The Liver

HST.035

Spring 2003

The liver is designed to maintain body's chemical and metabolic homeostasis

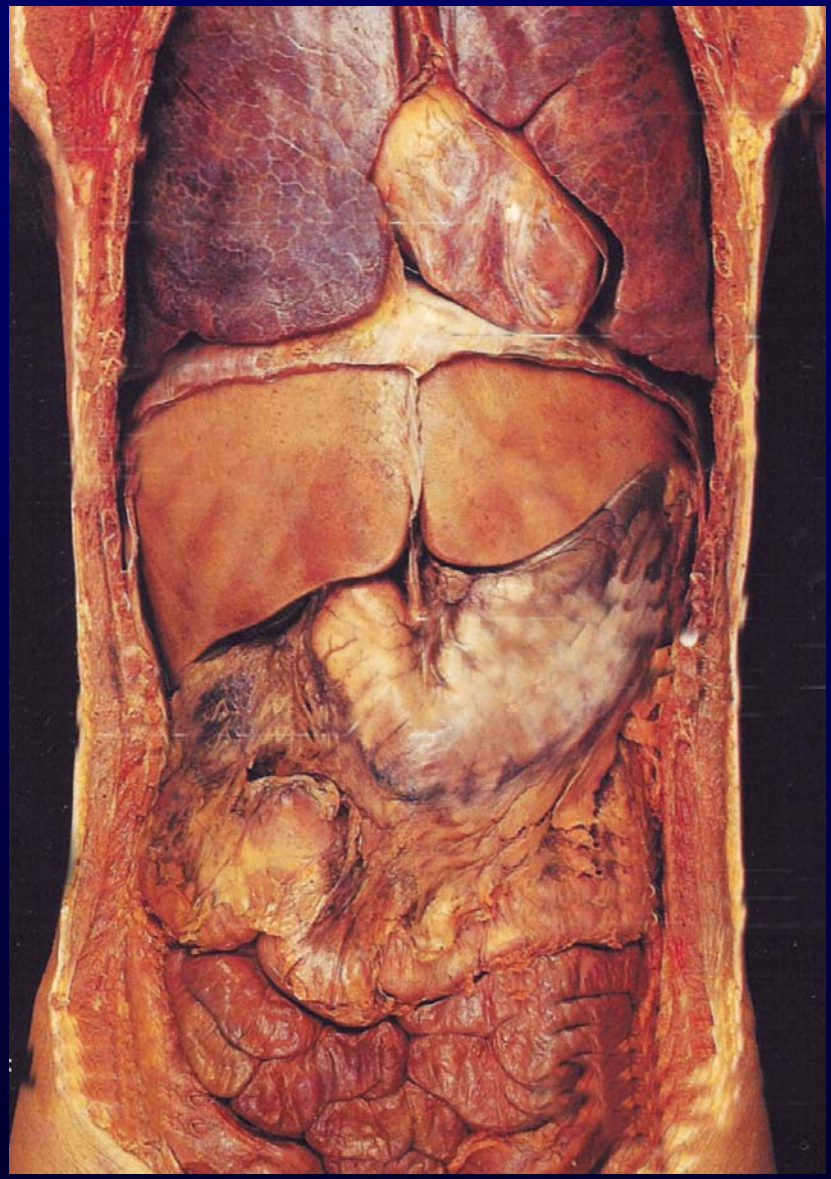
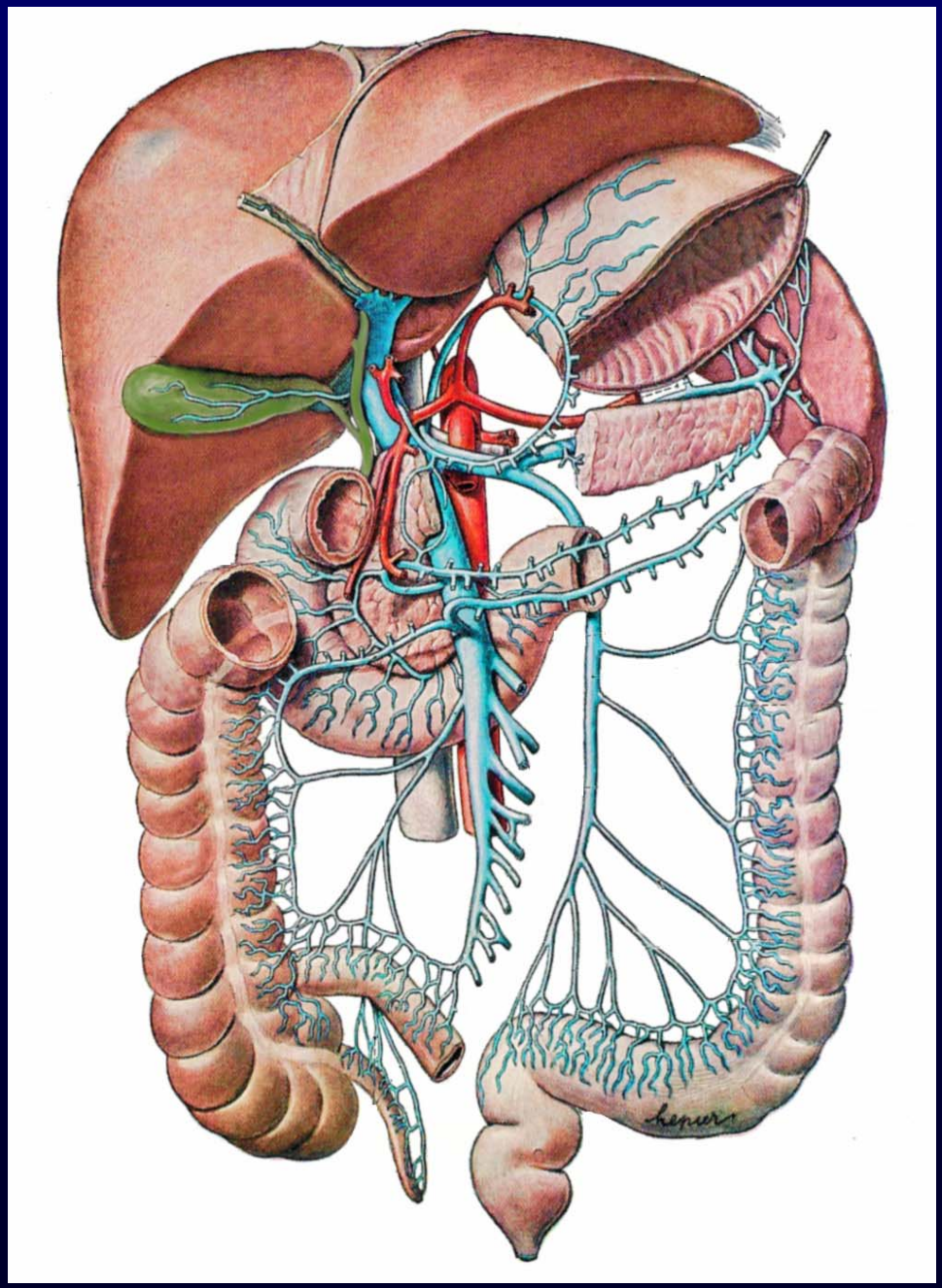
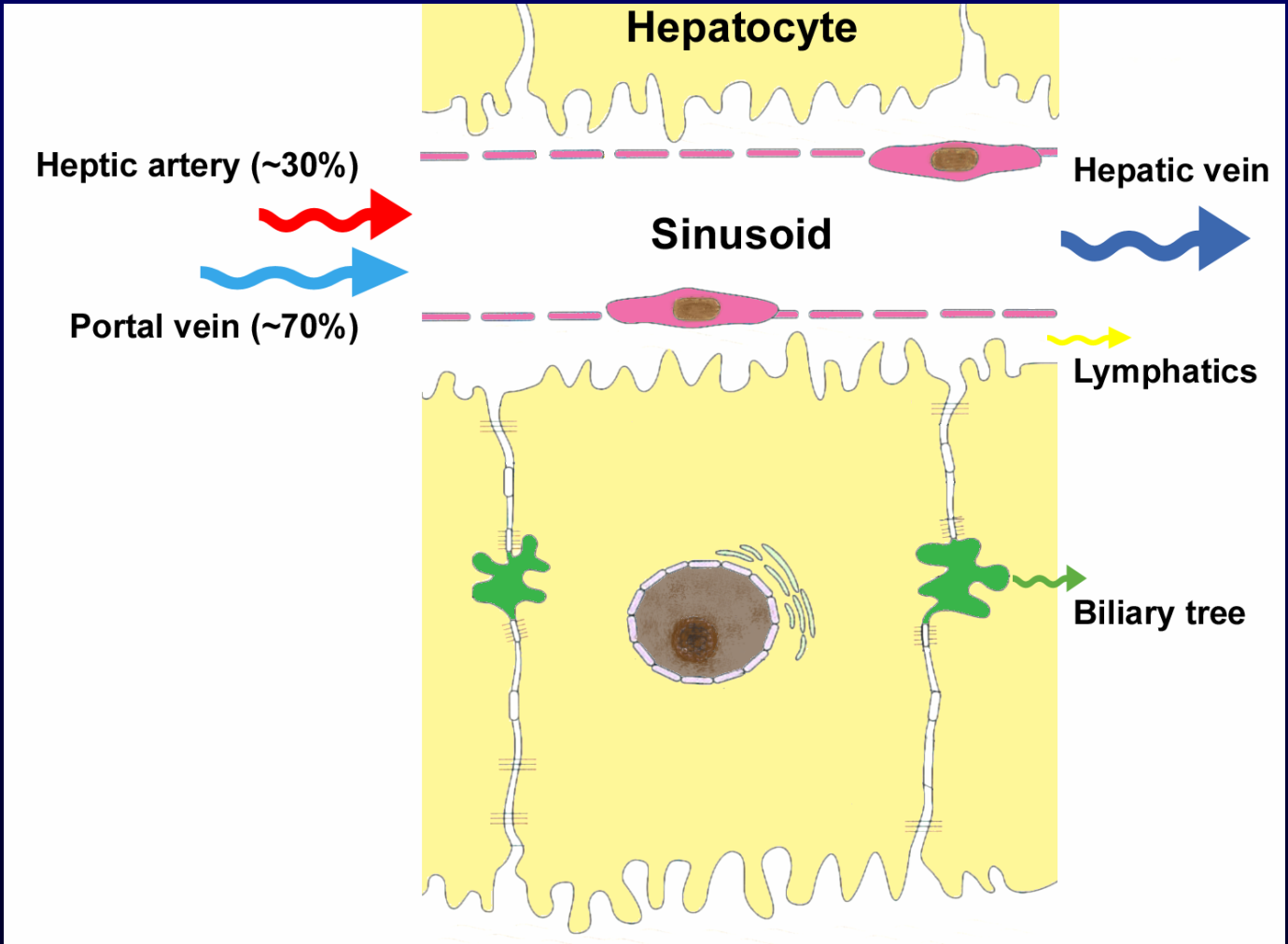


