

# Liver Disease

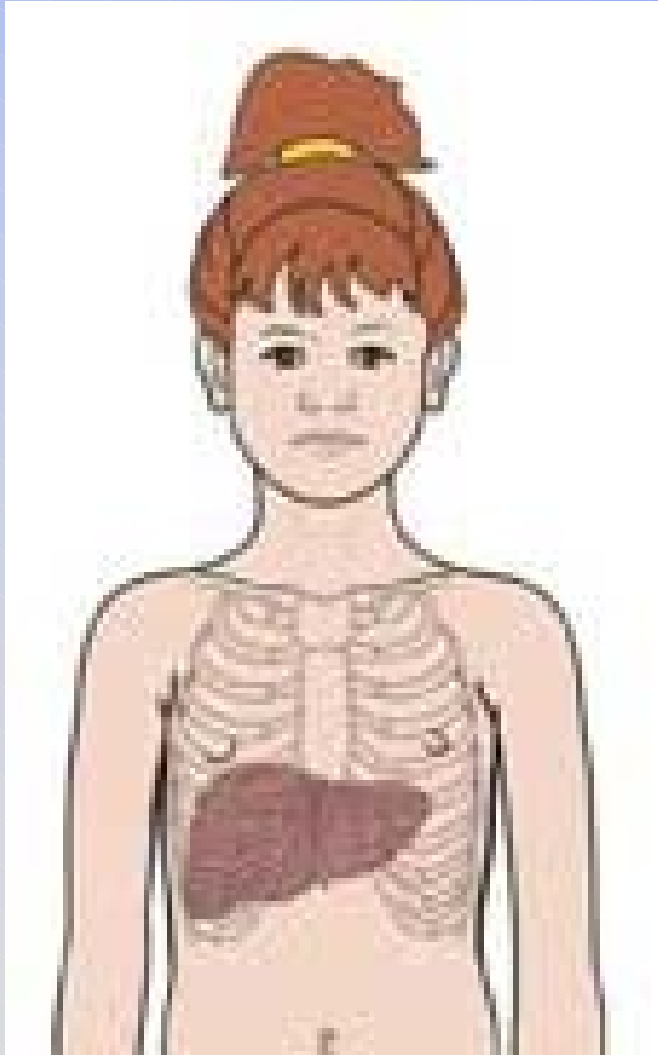
Medical Education Day  
Jeffrey P Schaefer, MD  
January 19, 2004

# Objectives

- Liver anatomy and function
- Manifestations of liver disease
  - symptoms
  - signs
  - common lab
- Common Presentations
- Therapy
- Prognosis

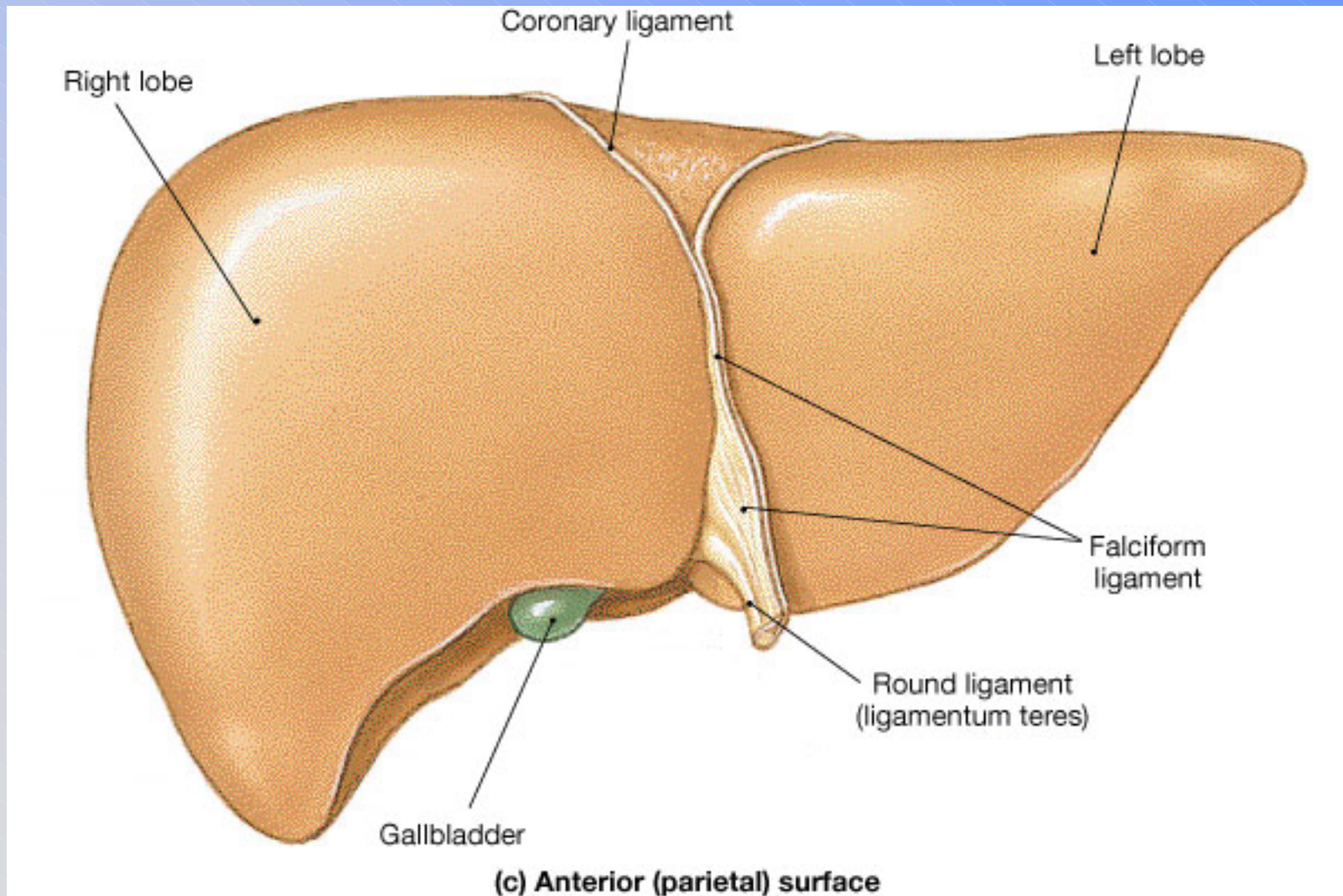
# Anatomy

# Liver Anatomy

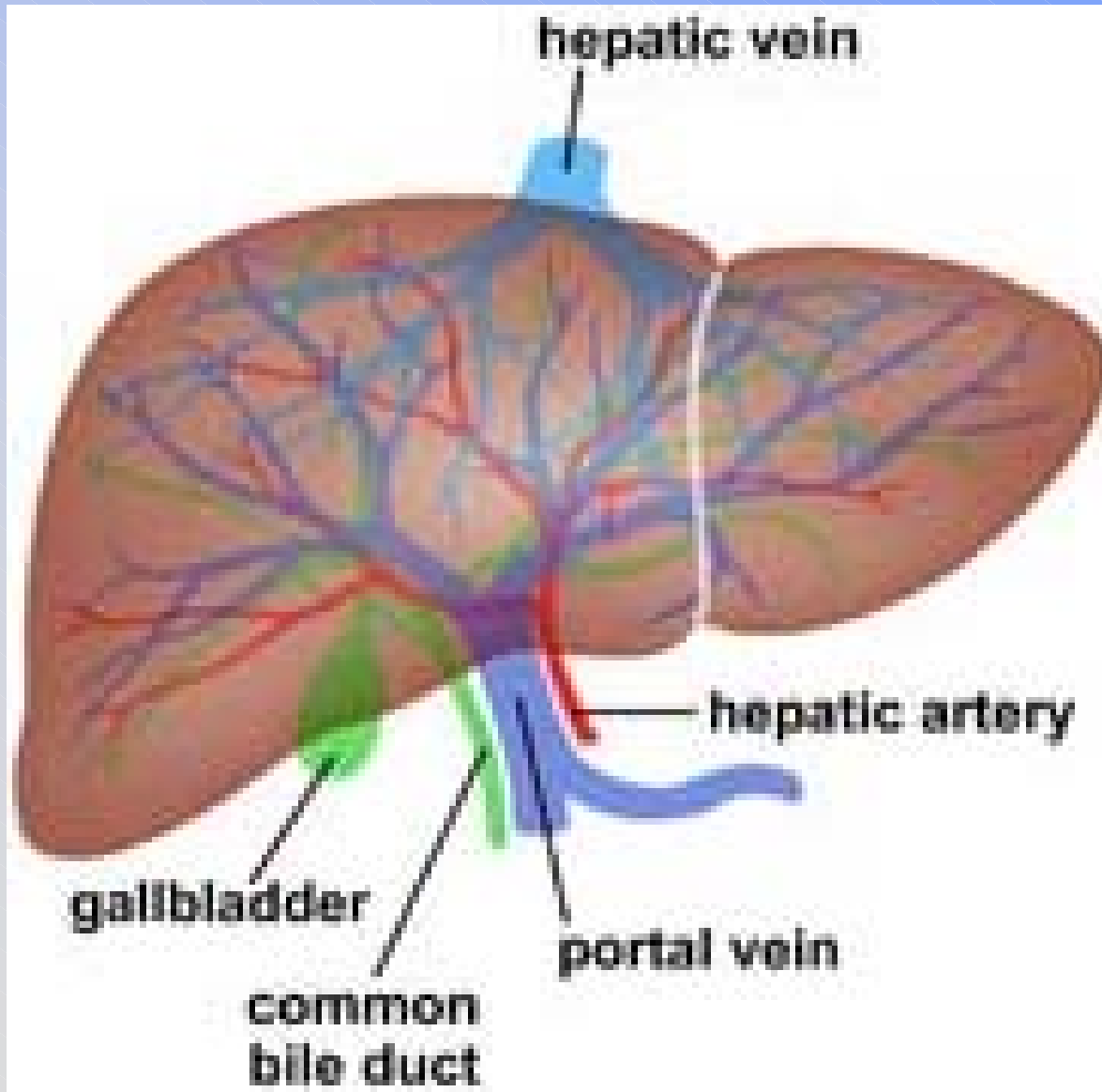


- right and left upper quadrants
- takes about 13% of blood supply

# Liver Lobes and Ligaments



# Liver Anatomy

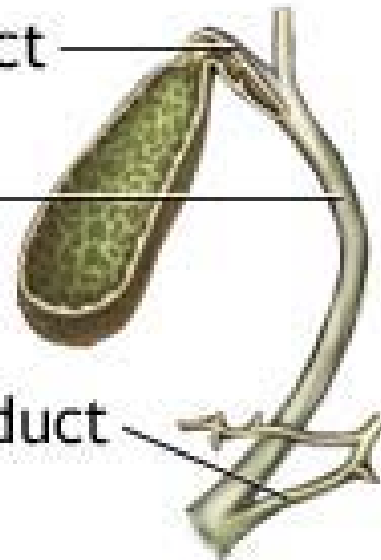


- dual blood supply
- portal vein from GI tract, pancreas, spleen
- artery from aorta

