

Anesthesia for Patients with Liver Disease

Michael O'Reilly, M.D., M.S.
Clinical Associate Professor
Department of Anesthesiology



Michael O'Reilly, M.D., M.S.
Director Liver Transplant Anesthesia
Department of Anesthesiology
University of Michigan





Why is This Important?

- Patients may have underlying liver disease
- Anesthesia care can have a direct impact
- Liver transplants “...one of the most demanding and intense anesthetic challenges...”

*Anesthesia care may directly
impact outcome*



"My heart is healthy, but my liver is shot to hell."

What Does the Liver Do?

■ Glucose homeostasis

- Storage and release of glucose
- Glycogen (75g; 24-48 hr supply)
 - » Important in acute starvation
- Gluconeogenesis (lactate, glycerol and amino acids)

*Beware hypoglycemia in patients
with liver disease*

What Does the Liver Do?

■ Protein synthesis

- Albumin less than $3.5 \text{ g}\cdot\text{dl}^{-1}$ indicates significant liver disease
- Albumin has a 23 day half-life
- Important when albumin is less than $2.5 \text{ g}\cdot\text{dl}^{-1}$

Beware dosing of drugs with significant protein binding; e.g. sodium thiopental

More About Protein Synthesis...

■ Coagulation

- **FACTORS:** Not affected until liver function dramatically decreased
 - » **BUT**, factor have short $t_{1/2}$
- **THROMBOCYTOPENIA:** from splenomegaly (from associated platelet sequestration)
- **FIBRINOLYSIS:** failure to clear activators

Dysfunctional clotting due to cellular and humoral components

More About Protein Synthesis...

- Hydrolysis of Ester Linkages
 - Decreased production of cholinesterases (pseudocholinesterase)
 - Ester linkages (Succinylcholine, mivacurium, ester local anesthetics)

Drug metabolism may be prolonged

Drug Metabolism

- Conversion of lipid soluble drugs to more water soluble less active substances
 - Microsomal enzymes
- Decreased function due to decreased hepatocytes and decreased blood flow associated with cirrhosis.
 - e.g. Morphine, alfentanil, pancuronium
- Enzyme induction causes cross-tolerance to other drugs