Image modified from Rohen and Yokochi, Color Atlas of Anatomy, Igaku-Shoin, 1988.



Modified image produced based on Clemente, Anatomy, Urban & Schwarzenberg, 1987.

Parenchymal Microcirculation



Parenchymal Microanatomy

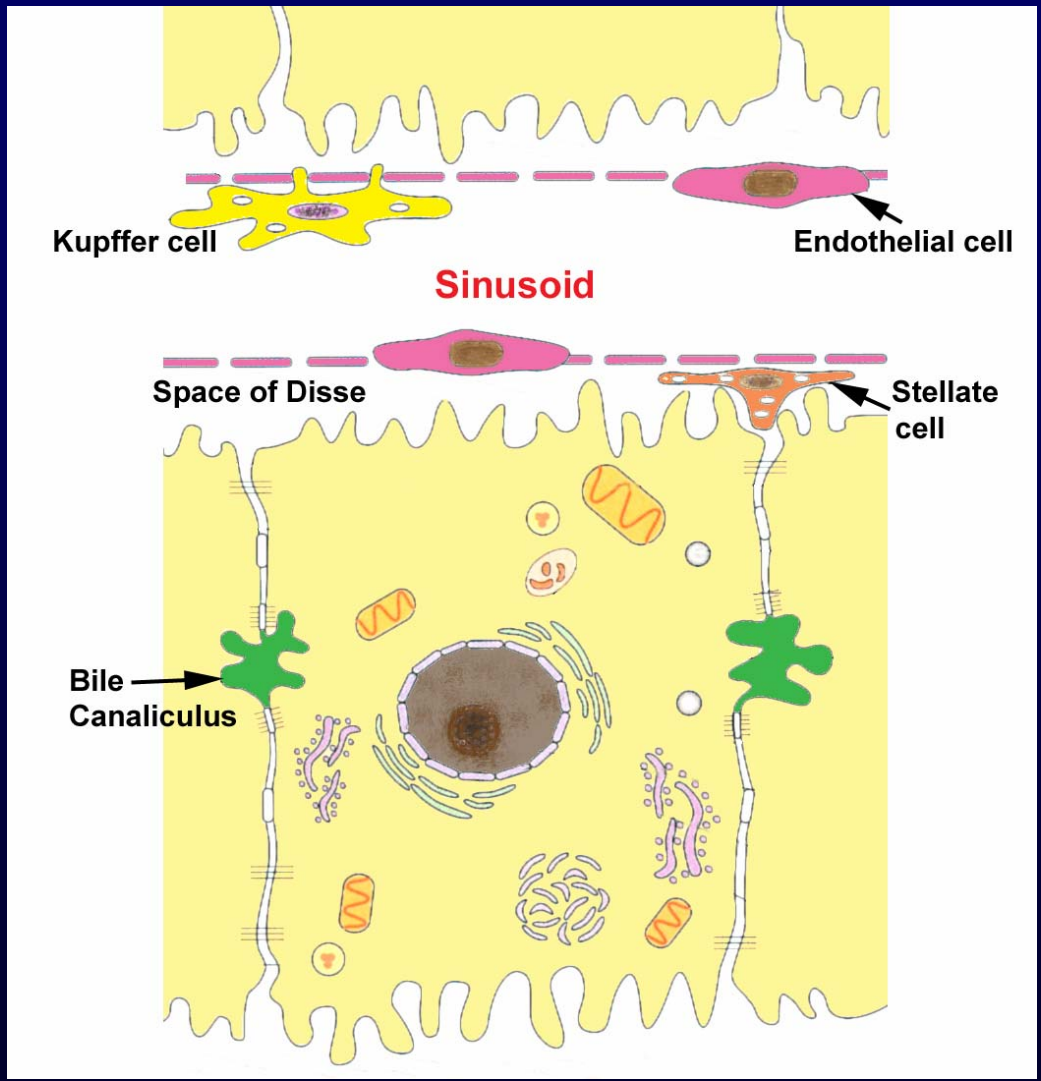
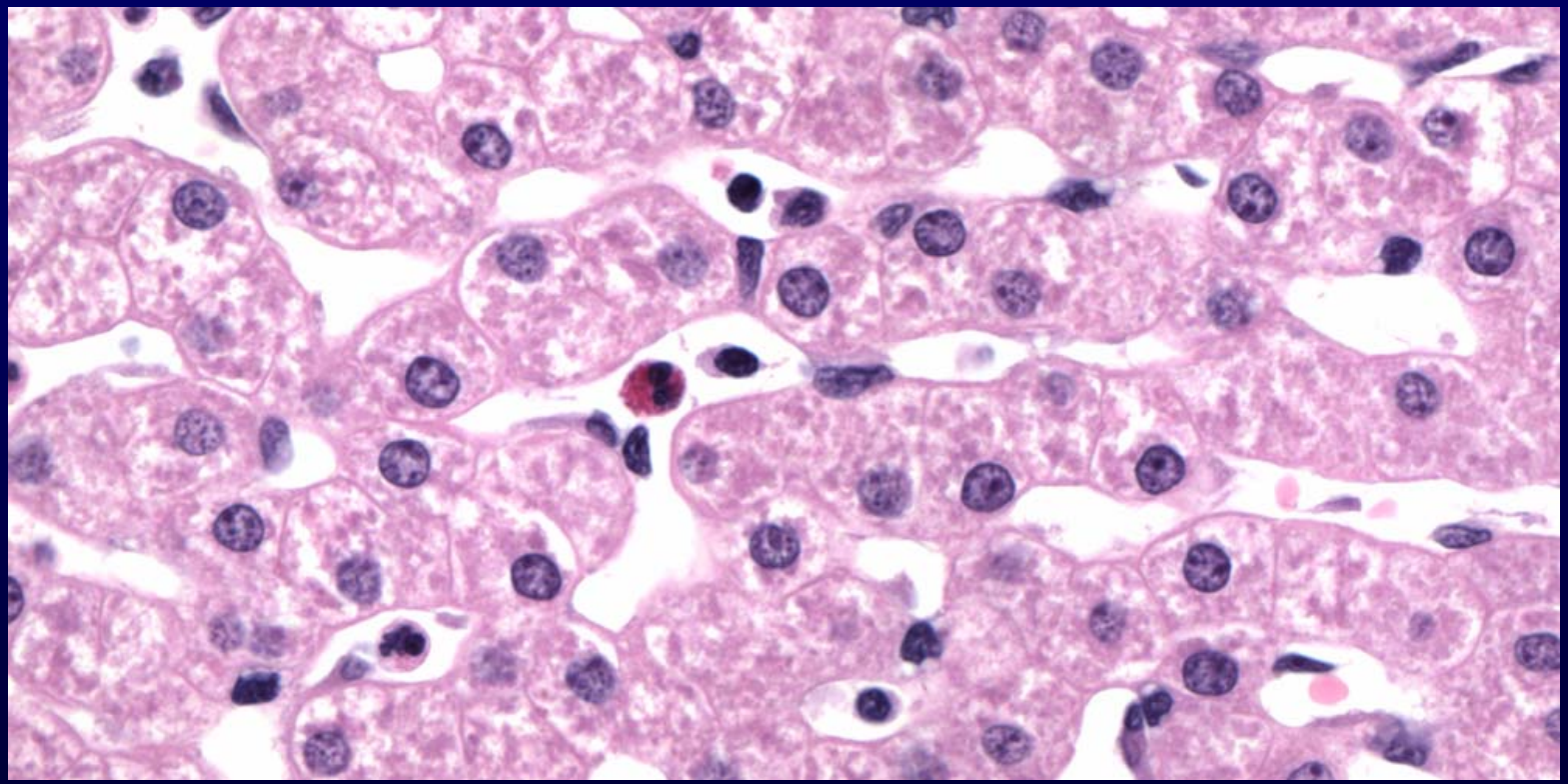


Image redrawn based on O'Grady et al., Clinical Hepatology, Mosby, 2000.