Cystic duct

Common  
bile duct

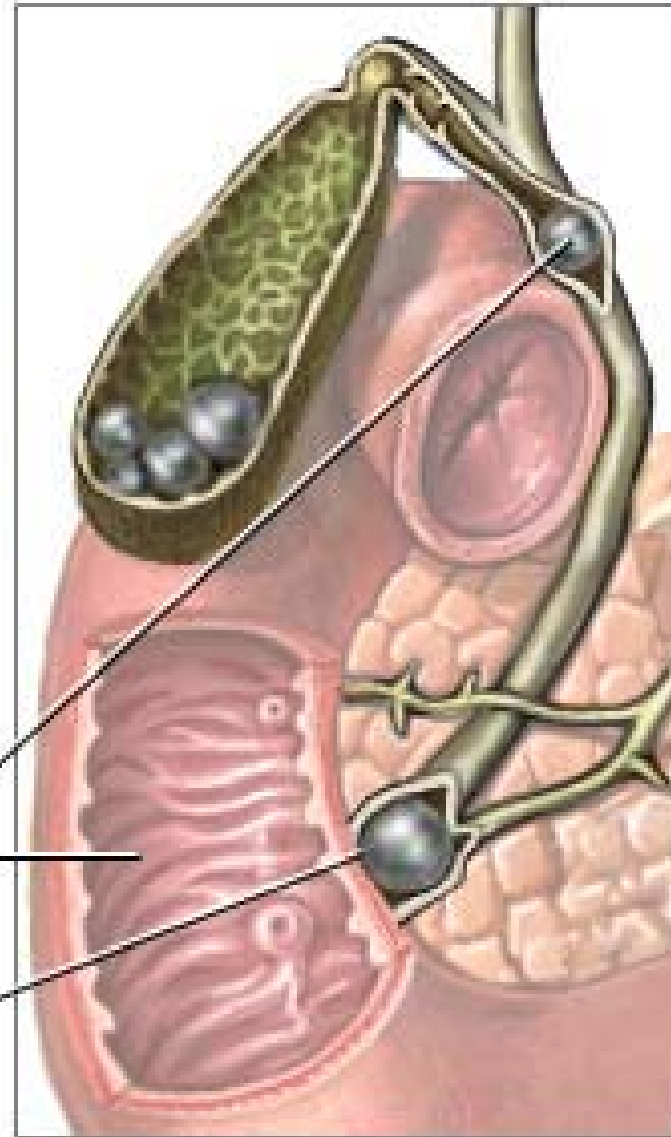
Pancreatic duct



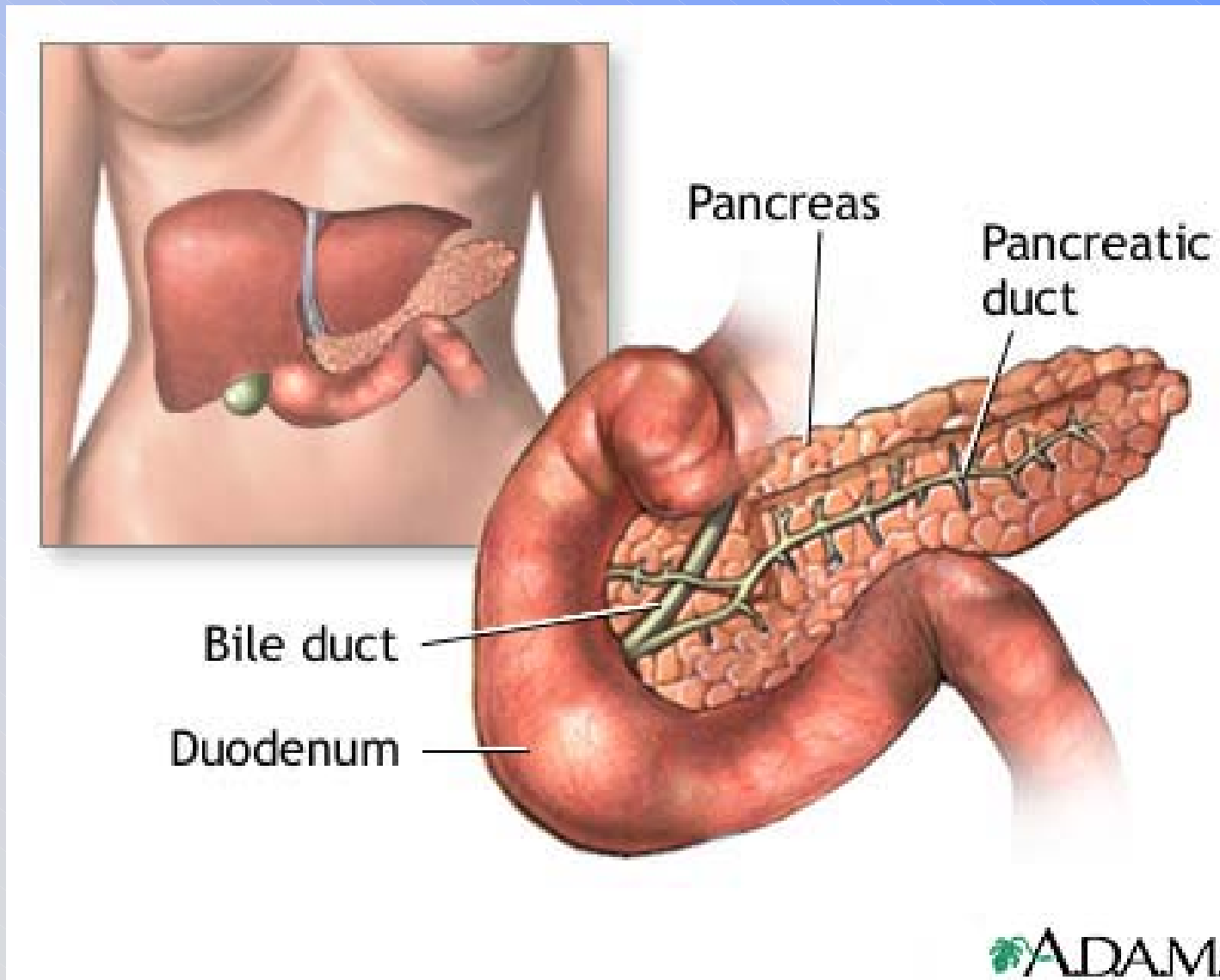
Gallstone blocking  
common bile duct

Duodenum

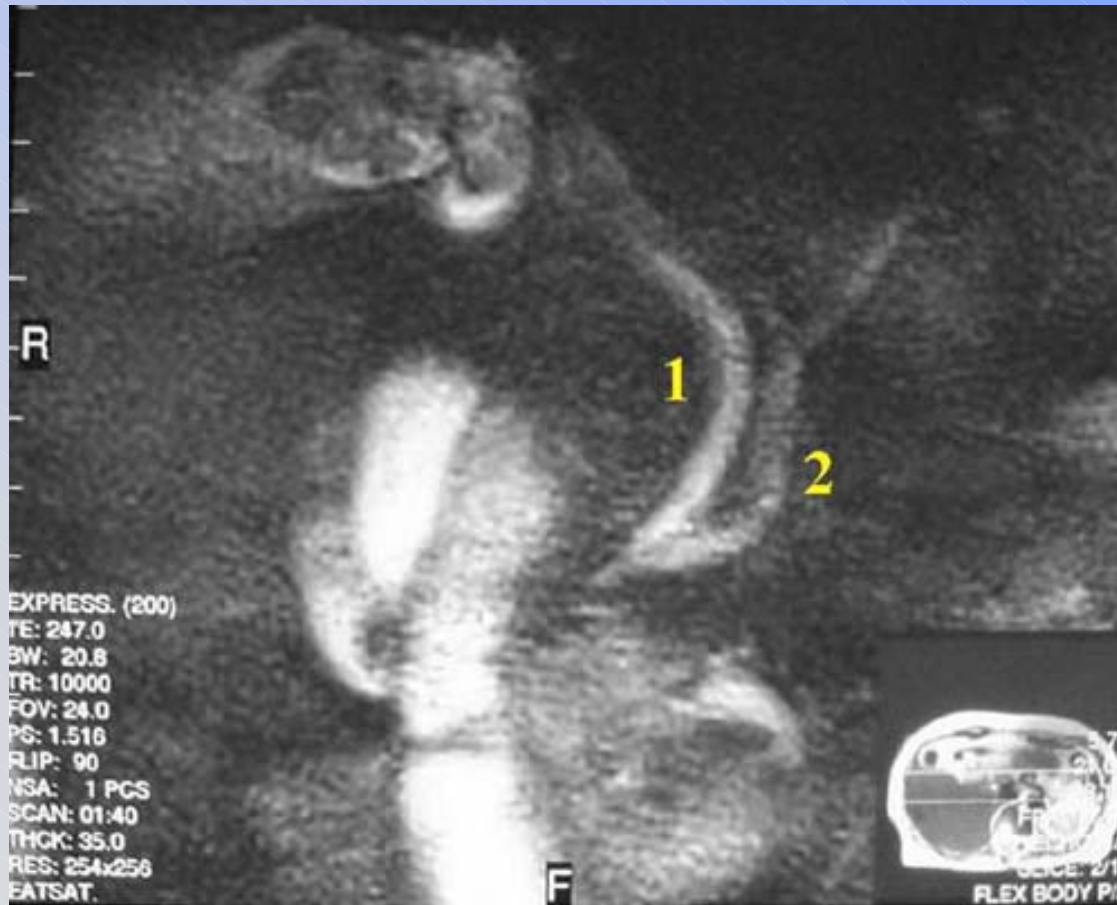
Gallstone blocking  
common bile duct  
and pancreatic duct



