



Potential Implications of Elevated Liver Enzymes



**NATIONWIDE
CHILDREN'S**

When your child needs a hospital, everything matters.SM

What are elevated liver enzymes?

Transaminases, or “liver enzymes” – alanine aminotransferase (ALT) and aspartate aminotransferase (AST) – are often checked during routine blood tests or may be tested in response to a patient’s specific signs or symptoms. Elevated transaminases may indicate inflammation of, or damage to the liver. Due to normal cell turnover, detectable serum levels of ALT and AST are normal in all patients. However, when the liver is inflamed or damaged, higher than usual amounts of these enzymes can leak from the hepatocytes (liver cells) into the bloodstream. The half life of these transaminases is short (1-2 days), so a persistent elevation indicates ongoing tissue damage.

It is critical to remember that, although ALT and AST are often called “liver function tests,” transaminases are not tests of liver *function*. They are indicators of cellular *injury*. Furthermore, while these enzymes are referred to as “liver enzymes,” this is also a misnomer since they can be released from other tissues as well, for example skeletal muscle. Therefore, elevated transaminase levels – especially AST, which is less specific for liver injury – can be indicative of diseases in other organs (e.g., muscular dystrophy and other myopathies, hemolytic conditions, pancreatitis, etc.). In many cases, elevated transaminases are temporary and do not necessarily indicate serious disease. If the elevation persists, however, a work-up is indicated.

Why test for elevated transaminases?

Physicians may elect to send serum enzyme testing for any of the following reasons:

1. Routine lab testing in asymptomatic patients (e.g., annual checkups)
2. Monitoring a patient taking medication known to possibly injure the liver
 - Antibiotics effective against β -lactamase-producing bacteria (oxacillin, nafcillin, macrolides)
 - ADHD medications and other psychotropic drugs
 - Minocycline (treatment of acne)
 - Thiopurines (treatment of inflammatory bowel disease)
 - Statins (treatment of dyslipidemia or hypercholesterolemia)
3. Assessing overweight and obese children at risk for non-alcohol fatty liver disease
4. Follow-up monitoring of a patient with a family history of liver disease
5. Testing a patient with symptoms indicative of liver damage or dysfunction

How high is too high?

ALT and AST 1.5 to 2 times higher than normal levels are cause for concern. Normal variation exists based on age, race and sex. Additionally, a cirrhotic patient or a patient in liver failure can have normal transaminase levels due to decreased hepatocyte mass. The following normal values are just examples and vary between laboratories. It is important to remember that infants and young children are generally expected to have lower transaminase serum levels; thus, even values that are “technically” within the normal range may still raise suspicion, for example an ALT or AST level of 40-60 IU/L in an infant with clinical signs or symptoms of liver disease.

Enzyme	Normal Range (IU/L)	Half-life	Source
ALT*	7 – 55	2 days	Liver, muscles, heart, kidney, pancreas, spleen, lung, *more liver-specific
AST+	1-13 yrs: 8 – 60 >13 yrs: 8 – 48	1 day	Liver, muscles, heart, brain, kidney, red blood cells, +often also elevated in muscle diseases, hemolytic conditions

What other tests can physicians order?

If transaminases are elevated, you should first retest them and may also order a creatine kinase level (see below). If ALT and AST are persistently elevated, consider ordering additional tests:

Test	Reason
Creatine kinase (CK)	Muscle injury, muscular dystrophy, other disorders
Serum albumin	Liver function
Serum bilirubin (total and direct)	
Prothrombin time (INR)	
Alkaline phosphatase (ALP)	Cholestasis, disease of the biliary system
Gamma-glutamyl transpeptidase (GGT)	
Ultrasound (ideally with Doppler) of abdomen or right upper quadrant	Assess for liver size, appearance (echogenicity, surface texture) of liver parenchyma, gallbladder wall, gallbladder or bile duct stones, obstruction/narrowing of hepatic vessels, abdominal masses, ascites, etc.

Refer to a specialist when:

1. There is evidence of impaired liver synthetic or metabolic function (elevated bilirubin, PT/INR, ammonia, low albumin)
2. There is evidence of cholestasis (elevated direct bilirubin, alkaline phosphatase, GGT)
3. There is evidence of portal hypertension (low platelet count or albumin, ascites on ultrasound)
4. The patient is a neonate or infant
5. **REFER IMMEDIATELY** if the patient also has *any* of the following symptoms:
 - Unexplained fever
 - Jaundice
 - Coagulopathy (prolonged bleeding, easy bruising)
 - Distended abdomen
 - Lethargy
 - Altered mental status
 - Nausea or vomiting

Key Features of Patient History and Symptoms for Diagnosis

Elevated transaminase levels in combination with other symptoms and patient history can facilitate diagnosis. Some examples of symptom constellations and suspected diagnoses include:

- ↑ AST/ALT + pruritus + other markers of cholestasis → bile duct problem?
- ↑ AST/ALT + prolonged bleeding / easy bruising / nosebleeds / gum bleeds → liver synthetic dysfunction? cirrhosis, portal hypertension, thrombocytopenia?
- ↑ AST/ALT + abdominal distension (ascites) → cirrhosis, liver synthetic dysfunction, venous thrombosis or stenosis?
- ↑ AST/ALT + mild abdominal pain + nausea/malaise +/- rash → viral or autoimmune hepatitis?
- ↑ AST/ALT + neurological/behavioral symptoms (especially in teenagers) → Wilson disease?
- ↑ AST/ALT + jaundice + coagulopathy → acute liver failure?
- ↑ AST/ALT + family history of early or non-smoker emphysema → α -1 antitrypsin deficiency?

What are the causes of elevated liver enzymes?

The most common causes of elevated liver enzymes are:

- Hemolysis of the blood sample from a difficult blood draw or delay in processing the sample
- Medications, including over-the-counter pain medications such as acetaminophen and ibuprofen
- Viral hepatitis A, B, C, EBV, CMV or nonspecific viral illness
- Non-alcoholic fatty liver disease (NAFLD)

Other causes of elevated transaminases that might be diagnosed by a specialist include:

- α -1 antitrypsin deficiency
- Wilson disease
- Autoimmune hepatitis
- Liver cancer
- Hemochromatosis
- Non-hepatic conditions (pancreatitis, celiac disease, myopathy, hemolytic disorder, renal disease, etc.)

What other tests might a specialist conduct?

- Specific genetic/metabolic tests (blood, urine, tissue)
- CT scan
- MRI scan
- Liver biopsy

The Liver Center at Nationwide Children's Hospital

An integral part of the Division of Gastroenterology, Hepatology and Nutrition, the Liver Center provides a range of specialized inpatient and outpatient services for children with inherited or acquired conditions. Nationwide Children's is also approved by the United Network for Organ Sharing (UNOS) as a liver transplant center.

Liver problems can be life threatening and life changing. Quick evaluation, correct diagnosis and early treatment can impact long-term health, so the Liver Center physicians are committed to seeing all outpatient referrals within 48 hours. Contact us to learn more, or visit NationwideChildrens.org/Liver.

Referrals and Consultations

Online: NationwideChildrens.org/GI

Phone: (614) 722-6200 or (877) 722-6220 | Fax: (614) 722-4000

Physician Direct Connect Line for 24-hour urgent physician consultations:
(614) 355-0221 or (877) 355-0221.

