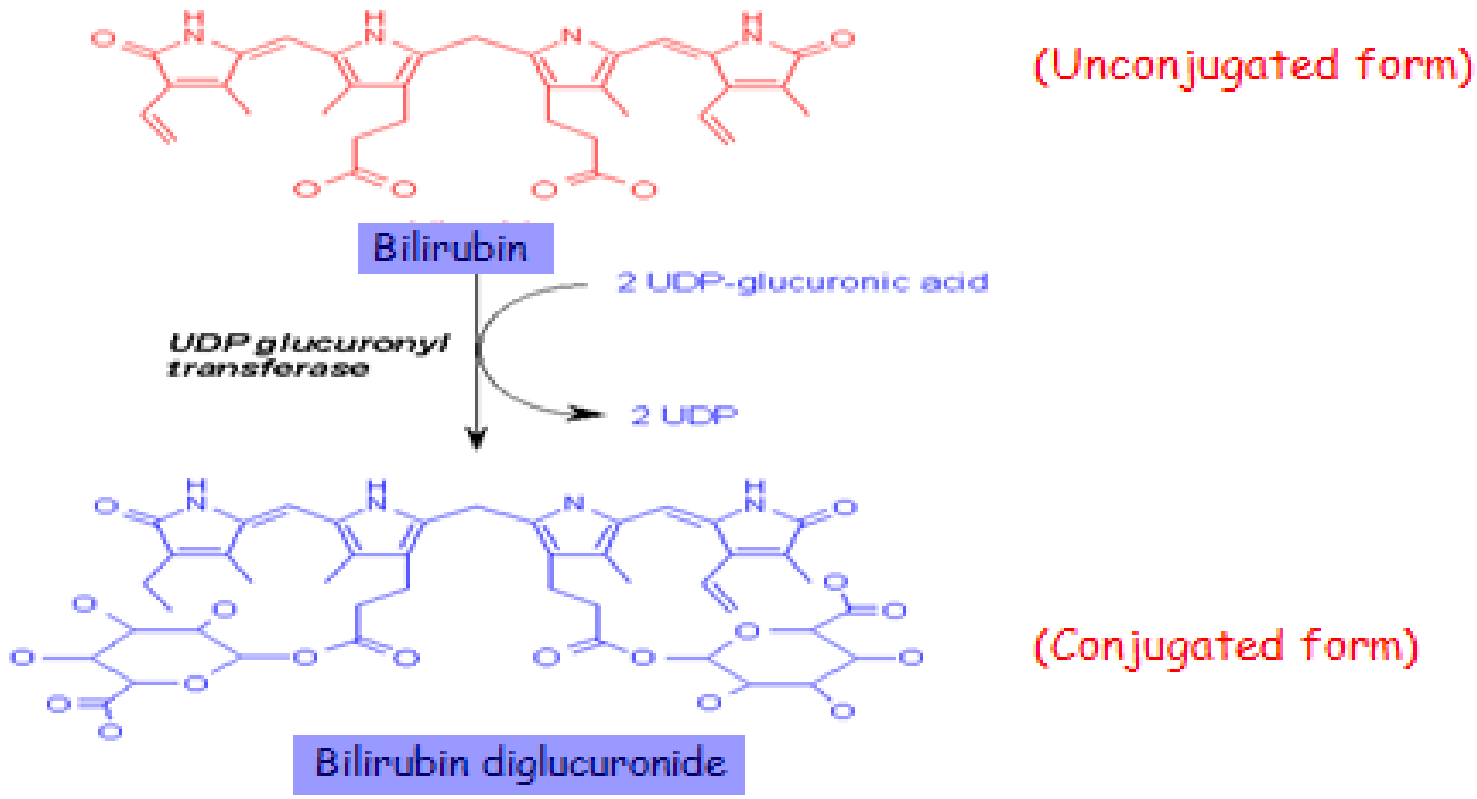

Heme
Bilirubin
Heme oxygenase (NADPH + 0_2)
Fe
CO
Biliverdin reductase (NADH or NADPH)
Biliverdin
M = CH_3
V = $CH=CH_2$
P = CH_2CH_2COOH