# Pancreas and Pancreatic Duct



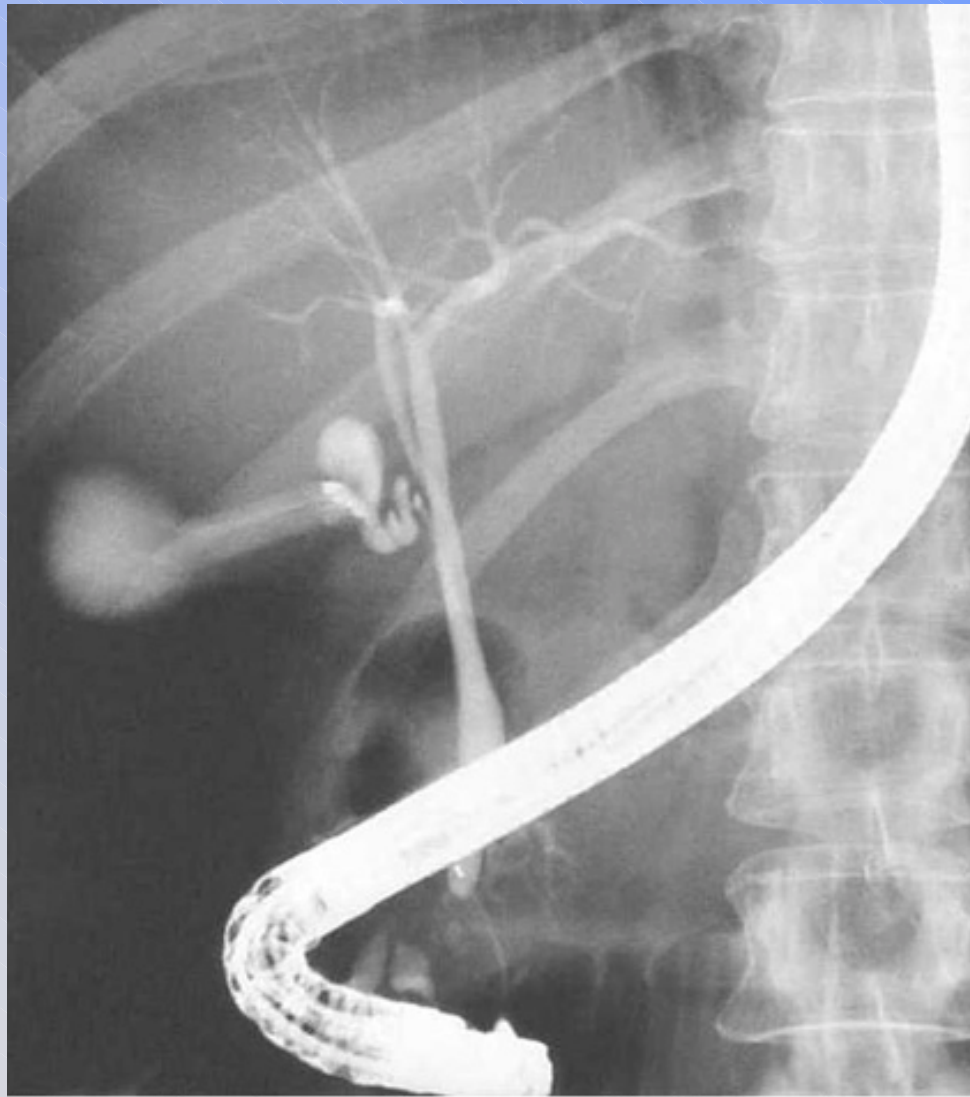
# MRCP - bile and pancreatic duct



- common bile duct and pancreatic duct join prior to duodenum

**Normal bile (1) and pancreatic (2) duct on MRCP.**

# ERCP of Biliary Tree



Normal endoscopic retrograde cholangiogram.

# The Liver has Many Functions

- Nutrition
  - stores glycogen (glucose chains)
  - releases glucose when if no insulin
  - absorbs fats, fat soluble vitamins
  - manufactures cholesterol
- Bile Salts
  - breakdown product of Hemoglobin
  - dissolves dietary fats (detergent)

# Liver Function

# The Liver has Many Functions

- Clotting Factors
  - manufactures most clotting factors
- Immune function
  - Kupffer cells engulf antigens (bacteria)
- Detoxification
  - drug excretion (sometimes activation)
  - alcohol breakdown
- Manufactures Proteins
  - albumin
  - binding proteins

# Liver Disease

- Hepatocellular disease
  - diseases of the liver cells
- Cholestatic
  - diseases of the biliary tree
- Two broad categories
  - some diseases include one or both types
  - clinical features within type may be similar irrespective of the specific disorder

# Liver Disease

# Hepatocellular Disease - symptoms

- patient may have no symptoms
- fatigue, malaise
- anorexia, nausea
- jaundice
- pruritus
- easy bruising and bleeding
- hematemesis
- abdominal pain, swelling
- day night reversal, confusion, coma

# Cholestatic Disease - symptoms

- patient may have no symptoms
- fatigue, malaise
- anorexia, nausea
- jaundice
- +++ pruritus
- +++ abdominal pain and pancreatitis
- +++ gray or clay-colored stools

# Signs of liver disease

- no abnormalities
- hepatic enlargement
- tender liver due to capsule distention
- nodular liver
- shrunken liver
- jaundice
- edema
- relative hypotension and tachycardia
- can be afebrile, hypo or hyperthermic

# Signs of liver disease

- spider angiomata
- palmar erythema
- nail clubbing
- Dupuytren's contracture
- gynecomastia
- testicular atrophy
- splenomegaly
- fetor hepaticus
- asterixis

