

Work up of the Asymptomatic Patient with Liver Enzyme Abnormalities

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Conflicts of Interest

- None

Objectives

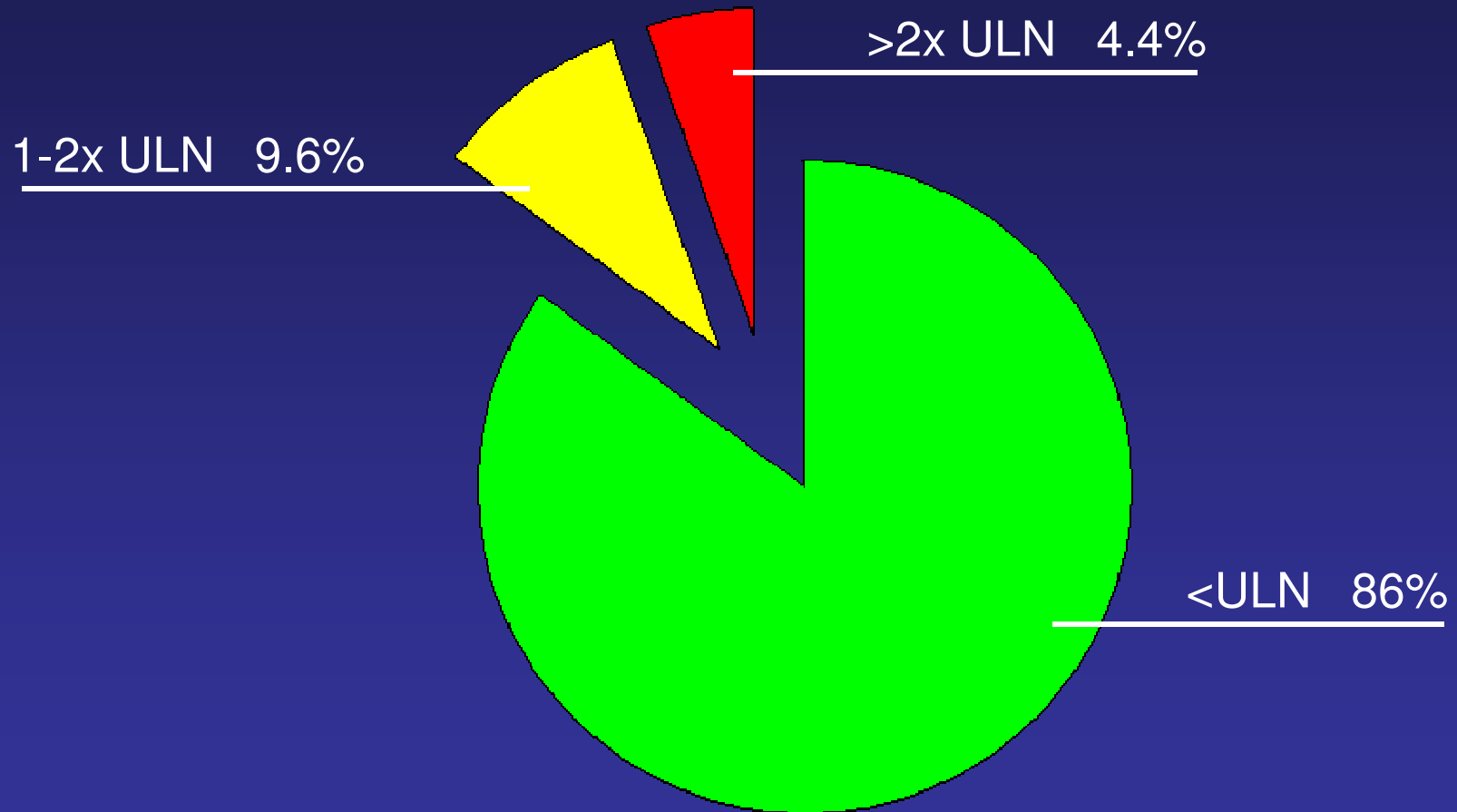
1. Appreciate why it is important to screen for liver disease.
2. What screening tests?
3. How to determine whether the patient has liver disease?
4. Characterize the nature of the liver disease
5. Develop a reasonable differential diagnosis

Why is it important to screen for
liver disease?



