Abnormal LFT's: Patient Evaluation

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Abnormal LFT's: Goals
At the end of the session, you should:

- Recognize when abnormal liver tests are significant
- Determine the most probable cause (s) for the abnormality in your patient
- Choose the appropriate diagnostic strategy
- Refer to a specialist in a timely fashion

Abnormal LFT's: definitions

- What are "liver function tests"?
  - "Hepatic (liver) panel/profile"
  - Albumin, PT: synthetic function
  - Bilirubin: detoxification of metabolites and transportation of organic ions
  - Indicate severity (ex. Child's score)
- Which tests are the indicators of injury or damage?
  - Aminotransferases (ALT, AST)
  - Alk Phos
  - GGT

Abnormal LFT's: definitions

- ALT and AST
  - Markers of hepatocellular necrosis
  - Damage or destruction of tissue rich in AST and ALT or changes in cell membrane permeability allowing leakage into serum
  - AST (cytosol and mitochondria): liver, cardiac and skeletal muscle, kidneys, brain, pancreas, lungs, WBC's, RBC's
  - ALT (cytosol): mostly liver

Abnormal LFT's: definitions

AST and ALT:

- Do the levels of elevation mean anything?
  - how normal is "normal"?
  - "know your ALT"
- AST/ALT

Abnormal LFT's: definitions

- Alkaline phosphatase
  - Liver, bone, intestine, kidney, placenta and WBC's
  - 5'nucleotidase or GGT to establish liver origin
- Elevated Alk Phos mechanism: induction of enzyme synthesis and release (regurgitation) into the circulation

Abnormal LFT's: definitions

- Alk Phos ↑ : What does it mean?
  - Cholestasis
  - Infiltrative disease
- Significant levels: > **1.5** X ULN
  - Pregnant and older women have higher values
- GGT – cell membrane of kidney, pancreas, liver, spleen, heart, brain and seminal vesicles

Abnormal LFT's: What to do?

- Document chronicity and liver origin
- Is it significant?
- History and physical exam
- Now what?

Case # 1:
Elevated ALT and AST

Case # 1

A 46 y/o female is found with elevated ALT and AST during testing for insurance purposes. Her history reveals transfusions for an ectopic pregnancy 30 years ago, “social” alcohol use, no history of hepatitis and no use of illicit drugs. She has no symptoms except mild joint aches.

On physical exam she is overweight, with a BP of 150/90. No other significant findings are noted.

Case # 1

CBC, CMP, cholesterol and triglycerides show the following abnormalities:

Cholesterol – 280 mg%

ALT - 89

AST - 78

What are your possible diagnosis?

How to confirm it?

Case # 1

Dx	Test
Chronic viral hepatitis	**HCVab** **HBsAg, HBsAb, HBcAb**
NAFLD	
Autoimmune hepatitis	**s PEP**