# Spider Angiomata

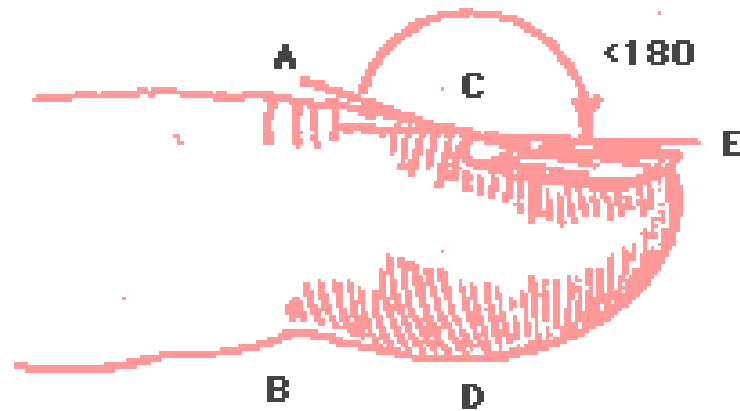


# Spider nevi

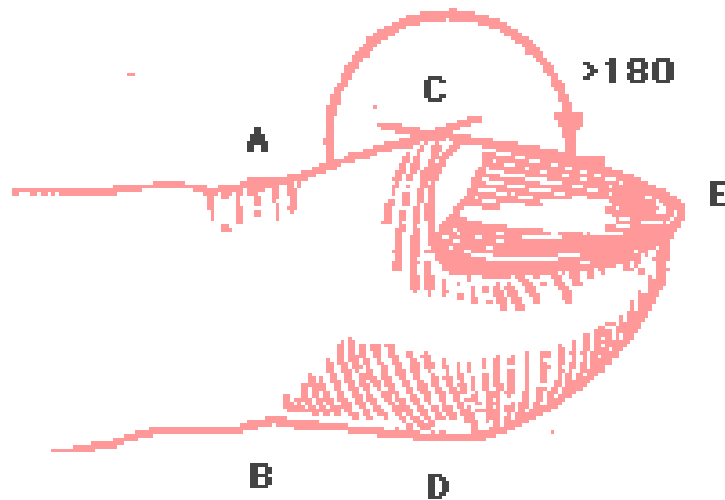


4547

# Nail Clubbing



Normal



Clubbing



# Dupuytren's contracture



# Jaundice



CUSTOM MEDICAL  
STOCK PHOTO

CMSP  
www.cmsp.com

To License Image Call: 773-287-8100 or 800-273-2677

# Juandice



# Ascites



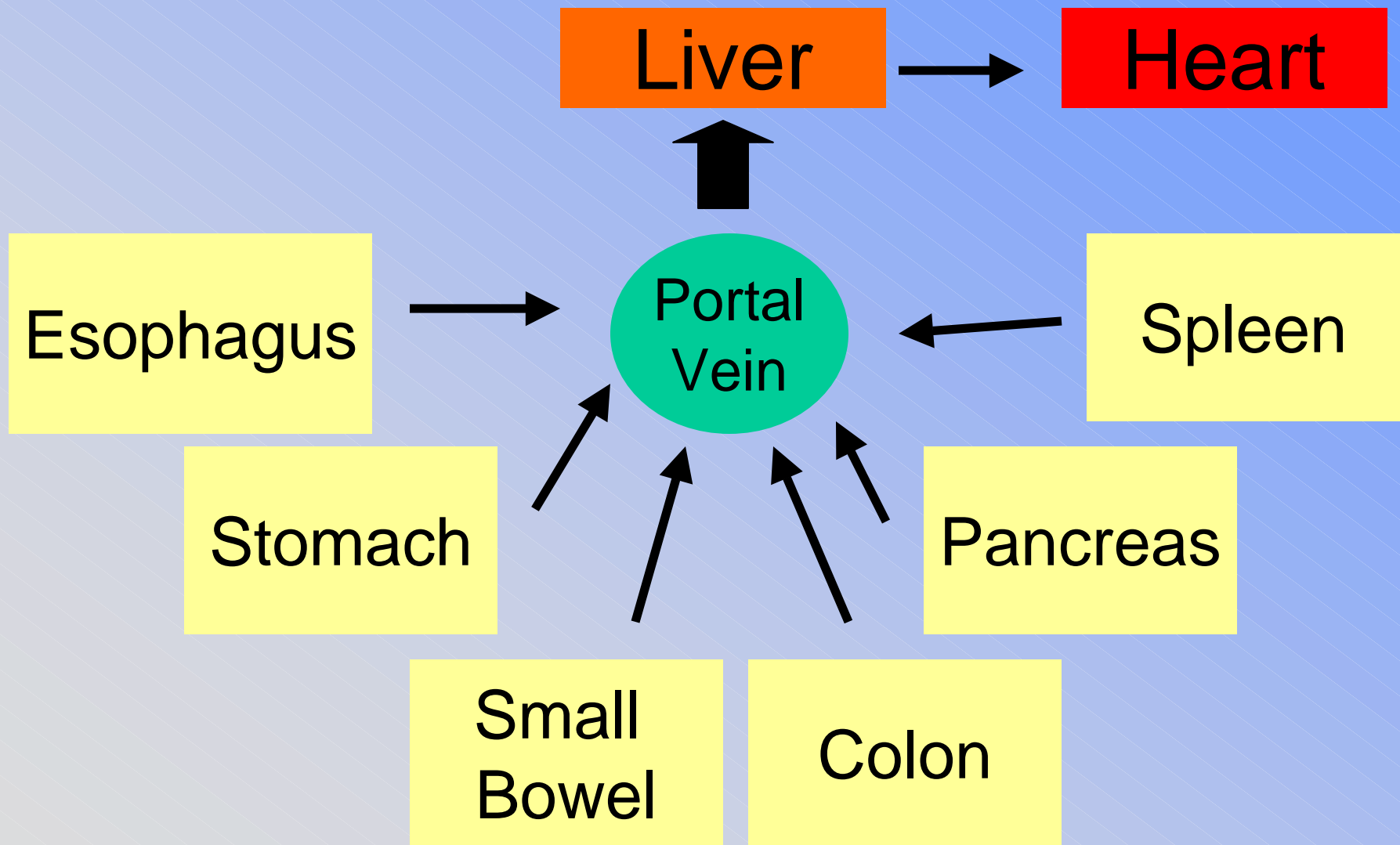
Medstudents

<http://www.medstudents.com.br>

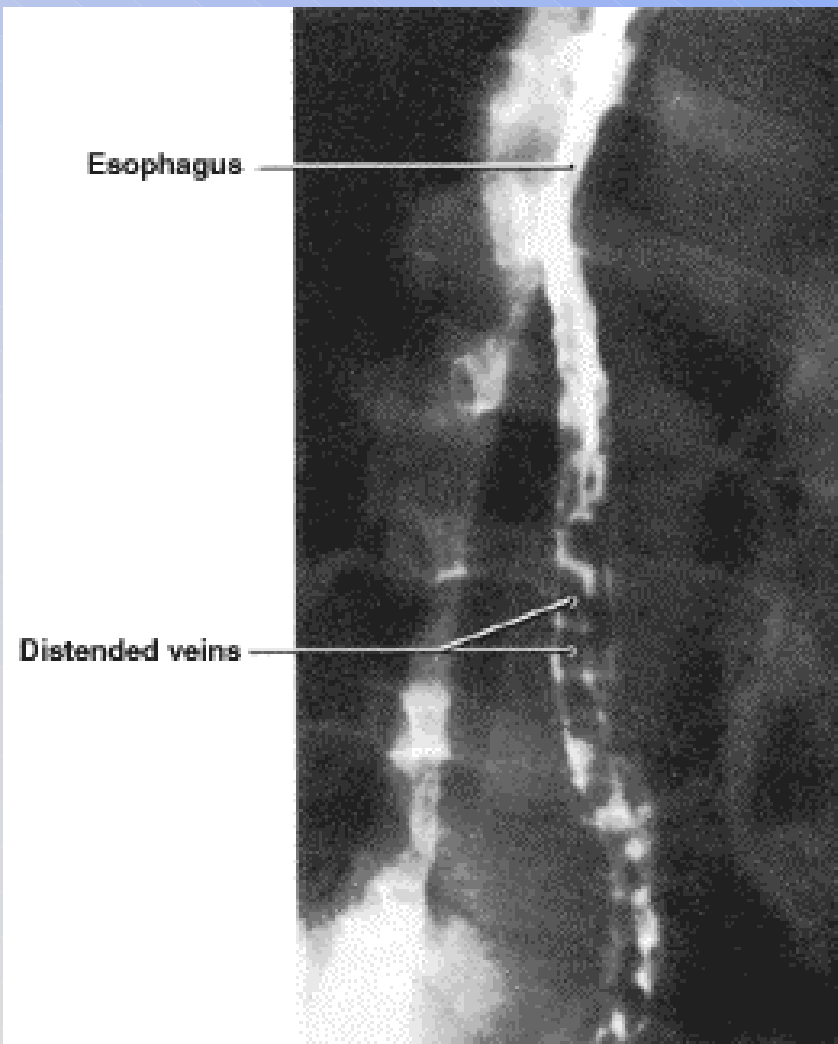
# Ascites



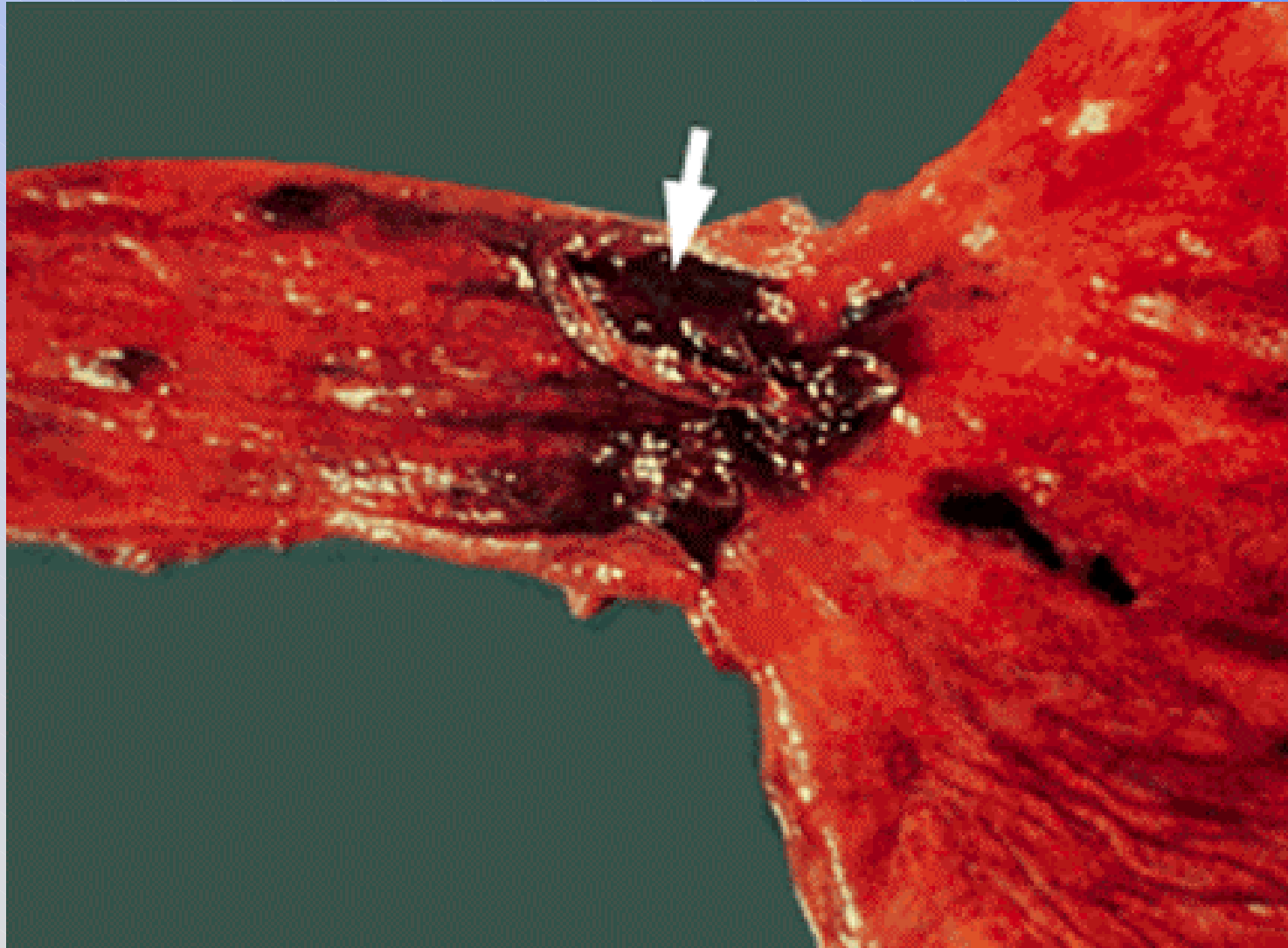
# Portal Hypertension



# Esophageal Varices



# Esophageal Varices



# Banding of Esophageal Varix



# Non-specific Laboratory Findings

- Anemia
- Low platelets
- Hyponatremia
- Hyperbilirubinemia
- Low albumin
- Elevated liver enzymes
- Elevated I NR
- Elevated ammonia
- Elevated creatinine (hepato-renal)

# Liver Enzymes

- Suggests hepatocellular disease
  - ALT Alanine amino transferase (SGPT)
  - AST Aspartyl amino transferase (SGOT)
- Suggests cholestatic disease
  - ALP Alkaline Phosphatase
- GGT gamma glutamyl transferase
  - non-specific test
- Enzymes have alternate sources
  - ALP (placenta, bone)

# Liver Function

- Liver function tests
  - INR
  - albumin
  - bilirubin
  - (distinguished from liver enzyme)

# Common Hepatocellular Diseases

- Infections
  - viral hepatitis
- Toxins
  - acetaminophen, methotrexate, halothane
  - alcohol
  - poisons (tetra hydrochloride)
  - herbals
- Non-alcohol Fatty Liver
  - diabetes, obesity
  - idiopathic

# Differential Diagnosis

# Common Hepatocellular Diseases

- Autoimmune
  - autoimmune hepatitis
  - secondary hepatitis
  - granulomatous hepatitis
- Metabolic
  - hemochromatosis
  - Wilson's disease
  - amyloidosis
- Shock Liver
- Fatty Liver of Pregnancy