Benjamin Rubinenko 1990

Aminotransferase Elevations in the General Population



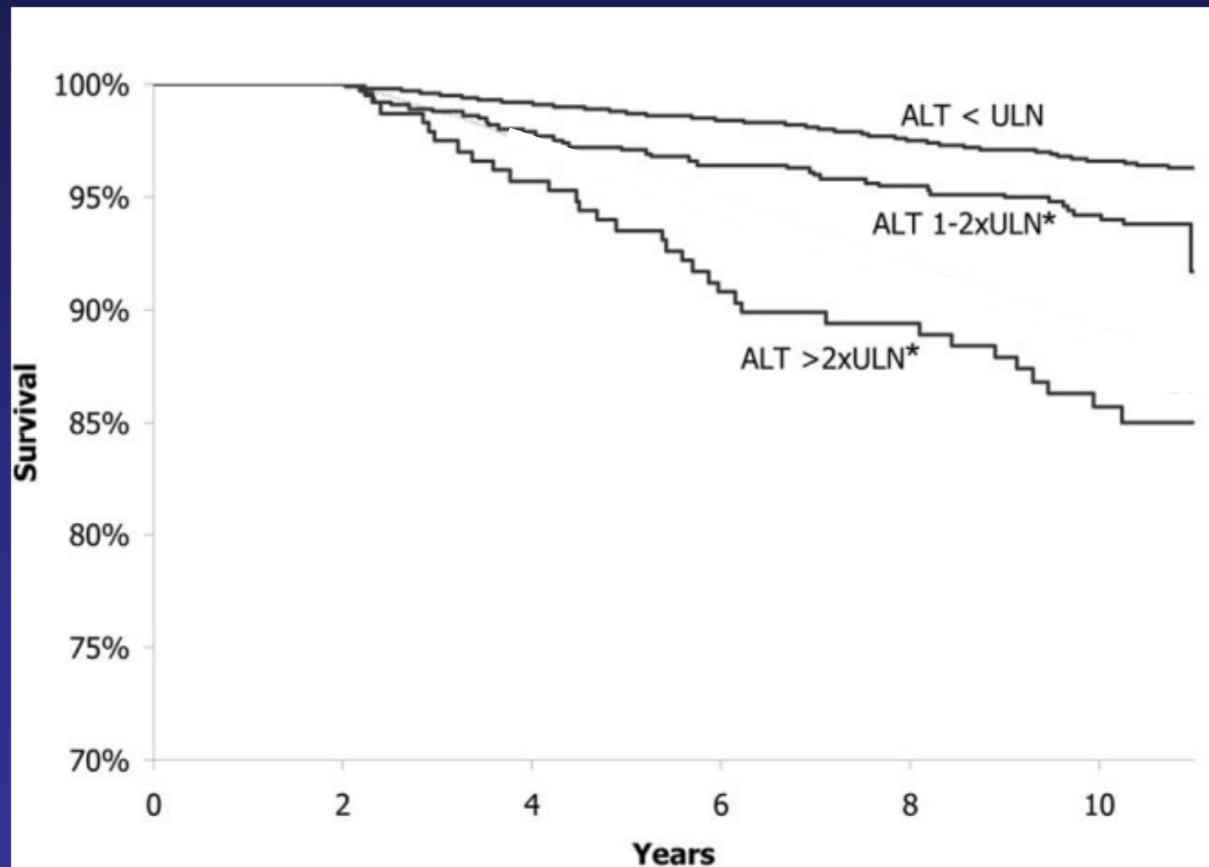


Fig. 2. Kaplan Meier survival of Olmsted County residents by ALT results.

* Indicates P 0.01 in comparison with the ULN group in each panel.