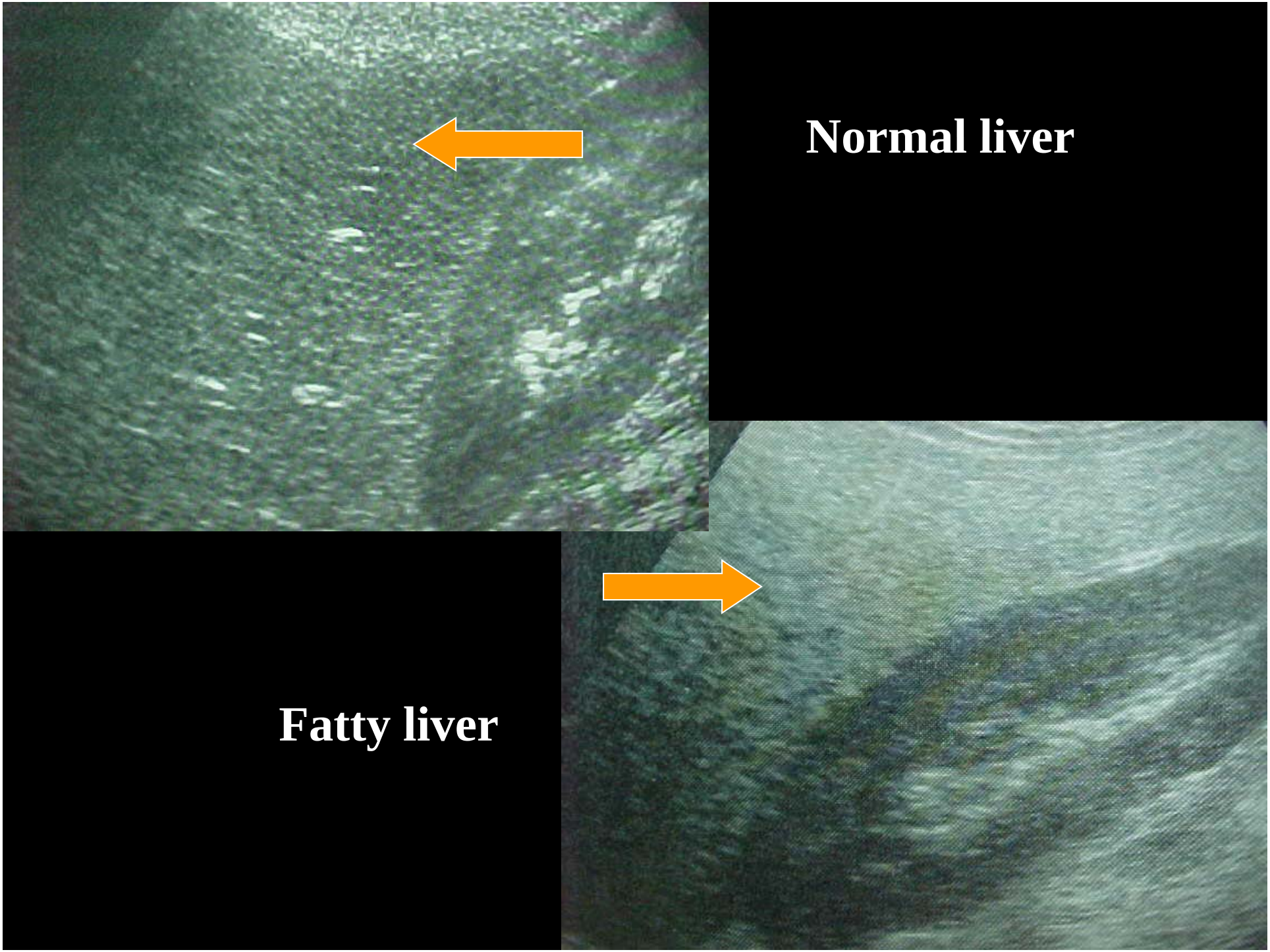
Any other ideas?

Case # 1

- Hepatitis serology is negative
- sPEP is normal
- Would you:
  - Do an ultrasound?
  - Do a liver biopsy?
  - Or?
- Would you give her statins?

Some facts about NAFLD

- Most common liver disease
  - 24% of population (NHANES III)
- Ranging from steatosis through steatohepatitis (NASH) to cirrhosis
- Associated factors: obesity, dyslipidemia, metabolic syndrome, diabetes
- No proven therapy
- Important predictor of CAD and diabetes
  - do not ignore the ALT!!!