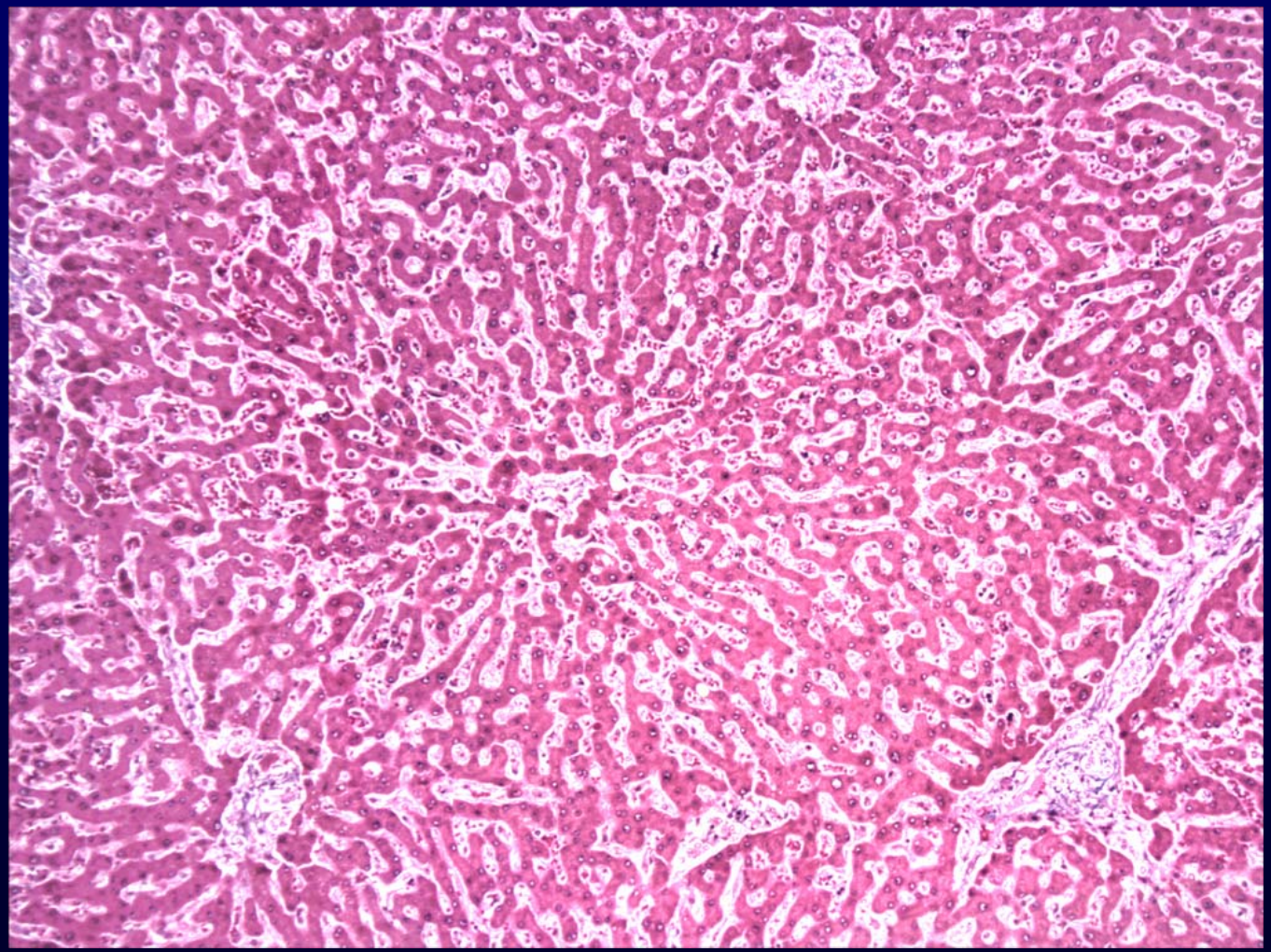
Parenchymal Microanatomy



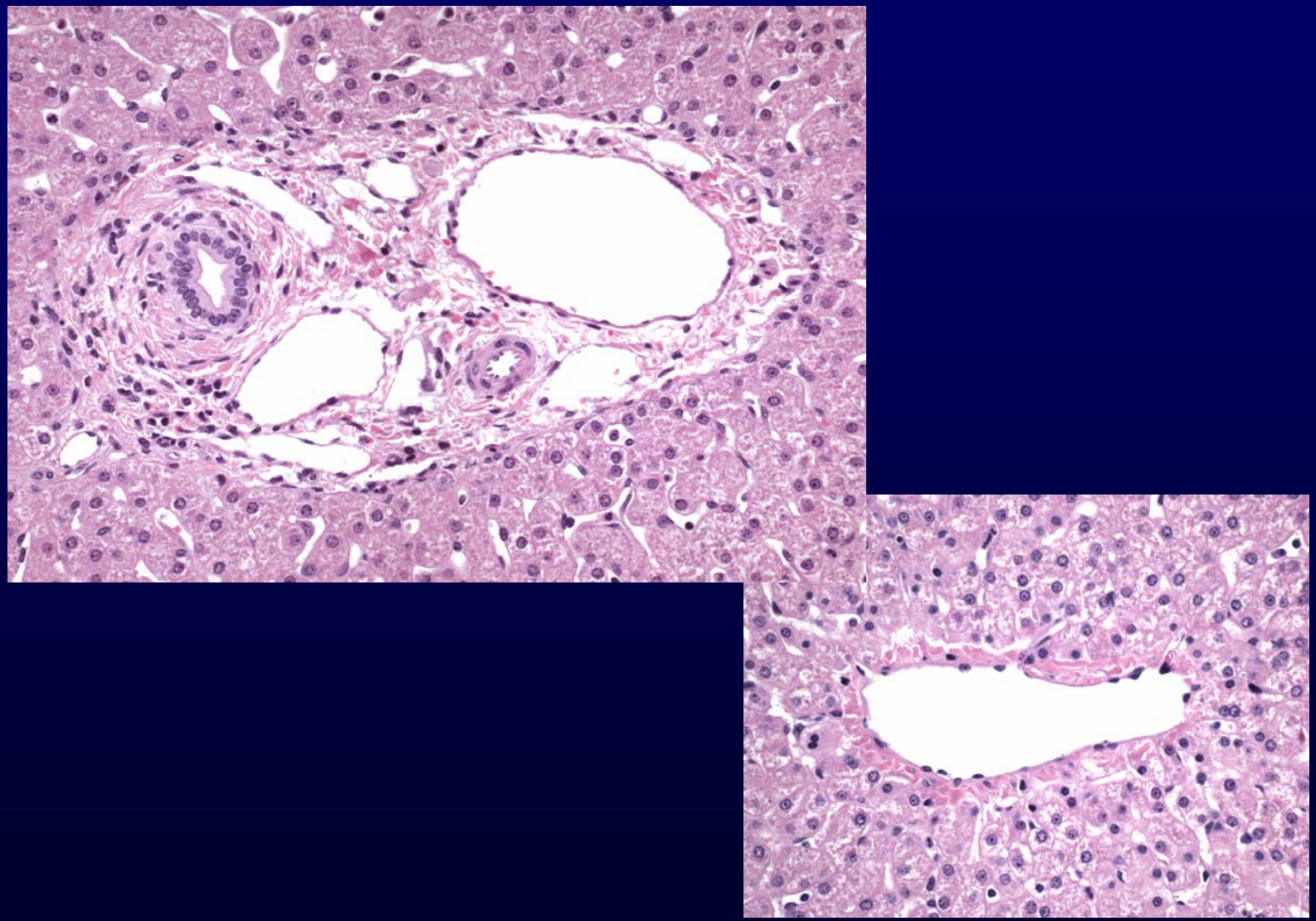
Lobular Microanatomy

Please see Junqueira & Carneiro. *Basic Histology: Text and Atlas*. 10th edition. McGraw Hill. 2003. ISBN: 0071378294.