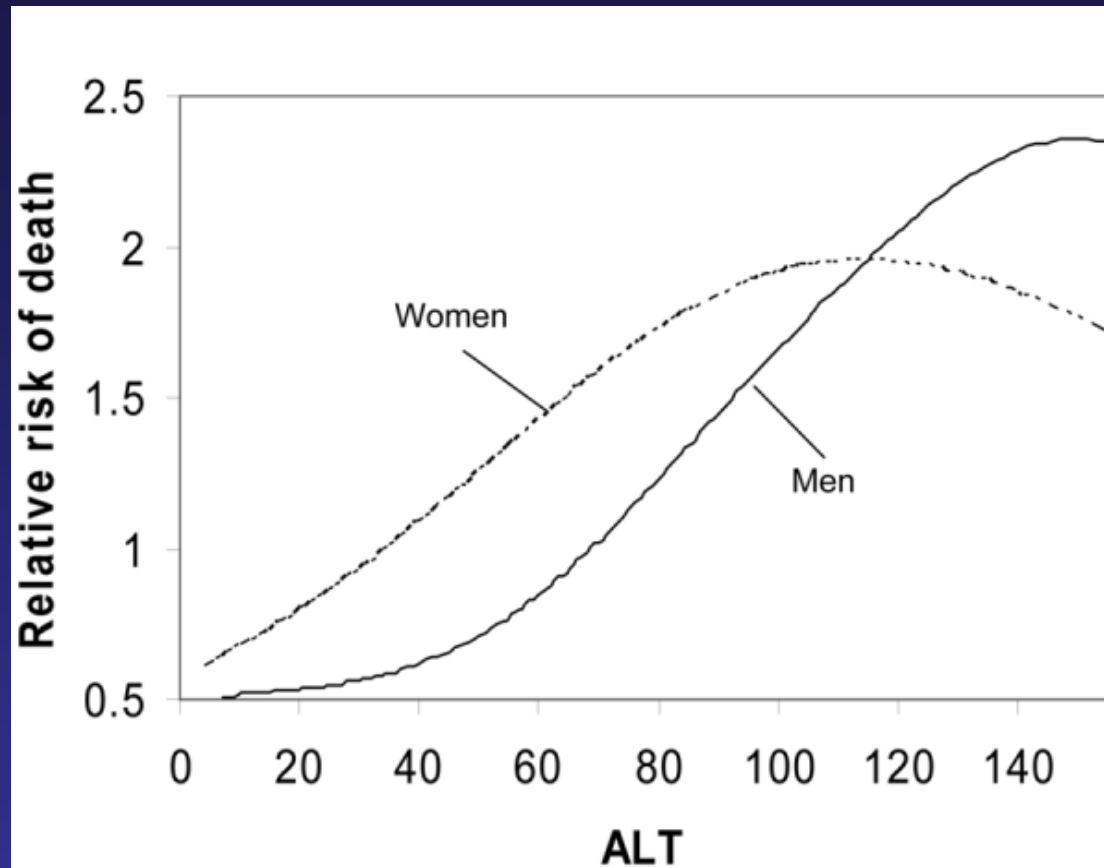


Fig. 3. Relative risk of death according to the aminotransferase level.

Message

1. Aminotransferase abnormalities are common (~ 15%).
2. Elevated aminotransferases are associated with increased mortality.

Which screening tests?

Suggested Screening Profile:

Liver Enzyme Tests

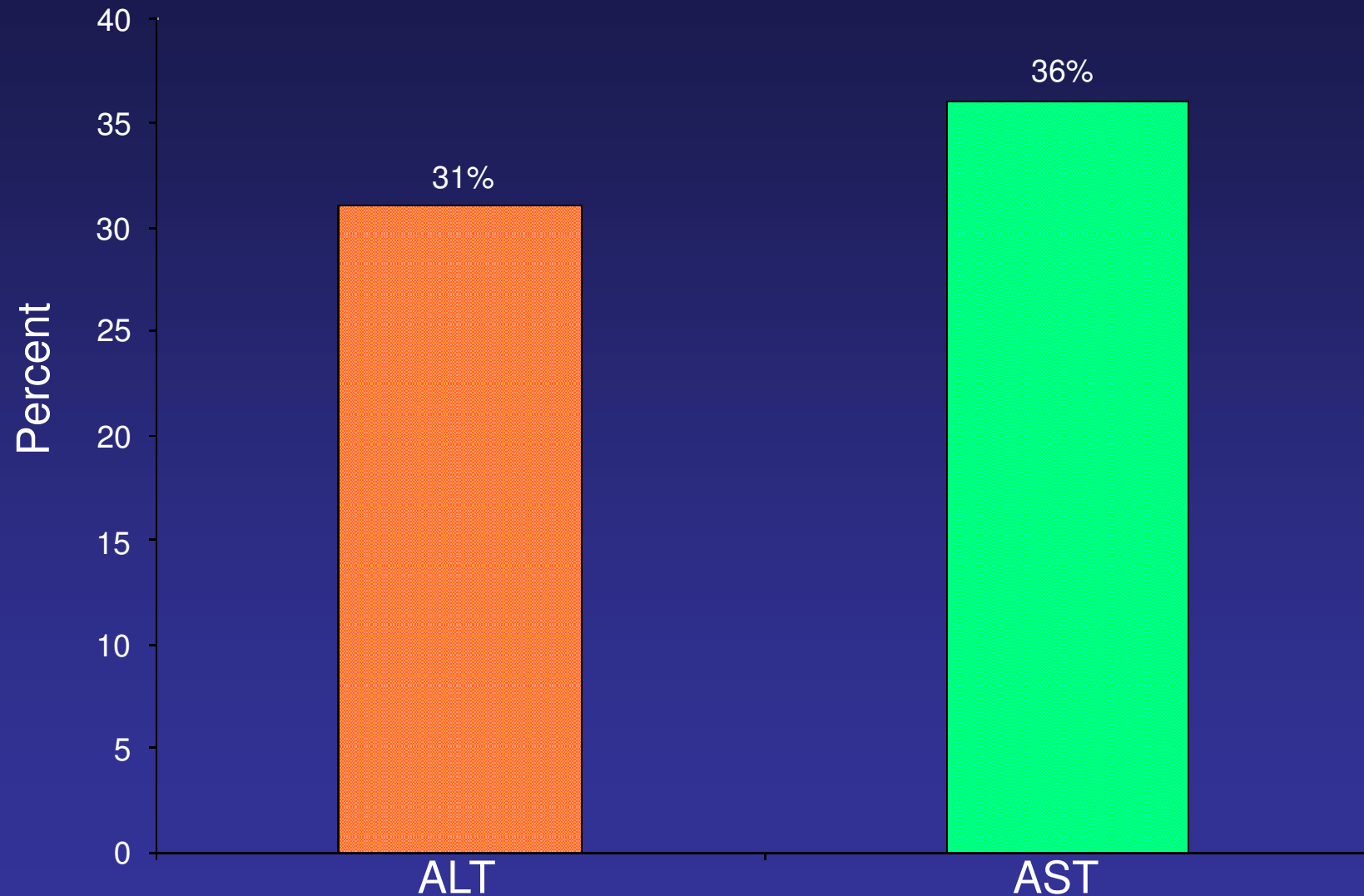
- Alanine Aminotransferase (ALT)
- Aspartate Aminotransferase (AST)
- Alkaline Phosphatase (AP)
- Gamma Glutamyltransferase (GGT)