Bilirubin metabolism



BDG = Bilirubin diglucuronide, UDP-G = Uridine diphosphate – glucuronate
UDP-GT = UDP-glucuronyltransferase

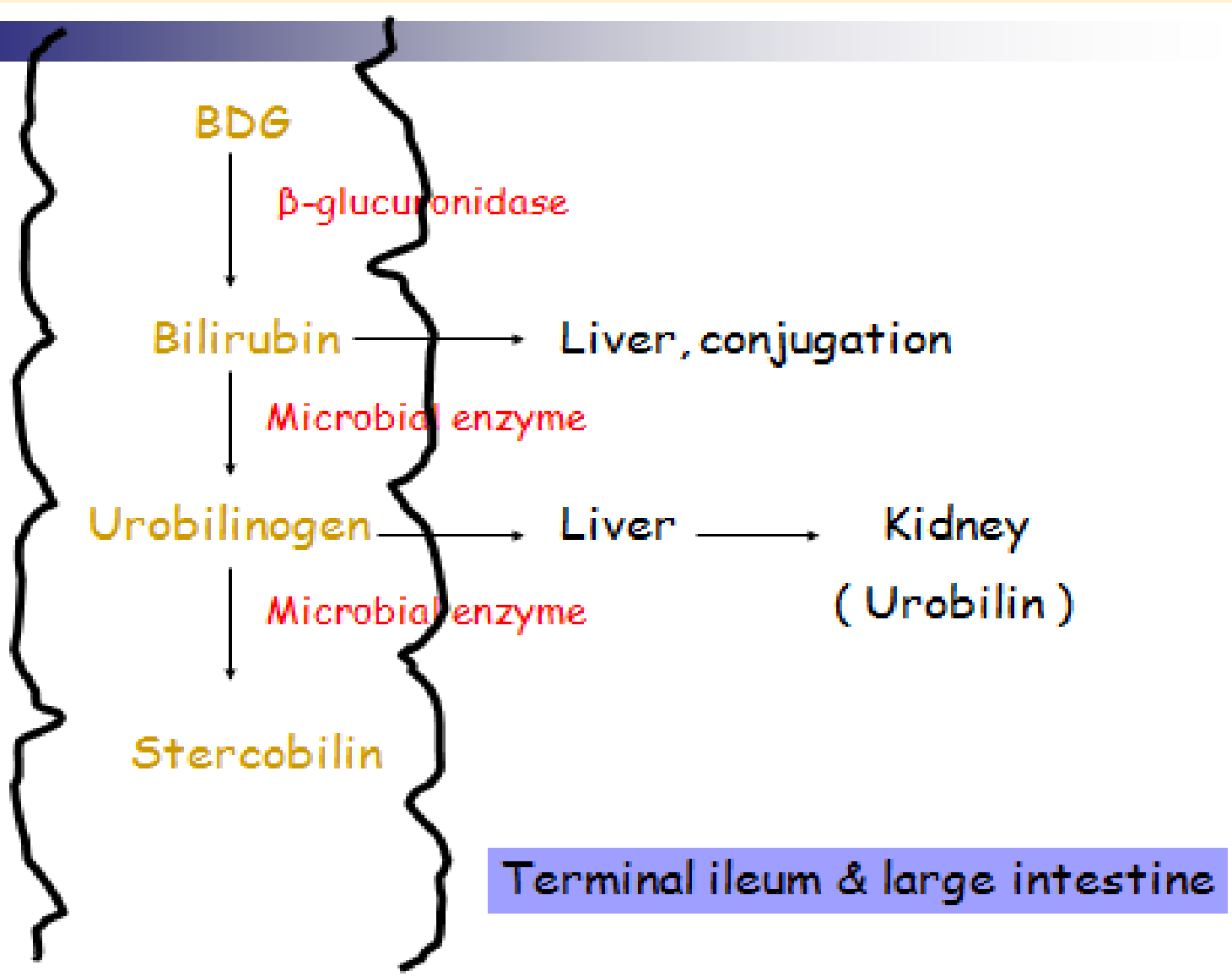
Bilirubin metabolism



(Unconjugated form)