Lobular Histology



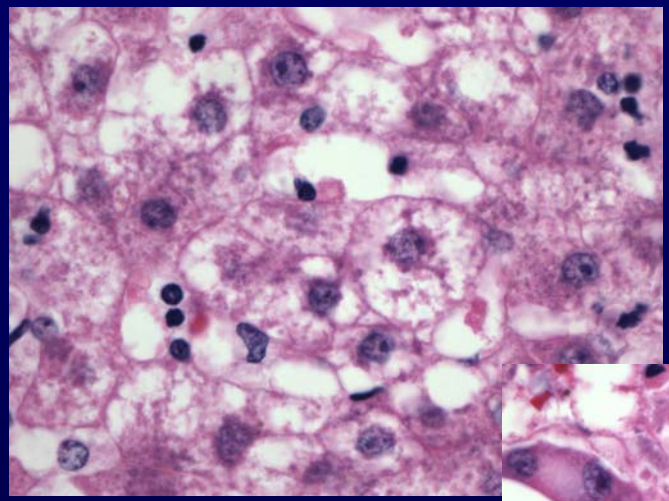
Portal Tract and Central Vein

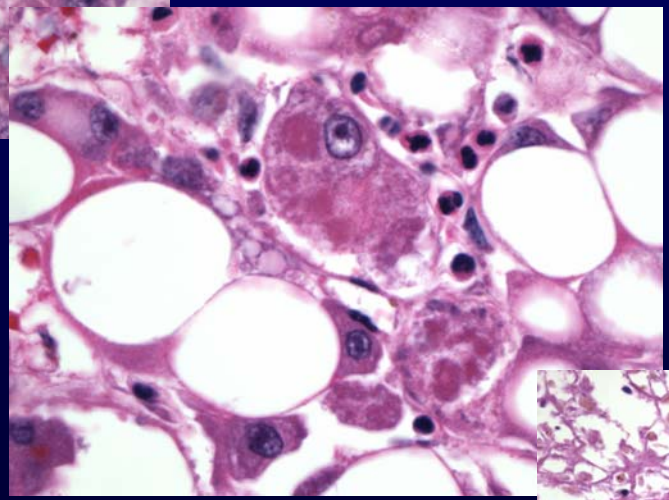


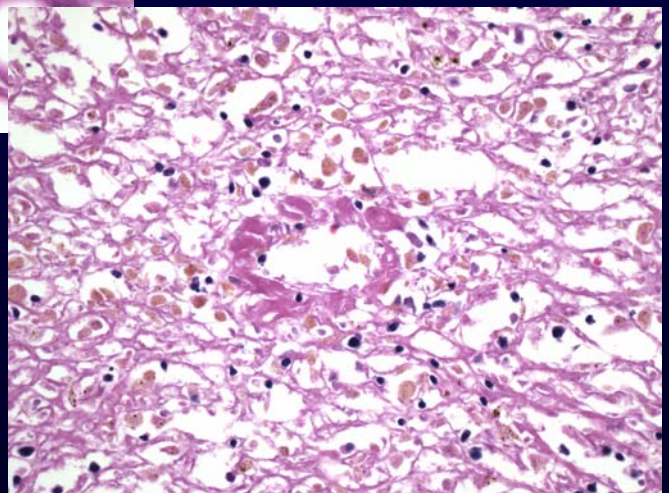
Morphological Patterns of Hepatic Injury

- Hepatocellular degeneration and intracellular accumulation
  - *Ballooning and foamy degeneration*
  - *Steatosis*
- Necrosis and apoptosis
  - *Councilman bodies (apoptotic hepatocytes)*
  - *Zonal necrosis*
  - *Massive necrosis*
- Inflammation (hepatitis)
- Regeneration
- Fibrosis
  - *Cirrhosis*

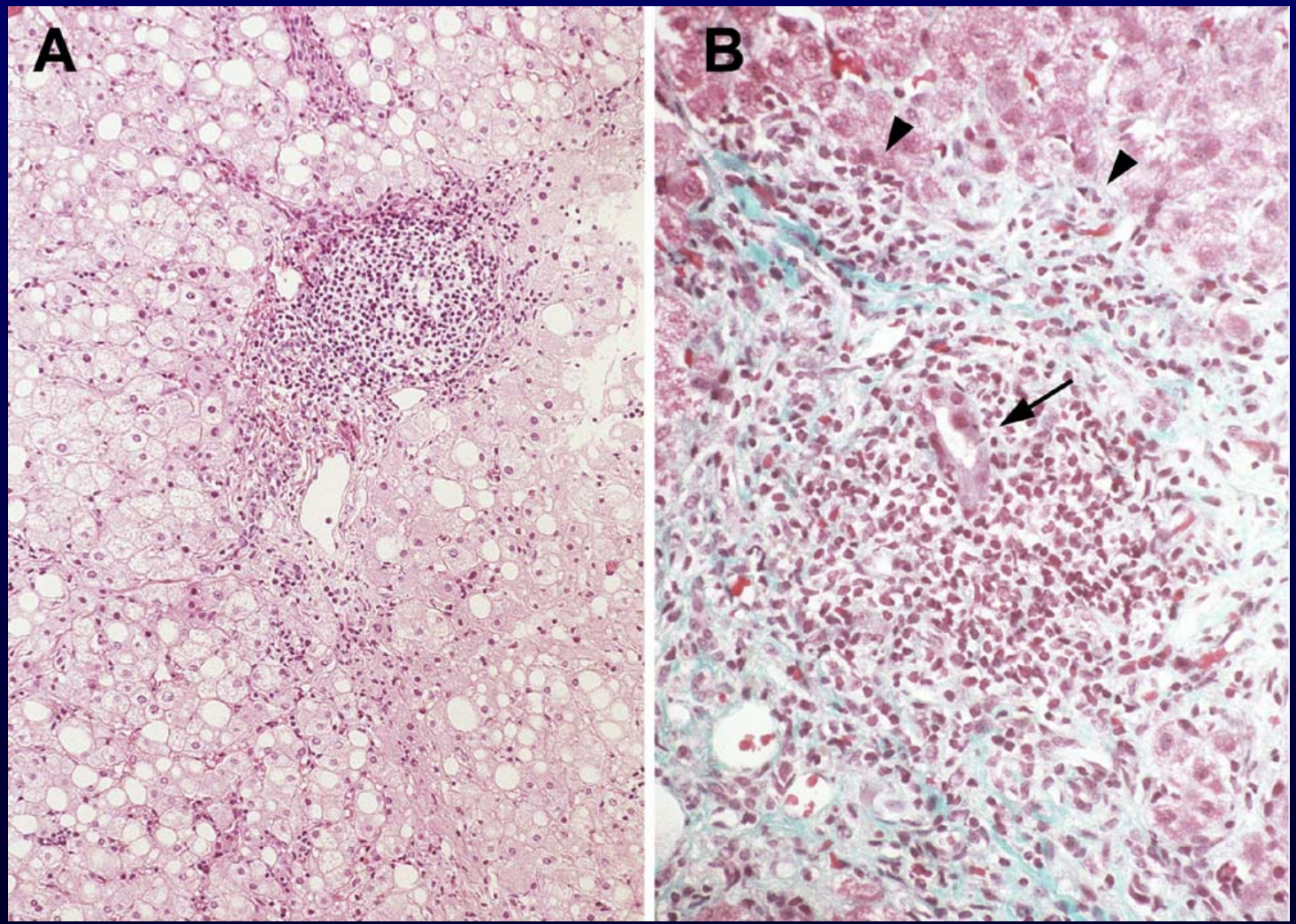
Morphological Patterns of Hepatic Injury: *Hepatocellular Damage*



