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UNIVERSITY OF MIAMI HEALTH SYSTEM

ELEVATED LIVER ENZYMES

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Financial Disclosures

- None

Objectives

1. Identify the components of the liver biochemistry profile and understand their meaning if abnormal
2. Identify and understand the significance of the true liver function test “LFTs”
3. Develop a differential diagnosis for abnormal liver biochemistries, including AST and/or ALT >1000
4. Follow an organized approach to evaluate abnormal liver biochemistries

Introduction

- Evaluation of abnormal liver enzymes in an otherwise healthy patient may pose challenge to most experienced clinician
- May not be necessary to pursue extensive evaluation for all abnormal tests, due to unnecessary expenses and procedural risks
- On the other hand, failure to investigate mild or moderate liver enzyme abnormalities could mean missing the early diagnosis of potentially life-threatening, but otherwise treatable conditions
- Liver enzymes are readily available and included in many routine labs
- Estimated that 1%-9% of asymptomatic patients have elevated liver enzyme levels when screened with standard “liver function panels”
- All persistent elevations of liver enzymes require methodical evaluation and appropriate working diagnosis

Introduction

- The following tests are recommended by the American Association for the Study of Liver Disease (AASLD) and the National Academy of Clinical Biochemistry (NCAB) to be used to evaluate patients with known or suspected liver disease

- Aspartate aminotransferase (AST)

- Alanine aminotransferase (ALT)

- Alkaline phosphatase (ALP)

- Total bilirubin

- Direct bilirubin

- Total protein

- Albumin

- Prothrombin time (PT)/INR

Markers of hepatocellular injury

Markers of cholestasis

True liver function tests (“LFTs”)



Lab Orders



- **Comprehensive Metabolic Panel (CMP)**
 - Total protein, albumin, globulin, AST, ALT, alk phos, total bilirubin
- **Hepatic Function Panel (7) - (LabCorp)**
 - Albumin, total bilirubin, direct bilirubin, AST, ALT, alk phos, total protein
- **Hepatic Function Panel (Quest Diagnostics)**
 - Total Protein, albumin, globulin (calculated), albumin/globulin ratio (calculated), total bilirubin, direct bilirubin, indirect bilirubin (calculated), alkaline phosphatase, AST, ALT

True Liver Function Tests (“LFTs”)

- Albumin
- INR
- Bilirubin

- **Hepatic Function Panel (7) - (LabCorp)**

- Albumin, total bilirubin, direct bilirubin, AST, ALT, alk phos, total protein

- **Hepatic Function Panel (Quest Diagnostics)**

- Total Protein, albumin, globulin (calculated), albumin/globulin ratio (calculated), total bilirubin, direct bilirubin, indirect bilirubin (calculated), alkaline phosphatase, AST, ALT

Investigation of abnormal liver biochemistries

1. Repeat testing to confirm isolated liver enzyme abnormality in otherwise healthy patient
 - Unless clinical context points toward obvious etiology (e.g. abnormal AST/ALT coinciding with start of new medication)
2. History and physical exam
3. History and physical exam
4. History and physical exam
5. Detailed laboratory workup
6. Abdominal imaging
7. Liver biopsy

Investigation of abnormal liver biochemistries

- If abnormality persists, further evaluation should be based on
 - 1) Pattern of liver injury
 - 2) Magnitude of enzyme elevation

Pattern of Liver Injury

Liver Disease Category				
Liver Biochemistry	Hepatocellular	Cholestatic	Mixed	Isolated hyperbilirubinemia
AST/ALT	++	wnl/+	++	wnl
Alk phos	wnl/+	++	++	wnl
Bilirubin (total)	wnl/+ to ++	wnl/+ to ++	wnl/+ to ++	+ / ++

Pattern of Liver Injury

R ratio

$$\frac{\text{ALT value / ALT ULN}}{\text{Alk Phos value / Alk Phos ULN}}$$

>5 Hepatocellular liver injury

2 – 5 Mixed pattern

<2 Cholestatic liver injury

Evaluation of liver enzyme elevations

Complete History

- (1) Patient age and ethnicity
- (2) Presence of signs/symptoms of chronic liver disease
 - Pruritus, jaundice, ascites, encephalopathy, GI bleeding
- (3) Risk factors for viral hepatitis
 - IV/intranasal drug use, body piercings, tattoo, sexual history, transfusion hx
- (4) Presence of comorbid conditions
 - Type 2 DM, HTN, HLD, obesity (NALFD); autoimmune dz (autoimmune hepatitis); emphysema (A1AT); neuropsychiatric symptoms (Wilson dz)

Evaluation of liver enzyme elevations

Complete History

- (5) History of EtOH consumption, medication use, and toxin exposure
- (6) History of other autoimmune disorders
 - Autoimmune hepatitis, PBC
- (7) Family history of genetic conditions predisposing to liver disease
 - Hemochromatosis or Wilson disease
- (8) History of chronic diarrhea or inflammatory bowel disease (IBD)
 - IBD, celiac sprue, thyroid disorders, etc
- (9) Presence of signs/symptoms of heart failure
 - Congestive hepatopathy

Liver Biochemistries

Hepatocellular Injury

- **AST**
- **ALT**
- **LDH (lactate dehydrogenase)**

Cholestasis

- **Alkaline phosphatase**
- **Bilirubin**
- **Gamma-glutamyltransferase (GGT)**
- **5'-nucleotidase**

Liver Function Tests

- **Albumin**
- **INR**
- **Bilirubin**

Serum Aminotransferases

- Collectively most sensitive marker of hepatocellular injury
- Aspartate aminotransferase → AST (formerly SGOT)
- Alanine aminotransferase → ALT (formerly SGPT)
- Important contributors to citric acid cycle

AST

- Found in cytosol and mitochondria
- Widely distributed throughout the body: **Liver** > cardiac muscle > skeletal muscle > kidney > brain > pancreas > lung > leukocytes > erythrocytes

ALT

- Found in cytosol
- Exists mainly liver, but exists in low concentrations in kidney, heart, and skeletal muscles
- More specific indicator of liver injury than AST

