It's important to be able to distinguish

Diagnostic Studies - Then

- History
- Biopsy

Diagnostic Studies - Now

- History
- Biopsy
- Serum markers (AFP, CA19-9, CEA)
- Radiology
  - Ultrasound
  - CT
  - MRI
  - ERCP/EUS
- Liver colloid scan
Benign hepatic lesions are common
- Estimated incidence of 7-9%
- Broad differential
- Lesions may arise from:
  - Hepatocytes
  - Biliary epithelium
  - Mesenchymal tissue
- Frequently no symptoms attributable to lesion

Nonspecific Symptoms
- More Common
  - Vague epigastric or RUQ pain
  - Abdominal fullness
  - Nausea
  - Early satiety
  - Fever
  - Malaise
  - Weight loss
- Less Common
  - Diarrhea
  - Pancreatitis
  - Hemobilia
  - Anemia

Need to start with a good history
- Presence of underlying liver disease
- Age
- Gender
- Use of oral contraceptives
- Recent travel

Important Differential
- Hepatocellular carcinoma
- Cholangiocarcinoma
- Cystadenocarcinoma
- Fibrolamellar carcinoma
- Metastasis (colorectal, pancreatic, breast)

(Malignancy)

Most Common Benign Lesions
- **Solid Liver Disease**
  - Hemangioma
  - Focal Nodular Hyperplasia
  - Hepatic Adenoma
  - Nodular Regenerative Hyperplasia
- **Cystic Liver Disease**
  - Simple Cyst
  - Cyst adenomas
  - Polycystic Liver Disease
  - Choledochal Cyst
  - Infectious Cyst

Hemangioma
- Most common benign liver tumor
  (prevalence on autopsies 5-20%)
- Thought due to ectasia rather than hypertrophy or hyperplasia
- Some have estrogen receptors
- Accelerated growth with high estrogen states
  (puberty, pregnancy, OCP, androgen use)
- Female:male ratio 5:1 to 6:1
- Usually found in ages 30-70
Hemangioma - Histology
- Also called cavernous hemangiomas
- Multiple large vascular channels
- Lined by single layer of endothelial cells
- Supported by collagenous walls

Hemangioma - Presentation
- Commonly incidental finding
- Most < 5 cm and asymptomatic
- > 5 cm called giant hemangiomas
- Symptoms due to size and location
- Nonspecific abdominal pain
- Risk of spontaneous rupture < 1%

Kasabach-Merritt Syndrome
- Rare syndrome
  - Thrombocytopenia
  - Disseminated intravascular coagulation (DIC)
  - In association with a giant hemangioma
- Consumptive cascade triggered by
  - Surgery
  - Dental procedures
- Present with abdominal pain and bleeding within hemangioma

Hemangioma - CT Imaging
- Usually subcapsular region of right lobe
- Well-defined, hypodense mass
- May include
  - Calcifications
  - Areas of fibrosis
  - Diffuse central scarring

Hemangioma - MRI Imaging
- T1-weighted MR image shows a high-signal-intensity lobulated mass with central necrosis
- T1-weighted MR image shows the mass with the typical centripetal pattern of peripheral enhancement

Hemangioma - Tc99-RBC Scan
- CT scan shows a large mass with multiple hypodense regions in the left hepatic lobe
- Early perfusion planar images with decreased perfusion in the left lobe of the liver, with gradually increased radiotracer uptake
Hemangioma - Management

- In asymptomatic patients with clear diagnosis: No treatment necessary
- Equivocal cases: Biopsy may be warranted
- Significant symptoms or diagnostic uncertainty: Surgical resection

Surgery for Hemangioma

- Enucleation to preserve parenchyma
- Anatomic approach to resection if significant bleeding due to location
- Rare cases of transplantation for giant hemangiomas

Focal Nodular Hyperplasia (FNH)

- 8% of benign liver tumors (2nd most common)
- Prevalence 3% in population
- Predominantly in women in 3rd to 5th decade
- Female: male ratio 6:1 to 8:1
- No causal relationship
- Associated with OCP
  - Accelerating growth of already existing tumors
  - Does not cause new lesions
- Non-neoplastic hyperplastic response to congenital vascular malformation

FNH - Histology

- Benign cords of hepatocytes
- Fibrous septae radiating from a central scar
- Formed by
  - Biliary ductules
  - Cholangiolar proliferation
  - Surrounding inflammation
  - Malformed arteries and capillaries
  - Portal veins are absent

FNH - CT Imaging

- Presence of central scar as hyperechoic band
- Homogeneous and isoattenuating to liver parenchyma before contrast
- Bright on arterial phase