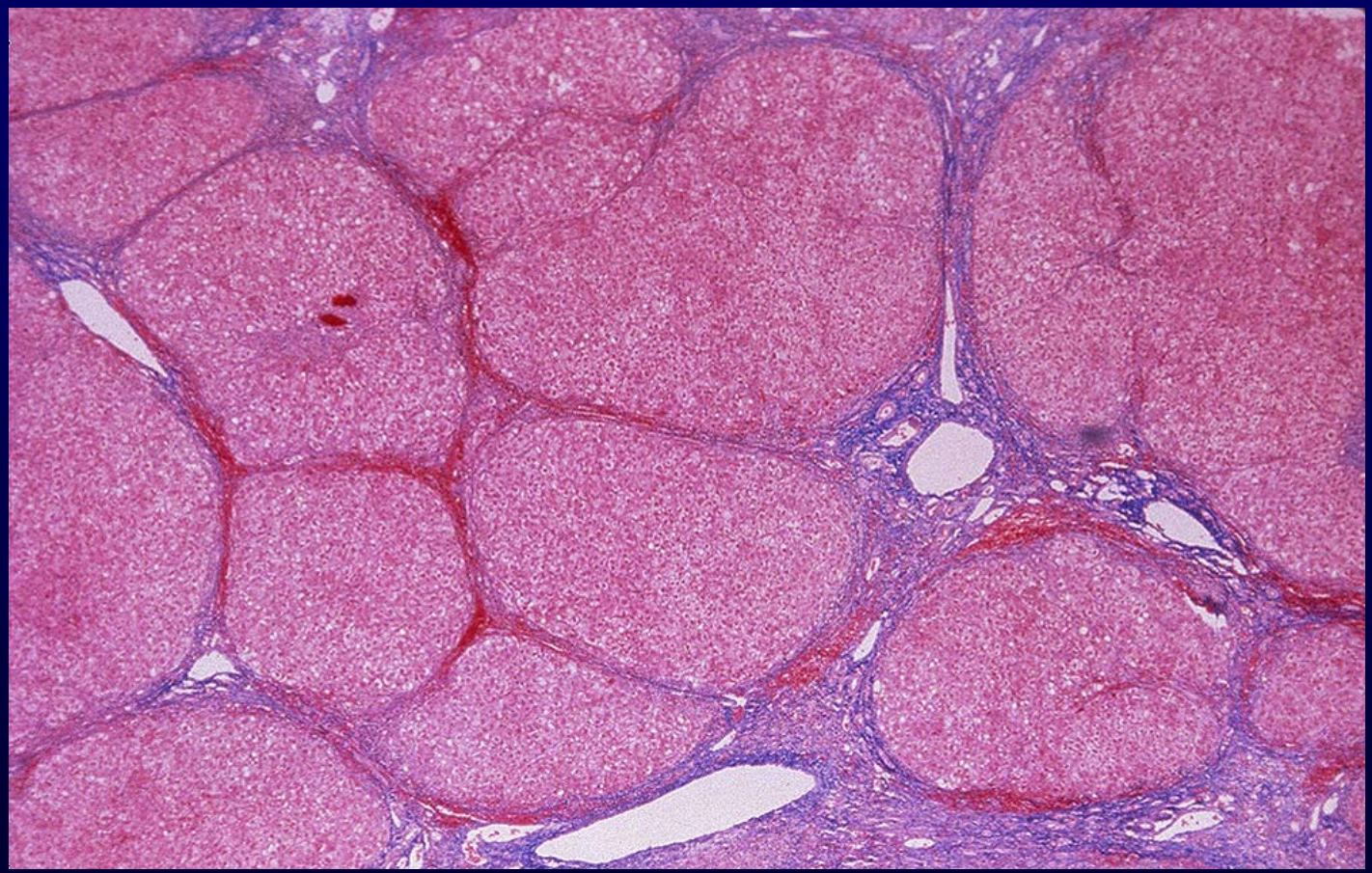




Morphological Patterns of Hepatic Injury: *Hepatitis*



Morphological Patterns of Hepatic Injury: *Cirrhosis (Regeneration + Fibrosis)*



Clinical Signs of Hepatic Injury

Please see O'Grady, John G. et. Al. *Comprehensive clinical hepatology*. Mosby, 2000. ISBN: 072343106X.

Clinical Signs of Hepatic Injury

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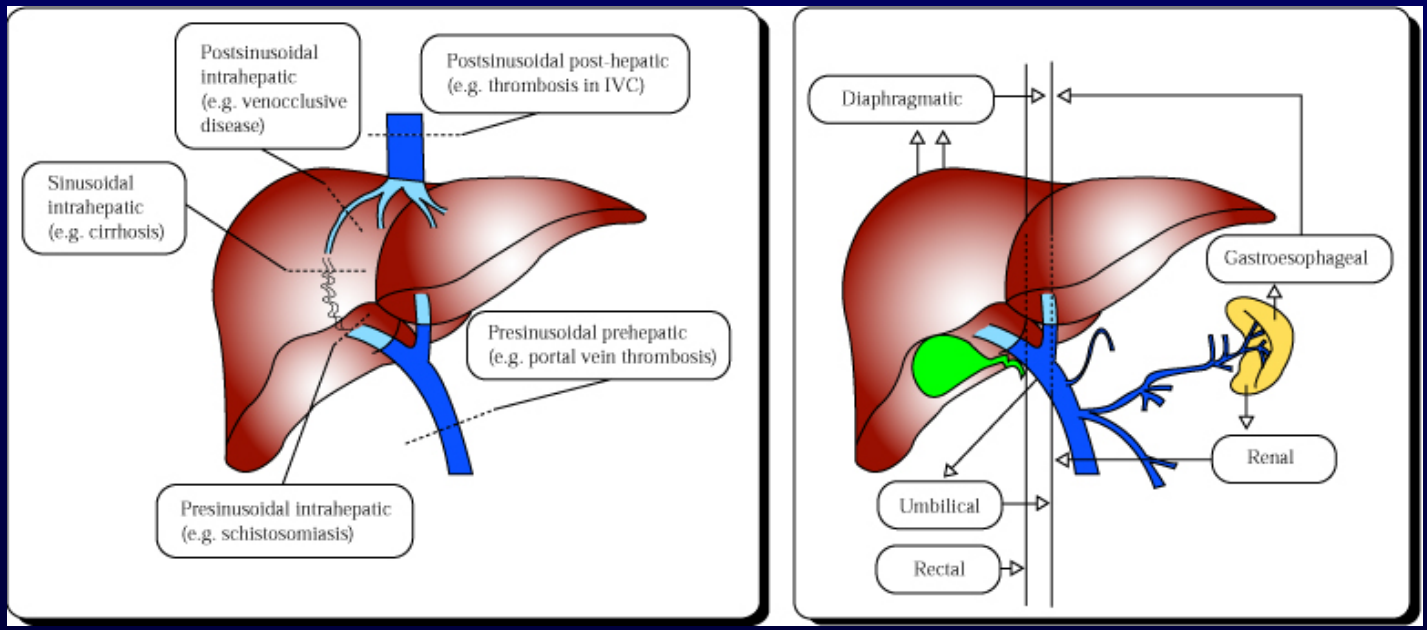
Portal Hypertension and Venous Collaterals



Portal Hypertension → Varices

Clinical Signs of Hepatic Injury

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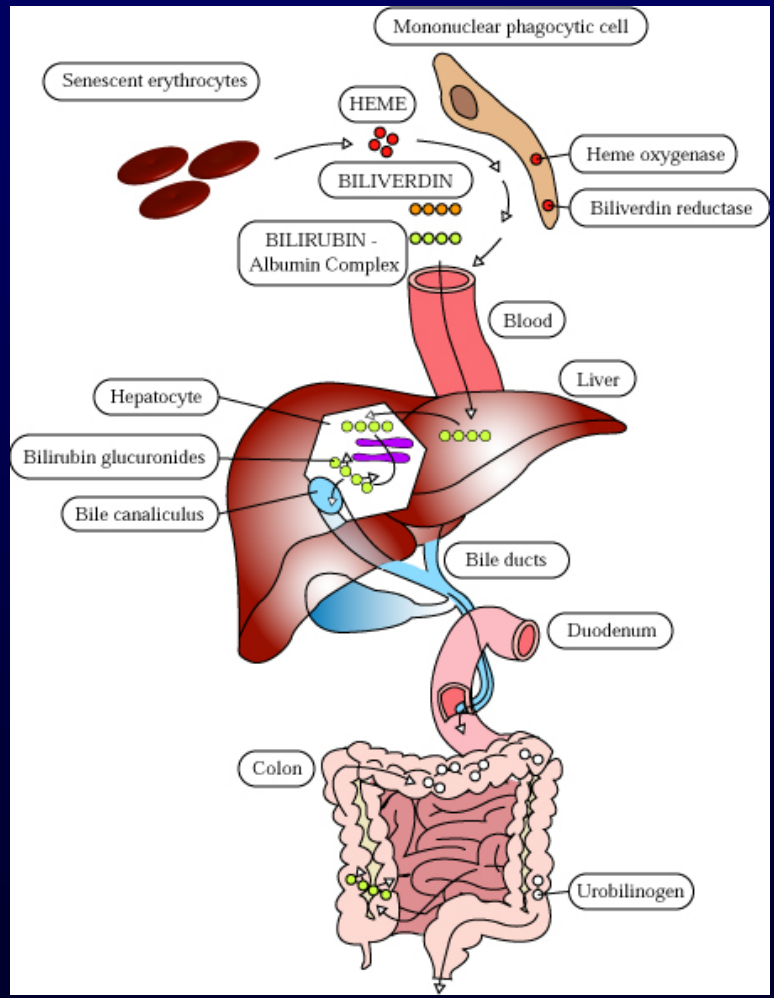
Bilirubin Metabolism and Elimination