### Herbal Supplements Associated with Hepatic Injury<sup>†</sup>

Product	Other names/toxins	Clinical manifestations	Pathologic findings
<b>Chaparral leaf</b>	Laurie tridentata "creosote bush" "grease wood" Nordihydroguaiaretic acid (HDGA)	ALT 10-20x normal; AST 7-10x normal; elevated bilirubin and prothrombin time; reversible; dose dependent	Acute and chronic liver injury: portal inflammation with bile duct proliferation; lobular necrosis and collapse
<b>Jin Bu Huan</b>	Lycopodium serratum Levo-tetrahydropalmatine	ALT/AST 10-20x normal; elevated bilirubin and prothrombin time; reversible	Acute and chronic liver injury: focal hepatic necrosis; eosinophilia; steatosis; bridging fibrosis and necrosis
<b>Germander</b>	Teucrium chamaedrys Teucrium polium	ALT/AST 5-10x normal; elevated bilirubin; reversible	Acute and chronic liver injury: hepatocellular necrosis; portal inflammation; fibrosis
<b>Mistletoe</b>	Viscum album	ALT/AST 5-10x normal; elevated bilirubin; reversible	Acute and chronic hepatitis: hepatocellular injury
<b>Skullcap</b>	Scutellaria sp.	ALT/AST 5-10x normal; elevated bilirubin; reversible	Acute hepatitis; hepatocellular injury
<b>Toxic alkaloids</b>	Symphytum (Comfrey) Senecio sp. Crotalaria sp. Heliotropium sp. Maté (Paraguay) tea Ackee Fruit Atractylis gummifera Callilepis laureola Cassia angustifolia (Senna) Cocaine (Erythroxyton coca) Valeriana officinalis Sassafras albidum Borago officinalis	ALT/AST 3-10x normal; elevated bilirubin; generally reversible; can be fatal; dose dependent	Hepatic venoocclusive disease; acute inflammation
<b>Pennyroyal</b>	Squawmint oil Hedeoma pulegoides Mentha pulegium Toxic terpenes, especially isopropylidene	ALT/AST 10-20x normal; associated with renal failure	Acute liver injury related to depletion of hepatic glutathione

<sup>†</sup>Adapted from Bashir, Lewis, Gastroenterol Clin North Am 1995; 24:957.

# Herbals and Liver Disease

# Common Cholestatic Diseases

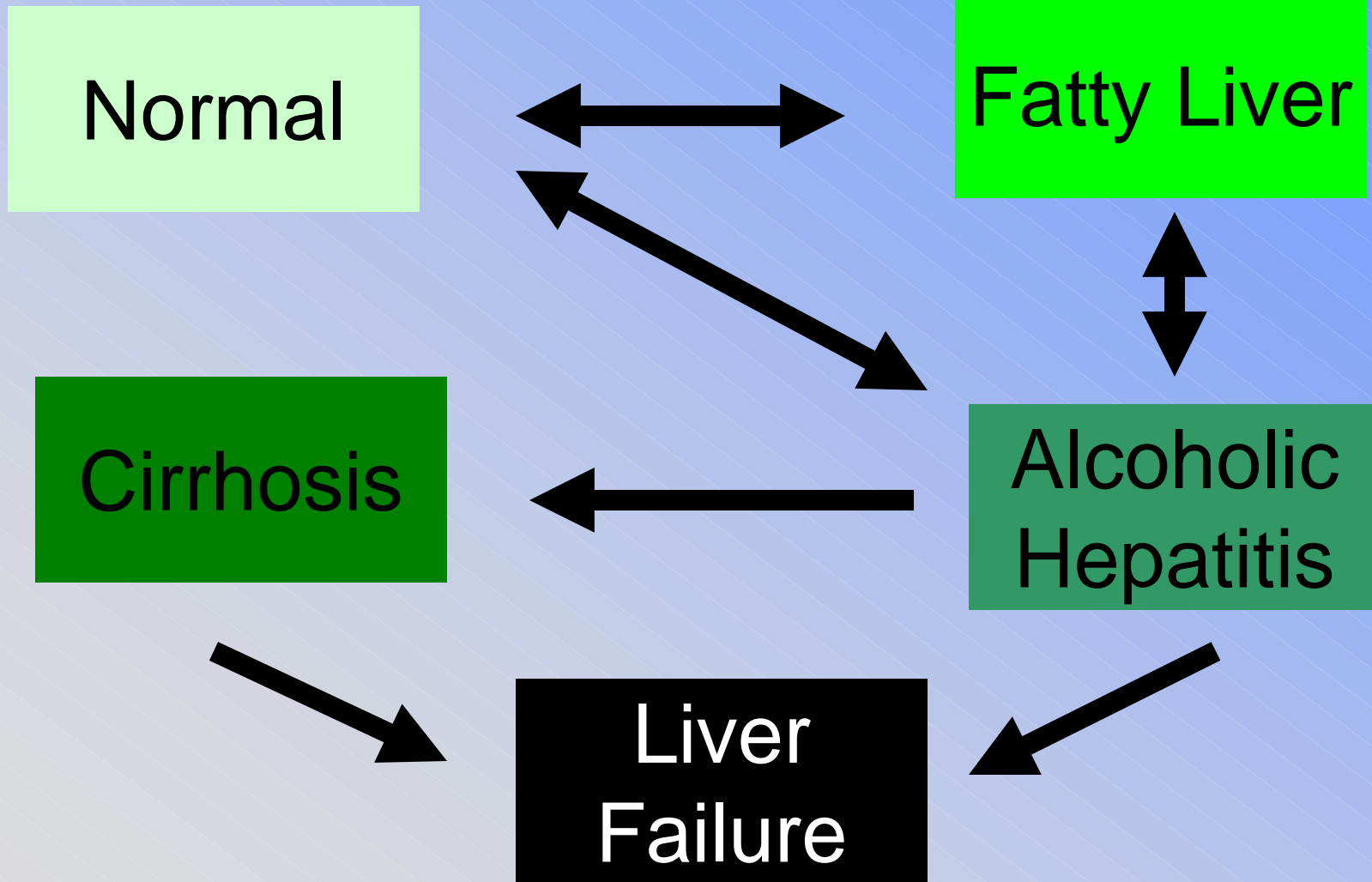
- Extrahepatic Biliary Tree Obstruction
  - choledocholithiasis
  - cholangiocarcinoma
  - pancreatic cancer
- Intra-hepatic Biliary Tree Obstruction
  - hepatocellular carcinoma
  - metastatic carcinoma
  - sclerosing cholangitis
  - primary biliary cirrhosis

# Cholestatic Diseases

- Intra-hepatic cholestasis
  - abscess: bacteria, fungi, protozoa, helminth
  - statins and just about any drug

# Progression of Liver Disease

# Liver Disease Pathogenesis



# How much alcohol?

- Threshold consumption
  - 80 gm/day for 10-20 years
    - 1 liter wine
    - 8 std sized beers
    - 1/2 pint hard liquor
- Among heavy drinkers
  - 230 gm / day x > 20 years
    - 80 % mod to severe fatty liver
    - 50 % cirrhosis or "precirrhotic" lesions

# CAGE Questionnaire

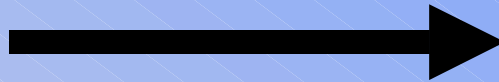
- Have you felt the need to **Cut** down drinking?
- Have you ever felt **Annoyed** by criticism of drinking?
- Have you had **Guilty** feelings about drinking?
- Do you ever take a morning **Eye** opener (a drink first thing in the morning to steady your nerves or get rid of a hangover?)

# CAGE

- Among alcoholics 50% will answer yes to at least two questions.
- Among non-alcoholics > 80% will answer no to all four questions.

# Liver Disease Pathogenesis

Normal

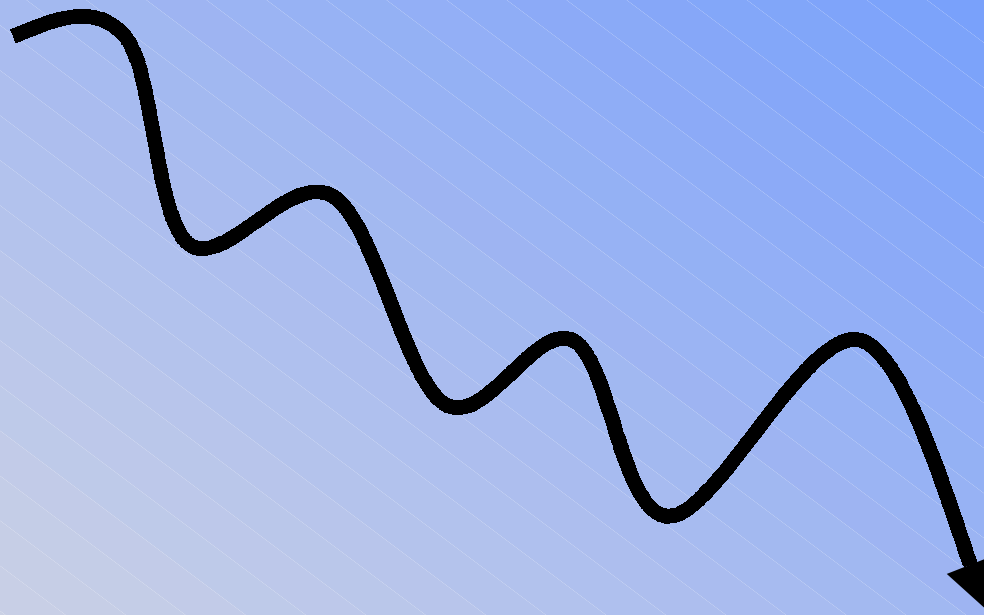


Liver  
Failure

Fast (days)  
versus  
Slow (years)

# Clinical Status in Liver Disease

Normal



Cirrhosis

# How Patients Present and Work-up

# Common Presentations

- Elevated Liver Enzymes
  - with / without symptoms
- Toxic exposure
  - acetaminophen
- Moderate Liver Disease
  - jaundice, ascites, edema
- Advanced Liver Disease
  - bleeding, confused, septic, renal failure
- Anatomical Liver Disease
  - abnormal u/s or CT (cholangitis, masses)

