KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Blood Chem Impaired Liver Function Review

MARKERS OF IMPAIRED LIVER FUNCTION

Marker	Value
ALT	High
AST	High
GGT	High
LDH	High
Alkaline phosphatase	High

AMINOTRANSFERASES (ALT AND AST)

- A group of enzymes that catalyze the interconversion of amino acids and oxoacids by the transfer of amino groups.
- ALT is a specific indicator of liver damage that is present in the highest amount in the liver.
- AST is present in tissues with high metabolic activity, including liver, heart, and kidney. It's not specific to the liver, but liver dysfunction is the most common cause of elevated AST.
- Elevated aminotransferases typically reflect abnormalities in liver cells or the bile duct.

GAMMA-GLUTAMYL TRANSFERASE (GGT)

- Primarily found in the hepatocytes and biliary epithelium. However, due to its presence in many tissues, it is not specific for liver and gallbladder disease.
- GGT and alkaline phosphatase levels increase in the blood with hepatobiliary obstruction
- Unlike alkaline phosphatase, GGT is not found in the bone.
- Primarily to confirm liver or gallbladder as a source of elevated alkaline phosphatase rather than breakdown in the bone.
- GGT is also a sensitive marker for metabolic dysfunction.

LACTATE DEHYDROGENASE (LDH)

- Primarily a marker for tissue or cellular damage.
- Not useful on its own as a marker of liver dysfunction but can help identify a pattern.

ALKALINE PHOSPHATASE

- Primarily a marker for liver and bone damage.
- When bone disease is excluded, an elevation of alkaline phosphatase suggests biliary obstruction, injury to the bile duct, epithelium, or cholestasis.
- Always retest to confirm high alkaline phosphatase.
- It is most likely marker of liver dysfunction when GGT is also high.
- If GGT is normal or equivocal, consider running alkaline phosphatase isoenzymes to see whether the elevation is coming from the intestine, the liver, or the bone.

LIVER FUNCTION MARKERS

Marker	Lab range	Functional range
ALT	0–50 IU/L	0–26 IU/L (men) 0–20 IU/L (women)
AST	0–40 IU/L	0–25 IU/L (men) 0–23 IU/L (women)
GGT	0–60 IU/L	0–29 IU/L (men) 0–21 IU/L (women)
LDH	119–226 IU/L	140–180 IU/L
Alk phos	39–117 IU/L	42–107 IU/L

LIVER DISEASE/ CAUSES OF ELEVATED LIVER ENZYMES

1. Chronic viral hepatitis

Form	Prevalence	Risk factors	Comments
Hepatitis C	1.8% of general population; rate much higher in people with known risk factors and ALT >40 IU/L	Blood transfusions (esp. before 1992), IV drug use, cocaine use, hemodialysis, organ transplantation, birth in endemic region	Many patients will have no symptoms or mild symptoms and only mildly elevated ALT/AST; if risk factors present, early testing warranted
Hepatitis B	0.2–0.9% of general population; as high as 20% after travel to endemic areas	Same as above; more commonly transmitted sexually than Hep C	Many patients will have no symptoms or mild symptoms and only mildly elevated ALT/AST; if risk factors present, early testing warranted