Normal liver
Fatty liver

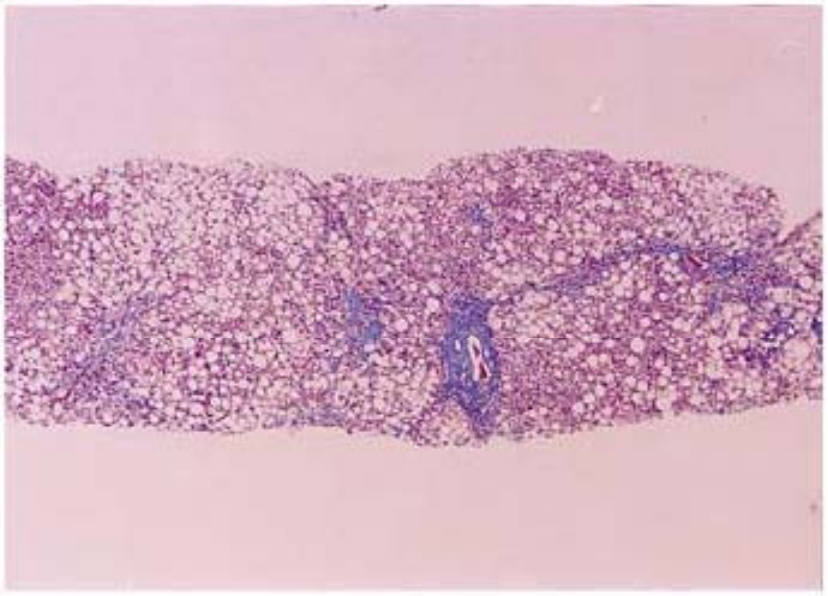
NAFLD and imaging

- > 33% fat for detection
- Steatosis vs NASH – no distinction

	Sensitivity %	PPV %
US	100	62
CT	93	76

Saadeh, Gastro 2002

Fatty liver



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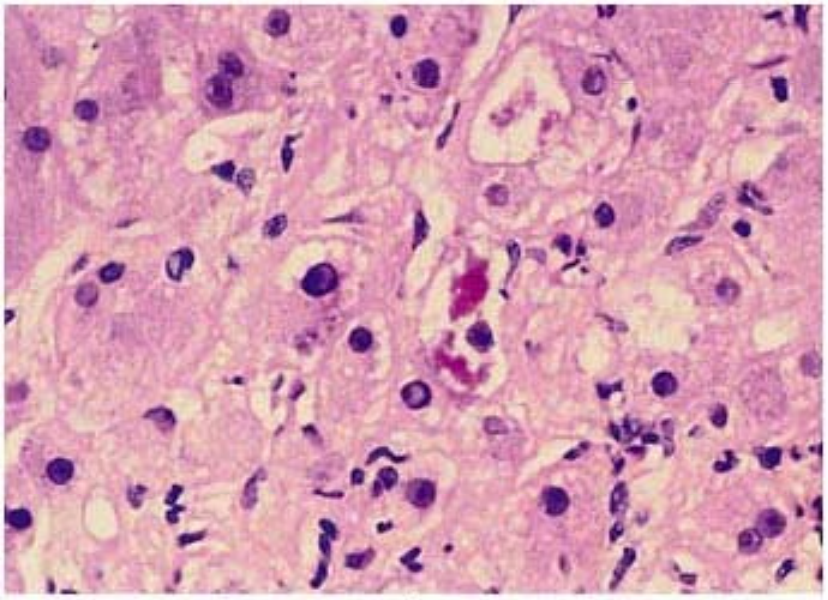

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Case # 2 :
elevated ALT and AST

Case # 2

The same 46 y/o lady now has the following lab results:

HCV ab – positive

HBV markers – negative

Case #2

You order?:

- HCV RIBA3
- HCV RNA
  - Qualitative
  - Quantitative
- HCV genotype
- Liver biopsy

Case #2

HCV RIBA 3	Only for neg RNA
HCV RNA qualitative	
HCV RNA quantitative	For prognostic and tx purposes
HCV genotype	To predict response to tx and duration
Liver bx	For prognosis and tx

Hepatitis C: some facts

- USA: 4 million infected
  - general prevalence 1. 8%
  - greater in Hispanics and blacks
  - general prevalence in PR 2.2%
- Slow evolution to cirrhosis (20%?) and end-stage liver disease
- Hepatocellular carcinoma a long-term complication (20% of cirrhosis)
- Most frequent cause for OLT in adults

Elevated aminotransferases: the common and not-so common

- Chronic viral hepatitis
- Alcoholic liver disease
- NAFLD
- Drugs
  - Many and any
  - 10% of "hepatitis"
  - 40% if > 40 y/o
- Autoimmune hepatitis
- The genetic:
  - Hereditary hemochromatosis
  - Wilson's disease
  - α-1 antitrypsin deficiency
- The rare: celiac disease
- The distractor: muscle disease

Abnormal enzymes: significance

- 81/1124 with negative markers:
  - 8 nl
  - 41 steatosis
  - 26 steatohepatitis
  - 4 fibrosis
  - 2 cirrhosis
    (Amer J Gastro 1999)
- 99/19877 donors (recruits) – 4 HBV, 4 HCV, 2 AIH, 87 no explanation (Dig Dis Sci 1993)

Abnormal enzymes: findings

- 149 asx – 64% fatty liver, 20% CAH/CPH, 6% cirrhosis, 4% A1ATD, 3.5% HHC
  (Scand J Gastro 1986)
- 5/36 – change in pre-bx diagnosis
  - 3 NASH to nl
  - 1 NASH to PSC
  - 1 ALD to nl
    (Amer J Gastro 2000)

Elevated aminotransferases: the initial tests

- HCV ab
- HBsAg, HBsAb, HBcAb
- s Fe and TIBC
- Ceruloplasmin (< 40 y/o)
- s protein electrophoresis

Case #3:
Elevated Alk Phos

Case # 3

A 50 y/o woman has history of intermittent RUQ pain for 6 months. She has now noticed dark urine for several days. No significant weight loss, no other complaints.

Physical exam shows an overweight woman in no distress, with mild jaundice.