Liver Function Tests

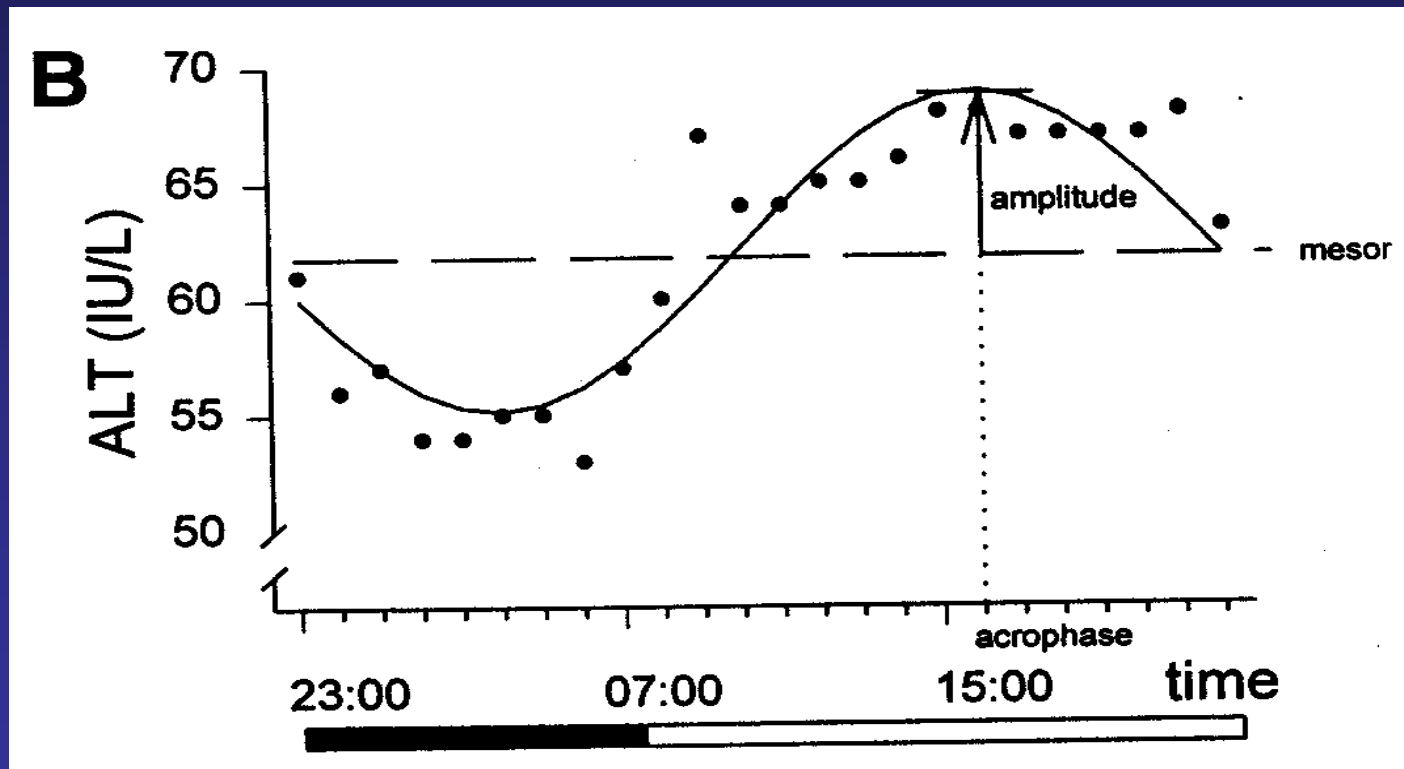
- Albumin
- Bilirubin
- INR

Does the Patient have Liver Disease?