FNH - MRI Imaging

- T1 (PV)
FNH - Presentation

- Most asymptomatic
  - > 5 cm, near capsule
- 10% have symptoms
  - RUQ pain
  - Epigastric pain
  - Normal LFT's
  - Spontaneous rupture is rare
  - No malignant degeneration

FNH - Management

- In asymptomatic patients with clear diagnosis: No treatment necessary
- Equivocal cases: Biopsy warranted
- Significant symptoms or diagnostic uncertainty: Surgical resection (or TACE)

FNH in High Estrogen States

- Controversial whether to stop OCP or avoid pregnancy
- Frequent ultrasounds during pregnancy and postpartum
- Postmenopausal women should be switched from oral estrogen to transdermal delivery to decrease first-pass hepatic metabolism

Hepatic Adenoma (HA)

- Rare hepatic tumor
- Predominantly in women 20-40
- Female: male ratio at least 4:1
- Strong association with oral contraceptive use
  - Incidence 3-4/100,000 vs. 1/100,000 in non-users
- More common with long-term high-dose estrogen, androgen, or anabolic steroid use
  - Withdrawal may induce tumor regression
- Also associated with:
  - Diabetes Mellitus
  - Glycogen storage diseases
    - Type I (von Gierke's disease) 50%
    - Type II storage disease 25%

Hepatic Adenoma - Presentation

- Most present with a small, asymptomatic lesion
- Multiple lesions in 10-30%
- Large (>5 cm) can be associated with RUQ pain, fullness or discomfort
- Hypervascular and lack of capsule → rupture
- Intra-tumoral 1/3, intraperitoneal in 2/3
- Malignant degeneration associated with larger tumors

Hepatic Adenoma

- 70-80% solitary
- Well-circumscribed
- Round
- Unencapsulated
- Often pseudocapsule
- Yellow-tan
- Intra-tumoral fat, necrosis, and hemorrhage common
**Hepatic Adenoma - Histology**
- Hypervascular tumors
- Benign proliferation of bile-producing hepatocytes
- No bile ducts can be seen
- Plates of cells separated by dilated sinusoids perfused by feeding arteries

**Sulfur Colloid Scan**
- FNH have Kupffer cells that pick up 99mTc-sulfur-colloid
- Adenomas do not
- If uptake is the same or above background, hepatic adenoma can be ruled out

**HA have variable appearance**
- Simple \(\rightarrow\) hypoechoic
- Hemorrhage/necrosis \(\rightarrow\) heterogeneous appearance

**Hepatic Adenoma - Management**
- Surgical resection
- Risk for:
  - Rupture
  - Malignant degeneration
  - Difficulty distinguishing from well-differentiated hepatocellular carcinoma
- Small asymptomatic lesions (<4-5 cm)
  - Discontinue estrogen
  - Serial imaging
  - AFP levels

**Surgery for Hepatic Adenoma**
- Enucleation with 1-2 cm margin
- Anatomic resection
- Hepatic artery embolization
- Transplantation
- Following rupture:
  - Acute treatment: hepatic arterial embolization
  - After recovery: formal resection

**Ruptured HA**
- Hematoma
- Adenoma
Nodular Regenerative Hyperplasia

- Benign proliferative process
- Normal hepatic parenchyma is replaced by nodules of hepatocytes with minimal associated fibrosis
- Nodules 1 mm to 1 cm
- No gender predilection
- Patients typically > 60
- Not pre-malignant

Nodular Regenerative Hyperplasia - Pathophysiology

- Hypercoagulability / Endothelial or Autoimmune Injury
  - Thrombosis
  - Sinusoidal Portal Venous Hypertension
  - Zone III Hepatocyte Atrophy
  - Compensatory Proliferation of Hepatocytes
  - Regenerative Nodules

Nodular Regenerative Hyperplasia

- Presentation
  - Most asymptomatic
  - May present with stigmata of portal hypertension
  - Normal LFT's (10-25% mild elevations in alkaline phosphatase)
  - Normal-sized liver
- Management
  - Prevent complications of portal hypertension
  - Given preserved synthetic function and encephalopathy rare
  - Portosystemic shunts

Simple Cyst

- Usually congenital
- Result from abnormal embryonal development of intrahepatic biliary ducts
- Fail to connect to their extrahepatic counterparts
- Form intraparenchymal cysts
Simple Cyst - Histology
- Single layer
- Cuboidal or columnar epithelium
- Minimal surrounding fibrous stroma
- Almost always contains clear, straw-colored serous fluid without bile

Simple Cyst - Presentation
- Solitary > 50%
- Asymptomatic > 90%
- Most < 5 cm
- Range up to 20 cm
- Usually incidental finding female patients > 40
- Symptoms related to mass effect
- Rarely, hemorrhage or infection