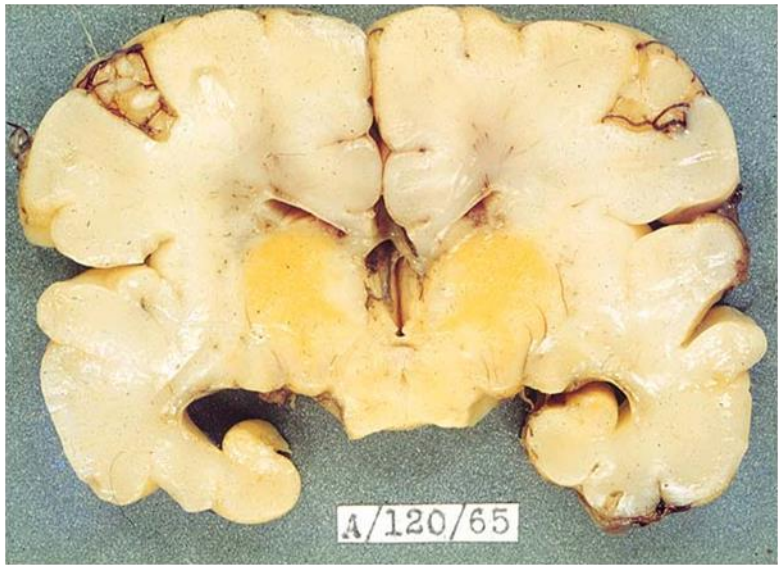
(Conjugated form)

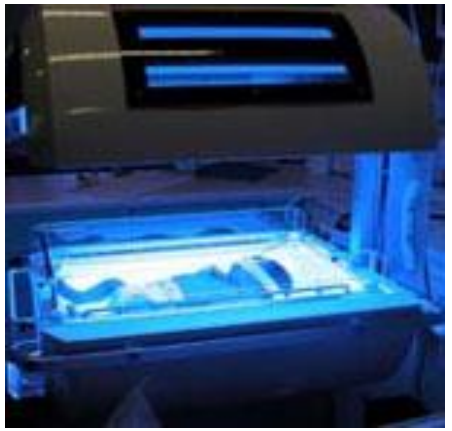
Enterohepatic circulation and excretion of bilirubin



Bilirubin toxicity (kernicterus)

Bilirubin encephalopathy leading to cerebral palsy or death





HDN= Hemolytic disease of the newborn

Routine liver function test (LFT)

	(Reference values)
• Cholesterol	127-262 mg/dl
• Total proteins	6.5-8.8 g/dl
Albumin	3.8-5.4 g/dl
Globulins	2.6-3.4 g/dl
• Total bilirubins	0.25-1.5 mg/dl
Direct bilirubin	0-0.5 mg/dl
Aspartate transminase (AST)	4-36 U/L
Alanine transminase (ALT)	12-32 U/L
Alkaline phosphatase (ALP)	42-121 U/L

Assessment of liver functions

Synthetic functions
Cholesterol
Total proteins
-- Albumin
-- Globulins

Hepatocellular damage
Aspartate transminase (AST)
Alanine transminase (ALT)

Excretory function
Total bilirubin
Direct bilirubin
Alkaline phosphatase (ALP)

Liver diseases

- Jaundice
- Hepatitis
- Cirrhosis
- Cholestasis

Jaundice

- Icteric sclera, total bilirubin > 3 mg/dl
- Direct or indirect hyperbilirubinemia
- Cause :
  - Pre- hepatic/ hemolytic jaundice
  - Hepatocellular jaundice
  - Post-hepatic/ cholestatic jaundice

Type of jaundice	Hemolytic	Hepatocellular	cholestatic
↑ TB	Indirect (TB < 5 mg%)	Both of them, vary (direct, indirect)	Both of them, vary (direct, indirect)
↑AST, ALT	Mild (AST only)	Moderate to marked	Normal to mild
↑ ALP	Normal	Normal to moderate	Moderate to marked
PT, PTT	Normal	Normal to prolong	Normal to prolong
Urine urobilinogen	Increase	Increase	Decrease
Urine bilirubin	Negative	Negative / Positve	Positive