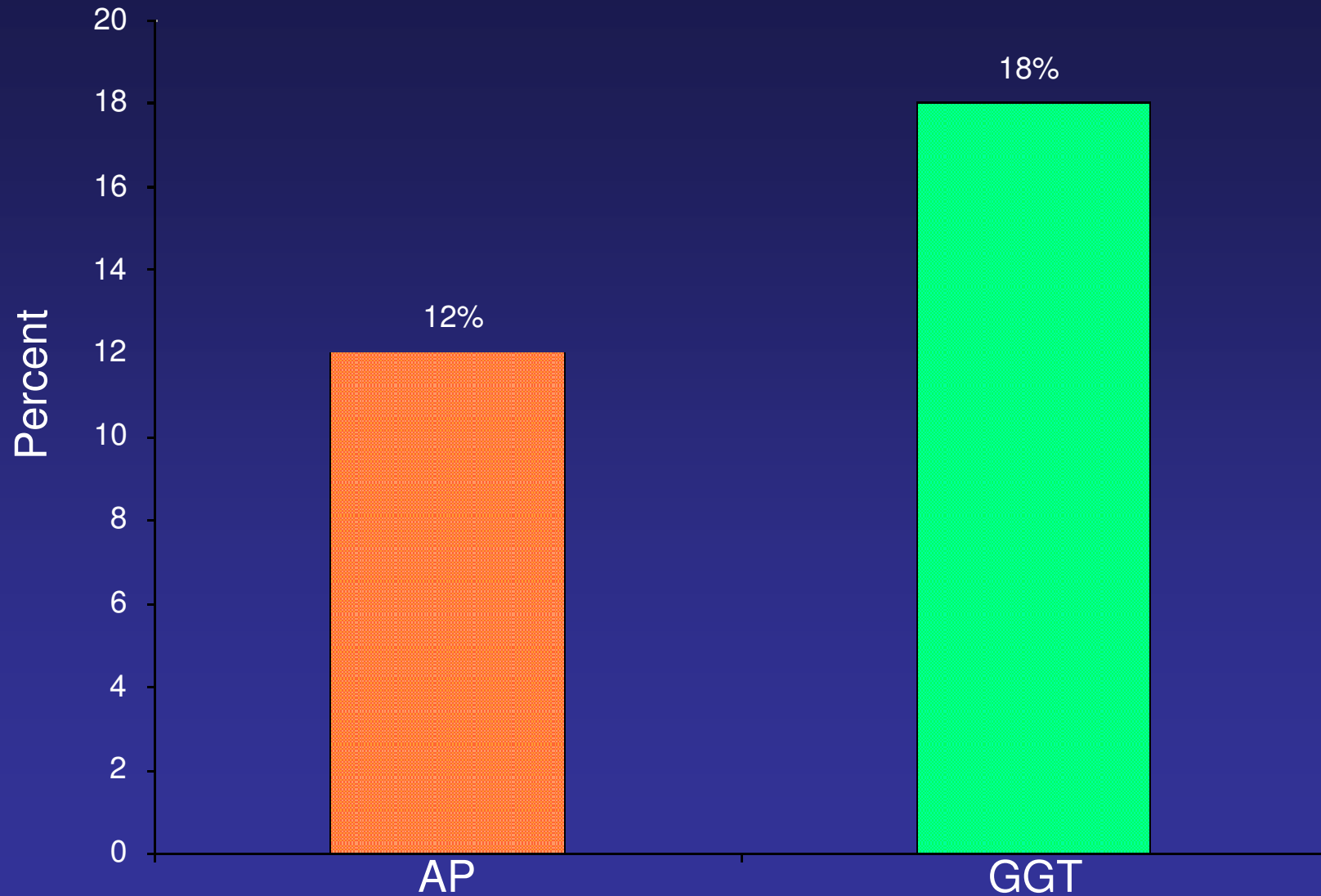
Reproducibility of Initially Abnormal ALT/AST Values



Increased ALT in Absence of Liver Disease -Time of Day



Reproducibility of Initially Abnormal AP/GGT Values



Elevated Alkaline Phosphatase in the Absence of Cholestasis

- Length of tourniquet application
- Delay in separation of sera
- Fatty meals in blood groups A and O (secretors of ABH red-cell antigens)

Message

1. Repeat abnormal LFTs within 2-3 wks and preferably in the AM.

Does the Patient have Liver Disease?

ALT (SGPT)	AST (SGOT)	ALK-PHOS	GGT
Liver	Liver	Liver	Liver
Skeletal M.	Cardiac M.	Bone	High TGs
	Skeletal M.	Placenta	Alcohol Drugs
	Kidney/Brain Pancreas/Lung WBC/RBC	Intestine	Cardiac/COPD Pancreas/DM Kidney

“Liver” Function

ALBUMIN	BILIRUBIN	INR
Liver	Liver	Liver
Kidney	Gilberts	Anticoagulants
Intestinal	Hemolysis/Drugs	Antibiotics
Nutritional	DJ/Rotors	Cholestyramine Nutrition Malabsorption

Does the Patient have Liver Disease?

Yes if :

1. If the abnormality is reproducible.
2. ALT increased (in absence of rhabdomyolysis).
3. Alkaline Phosphatase and GGT increased.
4. Combination of any two liver enzyme and/or function tests are abnormal.

Characterizing the Liver Disease

Is the Disease Hepatocellular, Cholestatic or Mixed?

