

Montefiore
THE UNIVERSITY HOSPITAL

 **EINSTEIN**
Albert Einstein College of Medicine
OF YESHIVA UNIVERSITY

Work up of the focal liver lesion

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World's Most Accurate Pie Chart



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- Incidental findings are common with increasing use of abdominal imaging
 - The goal of this lecture is to describe how to evaluate focal liver lesions and identify those lesions requiring further intervention

Focal Liver Lesions: Basic Concepts

- All solid liver lesions require investigation.
- Contrast enhanced, multiphase, cross sectional imaging is always required in the initial diagnostic work up.
- Histologic confirmation with a core or fine needle biopsy is usually not necessary and can be harmful

Differential diagnosis of hepatic mass lesions

	Hepatocellular carcinoma	Metastatic carcinoma	Hepatocellular adenoma	Focal nodular hyperplasia	Cavernous hemangioma	Simple cyst
Incidence/100,000*	1-4800*	8-20	1 ^Δ -4 [◇]	3-4	400-7500	170
Solitary	20-40 percent	5-10 percent	90 percent	90 percent	90 percent	?
Coexisting liver disease	HBV, HCV, cirrhosis, hemochromatosis	Uncommon in cirrhotic liver	None	None	None	None
Pathogenesis	HBV, HCV, alcohol, aflatoxin, cirrhosis	Hematogenous, lymphatic or direct spread	Estrogens, anabolic steroids	Congenital, ? estrogens	Congenital, estrogens	Congenital
Imaging[§]	US, CT	US, CT, CTAP	US, CT, 99mTc	US, CT, MRI, 99mTc	Dynamic bolus CT, 99mTc-RBC-SPECT scan, MRI	US, CT
Alpha-fetoprotein	>300-500 ng/mL	Normal	Normal	Normal	Normal	Normal
Characteristic gross features	Hemorrhage, necrosis; invasion/obstruction	Hemorrhage, necrosis; umbilicated	Hemorrhage, necrosis	Central scar	Blood filled "cyst"	Thin walled cyst with clear fluid
Characteristic microscopic features	"Thick" (>3-4 cells) trabeculae	Replacement of hepatocytes, by malignant cells no portal structures	"Neohepatocytes", normal cord structure, no portal structures	"Focal cirrhosis" with pseudoductiles	Blood filled spaces lined by single layer of flat epithelium	Simple cuboidal endothelium
Diagnosis[¶]	FNAB or core biopsy	FNAB or core biopsy	Imaging, biopsy	Imaging, biopsy	Imaging	Imaging
Treatment	"Curative resection" or ethanol injection if solitary, <5.0 cm; ? transplantation± chemoembolization	"Curative resection" if <3.0 cm and 3 or fewer nodules especially if large; otherwise periodic imaging; malignant potential	Discontinue estrogens/androgens; resect if possible, especially if large; otherwise periodic imaging; malignant potential	Discontinue estrogens; periodic imaging	Surgical resection only if symptomatic or >10.0 cm; discontinue estrogens; periodic imaging	Usually no treatment percutaneous aspiration or surgical enucleation if symptomatic

US: ultrasound; CT: computerized axial tomography; dynamic bolus CT: rapid sequential CT images taken at plane of the mass, with delayed images up to 20 minutes; CTAP: computerized axial tomography arteriogram; MRI: fast spin echo magnetic resonance imaging; 99mTc: 99mTechnetium labelled sulfur colloid scan; RBC-SPECT: 99mTechnetium tagged red blood cell study utilizing single photon emission computerized tomography; FNAB: fine needle aspiration biopsy for cytology.

* From autopsy series.

• Varies with geographic origin.

Δ Overall population.

◇ Females on birth control pills.

§ Most useful imaging technique with which to obtain a diagnosis.

¶ Definitive test required for confident diagnosis.

Adapted from: LaBrecque DR, Cakir-Yedidag A. *Management of Liver Neoplasms in Medical Management of Liver Disease*, EL Krawitt (Ed), Marcel Dekker, Inc. 1999, p.310.

Focal liver lesions Basic Concepts

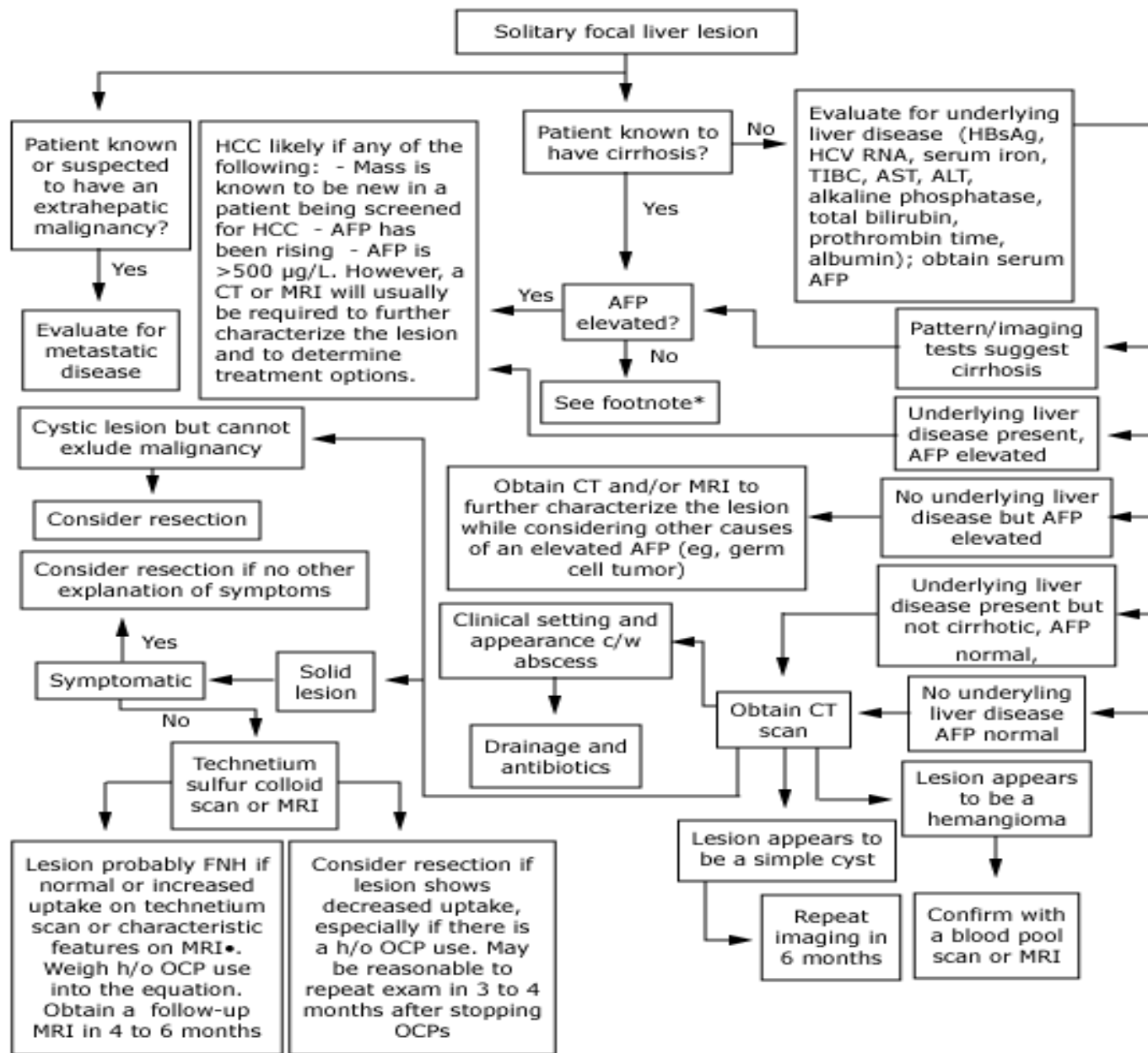
- Diagnostic evaluation utilizing a combination of history, physical, basic lab findings, and imaging has an accuracy of >99%, which exceeds the accuracy of either core biopsy or FNA.