Multiple factors may affect drug action

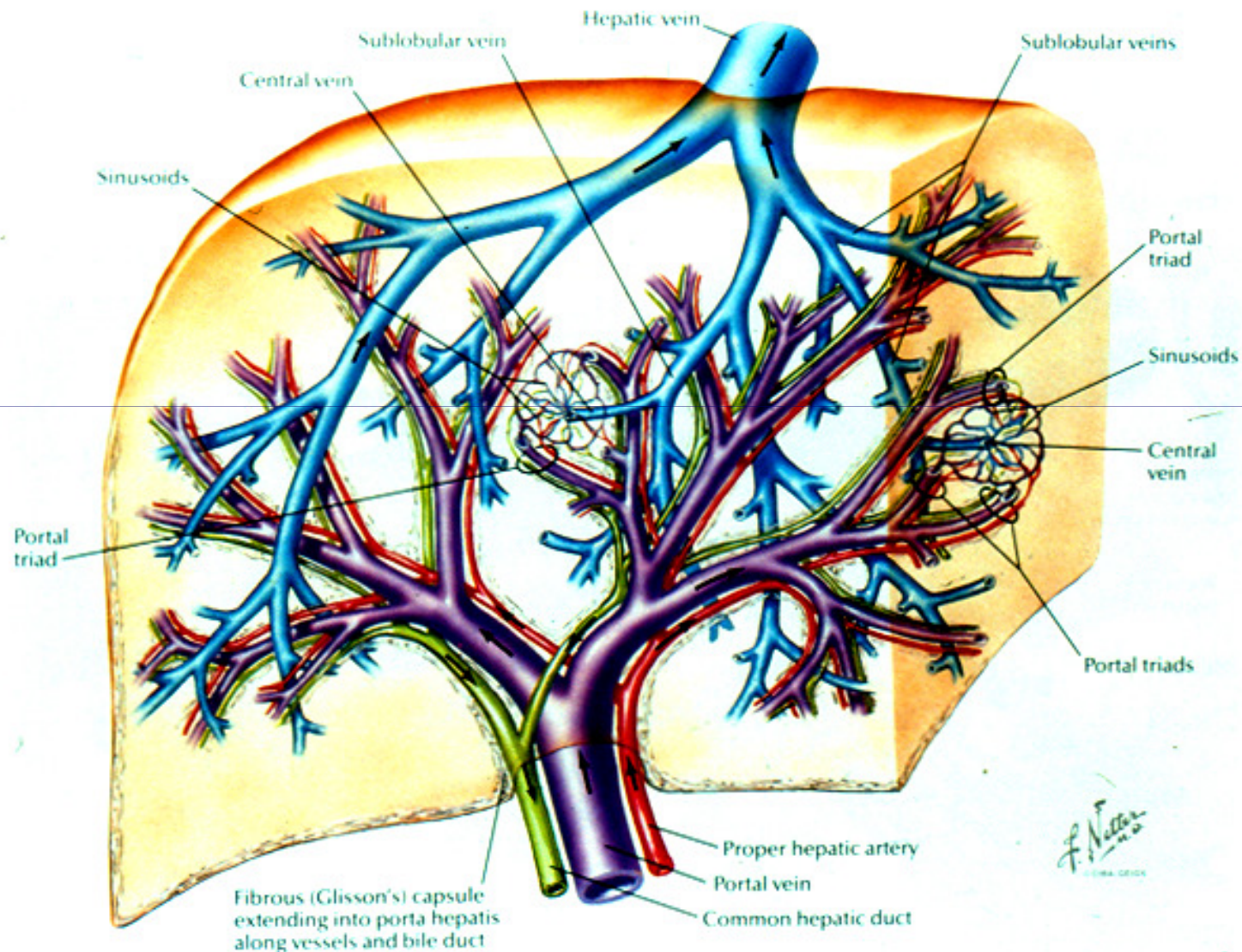
Bilirubin Formation and Excretion

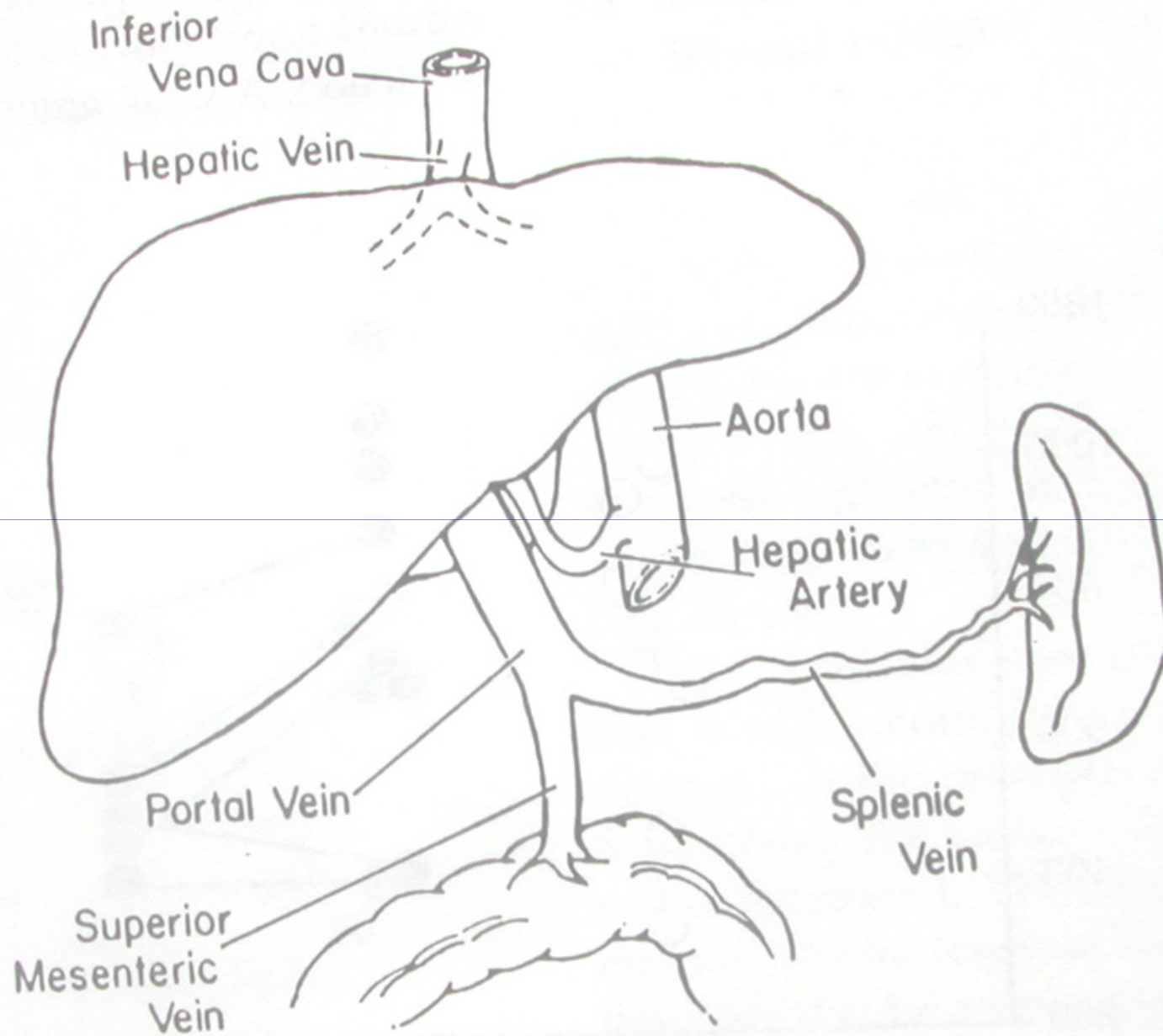
- **Produced by the breakdown of hemoglobin**
- **Transported to the liver bound to albumin (unconjugated) and not water soluble**
- **Conjugation (glucuronyl transferase) with glucuronic acid makes bilirubin water soluble.**
- **Most excreted in biliary canuli**

Hepatic Blood Flow

- Dual blood supply amounting to 25% of the cardiac output
 - 70% via portal vein (desaturated)
 - 30% hepatic artery

Intrahepatic Vascular and Duct Systems





What Determines Hepatic Blood Flow?

- Perfusion pressure(s)....
- ...versus (increased) splanchnic vascular resistance
 - Sympathetic control
 - » Hypoxemia
 - » Hypercarbia
 - » Catecholamines
 - » Beta blockers
 - Increases in CVP and therefore hepatic vein pressure
 - » Positive pressure ventilation
 - » Congestive heart failure
 - Cirrhosis itself
- Decreased delivery due to decreased cardiac output, no autoregulation

Impact of Anesthetic Drugs on Hepatic Blood Flow

- **Typically reduce blood flow 20-30%**
- **Mechanism not well understood**
- **Decreased perfusion, increased resistance**
 - or both**