Serum Aminotransferases

- Increases in serum aminotransferase levels reflect
 1. Damage to tissues rich in these enzymes
 2. Changes in cell membrane permeability to allow AST/ALT to leak into serum
- Degree of elevation does not correlate with extent of liver injury
- AST $\frac{1}{2}$ life < ALT $\frac{1}{2}$ life (ALT remains elevated longer)

PLEASE....PLEASE do not use the term “transaminitis”

Reference Range for ALT

- The upper limits of normal (ULN) for ALT in healthy adults^{1,2}
 - Males: 29 – 33 U/L
 - Females: 19 – 25 U/L
- ULN for ALT recommended to guide management decisions³ (HBV therapy)
 - Males: 35 U/mL
 - Females: 25 U/mL

ELEVATION OF SERUM AMINOTRANSFERASES

BORDERLINE

<2x ULN

MILD

2-5x ULN

MODERATE

5-15x ULN

SEVERE

>15x ULN

- Degree of elevation does not correlate with extent of liver injury
- Degree of elevation in AST and ALT can provide insight into etiology of liver injury
- Acute liver failure (ALF) is defined as rapid development of hepatocellular dysfunction (INR >1.5) and mental status changes (HE, any stage) in a patient without preexisting liver disease within 26 weeks of onset of illness...*regardless of ALT level*

ELEVATION OF SERUM AMINOTRANSFERASES

BORDERLINE

<2x ULN

- **Non-alcoholic fatty liver disease (NAFLD)**
- **Alcoholic liver disease**
- **Acute/chronic viral hepatitis**
- **Drug-induced liver injury (DILI)**
- **Autoimmune hepatitis**
- **Hemochromatosis**
- **Cirrhosis (of any etiology)**

MILD

2-5x ULN

- Wilson disease
- Alpha-1 antitrypsin deficiency
- Toxic/ischemic hepatitis
- Congestive hepatopathy
- Total parenteral nutrition (TPN)
- Budd-Chiari syndrome
- Hepatic artery injury/thrombosis
- Celiac disease
- Acute biliary obstruction
- Liver trauma
- Post-liver surgery
- Veno-occlusive disease (sinusoidal obstruction syndrome)
- Diffuse neoplastic infiltration of the liver
- Hyperemesis gravidarum
- HELLP
- Acute fatty liver of pregnancy
- Hemophagocytic lymphohistiocytosis

Nonhepatic Causes of Elevated Serum Aminotransferases

- Skeletal muscle damage (rhabdomyolysis)
- Strenuous exercise
- Cardiac muscle damage
- Thyroid disease
- Macro-AST
- Heat stroke
- Hemolysis
- Adrenal insufficiency
- Anorexia nervosa

ELEVATION OF SERUM AMINOTRANSFERASES

SEVERE
>15x ULN

- Acute viral hepatitis (especially HAV, HBV, HCV hepatitis)
- Ischemic hepatitis (“shock liver”)
- Vascular disorders (Budd-Chiari syndrome or acute hepatic artery occlusion)
- Toxin or drug-induced liver injury (DILI) (Acetaminophen, cocaine, flakka)
- Autoimmune hepatitis
- Acute biliary obstruction
- Diffuse neoplastic infiltration of the liver
- Wilson disease
- Rhabdomyolysis
- Heat stroke

MASSIVE
>10,000 UI/L

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AST:ALT ratio

ALT>AST

- Typical for most liver conditions, including chronic viral hepatitis and NAFLD

AST:ALT >1

- If AST >300 → consider alternative diagnosis than alcoholic liver disease
- If AST <300
 - AST:ALT >2 → suggestive of alcoholic liver disease (AST → **A** Scotch and Tonic)
 - AST:ALT >3 → highly suggestive of ALD
- Ratio results from deficiency of pyridoxal 5'-phosphate in pts with ALD
 - ALT synthesis in liver requires pyridoxal phosphate more than AST synthesis

The Alcoholic Liver Disease/Nonalcoholic Fatty Liver Disease Index (ANI)

- ANI is novel scoring system that accurately distinguishes alcoholic liver disease (ALD) from nonalcoholic fatty liver disease (NAFLD)
- Most accurate when MELD <20

AST: IU/l

ALT: IU/l

MCV: fL

Weight: kg lb

Height: m in

Gender: Male Female

Calculate ANI

ANI score:

Probability of Alcoholic Liver Disease: %

<https://www.mayoclinic.org/medical-professionals/model-end-stage-liver-disease/alcoholic-liver-disease-nonalcoholic-fatty-liver-disease-index>

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Lactate Dehydrogenase (LDH)

- Ubiquitous cytoplasmic enzyme
- LDH reversibly catalyzes conversion of lactate and NAD⁺ to pyruvate and NADH
- Serum LDH activity is very high in patients with ***ischemic hepatitis*** and ***neoplasms with hepatic involvement***
- ALT:LDH <1.5 → ischemic/toxic hepatitis
- ALT:LDH >1.5 → viral hepatitis

Sensitivity 94%
Specificity 84%

Workup for Elevated Serum Aminotransferase Levels

BORDERLINE

<2x ULN

- History and physical exam
- Discontinue all hepatotoxic medications and EtOH
- Assess for risk factors for fatty liver and viral hepatitis