Focal Liver Lesions Basic Concepts

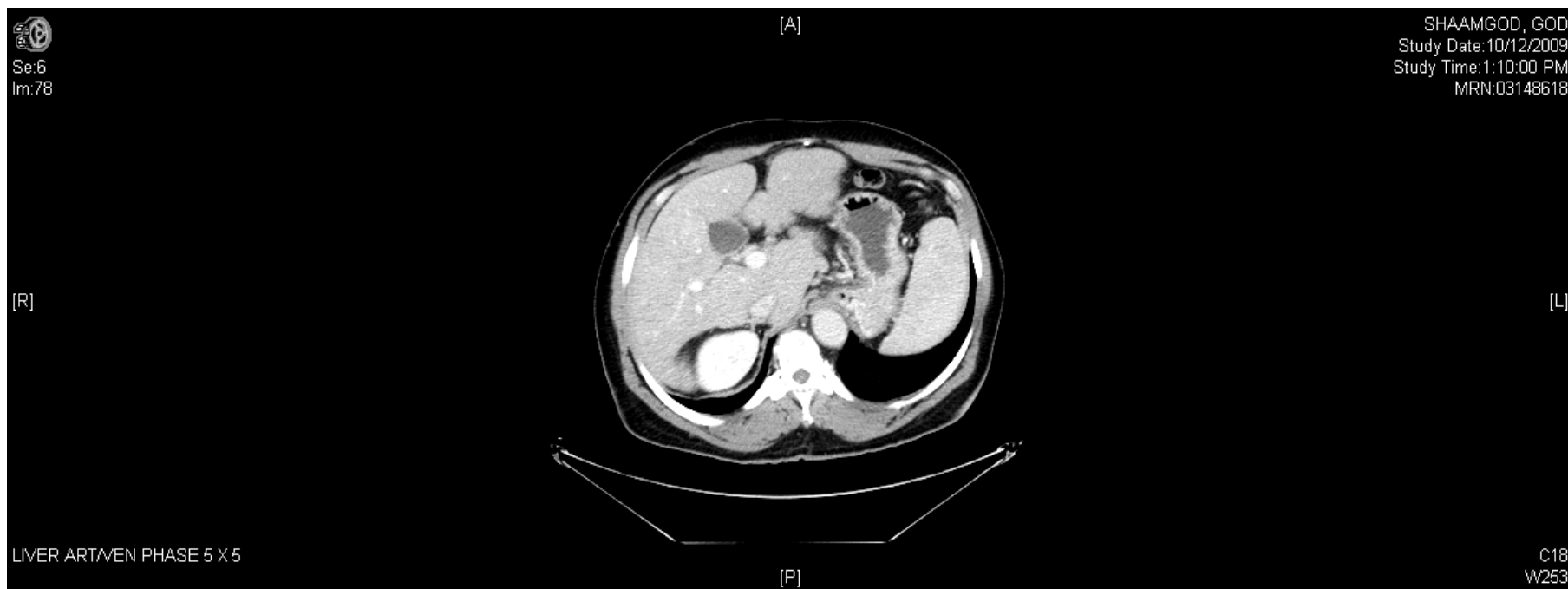
- Solid liver lesions in older patients are more likely to be malignant, with metastases more common than primary liver cancer in the absence of liver disease
- Solid liver lesions in patients with chronic liver disease (cirrhosis or active Hepatitis B) are more likely to represent primary liver cancer rather than metastases or benign tumors.
- In non cirrhotic patients, the most common solid liver tumor is hemangioma

Basic questions

- Is the lesion cystic or solid?
- Does the patient have risk factors for malignancy (age, prior malignancy?)
- Does the patient have known liver disease or risk factors for liver disease?



50 year old man comes to the ED with vague abdominal pain, has a CT with contrast which shows hypertrophy of the caudate lobe, slight nodularity of the spleen