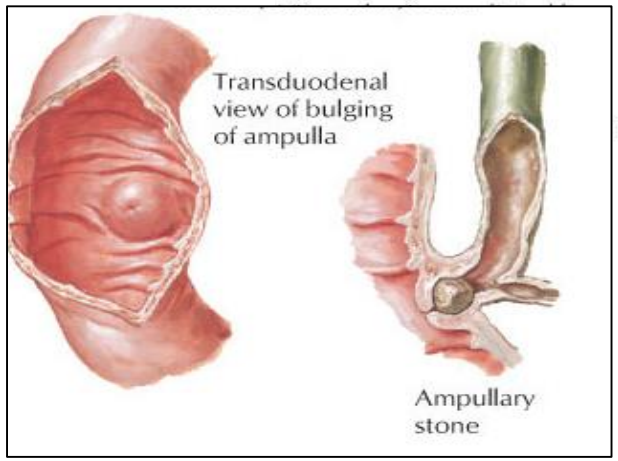
PT= prothrombin time, PTT= partial activated thromboplastin time

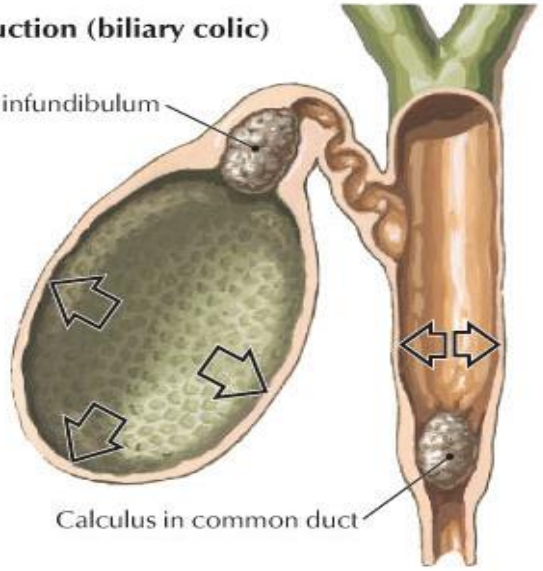
Cholestasis

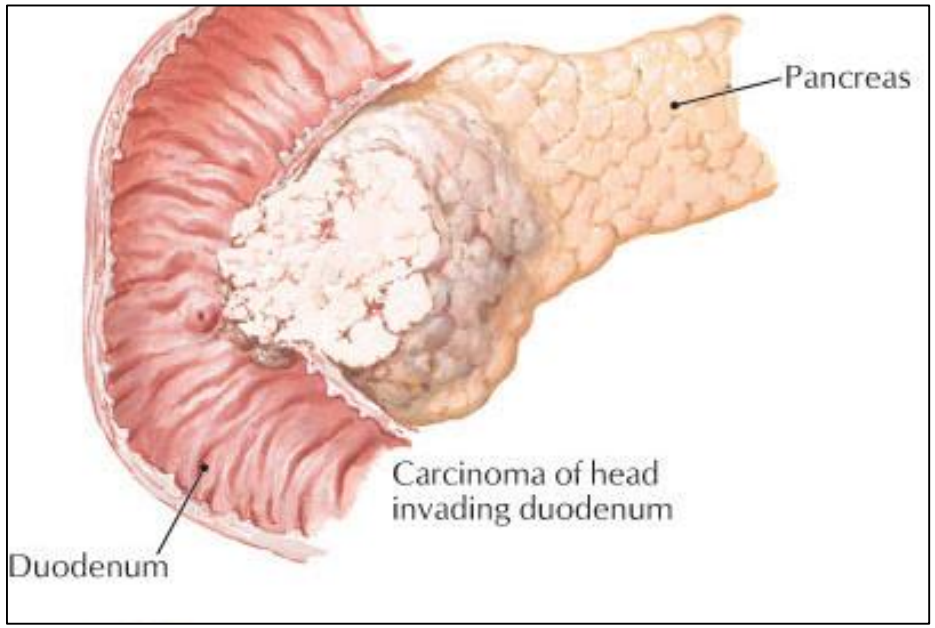
- Decrease of bile flow
- LFT profiles:
    -- Increased alkaline phosphatase (ALP)
    -- Direct hyperbilirubinemia