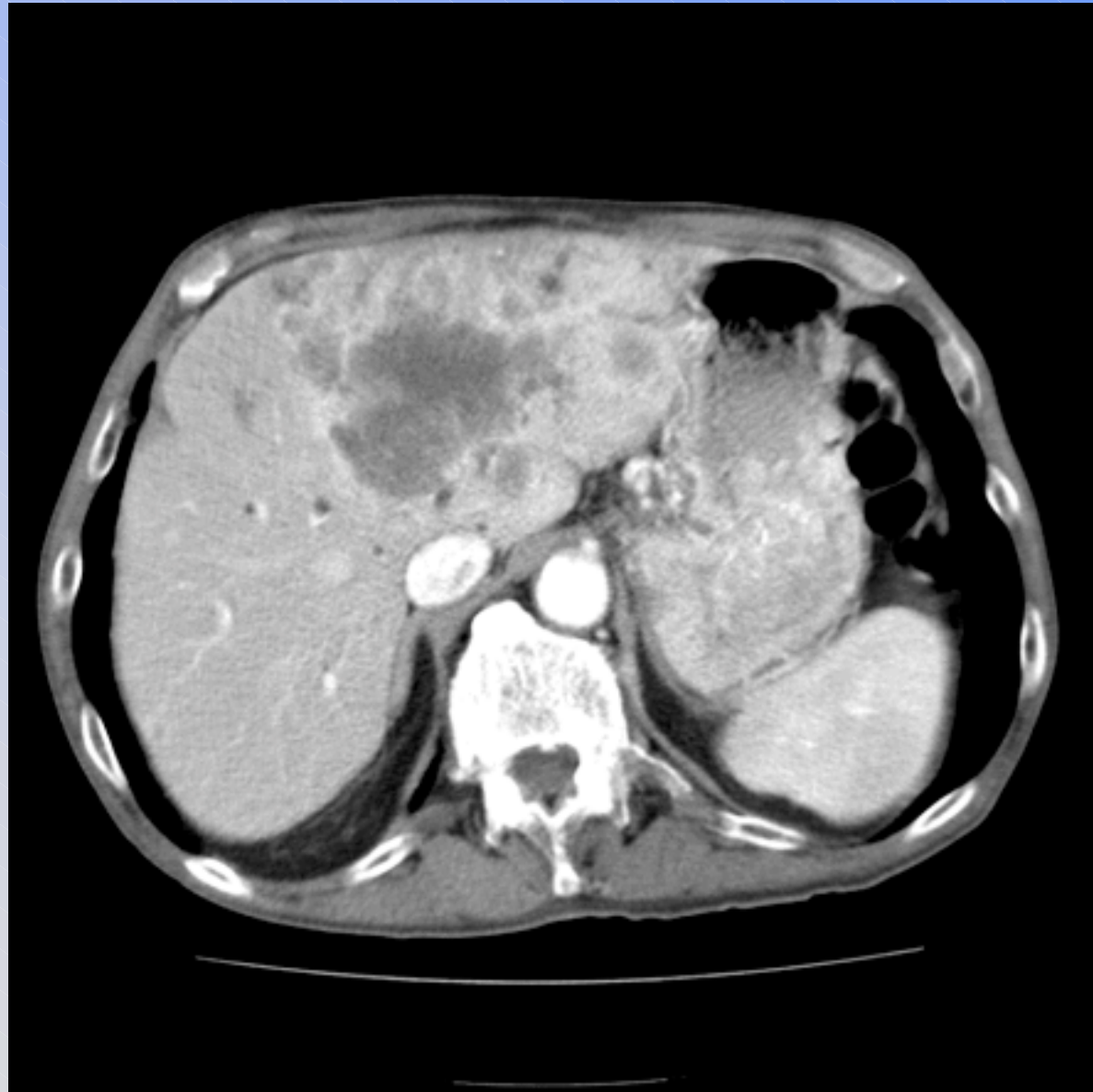
# Diagnostic Work-up

- History
  - exposures (alcohol, drugs, infection)
- Physical Examination
  - severity and chronicity
- Blood Work-up
  - enzymes and function
  - viral serology
  - auto-immune work-up
  - iron, sometimes copper
  - alpha-feto protein

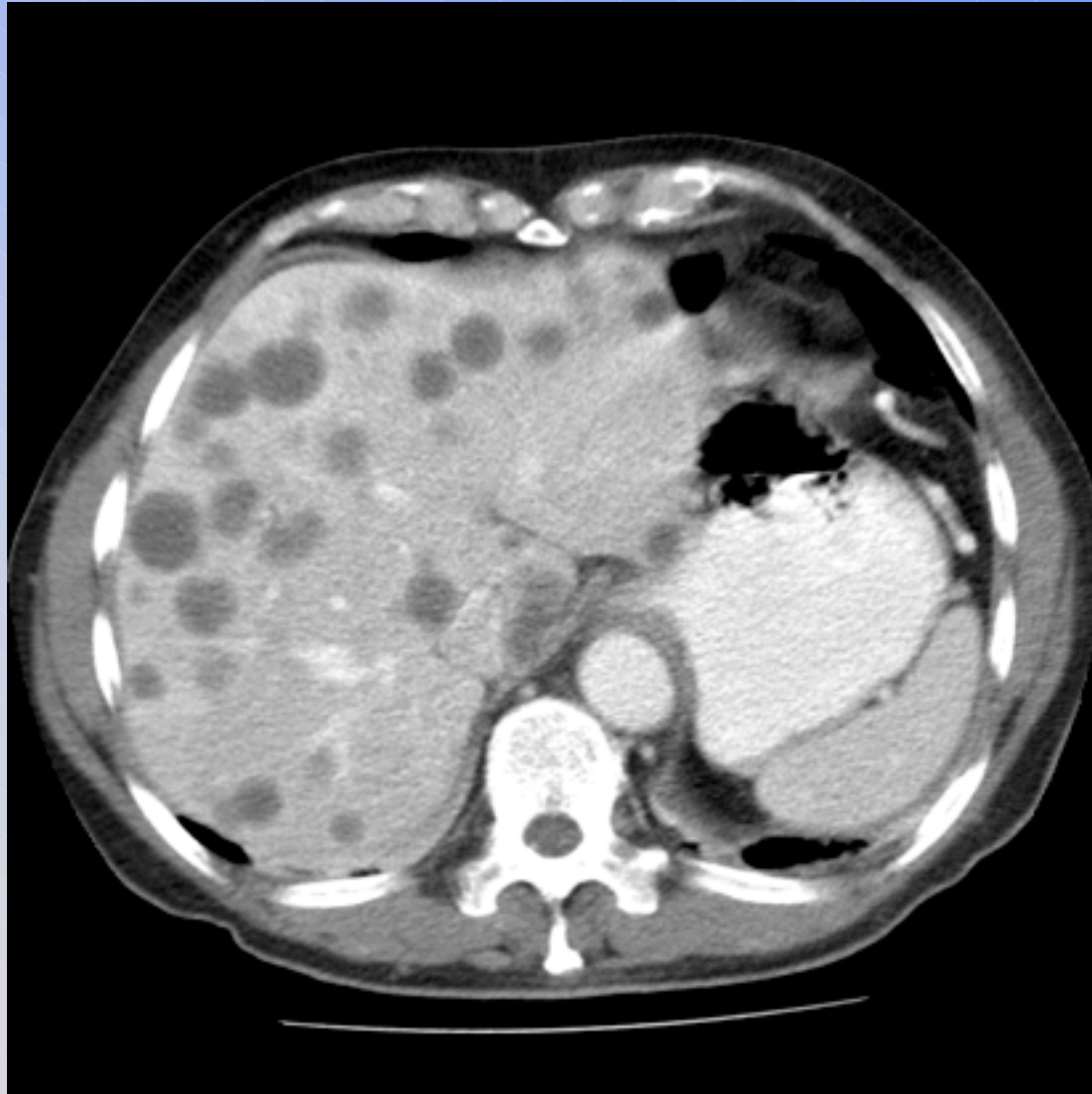
# Diagnostic Work-up

- Diagnostic Imaging
  - CT scan
  - Ultrasound
  - HI DA Scan
  - MRI / MRCP
- Biopsy and Paracentesis