Labs: Alk Phos – 300 , AST – 65, ALT- 70, T.Bili - 4.2

Case #3

- Your next step is:
- **Because you think she has:**

- US – cholelithiasis, CBD measures 1.5 cms and shows a stone distally
- ERCP – papillotomy and stone extraction performed uneventfully followed by lap chole

COMMON DUCT STONE


←STONE
SLUDGE

Case # 4:
elevated Alk Phos

Case # 4

A 50 y/o woman comes to your office because her gynecologist ordered some routine labs and found an elevated Alk Phos. She has history of hypothyroidism, on adequate replacemnet therapy.

Physical exam shows some palmar erythema, and a palpable liver.

Case # 4

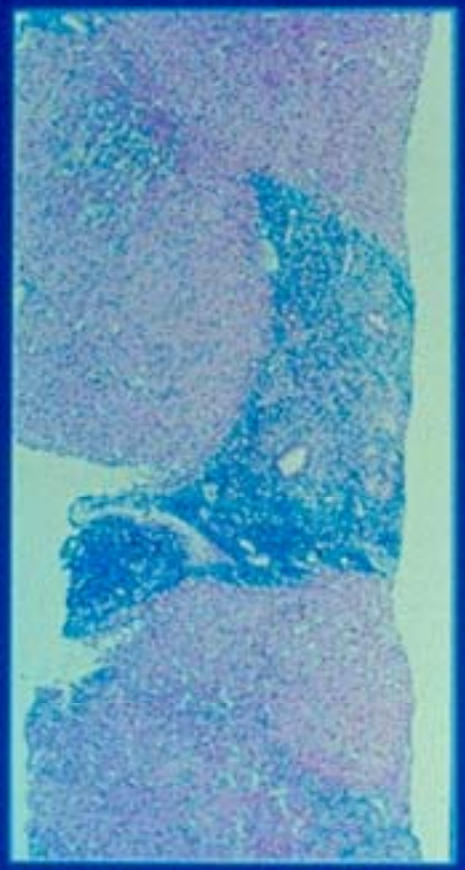
- Labs show:
  - Alk Phos - 350
  - T Bili - 1.0
  - ALT - 65
  - AST - 70
  - Cholest - 280

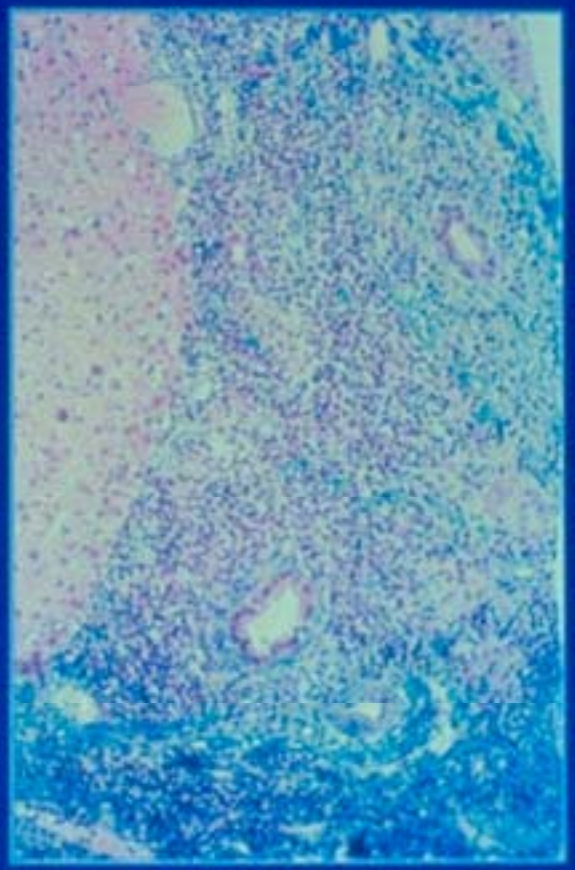
Case # 4

- Your next step is:

- Results of the tests are:
  - US – normal gallbladder and bile duct
  - AMA - 1:640
- Do you biopsy?

PRIMARY BILIARY CIRRHOSIS





Case # 5:
elevated Alk Phos

Case # 5

A 60 y/o male comes with RUQ discomfort and anorexia. He has noticed some recent constipation.

Physical exam shows an enlarged hard liver.

Labs show a Hgb of 11.3 gm%, and Alk Phos of 275.