- Classification
    -- Intrahepatic causes:
        Decreased secretion of bile to bile canaliculi
    -- Extrahepatic causes:
        Decreased secretion of bile to duodenum

Extrahepatic cholestasis



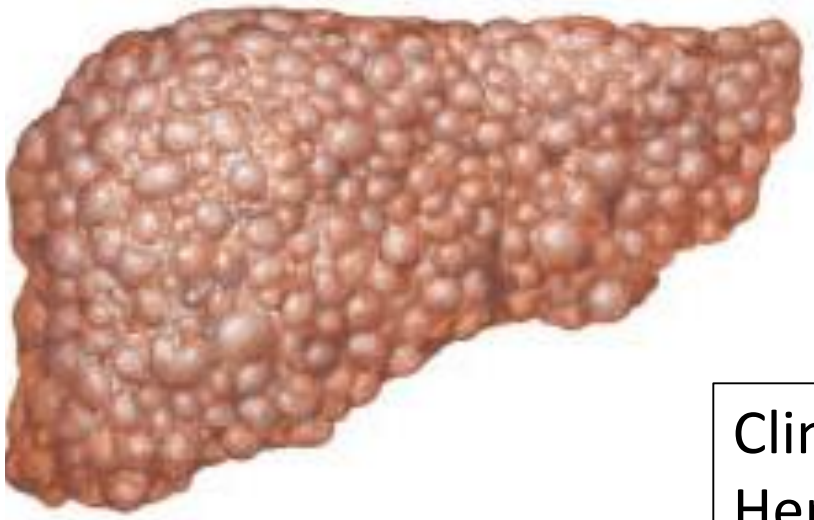




Netter's Clinical Anatomy, 2nd edition.

Cirrhosis

End stage of liver disease characterized by generalized liver fibrosis with regenerative nodules