Hepatocellular	Cholestatic	Mixed
ALT/Alk Phos > 4	ALT/Alk Phos < 2	ALT/Alk Phos 2-4
ALT/Alk Phos 240/180	ALT/Alk Phos 80/240	ALT/Alk Phos 80/180

ALT <40
Alk Phos <120

Developing a Differential Diagnosis for Hepatocellular Injury

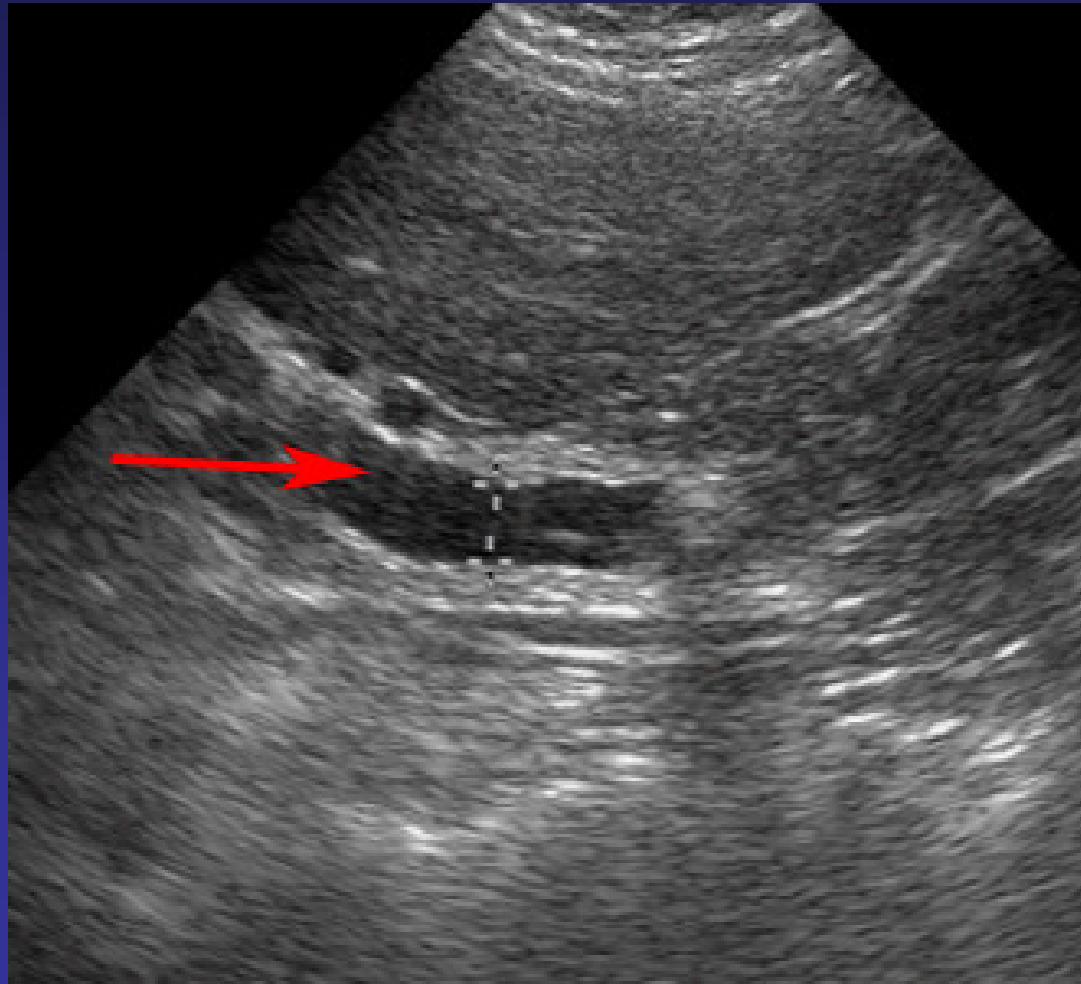
Differential Diagnoses of Hepatocellular Liver Injury (Hepatitis)

Condition	Key Diagnostic Clue
Alcohol	AST>ALT without cirrhosis/GGT
Drugs/Herbs/Toxins	Introduction within 3 mo.
Viral Infection	Acute: IgM Anti-HAV, IgM Anti-HBc, HCV-RNA, IgM Anti-HEV
	Chronic: HBsAg, Anti-HCV
NASH	Metabolic Syndrome/Ultrasound
Autoimmune CAH	Positive: ANA, ASMA
Hemachromatosis	Elevated Ferritin
Wilson's Disease	Low Ceruloplasmin