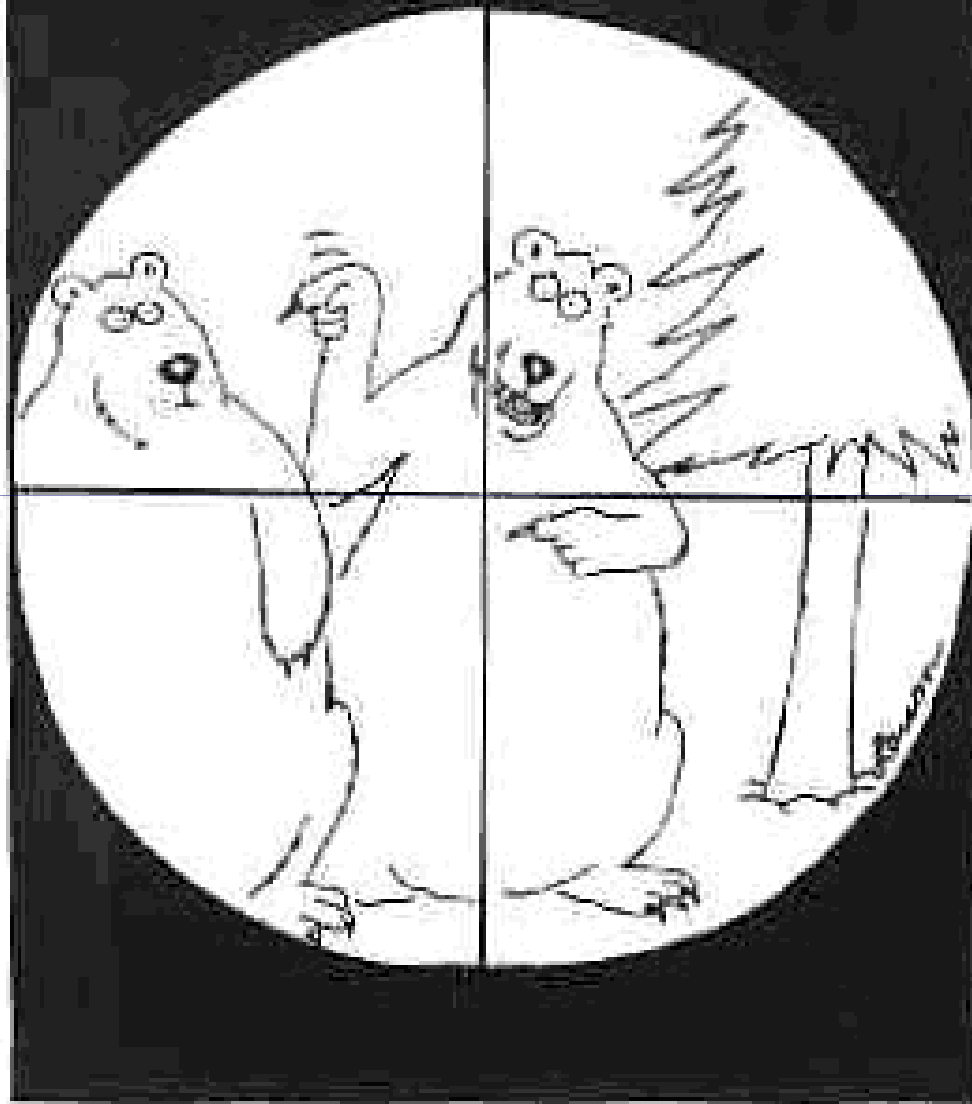
SURGEON



It's The Surgeon....

- Decreases in hepatic blood flow likely due to surgical manipulations

1981



Surgical Risk Based on Preoperative Evaluation of Liver Function

	Minimal	Modest	Marked
Bilirubin (mg/dl ¹)	<2	2-3	>3
Albumin (g/dl ¹)	>3.5	3-3.5	<3
Prothrombin time Prolongation(s)	1-4	4-6	>6
Encephalopathy	None	Moderate	Severe
Nutrition	Excellent	Good	Poor
Ascites	None	Moderate	Marked
(Data from Strunin. ¹⁰)			

The worse the liver function, the greater the surgical risk

Classification of Liver Disease

- **Parenchymal**

- Hepatitis
- Cirrhosis

- **Non-parenchymal (AKA cholestatic or extra-hepatic)**

- with obstruction
- without obstruction

Dysfunction

■ Prehepatic

- Blood transfusions
- Hemolysis
- Hematoma resorption
- *Increased unconjugated bilirubin; no change in enzymes*

■ Intrahepatic

- Drugs, sepsis, hypoxia, CHF, viruses
- *increased conjugated bilirubin AND increased aminotransferase enzymes*

■ Post Hepatic

- Obstruction
- *Increased conjugated bilirubin*
- *Increased alkaline phosphatase*

*N.B.: Enzymes are non-specific;
other organs produce the same enzymes when injured.*

Liver Function Tests: Bilirubin

- Bilirubin

Normal is 0.3 to 1.1. mg/dl

- Jaundice usually occurs once bilirubin exceeds 3 mg/dl

- Unconjugated bilirubin (the protein bound portion or the indirect bilirubin) cannot be excreted by the kidneys; conjugated or direct bilirubin can

- *Unconjugated bilirubin may increase with hemolysis.*
- *Increased conjugated bilirubin reflects a problem with secretion either due to hepatocellular disease or biliary tract obstruction.*
- *There is little correlation between the severity of liver disease and the level of bilirubin.*

N.B.: Enzymes are non-specific; other organs produce the same enzymes when injured.

Liver Function Tests: Transaminases

- Aspartate aminotransferase (AST - formerly called SGOT)
- Alanine aminotransferase (ALT - formerly called SGPT)
- Enzymes in hepatocytes released when damaged
- Not specific for liver damage

N.B.: Enzymes are non-specific; other organs produce the same enzymes when injured.

Liver Function Tests: Alkaline Phosphatase

■ Alkaline Phosphatase

- From cells in bile duct
- Even slight obstruction cause elevation
- Helps differentiate parenchymal disorders from those due to biliary obstruction
- Again, non-specific

N.B.: Enzymes are non-specific; other organs produce the same enzymes when injured.

Liver Function Tests: Albumin

- All albumin made in the liver
- Long half-life
- Marker for chronic problems

Liver Function Tests: Coags

- Short half-life
- Elevated in acute failure

Classification and Causes of Postoperative Liver Dysfunction

	Prehepatic	Intrahepatic	Posthepatic
Bilirubin	Increased (unconjugated fraction)	Increased (conjugated fraction)	Increased (conjugated fraction)
Aminotransferase enzymes	No change	Markedly increased	Normal to slightly increased
Alkaline phosphatase	No change	No change to slightly increased	Markedly increased
Prothrombin time	No change	Prolonged	No change to prolonged
Albumin	No change	Decreased	No change to decreased
Causes	Hemolysis Hematoma reabsorption Bilirubin overload from whole blood	Viruses Drugs Sepsis Arterial hypoxemia Congestive heart failure Cirrhosis	Stones Cancer Sepsis