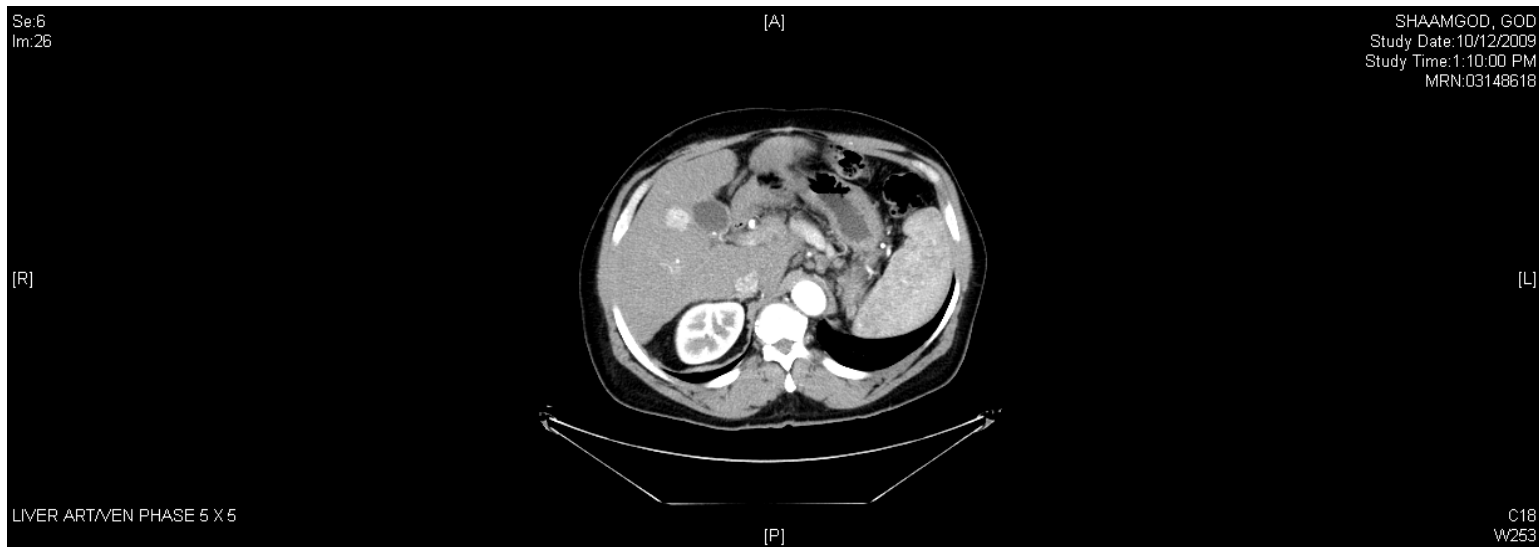


Normal bilirubin, normal Alk Phosph,
AST/ALT are moderately abnormal
WBC normal, Platelets 100K

GI Evaluation

- HCV antibody positive
- Active virus confirmed by PCR
- AFP 100

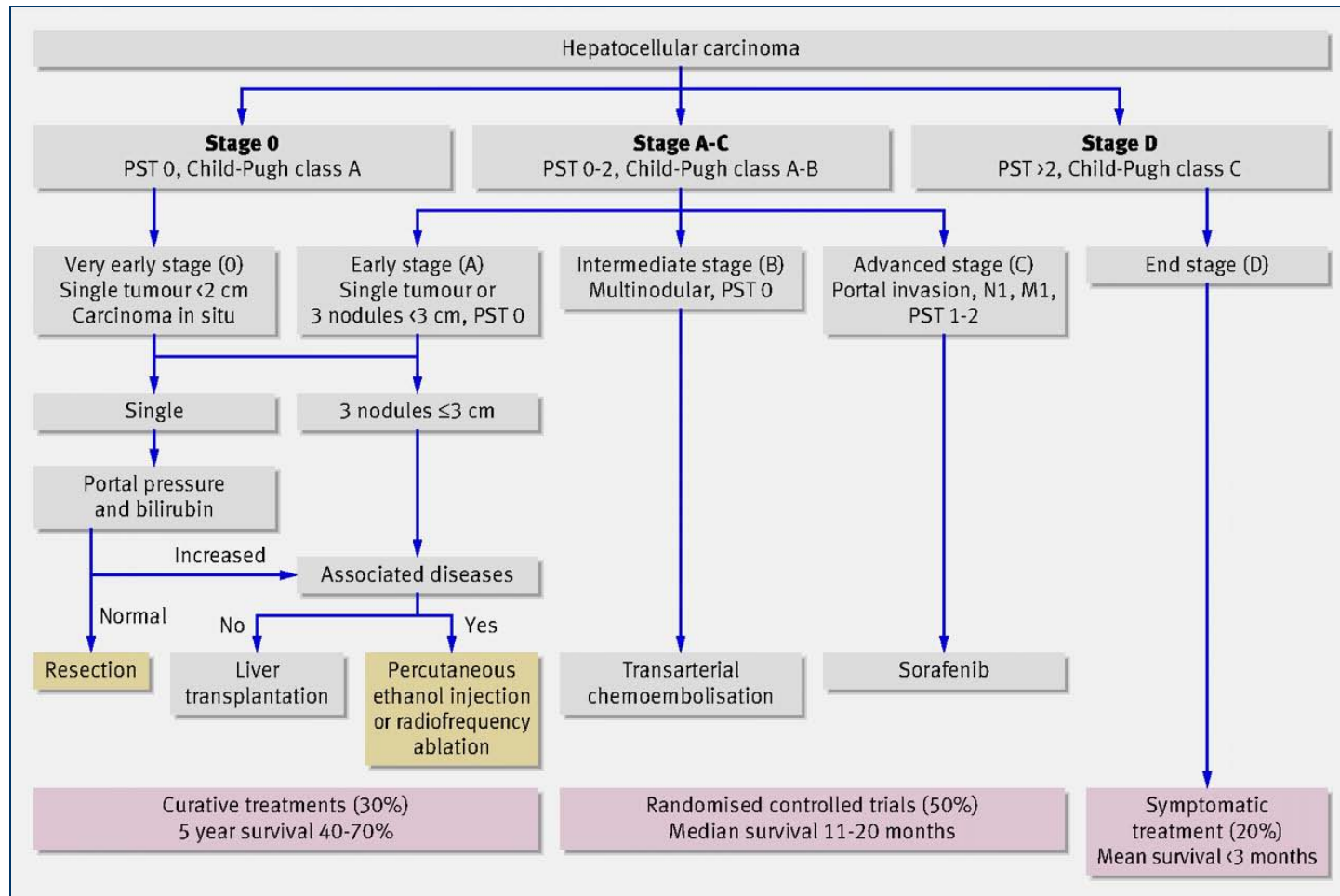
CT with liver protocol (multiphase contrast imaging)



AASLD Practice Guidelines For HCC Diagnosis of Lesions found on Screening in At Risk Groups

- Suspicious lesions less than 1cm : surveillance imaging only
- Typical lesions over 1cm can be diagnosed radiologically, without biopsy:
 - Multiphase imaging with two modalities increases the positive predictive value
 - If lesions are not typical in enhancement pattern on imaging, then biopsy is indicated, or document growth with serial imaging

Therapeutic Options In HCC



- 30 year old woman who is a student in an ultrasound technologist school underwent an abdominal ultrasound as part of a simulation session, was found to have a 5cm solid right lobe liver lesion

History

- She has no symptoms
- Currently on oral contraception
- No prior liver disease
- Lesion is solid on US



Differential Diagnosis of Solid Liver Lesions in Young Patients without Liver Disease

- Focal Nodular Hyperplasia
- Adenoma
- Hemangioma
- Less likely:
 - Well differentiated hepatocellular carcinoma
 - Hypervascular metastasis (renal cell, neuroendocrine tumor)