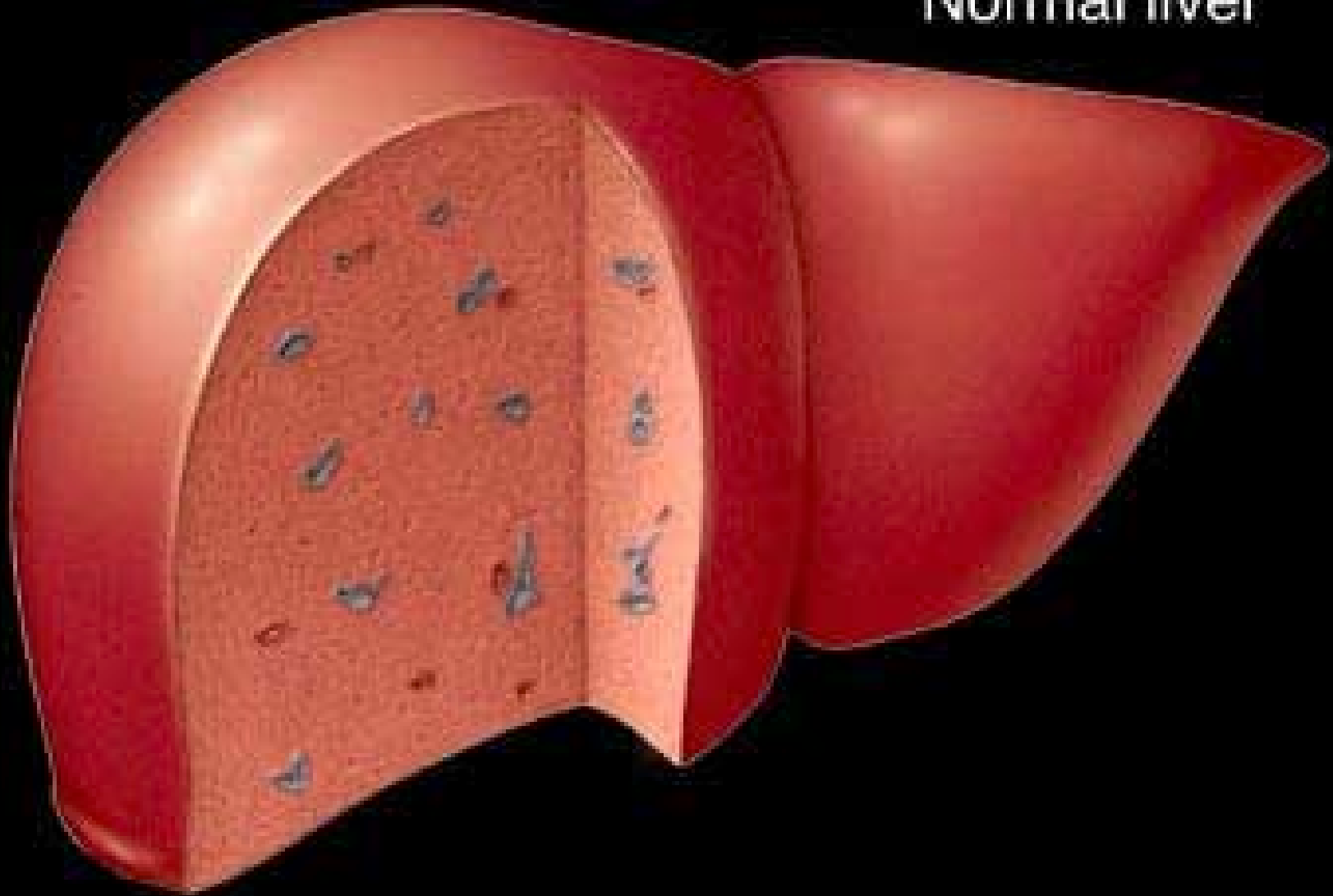
# Carcinoma in the Liver



# Metastatic Carcinoma



Normal liver



© 1998 Mayo Foundation for Medical Education and Research. All rights reserved.

# Cirrhotic liver





**Management**

# General Management

- Diet
  - no data to support low protein

# General Management

- Avoid toxins
  - acetaminophen (< 2 grams / day) \*AFP 2001 Nov
  - NSAIDs avoid
  - alcohol - abstain
  - statins - caution
  - opiates - caution
  - methotrexate
  - general anaesthesia may be risky

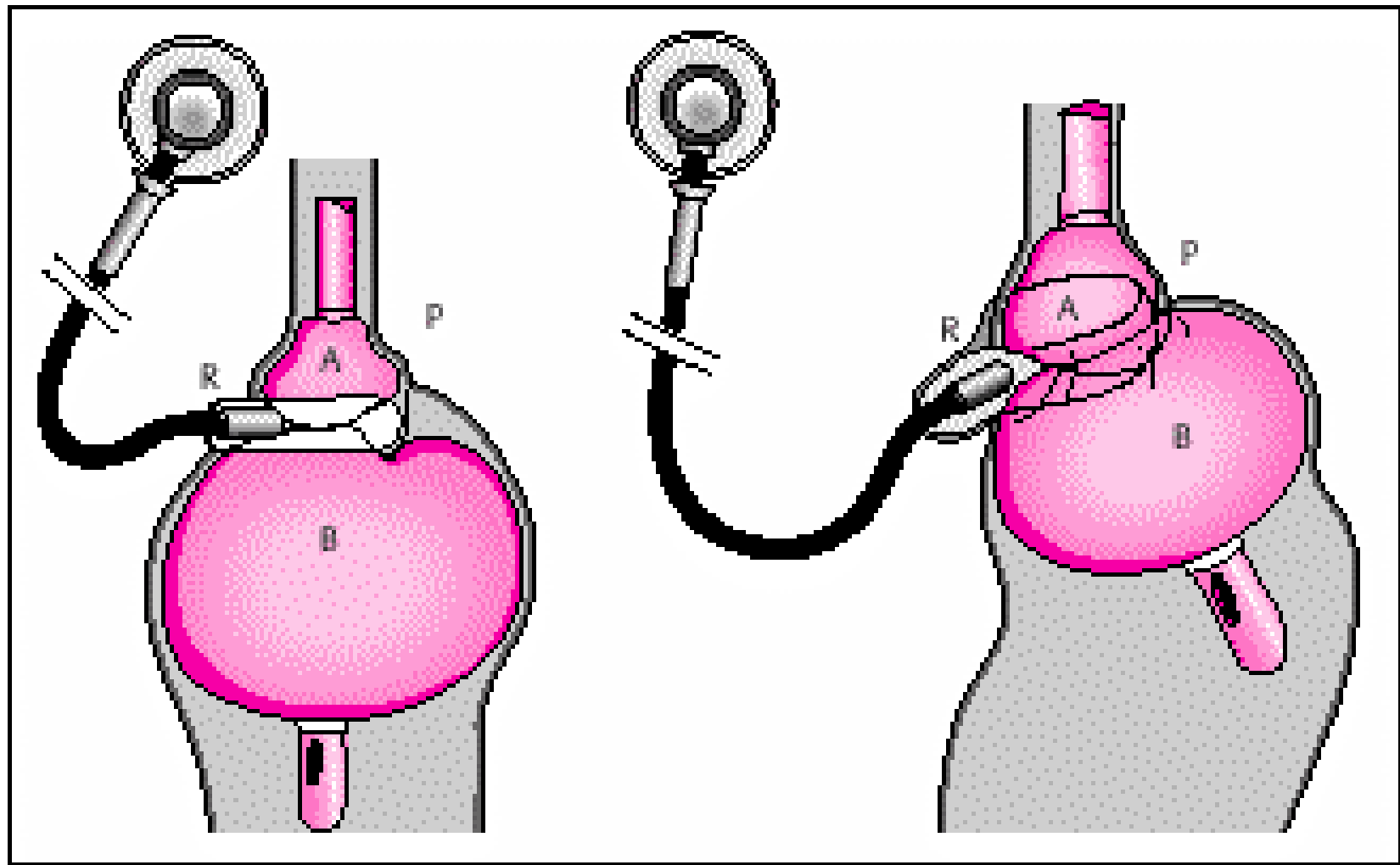
# General Management

- Ascites and Edema
  - salt restriction
  - diuretics
    - furosemide
    - spironolactone
  - water restriction if sodium < 125 mmol
  - paracentesis
    - diagnostic (SBP, tumor)
    - therapeutic
  - DAILY WEIGHTS!

# General Management

- Esophageal bleeding
  - prevention
    - beta-blockers & nitrates
  - correct coagulation defect
    - vitamin K
    - FFP
  - Octreotide - reduce portal pressure
  - Transfusion of Red Cells
  - Banding
  - Sengstain - Blakemore tubes

# Sengstakin - Blakemore



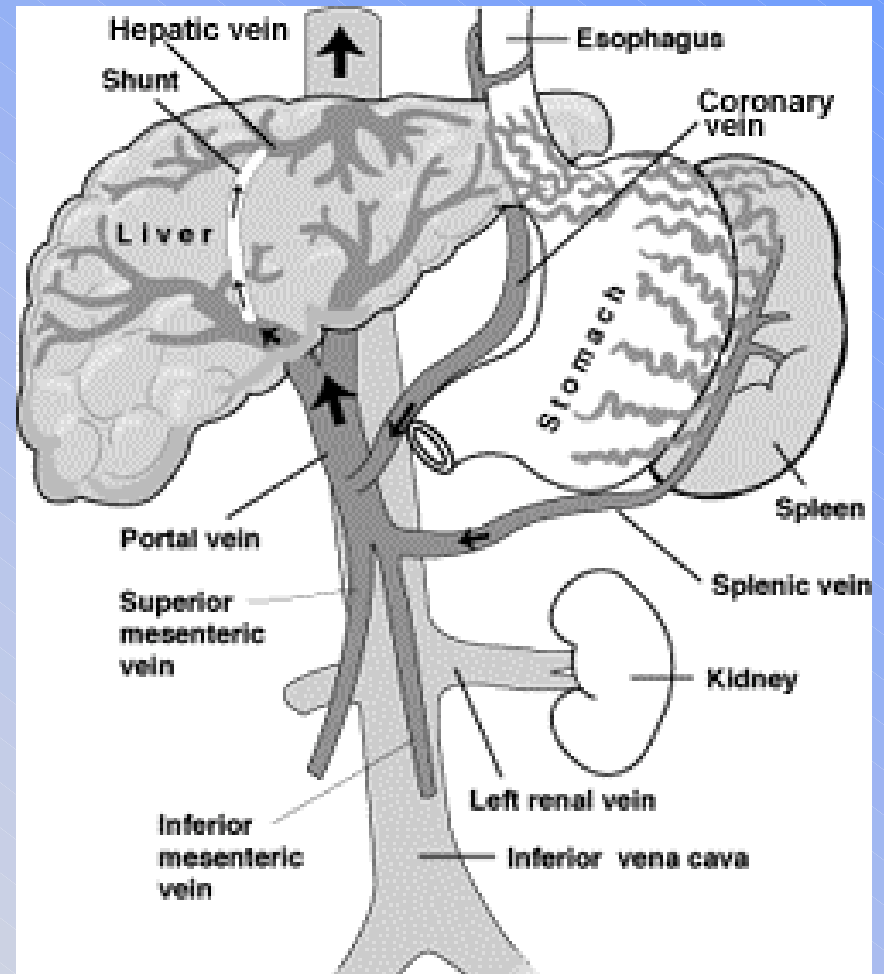
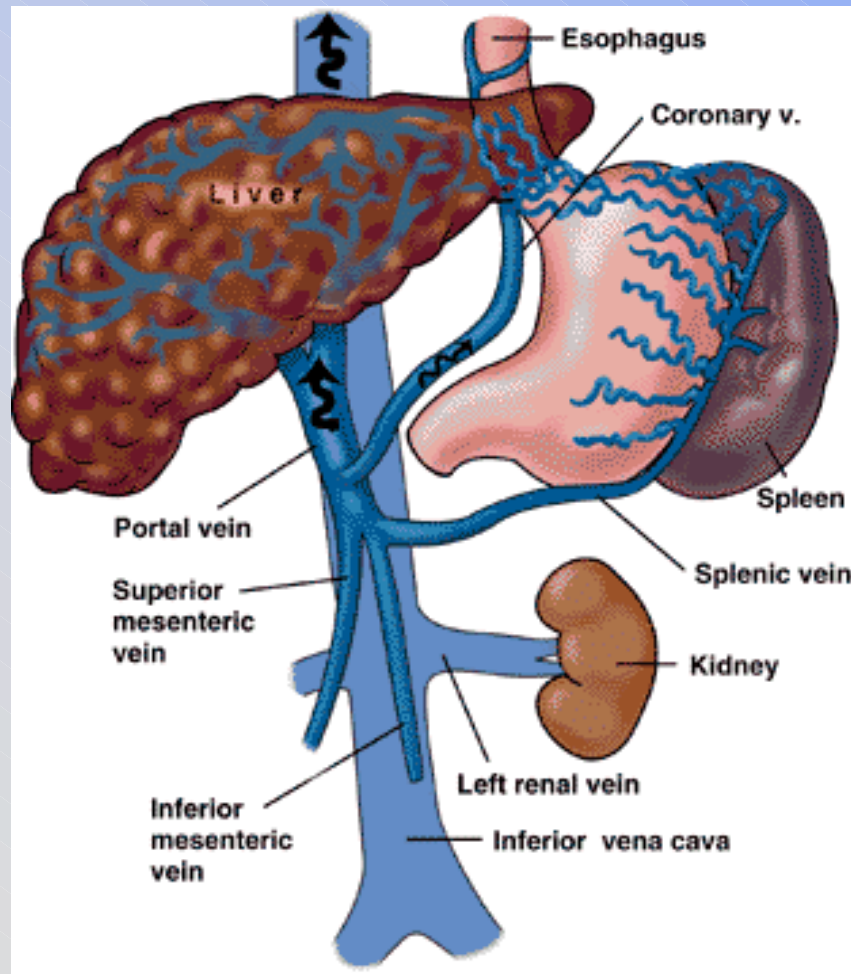
# General Management

