FIBROUS TISSUE

- portal triad
- central vein
- liver lobule
PORTAL
“TRIAD”

CENTRAL
VEIN
PATTERNS OF HEPATIC INJURY

• Degeneration:
  – Ballooning, “feathery” degeneration, fat, pigment

• Inflammation: Viral or Toxic
  – Regeneration
  – Fibrosis

• Neoplasia: 99% metastatic, 1% primary
BALOONING DEGENERATION
“FEATHERY” DEGENERATION
FATTY LIVER
“MICRO”-VESICULAR STEATOSIS
Obesity
Diabetes
Toxic

“MACRO”-VESICULAR STEATOSIS
“Golden” pigment stained with Prussian Blue stain to make it blue.  Hemosiderin?  Bile?  Melanin?
APOPTOSIS
INFLAMMATION

• PORTAL TRIADS (early)

• SINUSOIDS (more severe)
MILD “TRIADITIS”
More severe portal infiltrates with sinusoidal infiltrates also
Hepatic Regeneration

• The LIVER is classically cited as the most "REGENERATIVE" of all the organs!
FIBROSIS

• FIBROSIS is the end stage of MOST chronic liver diseases, and is ONE (of TWO) absolute criteria needed for the diagnosis of cirrhosis.

• What is the other?
CIRRHOSIS

- PORTAL-to-PORTAL (bridging)

FIBROSIS

- The “normal” hexagonal “ARCHITECTURE” is replaced by NODULES
CIRRHOsis

- Liver
- Alcoholic
- Biliary (Primary or Secondary)
- Laennec’s
- Advanced (kind of a “redundant” adjective)
- Post-necrotic
- Micronodular
- Macronodular
ALL CIRRHOSIS IS:

- IRREVERSIBLE

- The end stage of ALL chronic liver disease, often many years, often several months

- Associated with a HUGE degree of nodular regeneration, and therefore represents a significant “risk” for primary liver neoplasm, i.e., “Hepatoma”, aka, Hepatocellular Carcinoma
BLIND MAN's LIVER
Blind Man’s Diagnosis
portal triad

central vein

liver lobule
IRREGULAR NODULES SEPARATED BY PORTAL-to-PORTAL FIBROUS BANDS
TRICHRONE
CIRRHOSIS, TRICHRoME STAIIN
CIRRHOSIS, TRICHRHOME STAIN
DEFINITIONS:

• CIRRHOSIS is the name of the disease as demonstrated by the anatomic changes

• LIVER FAILURE is the series and sequence of abnormal pathophysiologic events
Hepatic encephalopathy

Malnutrition

Skin spider angioma

Esophageal varices

Portal vein

Splenic vein

Splenomegaly

Periumbilical caput medusae

Ascites

Hepatic lymph

Hemorrhoids

Testicular atrophy
“SPIDER” ANGIOMA, CIRRHOSIS
Common Clinical/Pathophysiological Events

• Portal Hypertension  WHY? WHERE?
• Ascites  WHY?  (Heart/Renal?)
• Splenomegaly  WHY?  Hepatomegaly?
• Jaundice  WHY?
• “Estrogenic” effects  WHY?
• Coagulopathies (II, VII, IX, X)  WHY?
• Encephalopathy  WHY?
Hepatic Enzymology

- Transaminases (AST/ALT), aka (SGOT/SGPT), and LDH are "hepatic INTRACELLULAR" enzymes, and are primarily indicative of hepatocyte damage.

- Alkaline Phosphatase (AlkPhos), Gamma-GTP (Gamma-glutamyl transpeptidase), and 5’-Nucleotidase (5’N) are MEMBRANE enzymes and are primarily indicative of bile stasis/obstruction.
Intracellular = DAMAGE
AST/ALT/LDH
Membrane = OBSTRUCTION
AlkPhos/GGTP/5’N
Bilirubin: (0.3-1.2 mg/dl)

UN-conjugated (IN-direct)

Conjugated (direct)
JAUNDICE

- Hemolytic (UN-conjugated)
- Obstructive (Conjugated)
JAUNDICE

- Excessive production
- Reduced hepatic uptake
- Impaired conjugation

- Defective Transportation
Neonatal Jaundice

• Neonatal, **genetic**
  – Gilbert Syndrome
  – Dubin-Johnson Syndrome

• Neonatal, **NON-genetic**
  – MASSIVE differential diagnosis, i.e., everything
CHOLESTASIS

• Def: Suppression of bile flow
• Associated with membrane enzyme elevations, “primarily”, ie, AP/GGTP/5’N
• Familial, drugs, but bottom line is OBSTRUCTION
Bile “plugs” ,  Bile “lakes”
VIRAL HEPATITIS

• A, B, C, D, E
• They all look the same, ranging from a few extra portal triad lymphocytes, to “FULMINANT” hepatitis
• Associated with full recovery (usual), chronic progression over years leading to cirrhosis (not rare), risk of hepatoma (uncommon), or death (uncommon)
VIRAL HEPATITIS