- Best single next test is a multiphase MRI with gadolinium (Magnevist)
 - FNH and adenoma: rapidly enhancing and washes out quickly
 - FNH's have central scars
 - FNH v Adenoma can be further if necessary using specialized MRI contrast agents (Eovist-gadoxetic acid)
 - Hemangioma: centripetal enhancement pattern and delayed wash out

Diagnosis of Solid Liver Lesions in Young Patients

- Adenoma
- Hypervascular
- Purely a hepatocyte tumor, cold on nuclear sulfur colloid scan
- May cause pain and can bleed
- Malignant degeneration

Focal Nodular Hyperplasia

Hypervascular

Contains all the liver ultrastructure including RES and bile ductules (isointense on sulfur colloid scan)

May cause pain

Central scar

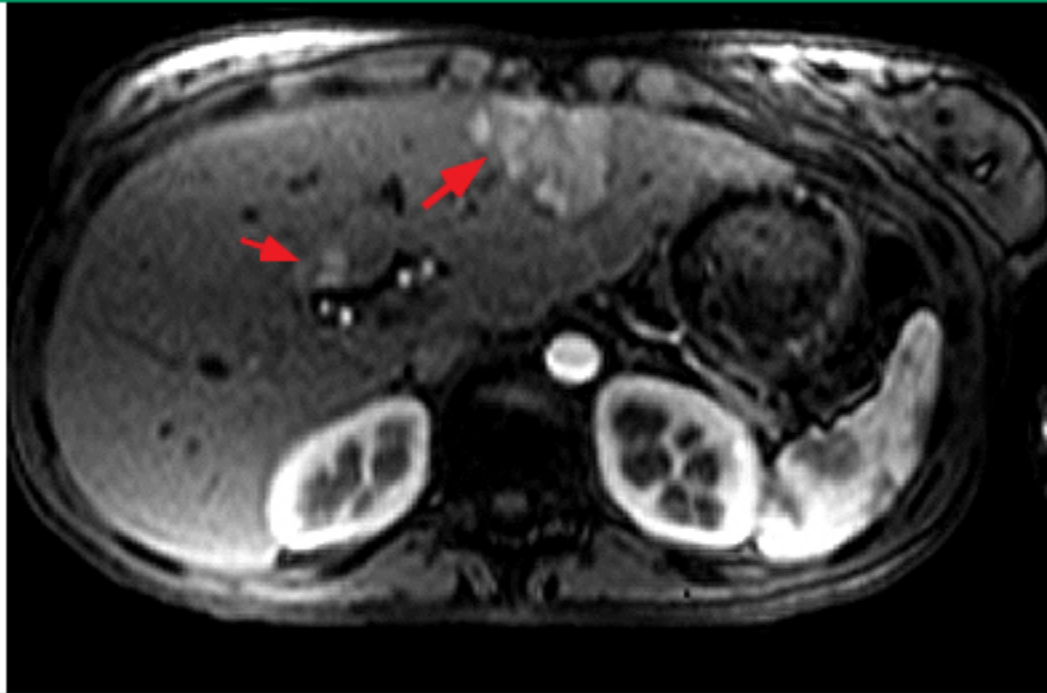
No malignant risk

Minimal bleeding risk

Hepatic Adenoma Demographics

- Most are solitary fat containing lesions
- Incidence is increasing
- Often found incidentally on imaging
- Usually in the right lobe
- Most common in young women
- Symptoms (pain, bleeding) are size related
- Multiple adenomas (adenomatosis) is a rare condition associated with Glycogen Storage Diseases

Hepatic adenomas



This gadolinium enhanced magnetic resonance image of the liver acquired during the early bolus phase of contrast administration demonstrates two enhancing masses in the liver, one in the left lateral segment, the second immediately anterior to the right portal vein (arrows). The enhancement characteristics are non-specific and are seen with any vascular tumor of the liver.

Courtesy of Jonathan Kruskal, MD.

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Hepatic Adenoma Association with Oral Contraception and Androgenic Steroids

- Association is well documented, but there are no large epidemiologic studies to quantify risk
- Mechanism of hepatocyte transformation is poorly understood, but there are identifiable oncogene mutations within adenomas that confer malignant risk.
- Risk of adenomas appears related to the duration of OC use (> 2 years) and estrogen component, but adenomas have been described with even 6 months of OC use.
- Regression can occur after discontinuation

Hepatic Adenoma Symptoms are Size and Location Related

- Pain related to capsular distension/compression
- Pain related to necrosis
- Pain related to intralesional bleeding
- Life threatening hemorrhage
 - Risk increased with size, symptomatic lesions, subcapsular location, long duration OC use.

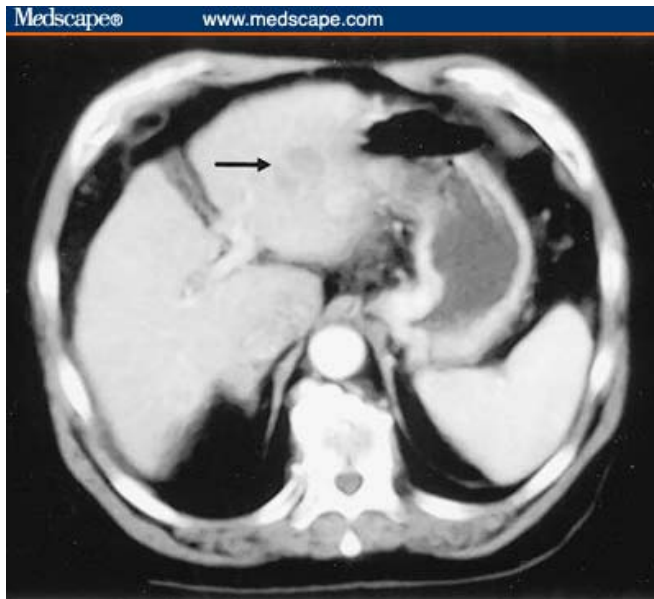
Hepatic Adenoma Management

- Small asymptomatic adenomas in women on OC: Resect or conservative management?
 - Risk of malignant degeneration and need for lifelong surveillance imaging and AFP screening
 - Major hepatic resection (lobectomy) is associated with 20-30% morbidity, which may not be reasonable in young women with asymptomatic benign tumors