Simple Cyst - Diagnosis
- USG usually sufficient
- CT and MRI
  - Thin wall
  - Without enhancement
  - Fluid-filled
  - No septations

Simple Cyst - Management
- Asymptomatic → no intervention
- Symptomatic
  - < 5 cm or poor operative candidate → aspiration followed by sclerosing agent (higher rate of recurrence)
  - > 5 cm → laparoscopic or open cyst unroofing (depends on location)
    - Cyst Fluid
      - Clear → no analysis
      - Bilious → inspect for duct and suture

Cyst Adenoma
- Incidence 50-1000 less common than simple cysts
- More common in women
- No association with oral contraceptives
- Can occur at extremes of age
- Most commonly present in fourth decade

Cyst Adenoma - Histology
- Multilocular
- Single layer epithelium
- Cuboidal or columnar
- Surrounded by thickened stroma
- Diagnosis made by presence of mesenchymal tissue
Cyst Adenoma - Presentation
- Internal septations
- Irregular borders
- Thick stromal layer
- Calcifications
- Mural nodules in walls

Cyst Adenoma - Management
- Benign but have potential to transform into cyst adenocarcinomas
  → should be resected when identified
- Malignant potential lies in the epithelium so they must be fully enucleated or resected

Multiple Cysts

Polycystic Liver Disease (PCLD)
- If multiple cysts, consider PCLD
- Inherited
- Autosomal dominant
- Found in association with renal cysts
- USG, CT or MRI
- Majority asymptomatic
- Preserved liver function
- Advanced disease
  - RUQ pain
  - Treat with aggressive cyst unroofing
  - Reduces cysts volume and symptoms
  - Rarely need liver transplant

Choledochal Cyst
- Congenital bile duct abnormality
- Cystic dilatation of the bile duct tree
- Extra- or intrahepatic ducts or both
- More prevalent in Asia
- Often anomalous junction between BD & PD → reflux/activation of pancreatic secretions
- Presentation: jaundice and fever

Variety of Choledochal Cysts
- Increased rate of cholangiocarcinoma
- Management:
  - Surgical excision
Carolí’s Disease
- Type V choledochal cyst
- Rare congenital abnormality
- Multifocal saccular dilatations of intrahepatic bile ducts
- Dilated ducts communicate with the normal ducts (in contrast to PCLD)
  - more prone to infections and stones
- No other associated hepatic abnormalities

Carolí’s Disease - ERCP

Carolí’s Disease - Presentation
- Presents in childhood or early adult life – 75% male
- Associated with renal disease (infantile medullary spongiosis)
- Carolí’s syndrome – associated with congenital hepatic fibrosis, occurs in 50% - autosomal recessive trait
- Usually do not have signs of liver failure or portal hypertension
- 7% develop cholangiocarcinoma

Carolí’s Disease - Management
- Ursodeoxycholic acid
- IV antibiotics and endoscopic or surgical stone removal for cholangitis
- Segmental liver resection for localized involvement
- Liver transplant for diffuse disease and recurrent cholangitis

Abscess – Infectious Cyst
- Pyogenic
- Amebic
- Fungal
- Echinococcal (Hydatid)
Pyogenic Abscess
- 10-15 cases per 100,000 hospital admissions
- Dropped as low as 8-15/100,000 but slowly increasing
- Previously
  - Most common patient 20’s or 30’s
  - Pyelophlebitis from complicated appendicitis
- Currently
  - 50-60’s
  - Biliary origin

Pyogenic Abscess
- Biliary obstruction
  - West – hepatobiliary malignancy
  - East – intrahepatic stones
- Pyelophlebitis
  - Any infectious order of the GI tract
  - Appendicitis, diverticulitis, etc.
- Direct extension
  - Gastric or duodenal perforation
  - Suppurative cholecystitis

Pyogenic Abscess
- Organisms
  - Aerobic – E coli, K pneumonia
  - Anaerobic – Bacteroides
- Presentation
  - Classic: fever, jaundice, RUQ pain (10%)
  - Additional: Malaise, fatigue, anorexia weight loss
- Treatment
  - Drainage – aspiration, percutaneous, surgical
  - Antibiotics

Pyogenic Abscess
- Parasitic Protozoan E. histolytica
- Typical patient in US
  - Hispanic male 20-40 years old
  - History of travel to endemic area (Mexico, SE Asia)
  - Male:female ratio 10:1
- Fecal-oral route of transmission
- Presentation similar to pyogenic abscess
- Most do not have detectable parasites in their stool
- Diagnosis by serological testing for antibodies
- Usually responds to antibiotics alone
- Typically does not require drainage