- Routine labs: CBC, CMP, PT/INR
- Additional labs: **“Rules of 3”**

- Imaging: Liver ultrasound with Doppler, Fibroscan, CT/MRI, MRCP, ERCP

- If workup negative, consider liver biopsy

MILD

2-5x ULN

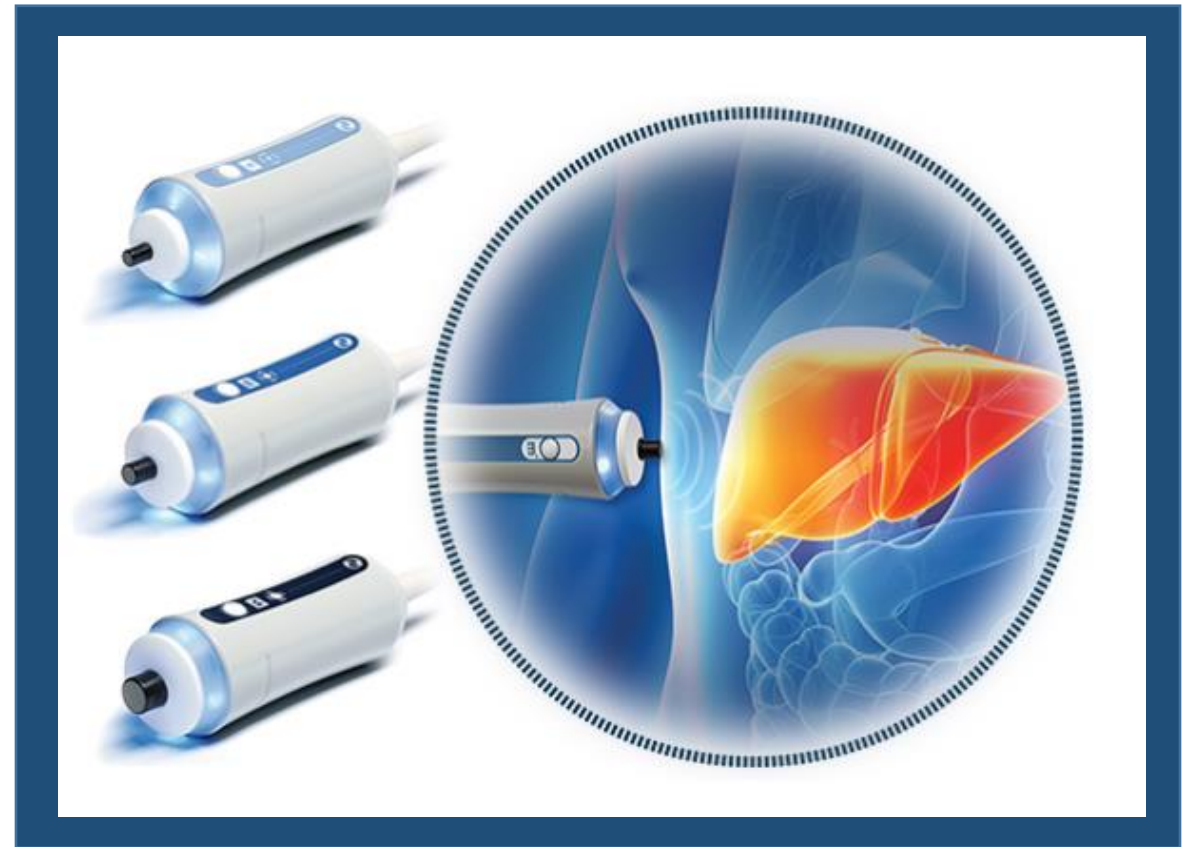
“Rules of 3”

- (1) Viral
 - i. HAV – HAV Ab IgM/IgG
 - ii. HBV – HBsAg, HBsAb, HBcAb IgM/IgG [HBV DNA if (+)]
 - iii. HCV – HCV Ab [HCV RNA if (+)]
- (2) Autoimmune
 - i. ANA (anti-nuclear Ab)
 - ii. ASMA (anti-smooth muscle Ab)
 - iii. AMA (anti-mitochondrial Ab)
- (3) Metabolic
 - i. Iron panel/ferritin (Hereditary hemochromatosis)
 - ii. Ceruloplasmin (Wilson disease)
 - iii. A1AT phenotype (A1AT deficiency)

FIBROSCAN

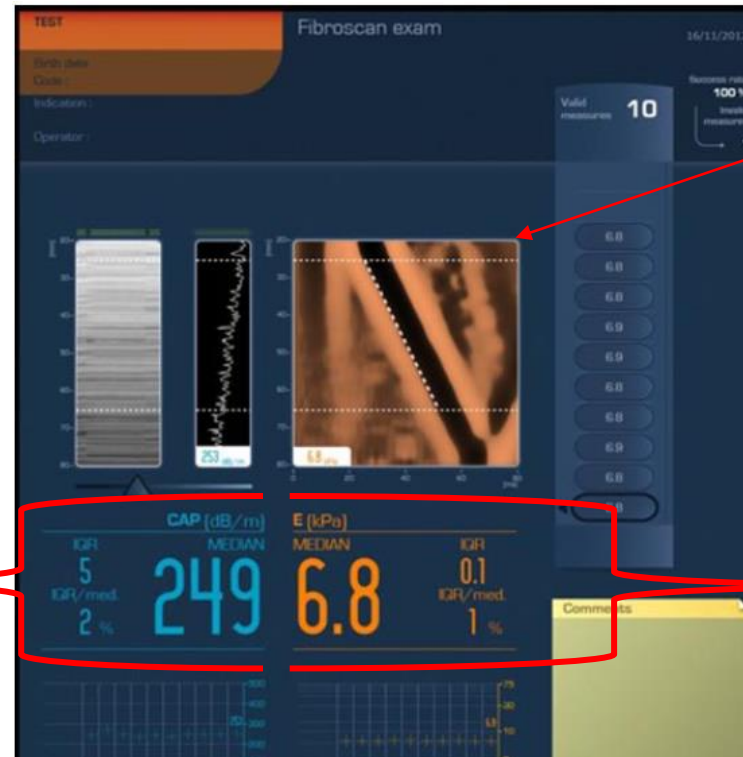
- Non-invasive device that assesses the “hardness” (or stiffness) of the liver using technique called transient elastography
- Liver hardness is evaluated by measuring the velocity of a vibration wave generated on the skin
- Because fibrous tissue is harder than normal liver, degree of hepatic fibrosis can be inferred from the liver hardness