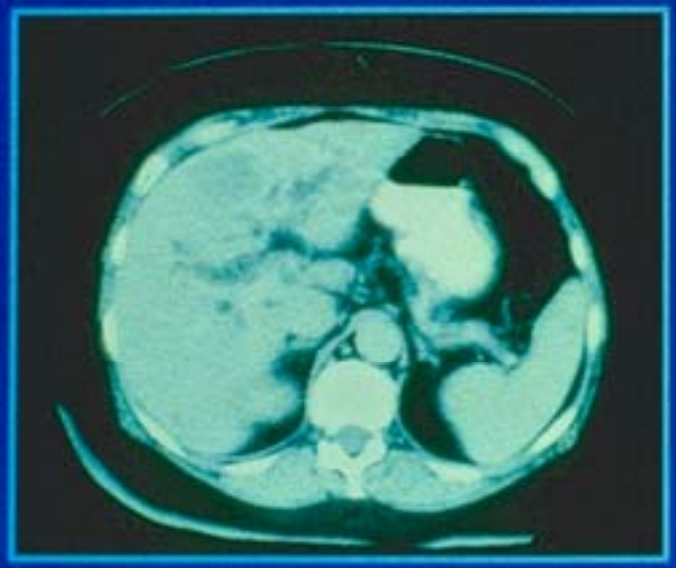
Case # 5

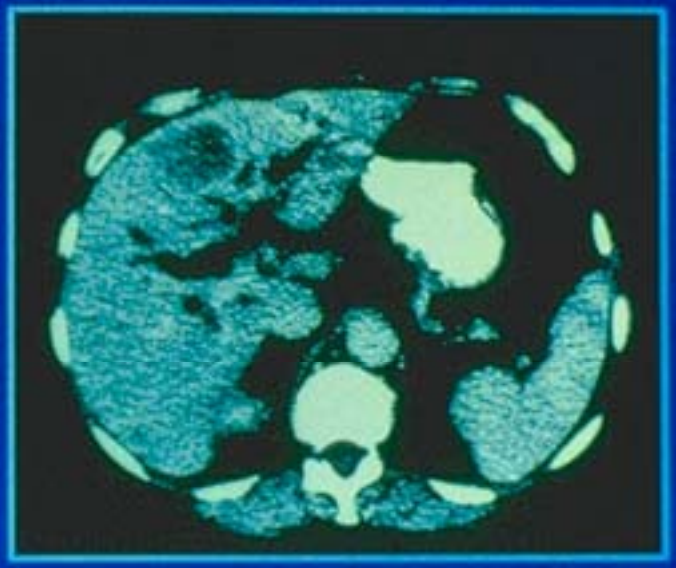
- You choose this test to investigate the cause of the abnormal Alk Phos:

- US or CT?

HEPATIC METASTASES

HEPATIC METASTASIS





Elevated alkaline phosphatase: Causes

- Liver/biliary vs other
  - 5’ –nucleotidase or GGT
- Chronic cholestasis
  - PBC
  - Bile duct obstruction
  - PSC
  - Adult ductopenia
  - Drug-induced
- Infiltrative diseases
  - Sarcoidosis
  - Other granulomatous diseases
  - Metastatic liver disease

Elevated alkaline phosphatase: what next?

AMA +

Liver bx

AMA –
US –
AP>1.5x uln

Liver bx
&
ERCP/MRCP

Elevated alkaline phosphatase: what next?

US: dilated ducts → ERCP

AP<1.5x uln, other tests nl → Observe

Abnormal liver tests: when to refer?

- For treatment decision of chronic viral hepatitis, including biopsy
- For biopsy and treatment of autoimmune liver diseases
- For ERCP/MRCP when indicated
- For liver biopsy of chronic significantly abnormal (>2xULN) liver tests
- For interventional evaluation of abnormal images (biopsy, arteriogram, etc)

When to biopsy?

Indications for Liver Biopsy

- Diagnosis, grading and staging of alcoholic liver disease, NASH and autoimmune hepatitis
- Grading and staging of chronic hepatitis B and C
- Diagnosis of hemochromatosis in index patients and relatives, quantitative iron

NEJM 2001;344:495-500

Indications for Liver Biopsy

- Diagnosis of Wilson's disease (quantitation of copper levels)
- Evaluation of cholestatic liver diseases PBC and PSC
- Evaluation of abnormal liver tests with negative or inconclusive serologic work-up
- Evaluation of effects of treatment regimens (ex. MTX for psoriasis)

NEJM 2001;344:495-500

Indications for Liver Biopsy

- Diagnosis of liver mass
- Evaluation of transplanted liver or donor liver
- Evaluation of FUO, with culture

NEJM 2001;344:495-500

Abnormal LFT's: Patient Evaluation Take-home points

- Abnormalities of ALT and AST are common
  - Medications are the first thing to look for
  - Fatty liver/NASH accounts for most of the others
- Ultrasound is useful
- Serious liver disease is frequently asymptomatic and must be considered in the patient with abnormal liver tests
- Chronic abnormalities may warrant a liver biopsy, but change of management is infrequent

Thank you!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