Fungal Abscess
- 10% of hepatic abscesses
- 80% due to Candida albicans
- Also Aspergillus or Cryptococcus
- Systemic fungal therapy and drainage
- Most develop mixed fungal and bacterial
- Mortality rate – 50%
Echinococcal (Hydatid) Cyst

- Endemic in certain parts of the world
  - S. America, N Africa, Australia, New Zealand
- Caused by tapeworms
  - *Echinococcus granulosus*
  - *Echinococcus multilocularis*
- Humans ingest the eggs through contact with sheep, cats, dogs, cattle, or contaminated water or food
- Can spread to lungs, brain, bones or bulbous oculi

- Cyst is composed of three layers
  - Outer pericyst
    - Compressed hepatic tissue
  - Endocyst
    - Inner germinal layer
  - Ectocyst
    - Translucent thin interleaved membrane

- Presentation
  - Eosinophilia (+)
  - Serologic tests
  - Anaphylactic shock due to cyst rupture into peritoneal cavity

- Treatment
  - Surgical Excision
  - Care to avoid spillage
  - Pre- and post-operative
    - Albendazole
    - mebendazole

Surgical Considerations
Surgical Approaches

- Non-anatomic resection
- Anatomic resection
- Transplantation
- Alternatives to resection
  (Ablative techniques)
  - TACE
  - RFA
  - Cryo
  - Ethanol

Evaluation of Hepatic Function

- Child-Pugh Score
  (Bili, Alb, INR, Ascites, Encephalopathy)
  - Child-Pugh A 10%
  - Child-Pugh B 30%
  - Child-Pugh C 80%

- Model for End Stage Liver Disease (MELD)
  (Bili, INR, Creatinine – range 6-40)
  - MELD < 9 0%
  - MELD ≥ 9 26%

Evaluation of Hepatic Function

- Functional testing (mostly Eastern nations)
  - Indocyanine green clearance
  - Galactose elimination capacity
  - Aminopyrine clearance

  - Useful for limited hepatic resections in estimating overall hepatic function
  - Do not evaluate functional reserve

Evaluation of Hepatic Function

- Clinical or radiological evidence of portal HTN
  - Splenomegaly
  - Abdominal collaterals
  - Grade II or III esophageal varices
  - Thrombocytopenia (PLT < 100)

- Biochemical evidence
  - Total bilirubin > 1 mg/dl
  - AST > 100 IU/L
  - ALT > ULN x2

Where can you cut?
Liver Remnant Volume

- Three-dimensional CT volumetrics
  - Preoperative measurement of functional liver remnant (FLR)
  - Outlining of hepatic segmental contours
  - Calculates volumes from surface measurements from each slice
  - Direct measurement of total liver volume is possible but is more accurately calculated from:
    \[ TLV (cm^3) = -794.41 + 1,267.28 \times BSA (m^2) \]
    
    \[ \text{CT measured FLR} / TLV = \text{standardized FLR} \]

Volume rendering

Defining vascular anatomy

Large Central Tumor

Resection

Planned

Actual
How much can you take?

- Significantly increased postoperative complications with FLR < 20% TLV for patients with normal underlying liver
- Liver failure follows FLR < 300 ml/m²
- Cutoff is 30-40% in chronic liver disease

The Effect of Steatosis

- Steatotic Liver: 14.7% mortality, 5.8% death from liver failure
- Normal Liver: 1.6% mortality, 0.6% death from liver failure

Subtract the amount of macrosteatosis to adjust for FLV.

What if the FLR is inadequate?

- Portal vein embolization (PVE) directed to the area of planned resection
- Induces hypertrophy in planned remnant
- Done in IR with coils or microparticles
- Increases volume and function of non-embolized segments, shown by:
  - Increased biliary excretion
  - Increased Tc-99m-galactosyl human serum albumin uptake

Pre- and post- PV embolization

- FLR/TLV ratio was 17.0% before and 25.1% after PVE
- Increase of 8.1%
- Allowed a successful right trisegmentectomy

Algorithm for Assessment of Hepatic Reserve

- Esnaola, 2008.
Role for Liver Transplant

- MELD score disadvantages those without significant biochemical dysfunction
- Need to apply for a MELD exception
- Acceptance varies between regions
- Alternatives
  - Less than optimal cadaveric donors
  - Living donors

Summary

- Broad range of benign liver tumors
- Different malignant potentials
- Some lead to poorer outcomes regardless of malignant potential
- Symptoms frequently not much help
- Important to distinguish through history, radiologic studies, and biopsy
- Management governed as much by anatomy and underlying state of liver as well as tumor histology
- Early referral to hepatobiliary/transplant