FIBROSCAN



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FIBROSCAN



• **Elastogram**

CAP

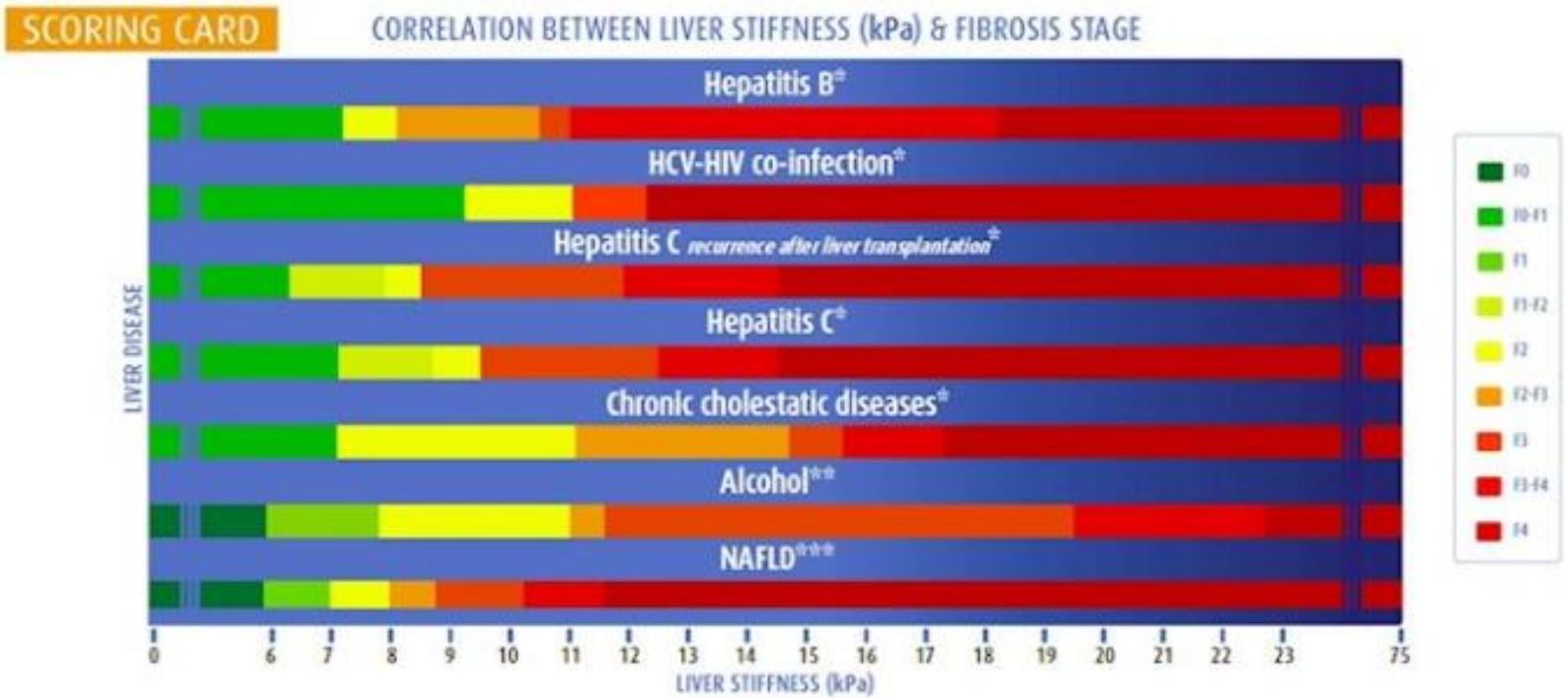
- Median (dB/m)
- IQR
- IQR/Median

Stiffness

- Median (kPa)
- IQR
- IQR/Median

1. ≥ 10 shots
2. Success rate $\geq 60\%$
3. Interquartile range (IQR) $\leq 25\%$

FIBROSCAN

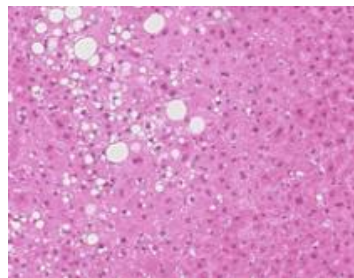


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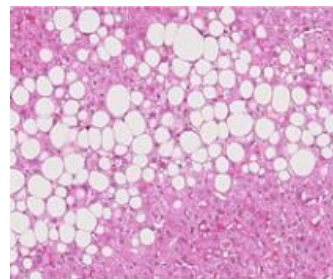
FIBROSCAN WITH CAP

- Controlled Attenuation Parameter (CAP) → measures steatosis
- Ranges 100 – 400 dB/m

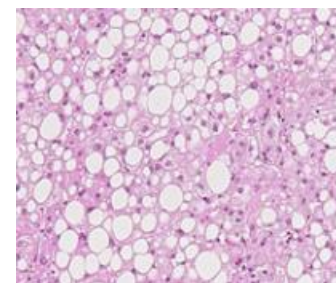
CAP Score	Steatosis Grade	Amount of Liver with Fatty Change (Steatosis)
238 – 260 dB/m	S1	11 – 33%
260 – 290 dB/m	S2	34 – 66%
>290 dB/m	S3	>66%



Grade S1



Grade S2



Grade S3

<https://livertox.nih.gov>



National Institutes of Health

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the National Institute of Diabetes and Digestive and Kidney Diseases



LiverTox

Clinical and Research Information on Drug-Induced Liver Injury

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Drug-Induced Liver Injury (DILI)

Antibiotics

- Amoxicillin-clavulanate (Augmentin)
- Minocycline
- Nitrofurantoin
- Sulfamethoxazole/trimethoprim (Bactrim)
- Sulfasalazine

Anti-arrhythmic

- Amiodarone
- Quinidine

Antimicrobial

- Isoniazid
- Ketaconazole
- Pyrizinamide
- Rifampin

Antihypertensive

- Hydralazine
- Methyldopa

Anti-epileptic

- Carbamazepine
- Phenytoin (Dilantin)
- Valproate (Depakene)

Immunosuppressant

- Azathioprine/
6-Mercaptopurine
- Infliximab (Remicade)
- Methotrexate

Misc...