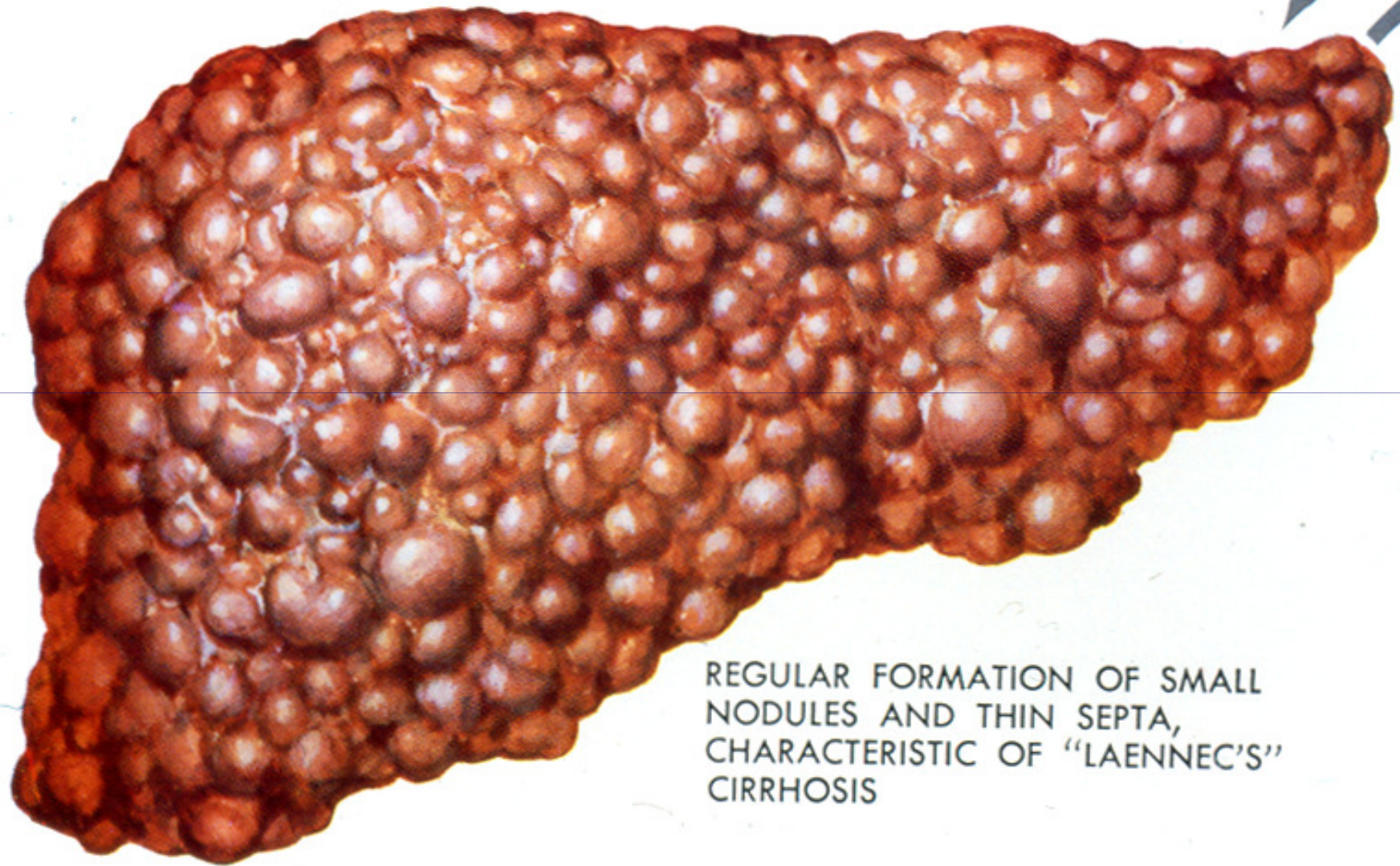
Drug Induced Hepatitis

- A variety of drugs can cause liver dysfunction
 - Histologically indistinguishable from viral hepatitis
- HALOTHANE HEPATITIS
 - Two types
 - » Mild increase in enzymes, thought due to decreased hepatic perfusion
 - » THE HALOTHANE HEPATITIS
 - Rare (1:22,000 TO 1:35,000) and severe
 - Immune mediated (?)
 - Acetylation of liver proteins → self becomes non-self

Cirrhosis

Causes

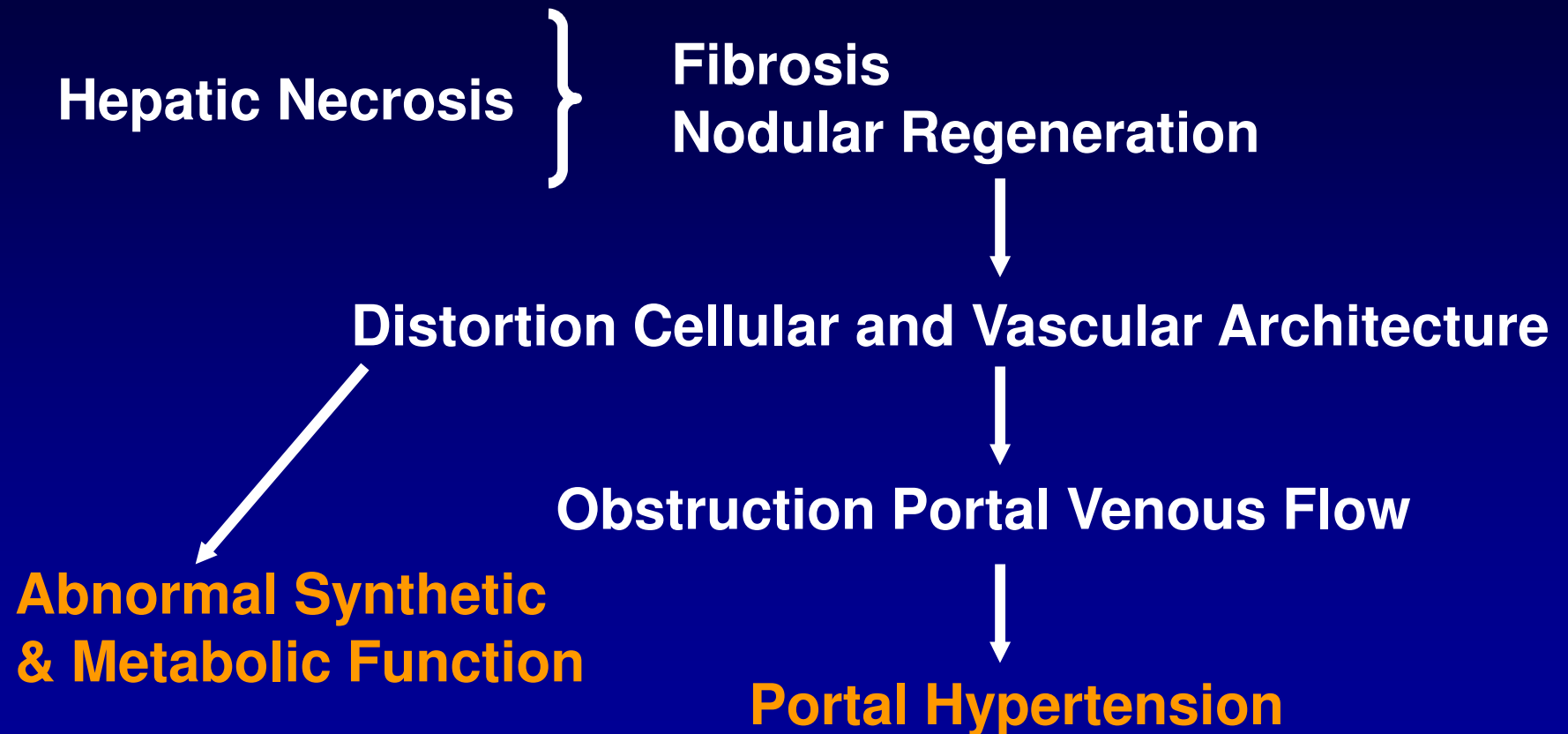
- **Alcohol - #1 Cause in U.S.**
 - (Laennec's Cirrhosis)
- **Chronic Active Hepatitis**
 - (Post Necrotic Cirrhosis)
- **Chronic Biliary Obstruction/Inflammation**
 - (Biliary Cirrhosis)
- **Chronic Right Sided CCF**
 - (Cardiac Cirrhosis)
- **Hemachromatosis**
- **Wilson's Disease**
- **α_1 - Antitrypsin Deficiency**