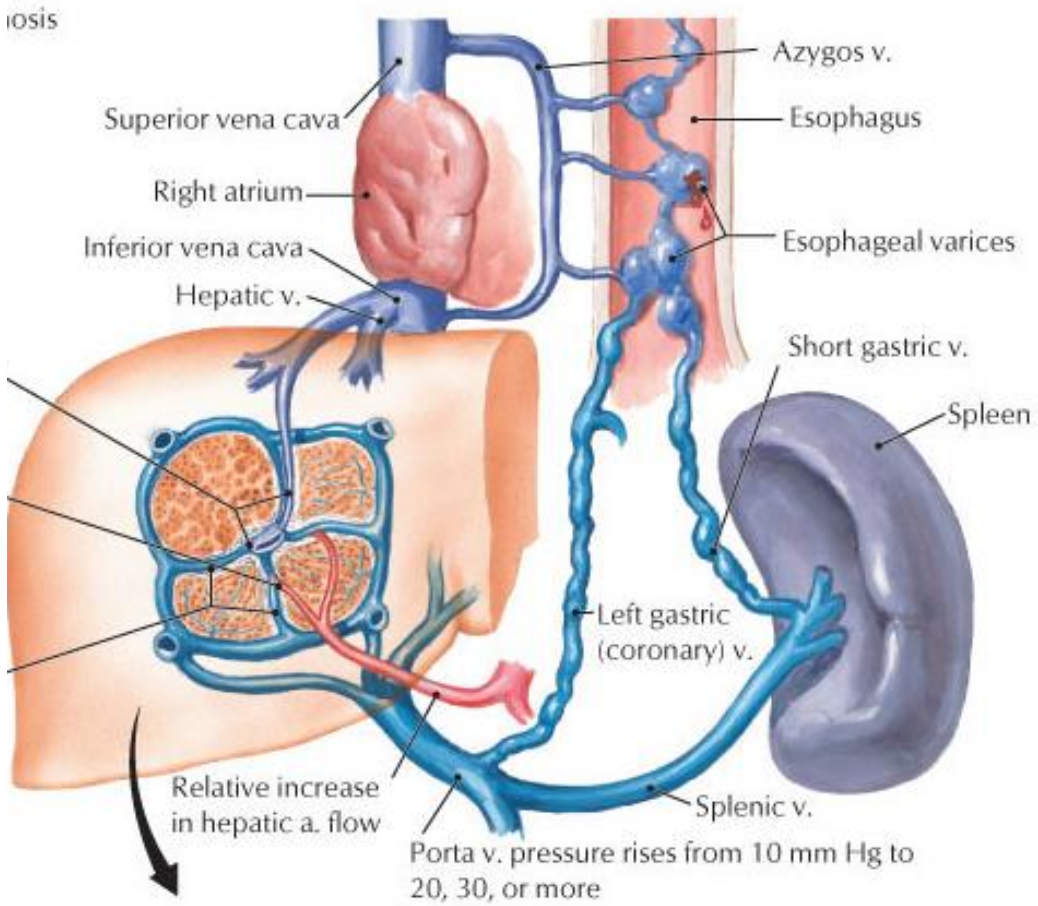
Gross view

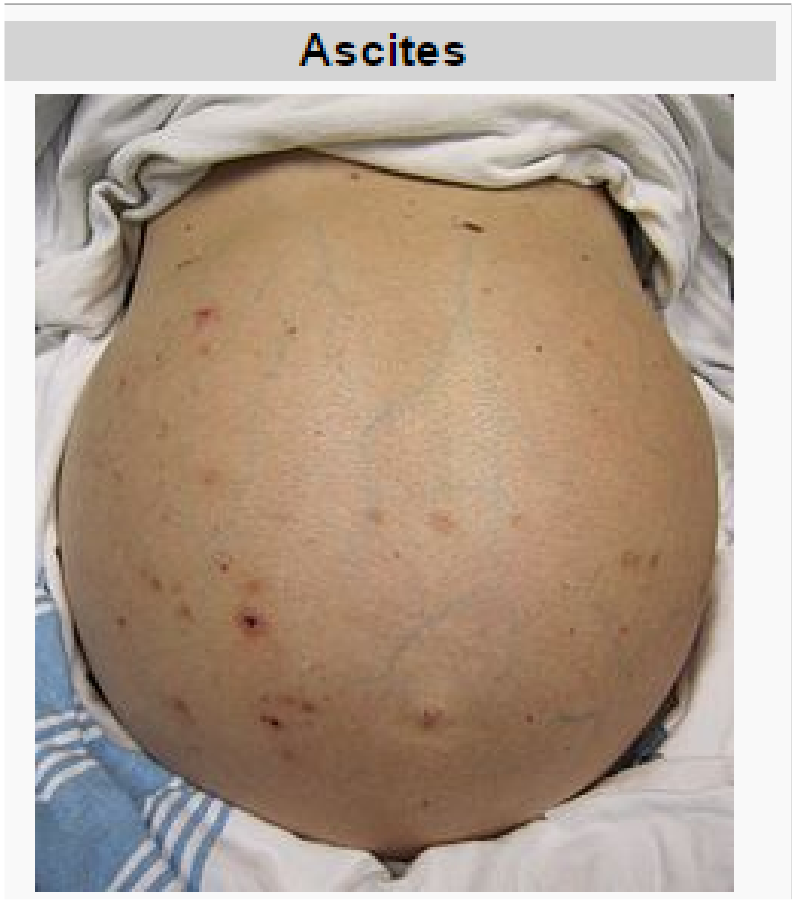
Commonly caused by chronic alcohol consumption and chronic viral hepatitis

Clinical features:
Hepatocellular insufficiency (impaired synthetic function)
Portal hypertension

Netter's Clinical Anatomy, 2nd edition.

Cirrhosis





Netter's Clinical Anatomy, 2nd edition.

References

- Marks' Basic Clinical Biochemistry, 2nd edition
- Lippincott's illustrated reviews, 5th edition
- BRS Biochemistry, Molecular Biology and Genetics, 6th edition