- Anabolic steroids
- Atorvastatin,
Simvastatin
- Dantrolene
- Diclofenac, Sulindac
- Disulfiram (Antabuse)

Non-invasive algorithms for gauging liver fibrosis in patients with NAFLD

(1) NAFLD Fibrosis Score – age, BMI, AST/ALT, plt, alb, DM

(2) Fibrosis-4 (FIB-4)

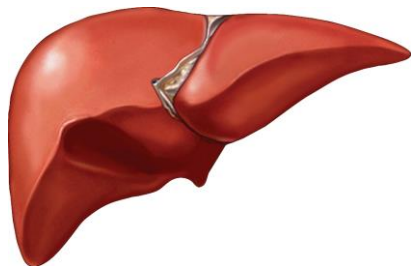
$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = \text{Yellow pill icon}$$

- **FIB-4 <1.45** → 90% negative predictive value for advanced fibrosis
- **FIB-4 >3.25** → 65% positive predictive value (97% specificity) for advanced fibrosis

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ENZYMES FOR DETECTION OF CHOLESTASIS

- Cholestasis develops from
 - (1) Defect in bile synthesis
 - (2) Defect in bile secretion
 - (3) Obstruction to bile flow
- Serum alkaline phosphatase (ALP) is traditional indirect marker of cholestasis
- Other enzymes that reflect that reflect cholestasis
 - 5'-nucleotidase
 - γ -glutamyltransferase (GGT)



ALKALINE PHOSPHATASE



- Group of enzymes that catalyze hydrolysis of organic phosphate esters at an alkaline pH
- Precise function is not yet known, but likely related to secretory activities of intrahepatic biliary epithelium
- Produced mainly in the liver (from biliary epithelium) and the bone
- Also found in smaller quantities in the
 - Intestine
 - Kidney
 - Placenta
 - White blood cells

ALKALINE PHOSPHATASE

- Normal distribution of the enzyme in the serum varies with age; normal serum range 20 – 140 IU/mL
- ALP activity 3x higher in young adults due to bone growth
- ALP activity 3-4x ULN in late pregnancy
- Intestinal contribution of ALP enhanced in patients with blood groups O and B after ingestion of fatty meals

ALKALINE PHOSPHATASE

- Elevation in ALP is not completely specific for cholestasis
- Mild elevation of ALP 2-3x ULN can be seen with almost any type of liver disease
- Elevations of ALP >4x ULN
 - Cholestatic liver disease
 - Infiltrative liver disease
 - Rapid bone turnover
- When alk phos is elevated in isolation, important to determine whether alk phos is of hepatic or non-hepatic origin
 - Obtaining additional enzyme testing with GGT and/or 5'-nucleotidase
 - Measurement of ALP isoenzymes using electrophoresis

5'-nucleotidase

- Enzymes found in the bile canalicular and sinusoidal membrane, but also found in the intestines, brain, heart, blood vessels, and pancreas
- Despite widespread distribution, ↑ serum levels of 5'-nucleotidase seen in pts with cholestasis similar to alk phos activity
- Negligible increase in pts with bone disease; therefore, used to confirm liver origin of ↑ alk phos in pts with suspected liver disease

Gamma Glutamyl Transpeptidase (GGT)

- Membrane-bound enzyme that catalyzes transfer of γ -glutamyl groups of peptides such as glutathione to other amino acids
- Abnormal values for GGT seen in same spectrum of disease as alk phos and 5'-nucleotidase
- GGT levels are increased in cholestasis and hepatocellular disease
- Not elevated in bone disease
- Elevated GGT has low specificity for liver disease
- Extensive evaluation of isolated elevated GGT in otherwise asymptomatic patient is not indicated

Non-Hepatic Causes of Elevated Alkaline Phosphatase

Physiologic

- Pregnancy
- Adolescence
- After fatty meal (blood type O and B)

Bone Disease

- Healing fractures
- Osteomyelitis
- Paget disease
- Vitamin D deficiency/Rickets
- Malignancy

Renal

- Renal failure

Heart

- Heart failure

Endocrine

- Hyperthyroidism
- Hyperparathyroidism

Malignancy

- Lymphoma
- Leukemia
- Renal cell carcinoma
- Multiple endocrine neoplasia

CAUSES OF ELEVATED ALKALINE PHOSPHATASE

Intrahepatic Cholestasis

- Drug-induced hepatitis
- Viral hepatitis (B, C)
- EtOH hepatitis
- Primary biliary cholangitis (PBC)
- Granulomatous liver disease
- Small duct PSC
- Autoimmune cholangiopathy
- Intrahepatic cholestasis of pregnancy (ICP)
- Infiltrative
 - Amyloidosis
 - Lymphoma
- TPN
- Cholestasis of sepsis
- Malignancy
- Genetic
 - Benign recurrent intrahepatic cholestasis (BRIC)
 - Progressive familial intrahepatic cholestasis (PFIC)

Extrahepatic Cholestasis

- Choledocholithiasis
- Malignancy
 - Pancreas
 - Gallbladder
 - Cholangiocarcinoma
 - Metastatic
- Large duct PSC
- Common hepatic/bile duct obstruction

WORKUP FOR CHOLESTASIS

Ultrasound

- Once alk phos confirmed to be of hepatic origin...
- Liver ultrasound to evaluate hepatic parenchyma and bile ducts
- Biliary dilatation suggests extrahepatic cause
- Non-dilated biliary systems suggest intrahepatic



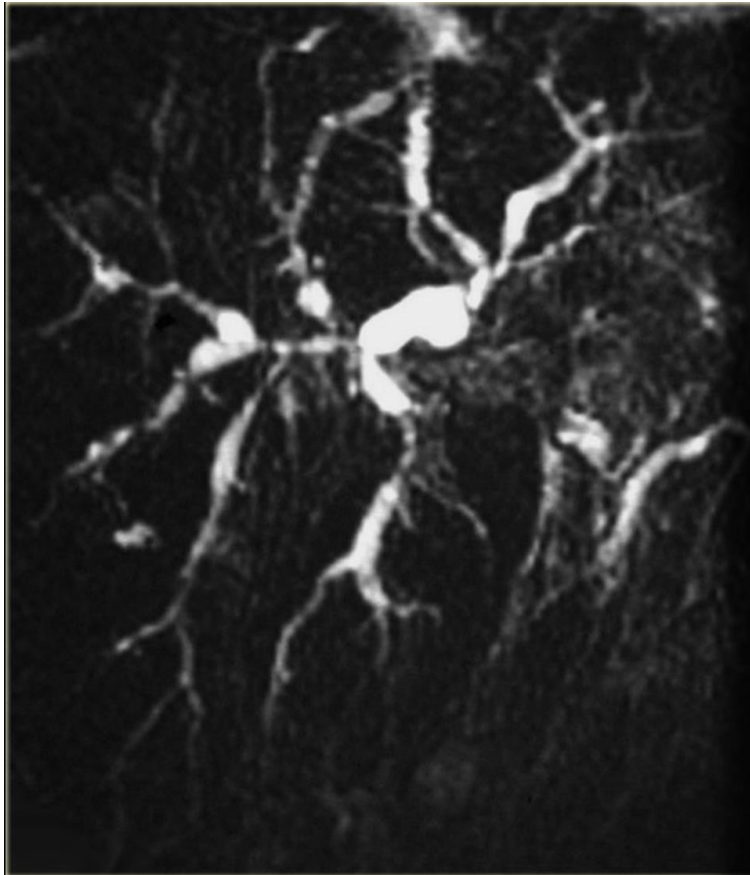
NORMAL ERCP



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Primary Sclerosing Cholangitis (PSC)