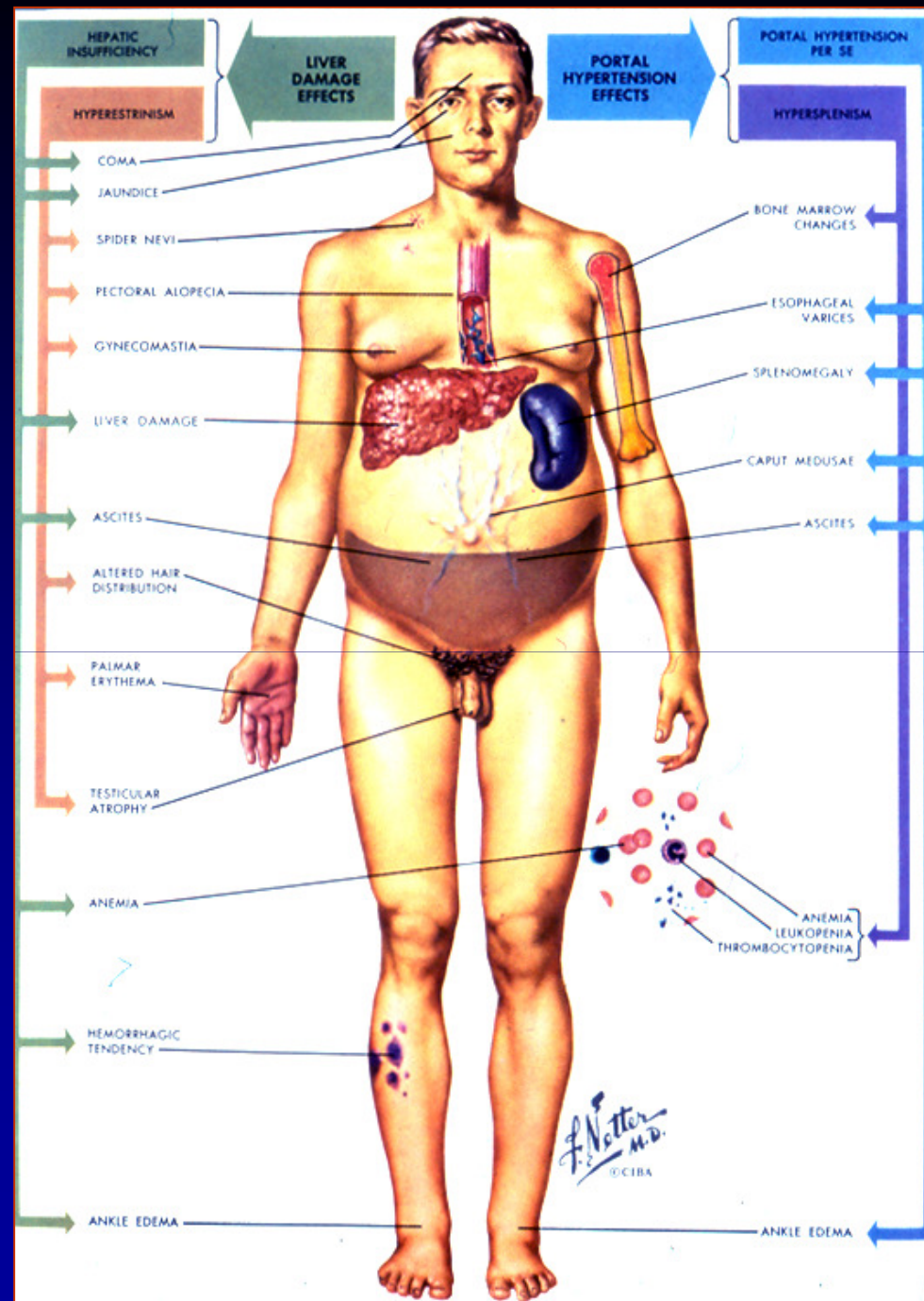


REGULAR FORMATION OF SMALL
NODULES AND THIN SEPTA,
CHARACTERISTIC OF "LAENNEC'S"
CIRRHOSIS

Cirrhosis

Anatomical Changes





Cirrhosis

- **Portal vein hypertension**
 - **Hepatomegaly +/- splenomegaly**
 - **Ascities**
 - **Gastrointestinal varices**
- **other effects**
 - **Increased cardiac output**
 - **Decreased peripheral vascular resistance**
 - **Hypoxemia...shunts (right to left)**
 - **Restrictive pulmonary disease due to ascities**
 - **Hepatic encephalopathy**
 - **Hepatorenal syndrome**
 - **Hepatopulmonary syndrome**
 - **Infections due to decreased immune function (EtOH)**
 - **Cardiomyopathy (EtOH)**
 - **Megoblastic anemia (EtOH)**