- Encephalopathy
  - minimize effects of liver disease
  - treat precipitants
    - sepsis
    - GI bleed
    - medications (over-diuresis)
  - avoid sedatives, hypnotics, opiates
  - lactulose
  - metronidazole
  - (diagnostic trial of flumazenil)

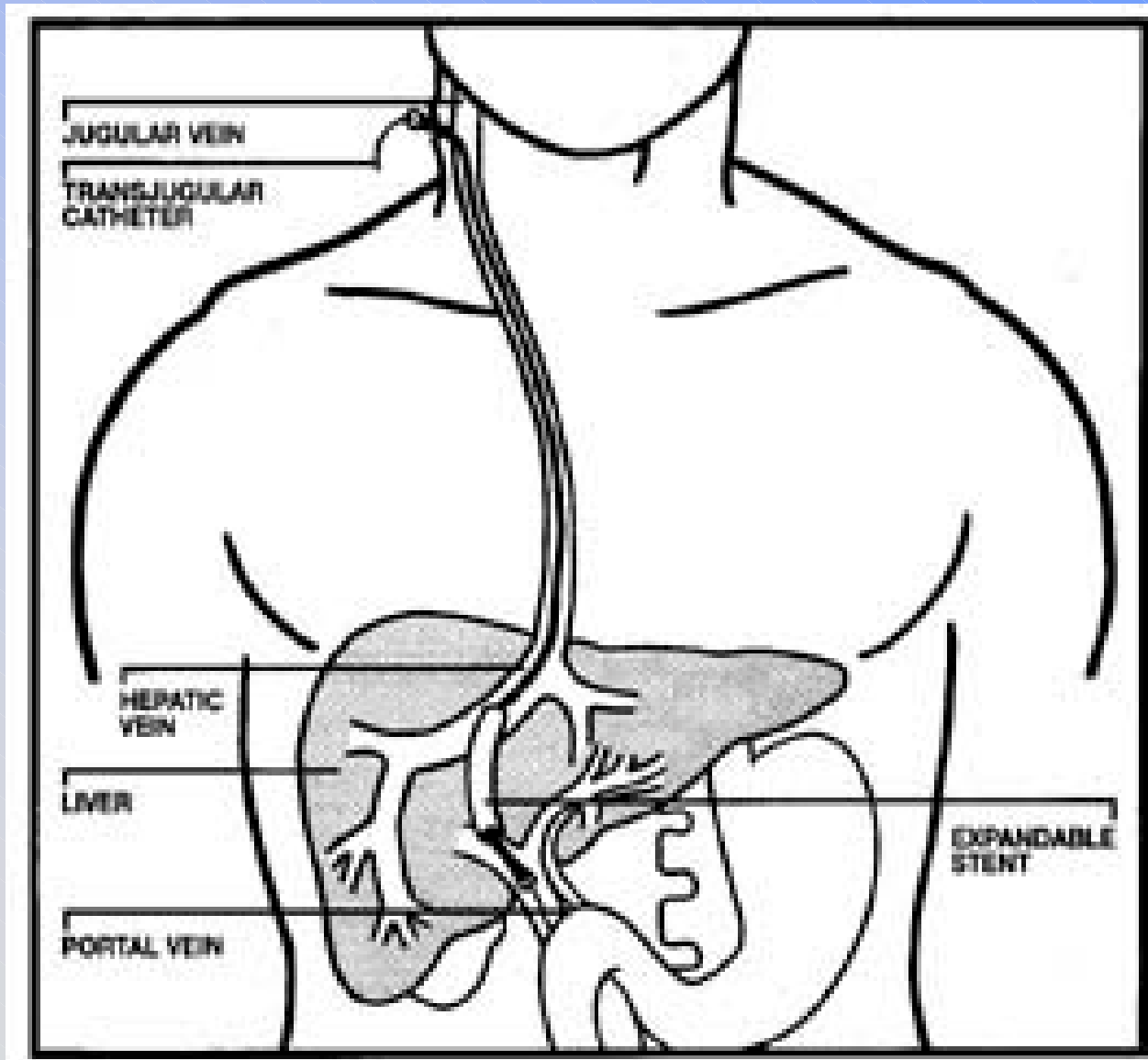
# General Management

- Renal Failure
  - trial of volume
  - avoid nephrotoxins
    - NSAIDs
    - IV contrast
  - avoid over-diuresis
  - avoid hypotension
- Hepato-renal Failure carries grave prognosis

# Transjugular Intrahepatic Portosystemic Shunt (TIPS)



# TIPS



# Specific Management

- Acetaminophen
  - N-acetyl-cysteine (NAC, Mucumyst)
- Hepatitis C
  - interferon
- Hemochromatosis
  - phlebotomies

# Specific Management

- Wilson's disease
  - penicillamine
  - trientine
  - zinc
- Autoimmune Hepatitis
  - corticosteroids (prednisone)
- Alcohol hepatitis
  - corticosteroids

# Specific Management

- Primary biliary cirrhosis
  - ursodeoxycholic acid (Ursofalk)
  - methotrexate
  - colchicine
  
- Choledocholithiasis
  - stone extraction with ERCP
  - cholecystectomy

# Transplantation

- Living Donor Liver Transplantation
  - pediatric recipient only
- Cadaveric Donor Transplants
  - Chronic hepatitis C or B — 28 %
  - Alcoholic liver disease — 16 %

## Uncommon Indications for Liver Transplantation†

Type of Disease	Causes	
<b>Hepatic tumors</b>	Carcinoid tumors Epithelioid hemangioendothelioma Fibrolamellar hepatoma Hepatic adenoma	Hepatoblastoma Hepatocellular carcinoma Pancreatic islet cell tumors
<b>Metabolic and genetic disorders</b>	Alpha-1-antitrypsin deficiency Cystic fibrosis Glycogen storage diseases I and IV Crigler-Najjar syndrome Familial hypercholesterolemia	Hemochromatosis Galactosemia Hemophilia A and B Byler's syndrome Homozygous hyperlipidemia
<b>Vascular disorders</b>	Budd-Chiari syndrome	Veno-occlusive disease
<b>Miscellaneous</b>	Adult polycystic liver disease Alagille syndrome Nodular regenerative hyperplasia Caroli's disease Severe graft-versus-host disease	Lymphangiomatosis Amyloidosis Sarcoidosis Hepatic trauma

†Adapted from Lopez, RR, Howard, TK, Villamil, FG, et al. Liver transplantation. In: Liver and Biliary diseases, Kaplowitz, N (Ed), 1996, p. 629, and Rosen, HR, Shackleton, CR, Martin, P, Med Clin North Am 1996; 80:1069.

# Contra-indications to Transplant

- Active alcohol or drug abuse
- HIV positivity
- Extrahepatic malignancy
- Infection outside the biliary tract
- Advanced cardiopulmonary disease
- Relative
  - Inadequate social or family support
  - Advanced age (over 65)

**TABLE 1**  
**Modified Child-Pugh Score**

<b>Parameters</b>	<b>Points assigned to laboratory values and signs*</b>		
	<b>1</b>	<b>2</b>	<b>3</b>
<b>Laboratory value</b>			
Total serum bilirubin level	<2 mg per dL (34 μmol per L)	2 to 3 mg per dL (34 to 51 μmol per L)	>3 mg per dL
Serum albumin level	>3.5 g per dL(35 g per L)	2.8 to 3.5 g per dL (28 to 35 g per L)	<2.8 g per dL
International Normalized Ratio	<1.70	1.71 to 2.20	>2.20
<b>Signs</b>			
Ascites	None	Controlled medically	Poorly controlled
Encephalopathy	None	Controlled medically	Poorly controlled

\* -- Based on total points, a patient with cirrhosis is assigned to one of three classes: Child class A = 5 to 6 points; Child class B = 7 to 9 points; Child class C = 10 to 15 points.

# Prognosis

- 1 Year Survival
  - Child Pugh A 80 - 100%
  - Child Pugh B 60 - 80%
  - Child Pugh C 35 - 45%

# Summary

- Anatomy and function predicts for clinical findings
- Many Liver diseases appear similar
- General and Specific Treatments

# Questions?

- note: patient photos are from internet
- [www.ucalgary.ca/~jpschaef](http://www.ucalgary.ca/~jpschaef)