MRCP



ERCP



PSC with Cholangiocarcinoma



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Bilirubin Metabolism

- Bilirubin is the end-product of heme catabolism occurring in the reticuloendothelial cells of the spleen and the liver



- Bilirubin exists in two forms
 - (1) Unconjugated (indirect bilirubin)
 - (2) Conjugated (direct bilirubin)
- Initially, bilirubin is unconjugated and insoluble in water
- Unconjugated bilirubin is bound to albumin and transported to the liver
- In the liver, bilirubin is conjugated with glucuronic acid by the enzyme *uridine-5'-diphosphate (UDP) glucuronyltransferase* and becomes soluble in water

Bilirubin Metabolism

- Conjugated bilirubin is actively transported across canalicular membrane of biliary system from plasma into bile through ATP-dependent transport protein and enters the small intestine
 - Only energy-dependent step in bilirubin metabolism and explains why even pts with fulminant hepatic failure have predominantly conjugated hyperbilirubinemia
- Once in bile, conjugated bilirubin passes freely until it reaches the distal ileum and colon



- Metabolism of urobilinogen (colorless)
 - (1) Oxidized by intestinal bacterial to **stercobilin** and excreted in feces giving characteristic brown color
 - (2) Excreted unchanged
 - (3) Absorbed passively by intestine into portal system
 - a) Portion participates in enterohepatic urobilinogen cycle
 - b) Remainder of urobilinogen transported to kidney and oxidized and excreted as **urobilin**, which gives urine its characteristic yellow color

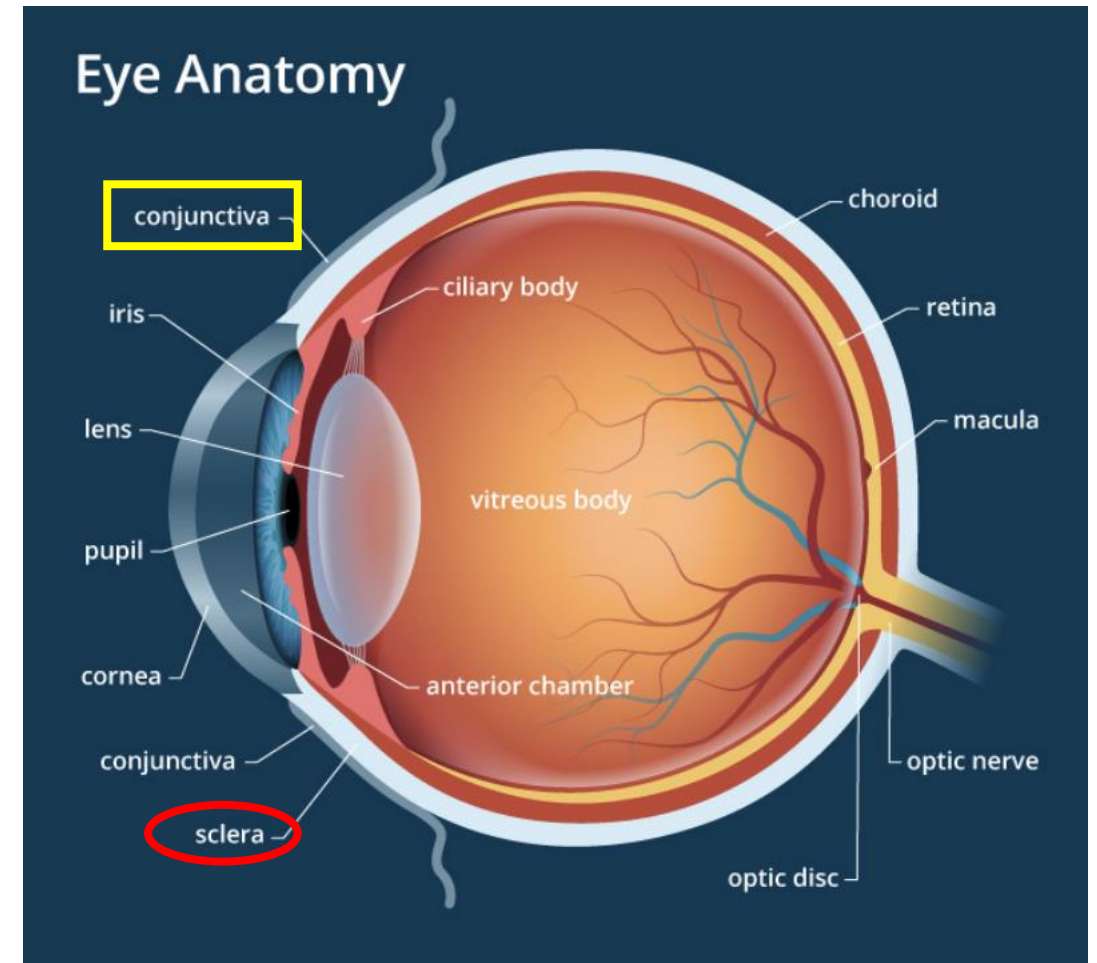
- Unconjugated bilirubin is never found in urine because in the serum it is bound to albumin and not filtered by the glomerulus
- Presence of bilirubin in urine indicates conjugated hyperbilirubinemia and suggestive of hepatobiliary disease

APPROACH TO PATIENT WITH HYPERBILIRUBINEMIA

- Causes of hyperbilirubinemia
 - (1) Overproduction of bilirubin secondary to excessive breakdown of hemoglobin
 - (2) Impaired hepatocellular uptake, conjugation, or excretion of bilirubin
 - (3) Regurgitation of unconjugated and conjugated bilirubin from damaged hepatocytes or bile ducts
- Jaundice develops under the tongue and in the eyes typically when total bilirubin ≥ 3.0 mg/dL
 - Does not differentiate between conjugated and unconjugated hyperbilirubinemia
- Tea- or cola-colored urine may indicate presence of bilirubinuria and thus conjugated hyperbilirubinemia