1. *Heme oxygenase* oxidizes heme to biliverdin
2. *Biliverdin reductase* reduces bilieverdin to *unconjugated*, water- insoluble bilirubin, which is carried in blood bound to serum albumin
3. Carrier-mediated transport of unconjugated bilirubin into hepatocytes
4. Bilirubin is *conjugated* to glucoronic acids by uridine diphosphate glucoronyltransferase (UGT) and conjugated bilirubin is transported into bile canaliculi by MRP2
5. Intestinal bacteria deconjugate and breakdown bilirubin into colorless urobilinogens, which are primarily excreted in feces



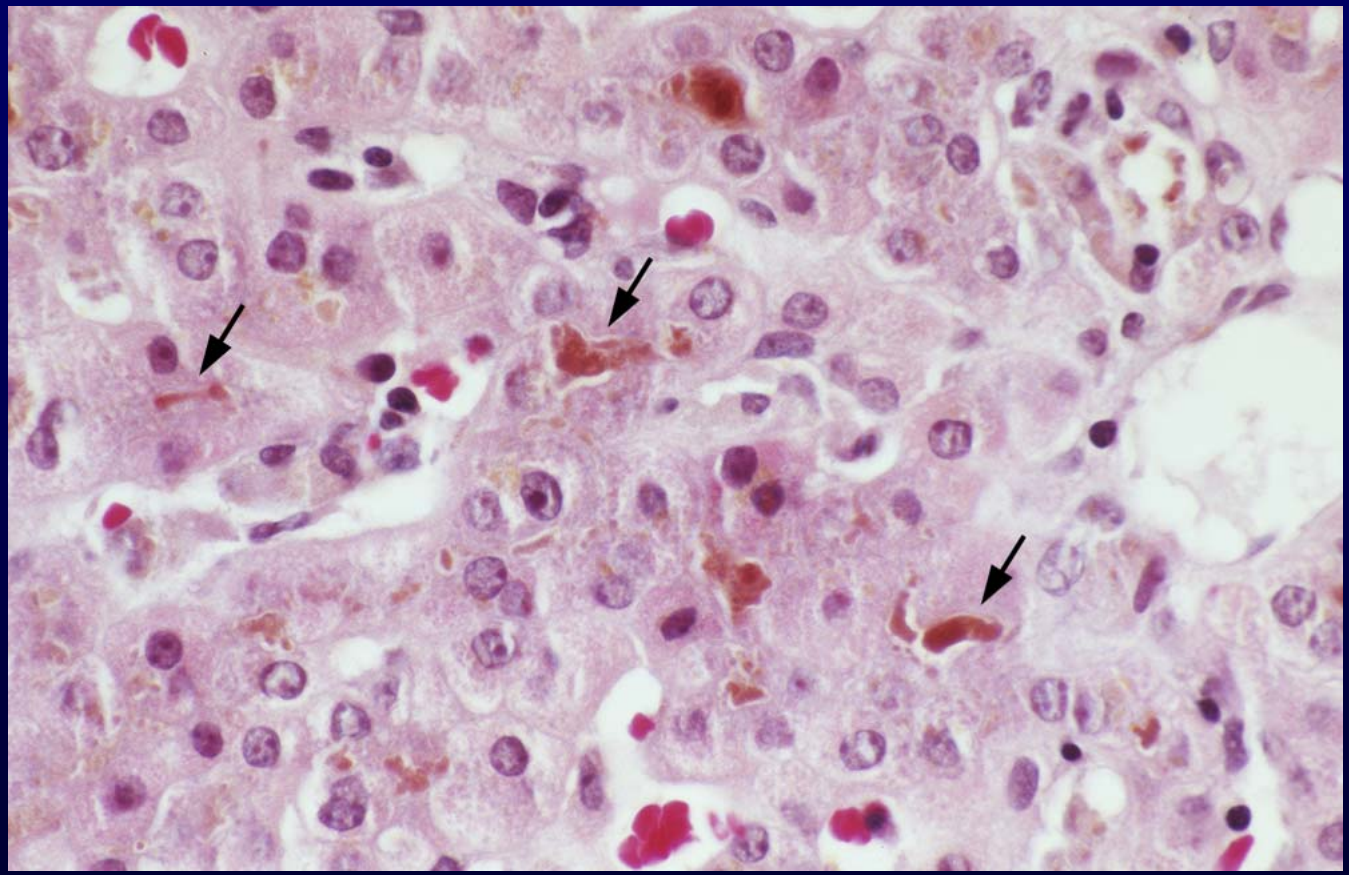
Causes of Jaundice

- **Disorders of bilirubin production or metabolism**
  - Unconjugated:
    - Overproduction (hemolysis, ineffective hematopoiesis)
    - Decreased conjugation (newborns, Crigler-Najjar, Gilbert)
  - Conjugated:
    - Impaired canalicular transport (Dubin-Johnson)

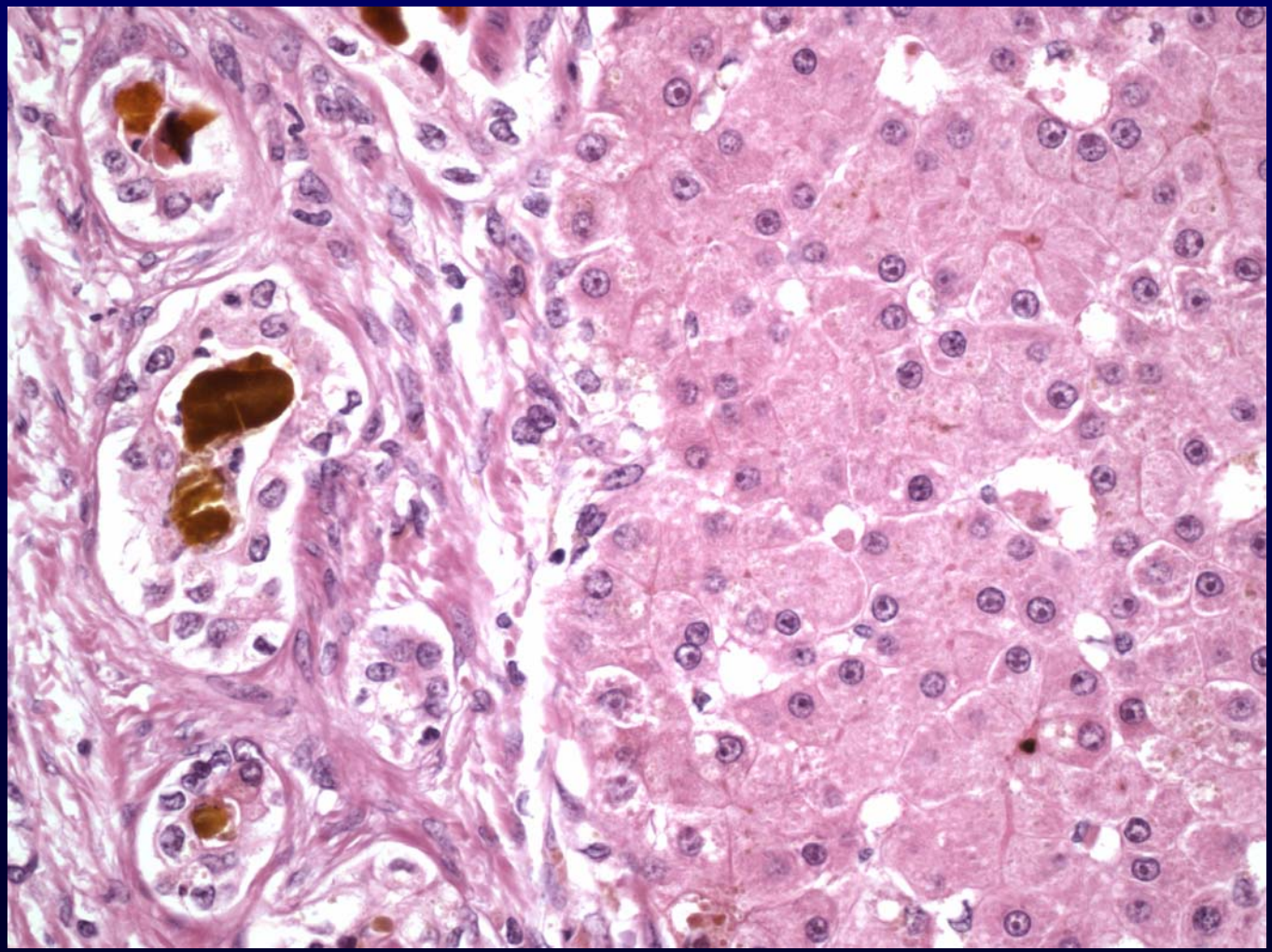
- **Liver diseases**
  - Acute or chronic hepatocellular injury
  - “Intrahepatic cholestasis”