Hepato-Renal Syndrome: Pathophysiology

- **Not entirely clear**
- **Vasoconstriction of the renal circulation leads to significant reduction in renal blood flow and glomerular filtration rate**
- **Chronic renal failure leads to portal hypertension, systemic hypotension, increased SVR and increased cardiac output**
- **Vasoconstrictive mechanisms activated**
 - **renin-angiotensin system**
 - **sympathetic nervous system**
 - **ADH are activated**

Hepato-Renal Syndrome: Clinical Manifestations

- **Acute renal failure associated with decompensated cirrhosis**
- **Presents as acute oliguria in patients with advanced liver disease with ascites and portal hypertension.**
- **Will occur in 10-40% of patients with cirrhosis and ascites**
- **Oliguria, very low sodium excretion, low urine output in the absence of diuretics, and a progressive rise in the plasma creatinine concentration.**
- **High mortality**

Hepato-Pulmonary Syndrome

- Triad
 - Liver failure
 - Increased alveolar-arterial gradient ($\text{PaO}_2 < 60$ mm Hg)
 - Evidence of intrapulmonary vascular dilatations
- Pathophysiology not well understood
- 8% of cirrhotics
- Intrapulmonary shunts
- Platypnea: Dyspnea improves when upright
- Orthodeoxia: Hypoxia worsens when lying flat

Portopulmonary Hypertension

- Vasoconstriction, endothelial and smooth muscle cell proliferation, thrombosis and fibrosis
- Pulmonary HTN mean PAP>25
- Pathologically indistinguishable from primary pulmonary hypertension

Pulmonary Hypertension

- 1205 liver transplants
- Pulmonary HTN mean PAP>25;
PVR >120
- 8.5% with pulmonary HTN
- Mild: 81
- Moderate: 14
- Severe: 12

*Ramsay et al. Liver Transplantation
and Surgery, Vol 3 No 5 (Sept), 1997*

Management of Patients with Liver Dysfunction

- Cross tolerance
- Coagulation and so forth
- Beware renal function

Management of Patients with Hepatic Failure

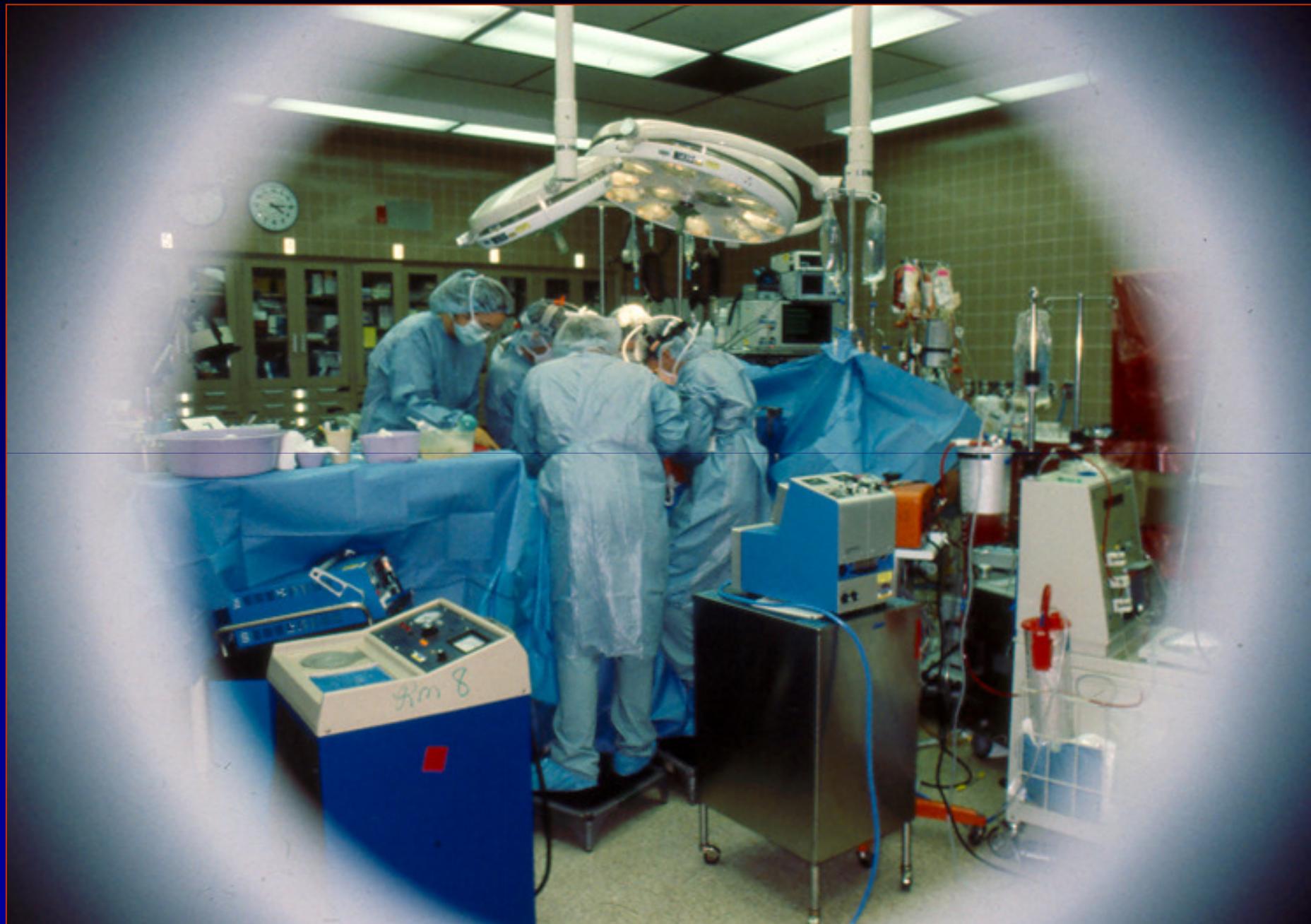
- Delay if possible
- May need to correct coags
- Patients may be sensitive to sedatives and depressant drugs
- Beware drugs that depend on hepatic metabolism
- Succinylcholine should not be a problem; 2 week half-life
- Measure glucose to avoid hypoglycemia
- Avoid hypotension (Dah!)
- Maintain urine output
- Regional OK, if coags ok