Conjunctival Icterus NOT Scleral Icterus

- “Scleral icterus” from histopathologic perspective is a misnomer perpetuated in medical textbooks
- Bilirubin has high affinity for elastin, which is an abundant protein in the conjunctivae NOT the sclera
- Correct term is **conjunctival icterus**

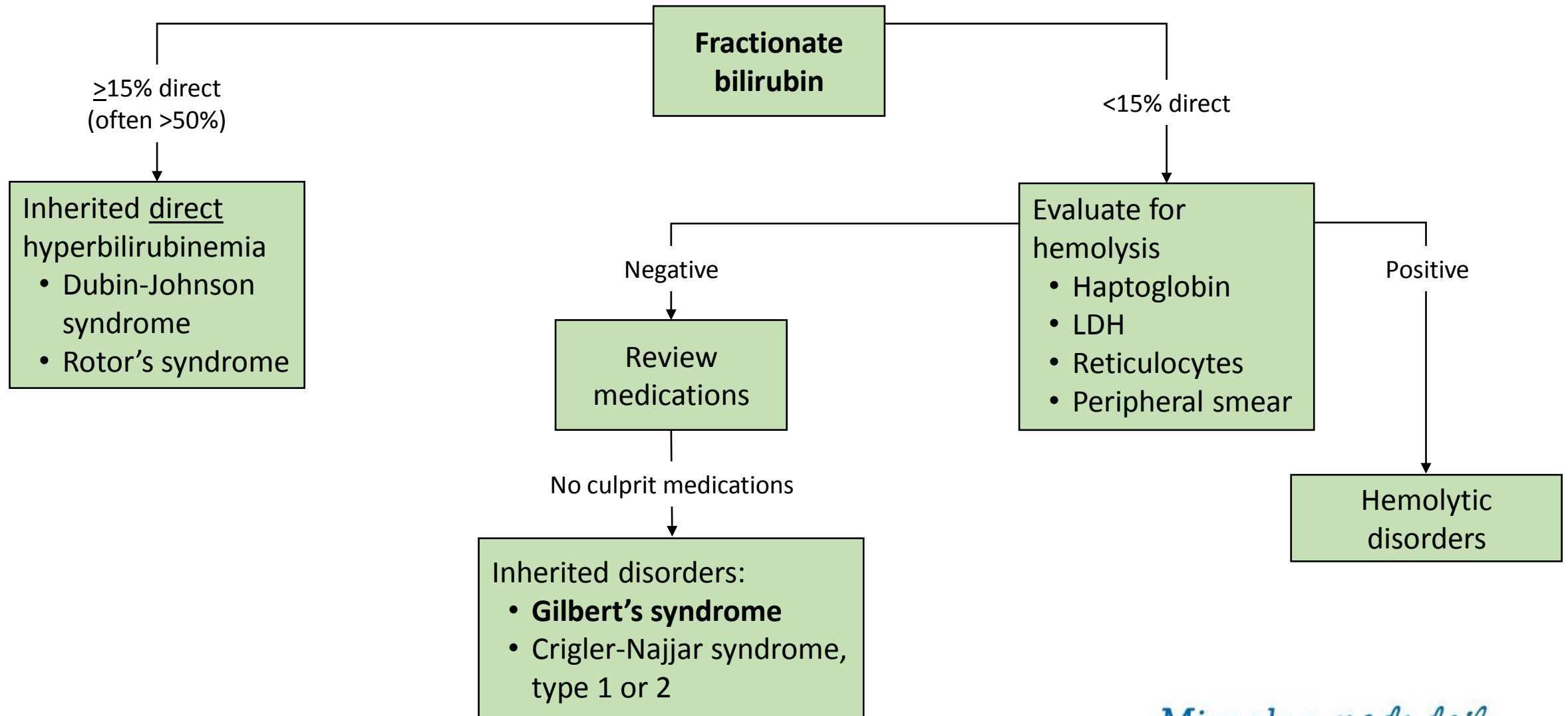


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Bilirubin

- Evaluation of patient with isolated hyperbilirubinemia is different than hyperbilirubinemia associated with hepatocellular or cholestatic process
- First step is to fractionate bilirubin
 - Unconjugated bilirubin → Indirect bilirubin
 - Conjugated bilirubin → Direct bilirubin
- In general, if direct bilirubin is <15% of total bilirubin → **INDIRECT HYPERBILIRUBINEMIA**

EVALUATION OF ISOLATED HYPERBILIRUBINEMIA



Albumin

- Protein that is produced exclusively in the liver
- Multiple biological actions
 - Maintenance of oncotic pressure
 - Binding of other substances (unconjugated bilirubin, fatty acids, thyroid hormones, and drugs)
 - Metabolism of compounds
 - Antioxidant properties
- Normal serum values for albumin 3.5 – 4.5 g/dL

Albumin

- Long half-life of 15-20 days; thus, changes are not good indicator of acute liver dysfunction
- Hypoalbuminemia is more common in chronic liver disorders, e.g. cirrhosis, due to reduced albumin synthesis
- Serum albumin level <3 g/dL associated with liver disease should raise suspicious for chronic liver disease +/- cirrhosis
- Although serum albumin concentration is considered marker of synthetic function of the liver, albumin concentrations may be reduced in many clinical situations
 - Nephrotic syndrome
 - Malabsorption
 - Protein-losing enteropathies
 - SIRS associated with chronic infections

Prothrombin time (PT) and INR

- Liver is major site of synthesis of all major blood coagulation proteins – Factors I, II, V, VII, IX, X, XII, XIII
 - Exception → Factor VIII is produced by vascular endothelial cells
- Blood clotting parameters used to measure liver function
- In significant liver injury, results in reduction in clotting factor production and subsequent coagulopathy → ↑ PT/INR
- Prolonged PT not specific to liver disease; may result from congenital or acquired conditions
 - Congenital deficiency of clotting factors
 - Consumption of clotting factors [disseminated intravascular coagulation (DIC) or severe GI bleeding]
 - Certain medications (coumadin)
 - Vitamin K deficiency