- **Obstruction of bile ducts** (“extrahepatic cholestasis”)
  - Gallstones
  - Other masses
  - Inflammation/infection

Intrahepatic Cholestasis



Extrahepatic Cholestasis



Viral Hepatitis

Hepatitis A

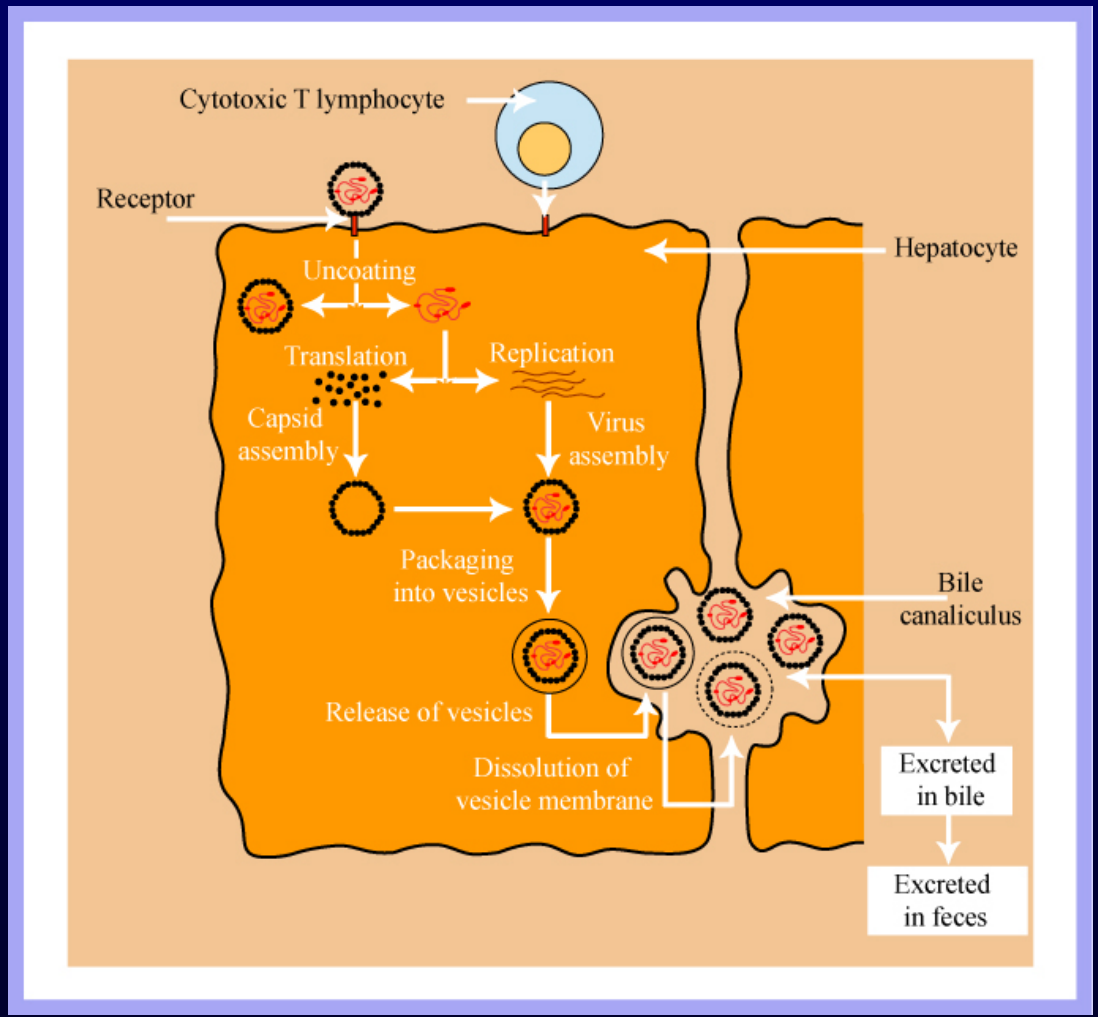
- The most common cause of viral hepatitis worldwide.
- Estimated 75,000 clinnical cases/yr in the US.

Please see O'Grady, John G. et. Al. *Comprehensive clinical hepatology*. Mosby, 2000. ISBN: 072343106X.

Clinical Characteristics of Hepatitis A

Please see O'Grady, John G. et. Al. *Comprehensive clinical hepatology*. Mosby, 2000. ISBN: 072343106X.

Pathogenesis of Hepatitis A



Hepatitis B

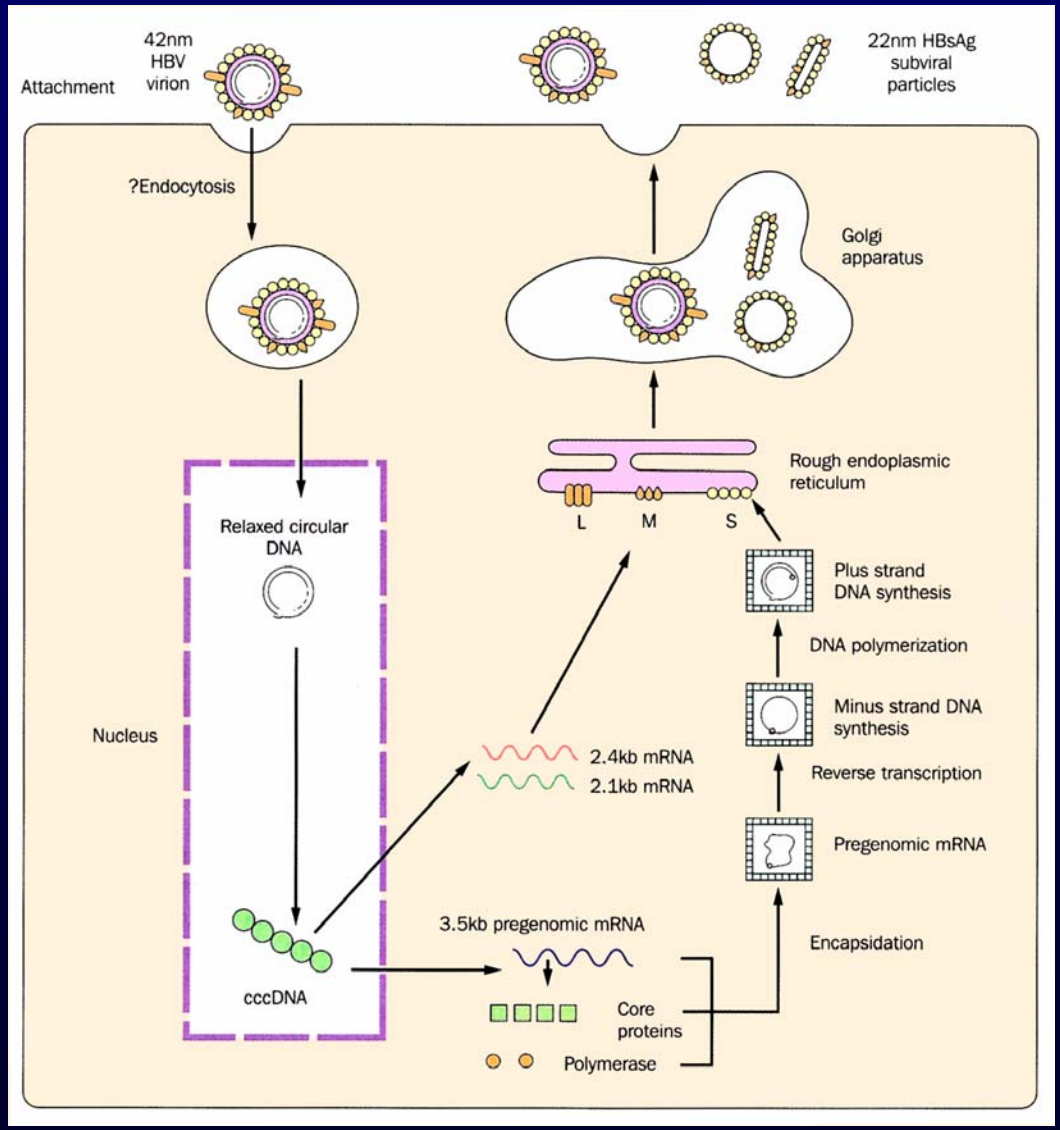
- ~300 million infected worldwide, of whom 250,000 die of complications.
- Sexual transmission is the major mode of spread in developed countries.
- Perinatal transmission occurs in 90% of infants born to HBeAg+ mothers.

Please see O'Grady, John G. et. Al. *Comprehensive clinical hepatology*. Mosby, 2000. ISBN: 072343106X.