Differential Diagnoses of Hepatocellular Liver Injury (Hepatitis)

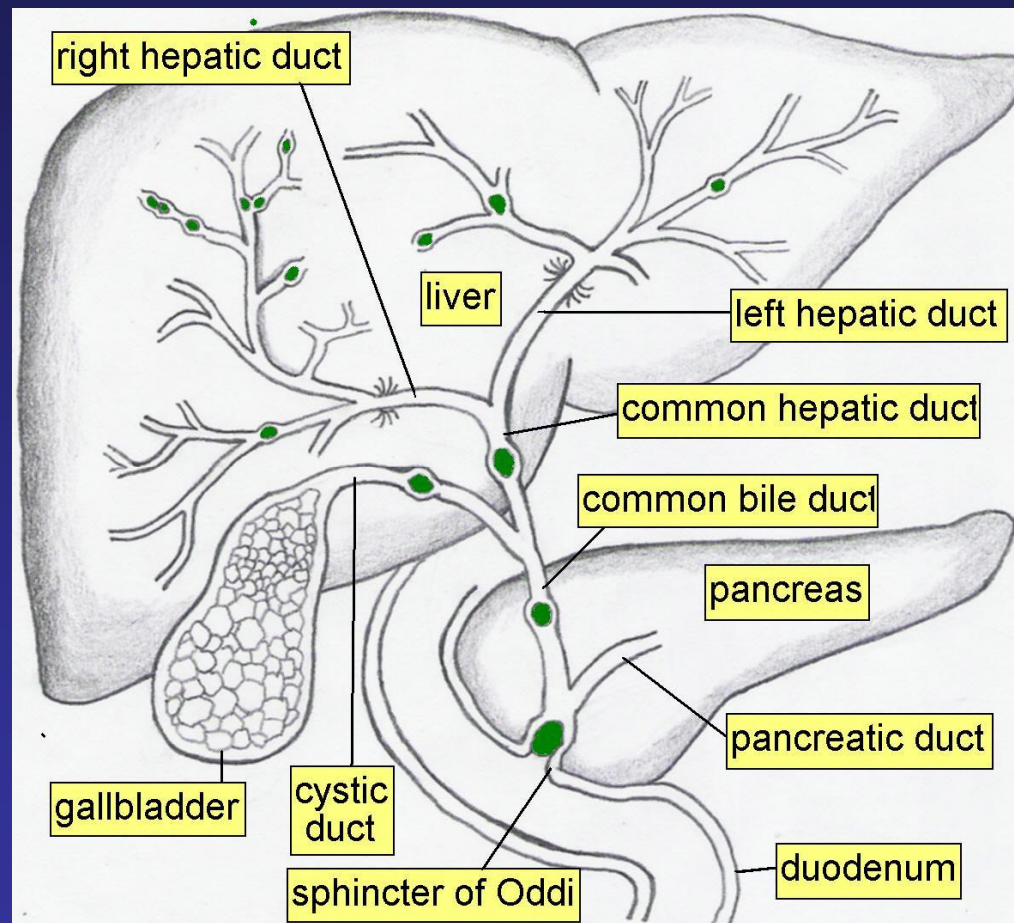
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Differential Diagnoses of Cholestasis



Cholestasis- Mechanical

Stones, Strictures, Tumors and Worms



Differential Diagnosis of Intrahepatic Cholestasis

Intrinsic	Infiltrative	Systemic	SOL
Alcohol	Fat	Sepsis/Abcess	Hematoma
Drugs	Granuloma	BS Syndromes	Cysts
Viral	Lymphoma	Paraneoplastic	Abscess
Autoimmune	Amyloid	Uremia/Dialysis	Tumor

Differential Diagnosis of Mixed Liver Enzyme Abnormalities

1. Drugs
2. Infection (HCV and CMV)
3. Infiltrative Disorders (granuloma, tumor)

Conclusions

- **Why:** Liver disease is common and a/w increased mortality
- **What Tests:** ALT, AP and Bilirubin
- **Liver Disease?:**
 - Repeat in 2 wks and AM
 - Consider non-hepatic causes
- **Type of Injury:** HC vs Cholestatic vs Mixed
- **Differential Diagnosis**

Questions?