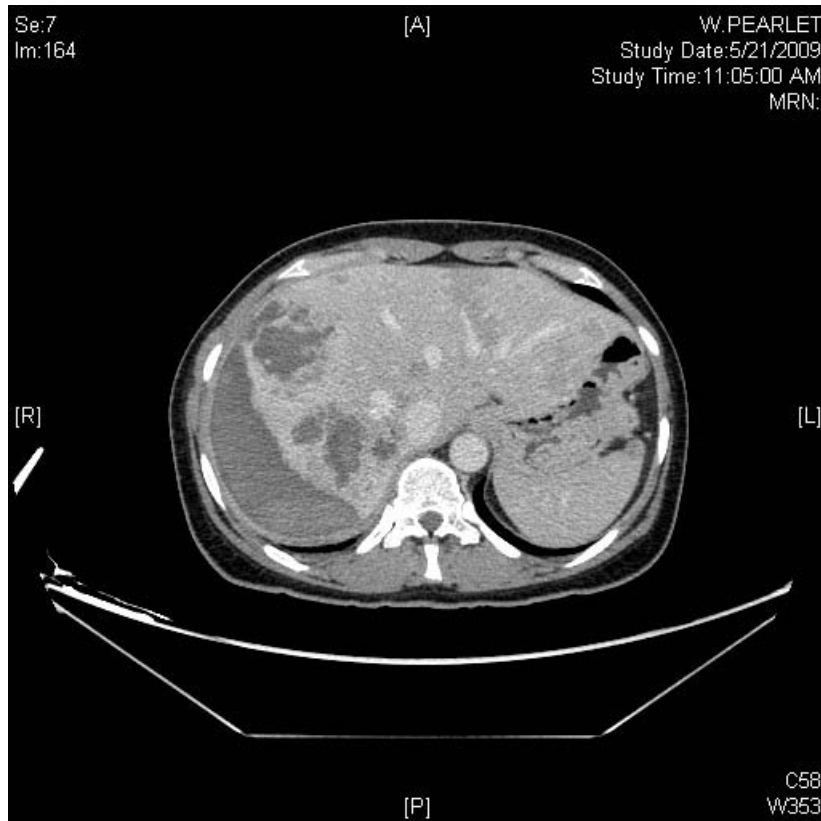
Montefiore Approach

- Resection of large (>5cm) or symptomatic adenomas
- Discontinuation of OC in asymptomatic smaller adenomas and counselling regarding options, including future pregnancy
- Patients with subcapsular lesions and those planning future pregnancy may be better served with resection

Minimally Invasive Hepatic Resection



Ruptured adenoma management



- Monitored setting of care, resuscitation and pain control
- Urgent embolization
- Elective resection after resolution of acute hematoma may permit more limited resection
- Urgent resection if ongoing bleeding

Focal Nodular Hyperplasia

- Thought to be a congenital vascular anomaly; associated with Osler-Weber-Rendu and liver hemangiomas (in up to 20%)
- Lesions classically (though not always) have a central scar containing an unusually large artery, with radiating branches to the periphery (Hub and spoke pattern)
- Lesion is a hyperplastic response to abnormal arterial flow
- Sinusoids, bile ductules, and Kupffer cells are present on histology

Focal nodular hyperplasia of the liver

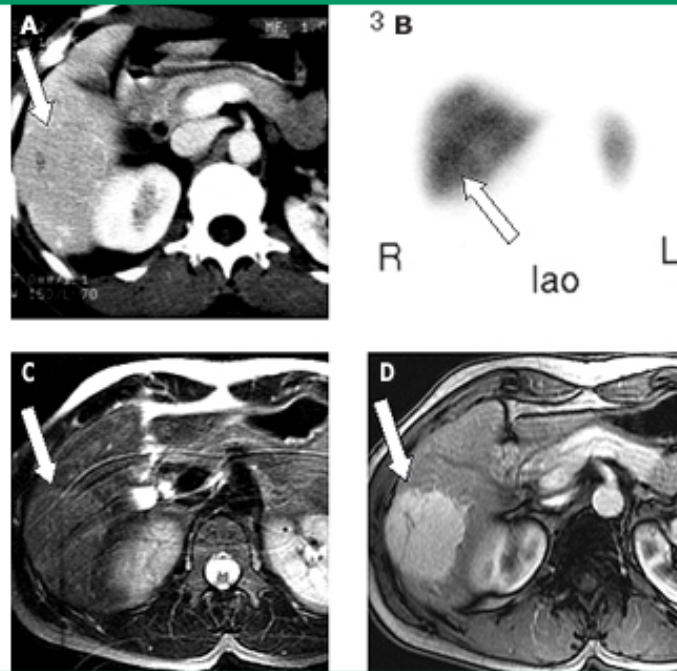


Surgical specimen showing a mass lesion within a noncirrhotic liver. Note the central stellate scar.

Courtesy of Frank A Mitros, MD.

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Focal nodular hyperplasia



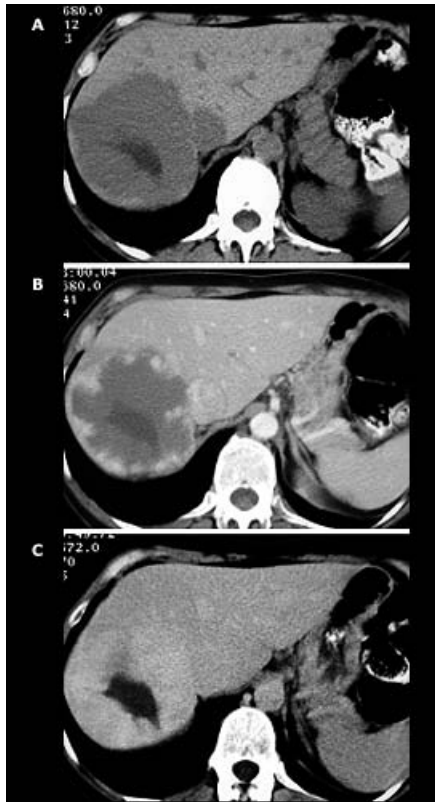
Radiologic findings of focal nodal hyperplasia in an asymptomatic 47-year-old woman. Panel A: Contrast-enhanced CT scan shows an area of slight heterogeneity (arrow) in the right lobe of the liver, but a discrete mass is difficult to identify. Panel B: Technetium-99 sulfur colloid scan shows uptake in the mass (arrow) similar to the rest of the liver. This finding is diagnostic of focal nodular hyperplasia. Panel C: T2-weighted MR image shows the mass (arrow) as slightly increased signal intensity. Panel D: Arterial-phase dynamic gadolinium chelate-enhanced T1-weighted gradient-echo MR image shows rapid intense enhancement of the mass (arrow), typical of focal nodular hyperplasia.

Courtesy of Eric Outwater, MD.