Clinical Outcomes of HBV Infection

Please see figure 19-9, pg. 858 of Cotran et al. *Robbins Pathological Basis of Disease*. 6th edition. WB Saunders 1999. ISBN: 072167335X.

Lifecycle of HBV



Modified from O'Grady et al., Clinical Hepatology, Mosby, 2000.

Hepatitis C

- The global prevalence of *chronic* HCV is ~3%.
- 4 million HCV carriers in US; 5 million in Europe.
- Transmission as a blood-borne pathogen.

Please see O'Grady, John G. et. Al. *Comprehensive clinical hepatology*. Mosby, 2000. ISBN: 072343106X.

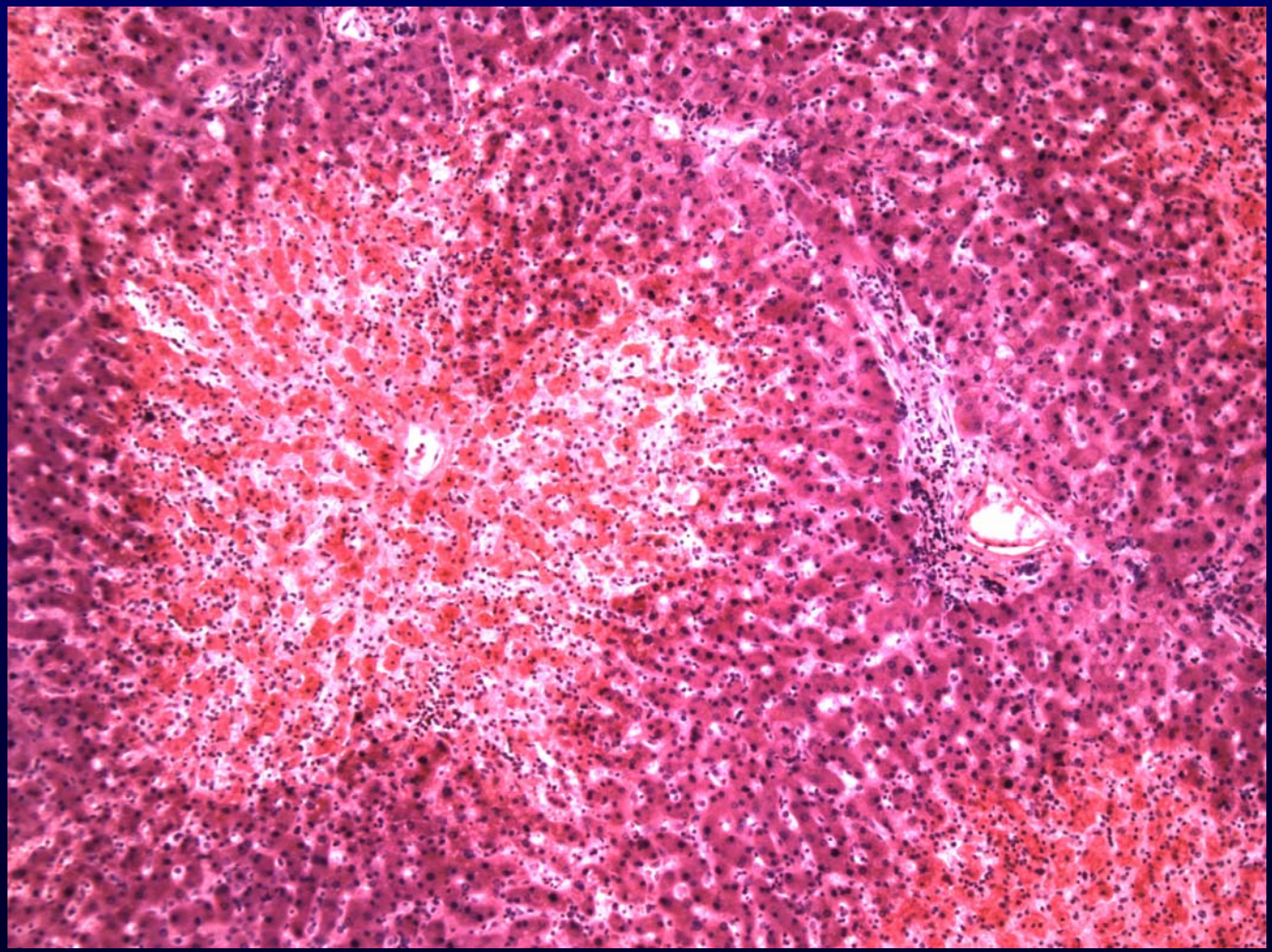
Clinical Outcomes of HCV Infection

Please see figure 19-12, pg. 860 of Cotran et al. *Robbins Pathological Basis of Disease*. 6th edition. WB Saunders 1999. ISBN: 072167335X.

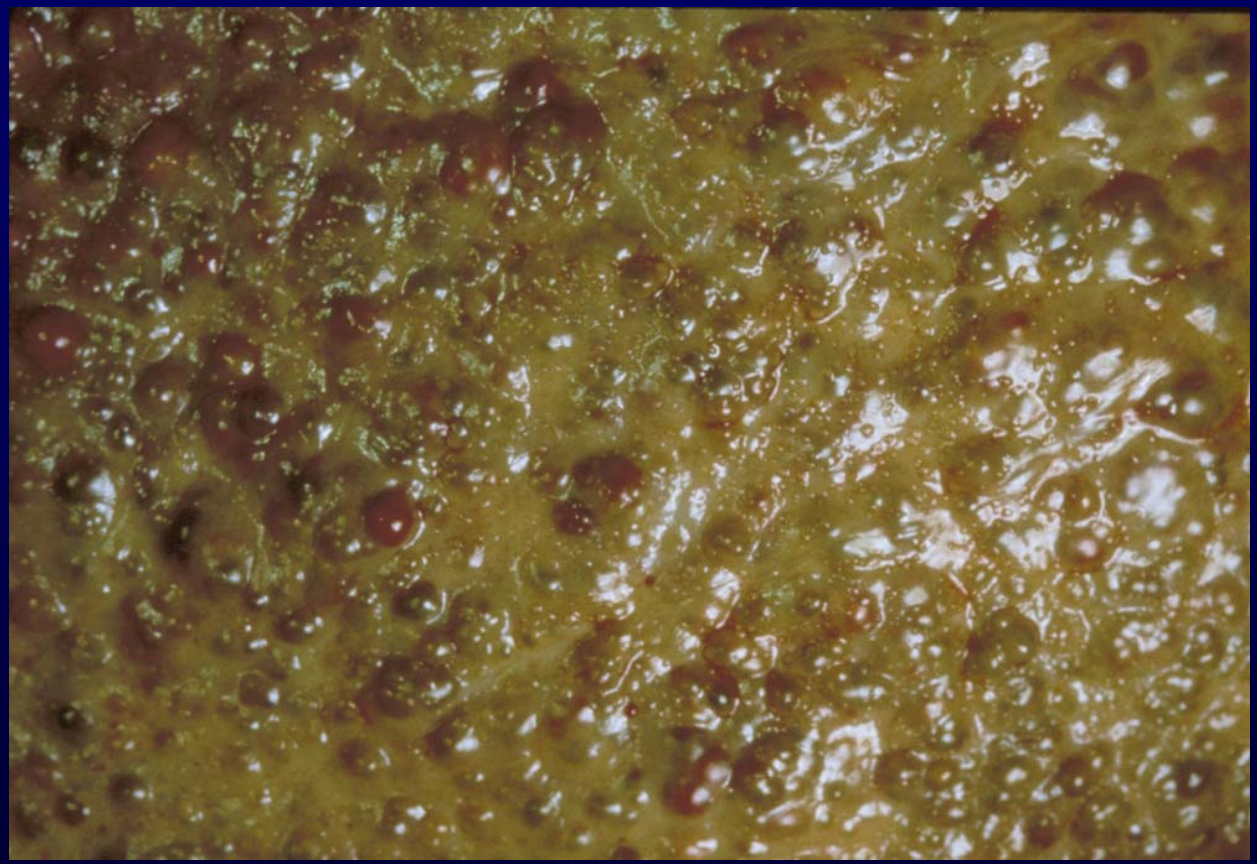
Drug and Toxin-Induced Liver Disease

Pattern of Damage	Example of Drugs
Microvesicular steatosis	Tetracycline, ethanol, aspirin
Macrovesicular steatosis	Ethanol, methotrexate
Centrilobular necrosis	Tylenol, rifampin
Massive necrosis	Halothane, isoniazid
Hepatitis	Isoniazid, methyldopa
Fibrosis	Ethanol, methotrexate
Granulomas	Sulfonamides, quinine
Cholestasis	Chlorpromazine, steroids

Drug and Toxin-Induced Liver Disease



Alcoholic Liver Disease



Alcoholic Liver Disease