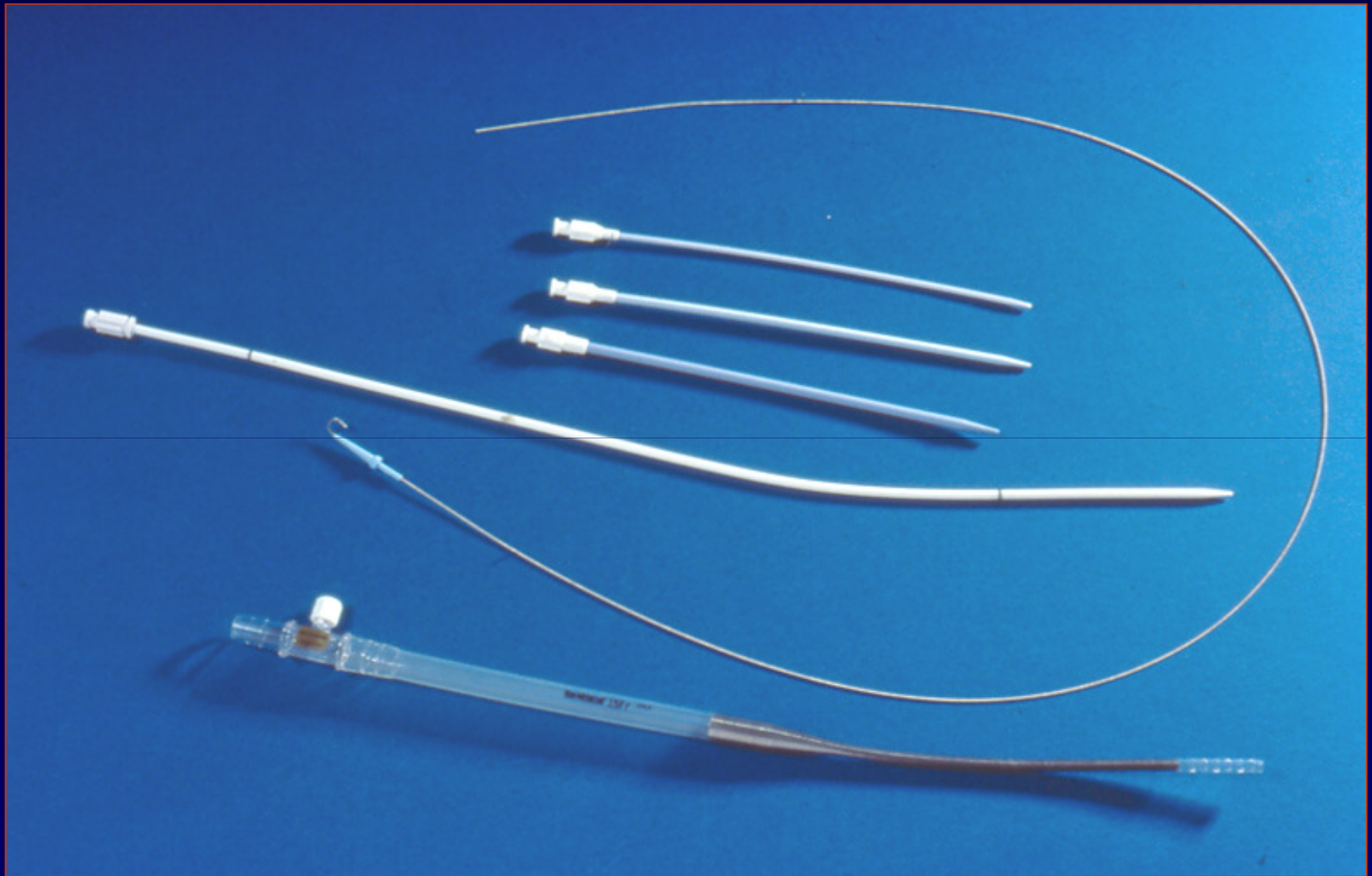
Management of Anesthesia for Intoxicated Patients