• Jaundice, urine dark, stool chalky
• Viral “prodrome”
• Upper respiratory infection
• All have multiple antigen (virus) and antibody (serology) serum tests
• “Councilman” bodies on biopsy are very very nice to find. Why?
Chiefly Portal Inflammation
FULMINANT HEPATITIS
“FULMINANT” Acute Viral Hepatitis
“Councilman” Bodies……Diagnostic? Probably!
LESS common than B (one fourth)
LESS dangerous than B in the acute phase
MORE likely to go chronic than B
MORE closely linked with hepatoma than B
NON-Viral hepatitides

- Staph aureus (toxic shock)
- Gram-Negatives (cholangitis)
- Parasitic:
  - Malaria
  - Schistosomes
  - Liver flukes (Fasciola hepatica)
- Ameba (abscesses)

- AUTOIMMUNE
- ALCOHOLIC HEPATITIS
DRUGS/TOXINS

• Steatosis (ETOH)
• Centrolobular necrosis (TYLENOL)
• Diffuse (massive) necrosis
• Hepatitis
• Fibrosis/Cirrhosis (ETOH)
• Granulomas
• Cholestasis (BCPs, steroids)
“Metabolic” Liver Disease

- **Steatosis** (i.e., “fat”, fatty change, fatty “metamorphosis”)
- **Hemochromatosis** (vs. hemosiderosis)
  - Hereditary (Primary)
  - Iron Overload (Secondary), e.g., hemolysis, increased Fe intake, chronic liver disease
- **Wilson Disease** (Toxic copper levels)
- **Alpha-1-antitrypsin** (NATURAL protease inhibitor)
- **Neonatal Cholestasis**
PAS positive inclusions with alpha-1-antitrypsin deficiency
INTRAHEPATIC BILE DUCTS
Points of Interest

• INTRA-hepatic vs. EXTRA-hepatic
• PRIMARY biliary cirrhosis is a bona-fide AUTOIMMUNE disease of the INTRA-hepatic bile ducts
• SECONDARY biliary cirrhosis is caused by chronic obstruction/inflammation/both of the intrahepatic bile ducts
• CHOLANGITIS, or inflammation of the INTRA-hepatic bile ducts, is associated with chronic bacterial (often gram negative rods) infections, or Crohns/Ulcerative colitis (IBD)
CIRCULATORY Disorders
Points of Interest

• Infarcts are rare. WHY?
• Passive congestion with “centrolobular” necrosis, is EXTREMELY COMMON in CHF, and a VERY COMMON cause of cirrhosis, i.e., “cardiac” cirrhosis
• Various semi reliable clinical and anatomic findings are seen with disorders of:
  – Portal Veins
  – Hepatic veins/IVC
  – Hepatic arteries
MISC.

• Hepatic Diseases are seen often with
  – Pregnancy
    • PRE-Eclampsia/Eclampsia (HTN, proteinuria, edema, coagulopathies, DIC)
    • Fatty Liver
    • Cholestasis
  – Transplant—Bone Marrow or other Organs
    • Drug Toxicities
    • GVH
BENIGN LIVER TUMORS

• .....are, in most cases, really regenerative nodules
• Have been historically linked to BCPs
• Can really be neoplasms of blood vessels also
MALIGNANT LIVER TUMORS

- 99% are metastatic, i.e., SECONDARY, esp. from portal drained organs
- Just about every malignancy will wind up eventually in the liver, like the lungs
- PRIMARY liver malignancies, i.e., hepatomas, aka hepatocellular carcinomas, arise in the background of already very serious liver disease chronic hepatitis/cirrhosis, are slow growing, and do NOT metastasize readily
- CHOLANGIOCARCINOMAS are malignancies if the INTRA-hepatic bile ducts and look MUCH more like adenocarcinomas than do hepatomas
HEPATIC ANGIOMA
HEPATOMA, or HEPATOCELULAR CARCINOMA
CHOLANGIOCARCINOMA
EXTRAHEPATIC BILE DUCTS & GALLBLADDER
MAIN CONSIDERATIONS

• Anomalies
• Stones (Cholesterol/Bilirubin) (Chole[docho]lithiasis)
• Inflammation (Cholecystitis/Cholangitis)
• Cysts
• Neoplasms
Anomalies

• Congenitally absent Gallbladder
• Duct Duplications
• Bilobed Gallbladder
• Phrygian Cap
• Hypoplasia/Agenesis
Phrygian Cap
Cholelithiasis

Factors

• Bile supersaturated with cholesterol
• Hypomotility
• Cholesterol “seeds” in bile, i.e., crystals
• Excess mucous in gallbladder
Cholesterolosis of gallbladder mucosa
Cholesterolosis of gallbladder mucosa
Cholecystitis

- Acute: fever, leukocytosis, RUQ pain
- Chronic: Subclinical or pain
- Ultrasound can detect stones well
- HIDA (biliary) nuclear study can help
- Go hand in hand with stones in gallbladder or ducts
- If surgery is required, most is laparoscopic
Choledochal Cysts

- Dilatations of the common bile duct usually in children.
Adenocarcinoma of the gallbladder