FNH Natural History and Management

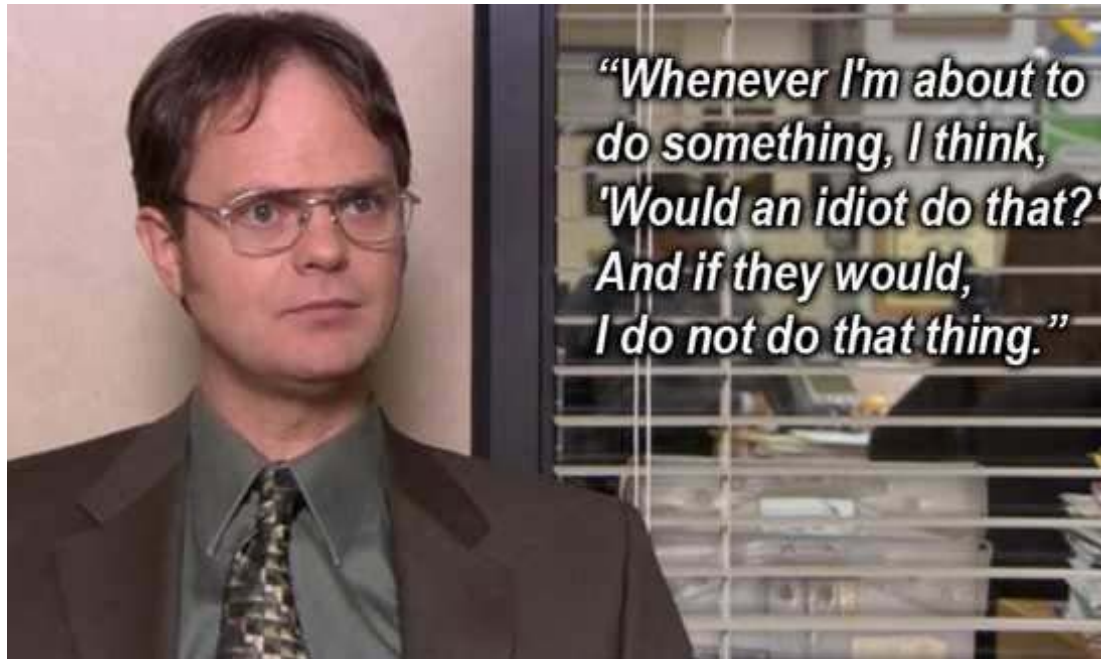
- Benign course, no malignant degeneration or bleeding
- Have been reported to increase in size during pregnancy
- May be responsive to estrogens, though discontinuation of OC is not a routine recommendation.
- No specific intervention is required, except possibly serial imaging for 6-12 months to confirm absence of changes

Hepatic hemangioma characteristics

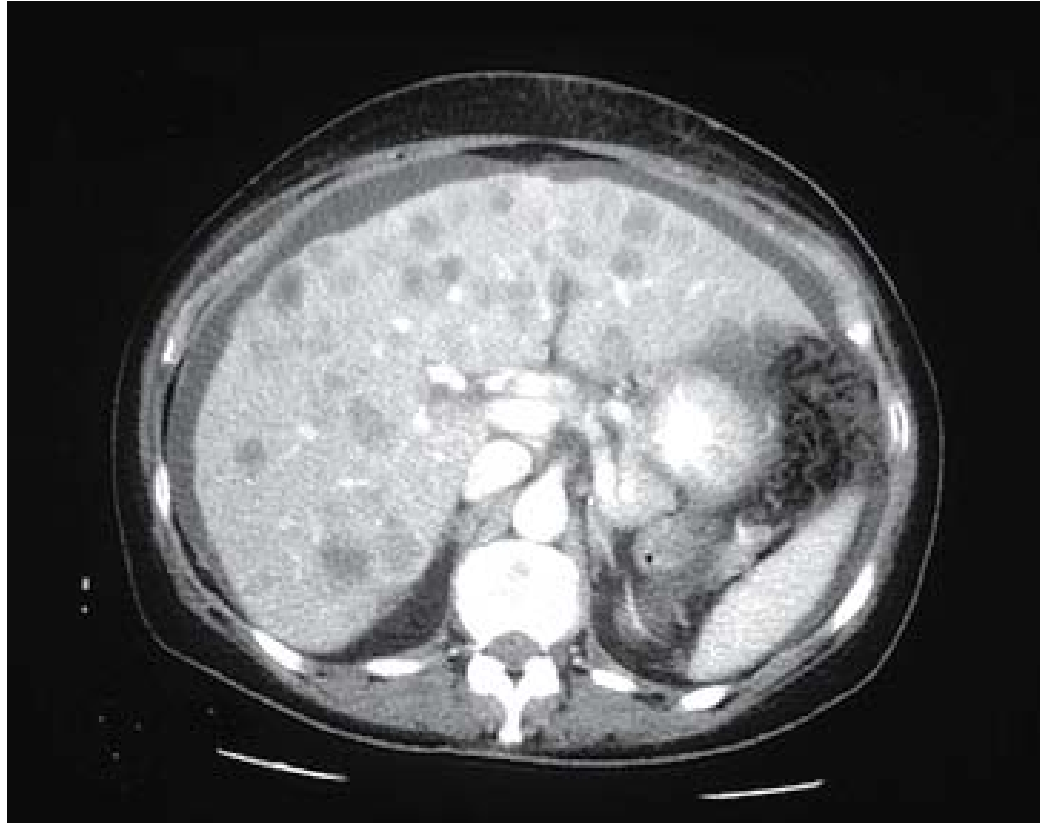


- Peripheral nodular enhancement on MRI
- Centripetal filling in on delayed phase
- Need for Tc99 RBC scan is low in the era of MRI
- Risk of extrahepatic hemorrhage low even with large lesions
- No intervention required in asymptomatic patients--Serial imaging to evaluate growth
- Symptoms may be caused by distention/compression when they reach large size, in which case resection may be indicated
- No role for embolization