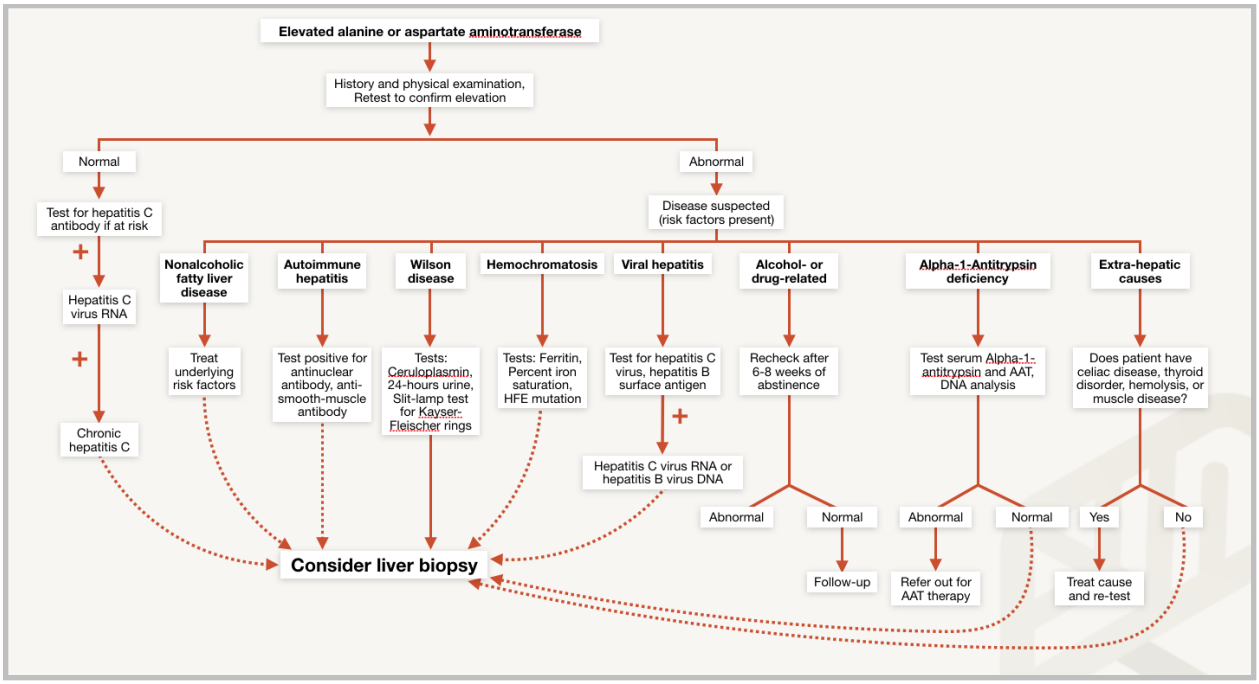
2. Iron overload
3. Alcoholic liver disease
    a. Risk**:** 10-plus years of more than 5 drinks, (12-ounce beer, 1.5 ounces of spirits, 5-ounce glass of wine)
4. Nonalcoholic fatty liver disease
    a. Risk factors include patients with components of metabolic syndrome: abdominal obesity, insulin resistance, hyperlipidemia, hypertension, certain medications (corticosteroids, tetracycline, valproic acid, amiodarone)
5. Autoimmune hepatitis
    a. More common in women and those with other autoimmune diseases
    b. Diagnosis by exclusion of viral hepatitis, pathologic findings, and presence of autoimmune markers such as antinuclear antibodies, smooth muscle antibody, liver-kidney microsomal antibodies
6. Wilson's disease
    a. Anyone under age 40 with abnormal liver enzymes should be evaluated, even in absence of neurologic or ocular findings; routine screening rarely helpful in patients over age 50.
    b. Genetic testing is of limited value because of large number of potential mutations of ATP7B gene;
    c. If a patient does have WD, screen family members
7. Alpha-1-antitrypsin deficiency
    a. A protease inhibitor made in the liver that protects both the liver and the lungs.
    b. Patients with emphysema or with a young sibling with liver failure are at higher risk.
    c. Common cause of liver disease in young children, but only a portion develop liver failure as adults
8. Drug- and toxin-related liver diseases

Risk factors	Comments
A variety of prescription and nonprescription drugs can damage the liver	NSAIDs
	Antibiotic
	Statins
	Valproic acid
	SSRIs
	PPIs
	Losartan
	Lisinopril
	Acetaminophen
	Some botanicals *(kava kava and germander)*
	Amiodarone
	Trazodone

9. Extrahepatic causes
    a. Thyroid disorders. Screen for thyroid antibodies and run full thyroid panel
    b. Celiac disease. Test tissue transglutaminase levels
    c. Hemolysis. Test LDH and haptoglobin levels, reticulocyte count; infection is a possible cause
    d. Muscular disorders. Test creatine kinase and aldolase levels; screen for SLE (systemic lupus erythematosus)

Hepatitis B, hepatitis C, iron overload, and nonalcoholic fatty liver disease are the most common causes of elevated AST and ALT. If you're able to exclude iron overload, hepatitis B, and hepatitis C, it is very likely that the patient has nonalcoholic fatty liver, especially if you can rule out Wilson's disease with copper, ceruloplasmin, and urine copper testing.

ALGORITHM FOR EVALUATING ELEVATED AMINOTRANSFERASES



If all known causes of elevated AST and ALT are ruled out and they remain elevated, you can monitor the patient for three to six months as you address other underlying causes that are identified in the case review. In many situations, you'll see the aminotransferases come down as you address those causes.