Prothrombin time (PT) and INR

- Deficiency in vitamin K-dependent clotting factors (II, VII, IX, X) results in prolonged PT/INR
 - Causes of vitamin K deficiency
 - Dietary insufficiencies
 - Fat malabsorption
 - Gut flora-altering antibiotics
 - Chronic cholestasis
- Vitamin K 10 mg IV daily x3
- Cholestasis results in prolonged PT/INR because
 - (1) Cholestasis causes ↓ bile flow
 - (2) ↓ Intraluminal bile salt concentrations
 - (3) Malabsorption of fat-soluble vitamins (A, D, E, K)

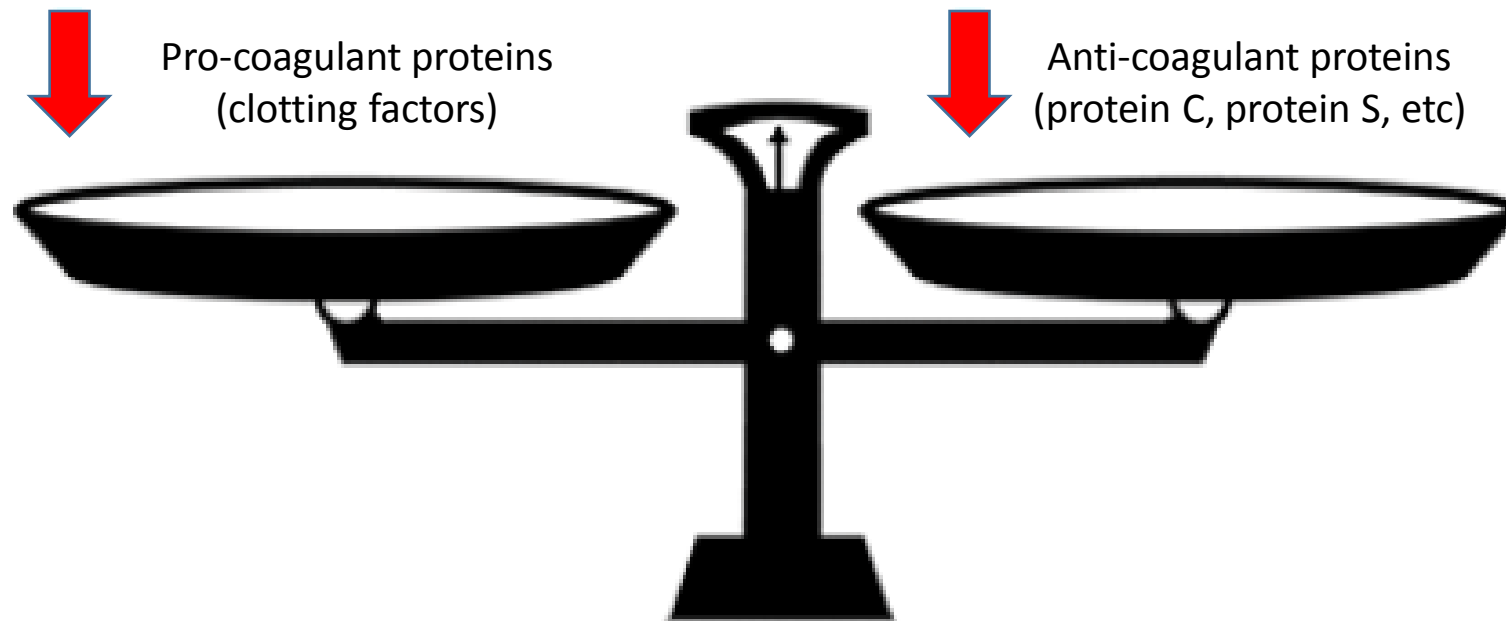
Prothrombin time (PT) and INR

- International normalized ratio (INR) devised and validated to standardize PT across laboratories in pts receiving anticoagulation therapy with vitamin K antagonists (e.g. Coumadin)
- INR is not accurate measure of bleeding risk in patients with cirrhosis; prolonged PT/INR does not accurately predict risk of GI bleeding
- Likewise, prolonged INR does not provide a protective role in development of DVT or PVT

Hematologic Disorders in Cirrhosis

- Pts with cirrhosis are in fragile continuum between ineffective hemostasis and inappropriate thrombosis

REBALANCED HOMEOSTASIS



Prognostic Markers of PT/INR

- Unlike albumin, PT is helpful in assessing acute liver dysfunction
- PT/INR has a high prognostic value and is included in multiple prognostication models
 - (1) King's College criteria (acute liver failure)
 - (2) Maddrey's discriminant function (alcoholic hepatitis)
 - (3) Child-Turcotte-Pugh score
 - (4) Model for End-stage Liver Disease (MELD) score

When to refer to Hepatology?

- When diagnosis is confirmed that requires specific treatment
- When diagnosis remains in question despite initial evaluation
- When evaluation reveals cirrhosis
- Before clinical course deteriorates (acute liver failure)

Liver Failure Team

Miami Transplant Institute's (MTI) Liver Failure Team was developed to share best practices and assist physicians treating patients suffering from complicated liver-related illnesses. Our team of experts is ready to assist Gastroenterologists, Hepatologists, and Primary Care Providers in deciding the best course of treatment, monitoring responses to those treatments, assisting in adjusting medications, and facilitating referrals for liver transplantation or arranging patient transfer, if necessary.

Contact The Liver Failure Team 24/7:
305-355-LIVR (5487)

Conclusion

- Asymptomatic abnormalities of liver biochemistries are not uncommon
- True LFTs include albumin, INR, and bilirubin
- Detailed physical exam and history is first step in evaluation of abnormal liver biochemistries
- Recognition of pattern of liver injury helps minimize differential diagnosis
- 3 most common causes of liver enzymes elevation EtOH toxicity, NAFLD, and DILI
- Rules of 3
 - (1) Viral hepatitis – HAV, HBV, HCV
 - (2) Autoimmune – ANA, ASMA, AMA
 - (3) Metabolic – iron/ferritin, ceruloplasmin, A1AT

THANK YOU

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