Intermission

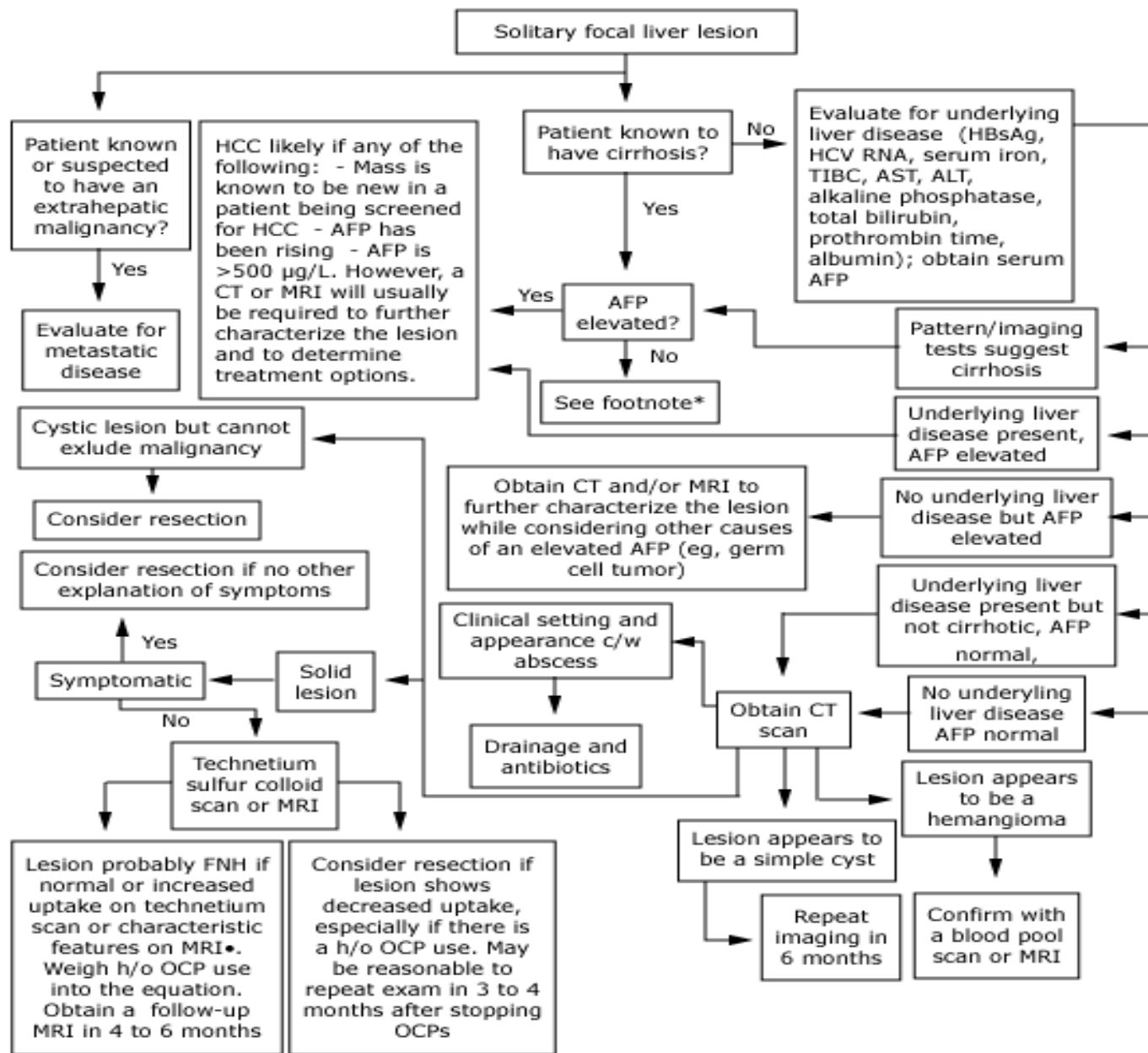


Liver metastases

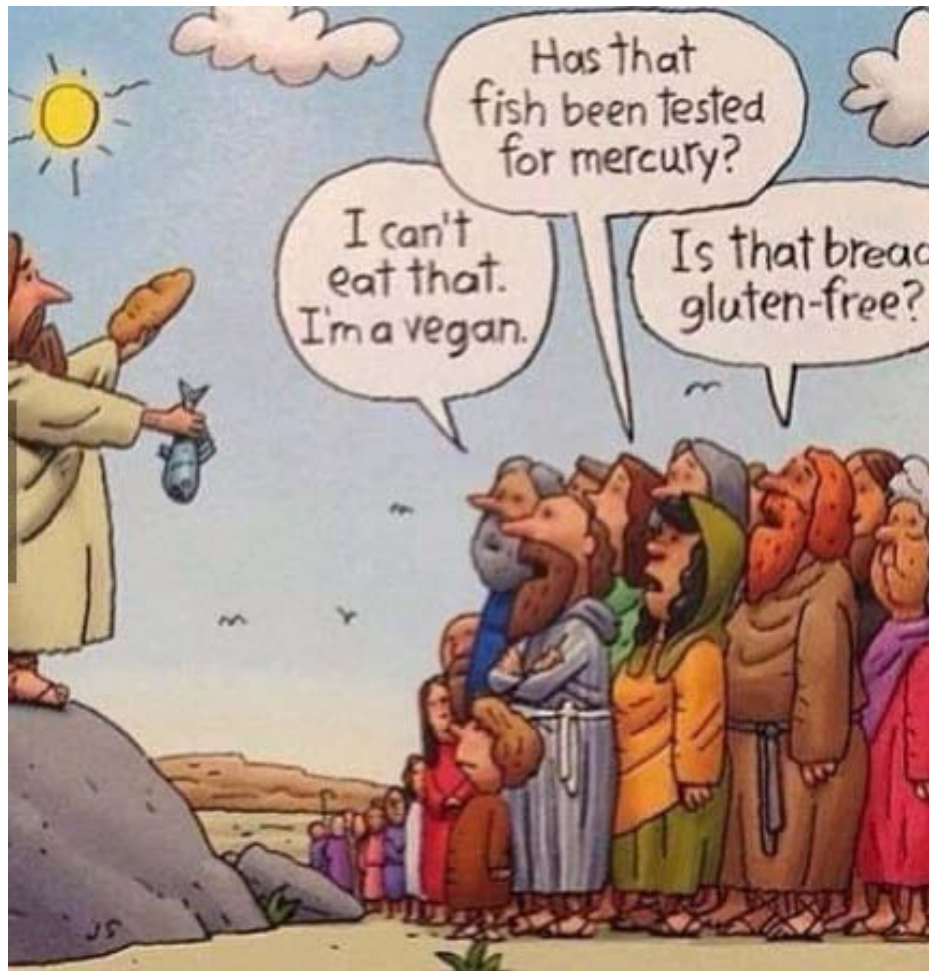


Suspected metastatic disease

- Multiple hypodense liver lesions on imaging or a focal liver lesion in a patient with known or suspected malignancy
 - Tumor markers
 - Evaluation for common sources of tumor
 - Colonoscopy, abdominal and chest imaging, mammography, directed nuclear scanning
- Histologic confirmation may be necessary if no primary is found (cancer of unknown primary)
- If patient has a known primary source and a liver lesion, PET can be helpful in certain tumor types that are PET avid



In conclusion...