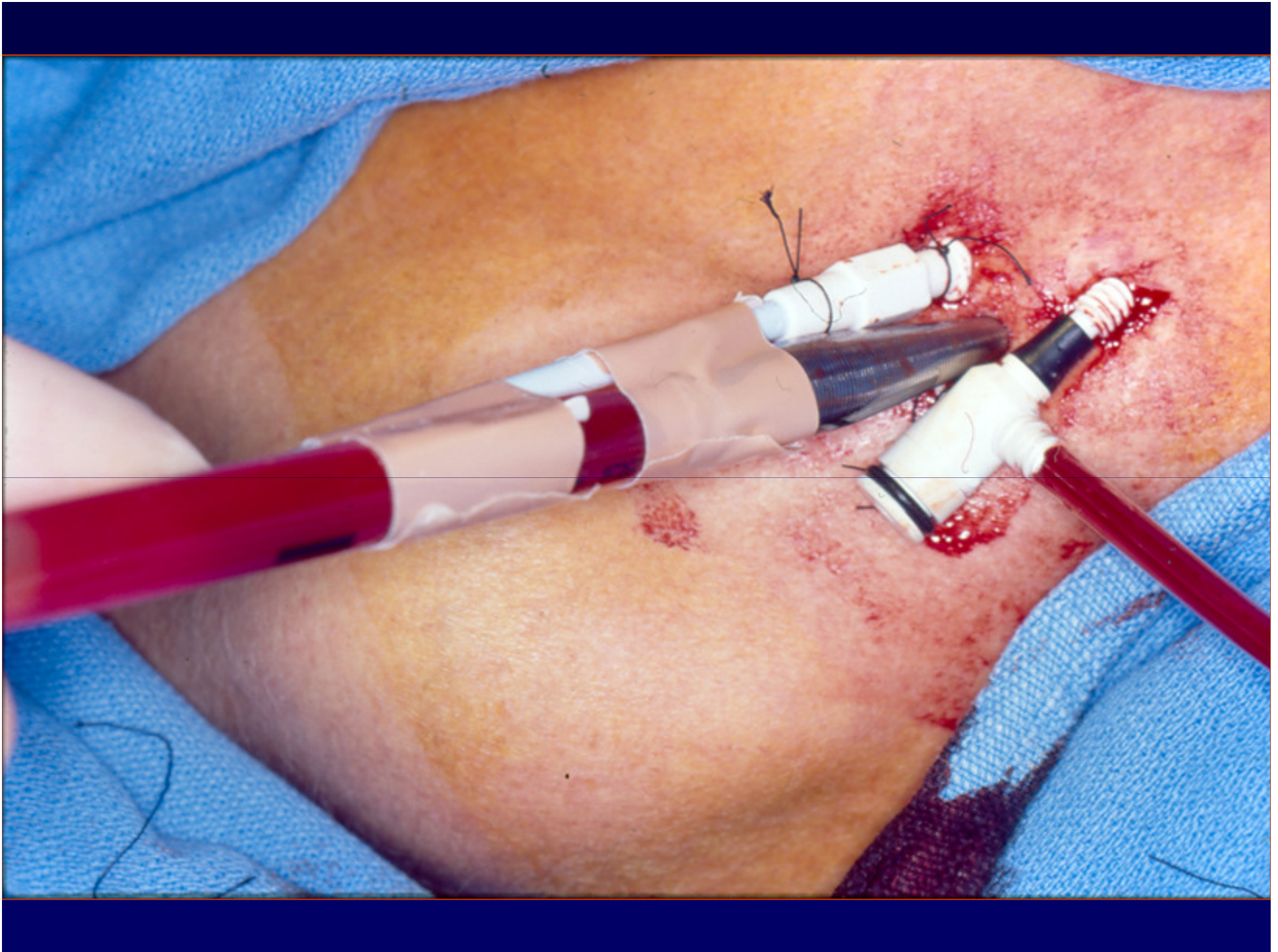
- They may already be there
- Aspiration risk



"That liver went to someone who doesn't have such a big yap."







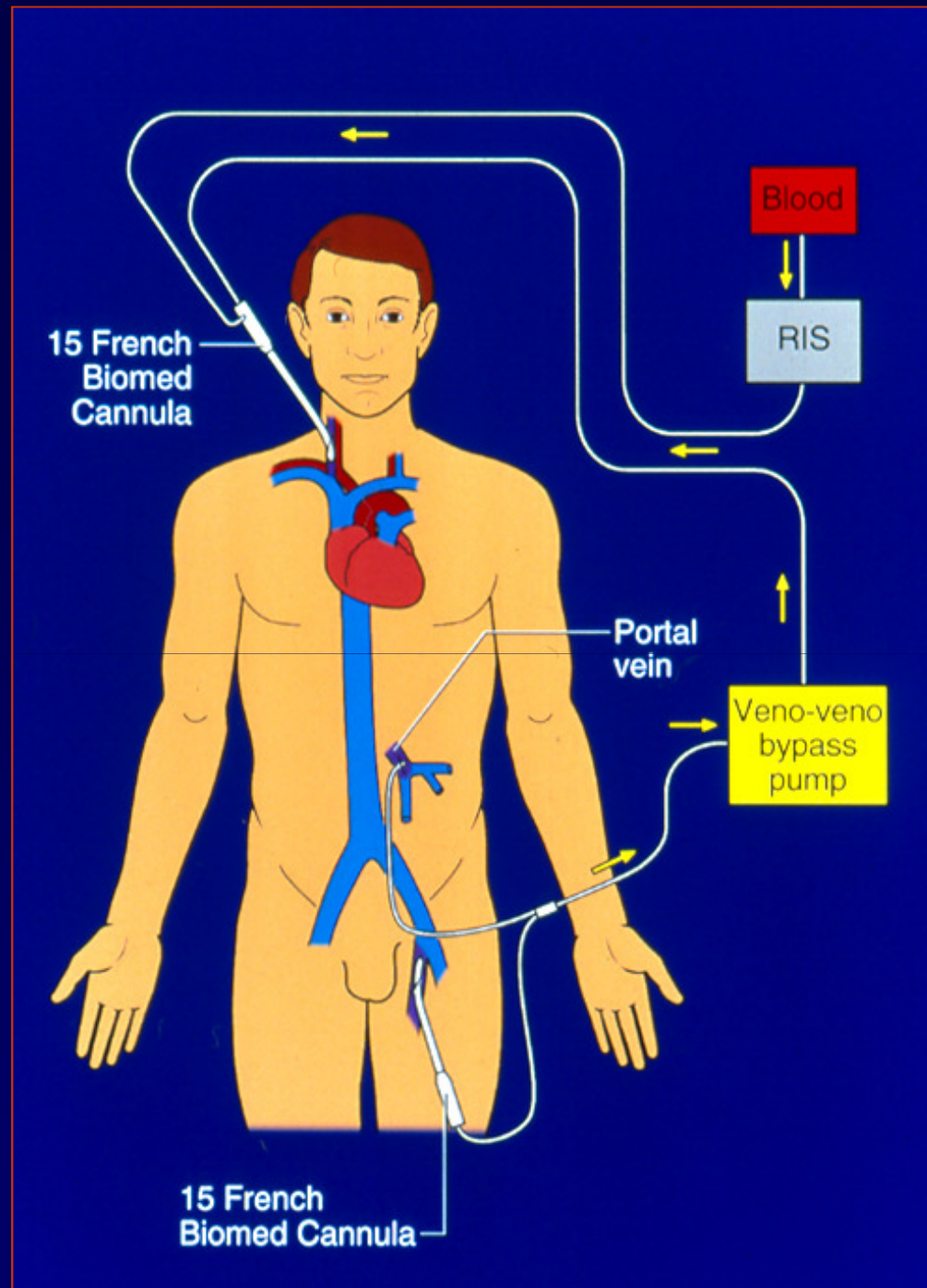












Management of Anesthesia for Patients with Diseases of the Biliary Tract

- Opioids and sphincter spasm
 - NTG
 - Glucagon
 - Naloxone
- Way overrated
- Most are done laparoscopically (cf MorCORE)



"Guacamole is the chopped liver of Mexico."

The New Yorker