Cystic lesions

Simple

Hydatid

Atypical

Polycystic
lesion

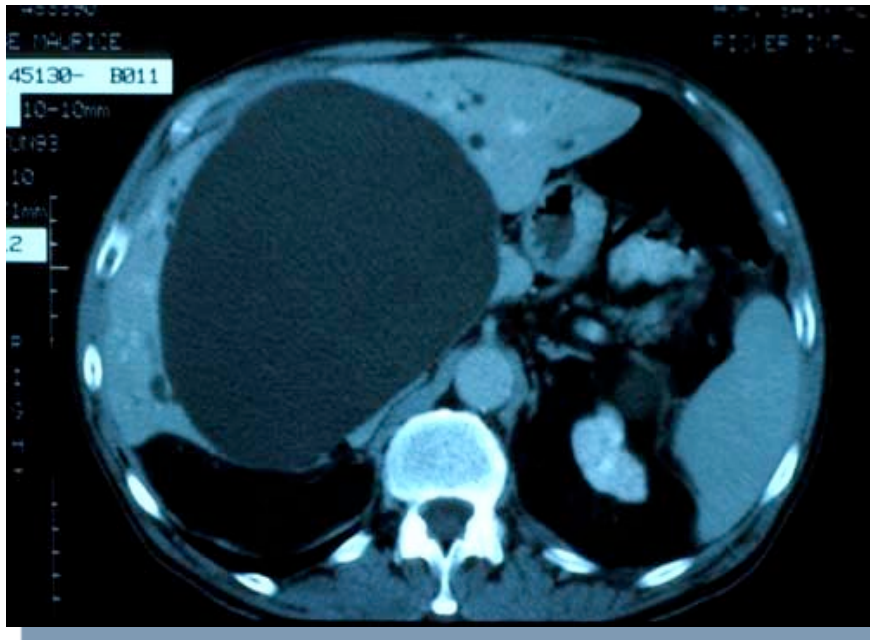
Pyogenic or amebic
abscess

Simple Cyst

- Liquid collection lined by an epithelium
- No communication with biliary tree
- Solitary and uniloculated
- Most of the time asymptomatic
- Symptoms can be related to
 - Intracystic haemorrhage
 - Infection
 - Rupture (rare)
 - Compression of adjacent structures



Simple Cyst



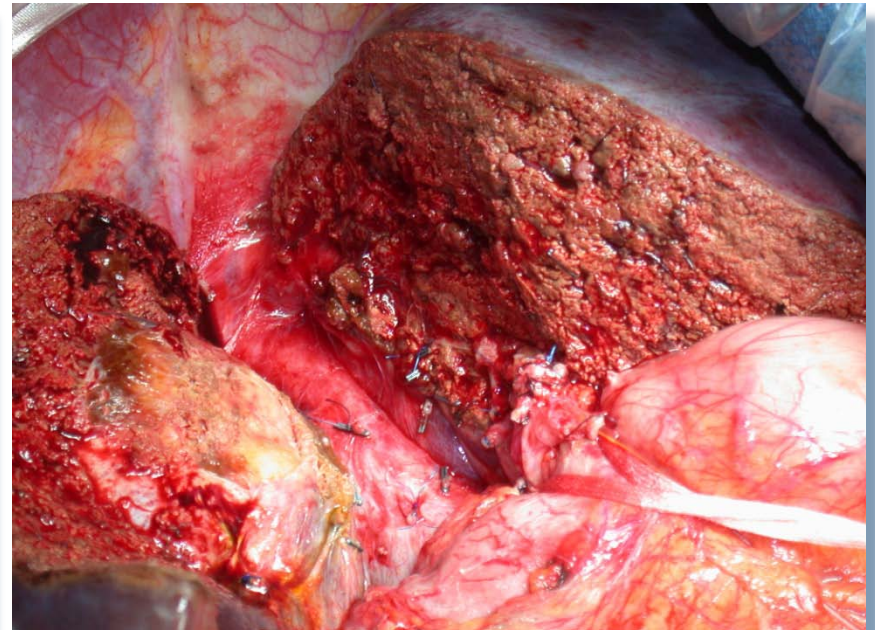
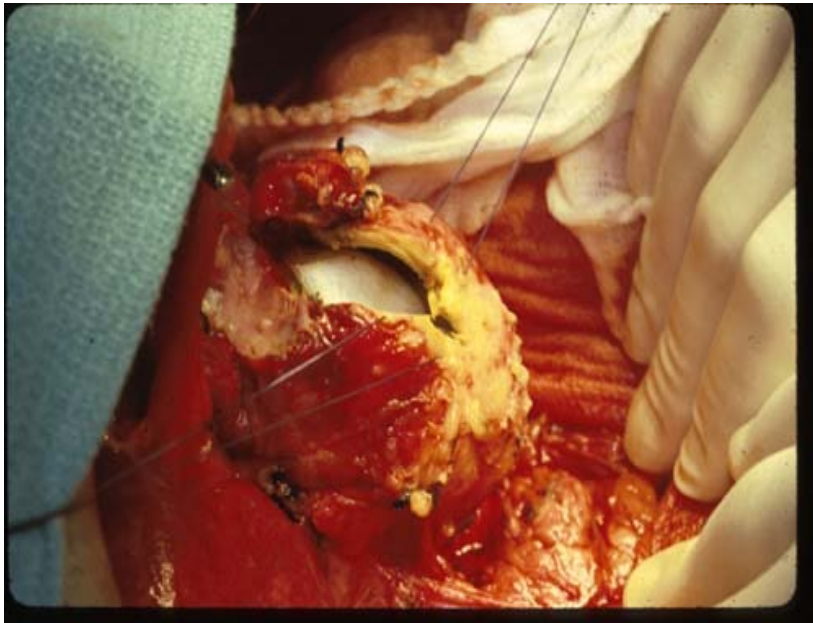
- No follow up necessary
- If doubt, imaging in 3-6 months
- If symptomatic or uncertain diagnosis (complex cystic lesion), then consider surgical intervention

Hydatid Cyst



- Echinococcus granulosus
- Endemic regions: Eastern Europe
- Patients may present with disseminated disease, or erosion of cysts into adjacent structures and vessels (IVC)
- Clinical diagnosis based on history, appearance, and serologic testing

Hydatid Cyst



Treatment: Marsupialization or resection,
albendazole

Liver Abscess

- High fever
- Leukocytosis
- Abdominal Pain
- Complex liver lesion
- History:
 - Abdominal or biliary infection
 - Dental procedure



Liver Abscess

- Initial empiric broad spectrum antibiotics
- Aspiration/drainage percutaneously
- Echocardiogram
- Operation if no clinical improvement:
 - Open drainage
 - Resection
- 4 weeks antibiotic therapy with repeat imaging