

American Association for the Study of Liver Diseases (AASLD) Practice Guidance on Initial Laboratory Assessment of Drug, Herbal and Dietary Supplement Induced Liver Injury

According to the AASLD, “there are currently more than 1,000 prescription medications available for use in the United States and more than 100,000 over-the-counter herbal and dietary supplements (HDS) available for purchase in retail stores and online. In addition, the average adult American receives more than six prescription medications per year. Many of these drugs and HDS products have been implicated as causes of drug-induced liver injury (DILI).”¹

The 2022 AASLD guidelines (expressed verbatim below) suggest the following for the laboratory assessment of DILI:¹

Clinically significant biochemical evidence of DILI is typically defined as meeting one of the following criteria:

- serum AST or ALT $>5\times$ Upper Limit of Normal (ULN), or ALP $>2\times$ ULN (or pretreatment baseline if baseline is abnormal) on two separate occasions;
- total serum bilirubin $>2.5\text{mg/dL}$ along with elevated AST, ALT, or ALP level; or
- INR >1.5 with elevated AST, ALT, or ALP.

In general, the pattern of injury can be categorized as primarily hepatocellular, with a predominance of transaminase (ALT, AST) elevation; cholestatic, with a predominance of ALP elevation; or mixed.

These patterns can be more precisely and quantitatively expressed through the R value at presentation ($R = (\text{ALT/ULN})/(\text{ALP/ULN})$) when:

- $R \geq 5$ identifies hepatocellular liver injury
- R value 2-5 identifies mixed liver injury
- $R \leq 2$ identifies cholestatic liver injury

When liver injury falls into hepatocellular or mixed categories, it may be important to exclude other causes of liver injury as listed in the table below:¹

Other Etiologies to Consider	Evaluation
Viral hepatitis (e.g., HAV, HBV, HCV, HEV, CMV, EBV, HSV)	HAV IgM, HBsAg, HCV RNA, HEV IgM, CMV PCR, EBV PCR, HSV PCR
Ischemia	History of hypotension, sepsis, or heart failure; echocardiogram
Autoimmune hepatitis	ANA, ASMA, IgG, liver biopsy
Alcoholic hepatitis	Clinical history, AST $>2\times$ ALT, serum PETH, urine ethylglucuronide
Drug/toxin (e.g. mushroom, APAP)	History, urine toxicology, serum APAP
Budd-Chiari	Doppler ultrasound (or CT or MRI)
Wilson disease	Ceruloplasmin, ALP :TB <4 , AST:ALT >2.2
Alpha-1-antitrypsin deficiency	A1AT level
Hereditary hemochromatosis	Ferritin, transferrin saturation
Fatty liver disease	History and imaging features
Celiac disease	Anti-TTG IgA
Rhabdomyolysis	CPK
Hypothyroidism/Thyrotoxicosis	TSH, free T4, T3

When liver injury falls into cholestatic category, it may be important to exclude other causes of liver injury as listed in the table below:

Other Etiologies to Consider	Evaluation
Choledocholithiasis	Doppler ultrasound
Primary biliary cholangitis	AMA, liver biopsy
Biliary strictures (e.g. primary sclerosing cholangitis)	Cholangiography
Pancreaticobiliary tumors	CT or MRI
Malignancy/infiltrating cancer (e.g. lymphoma)	LDH, imaging
TPN cholestasis	History
Bone disease	ALP isoenzymes

Additional proposed actions for patients with suspected DILI as outlined in 2022 AASLD guidelines:¹

When DILI is suspected based on clinical history, symptoms, and/or physical exam:

- Assess exposure to all prescription and over the counter medications, HDS products, and toxins, including start and stop dates, especially within the preceding 6 months
- Discontinue any non-essential medications and supplements

Search for injury patterns in LiverTox, PubMed:

- Latency (time to onset)
- Dechallenge (time to recovery)
- Clinical phenotype

Labcorp offers the following tests for use in the assessment of DILI:

Test Name	Test No.
Drug-Induced Liver Injury Profile	010045
Drug-Induced Liver Injury Pattern Assessment with Calculation of R Value	010035

Related tests:

Test Name	Test No.
ALT	001545
AST	001123
Alkaline Phosphatase	001107
Albumin	001081
Bilirubin, Total	001099
PT with INR	005199

References

1. Fontana RJ, Liou I, Reuben A, et al. AASLD Practice Guidance on Drug, Herbal and Dietary Supplement Induced Liver Injury. doi: 10.1002/hep.32689.

Visit the online test menu at **Labcorp.com** for additional test options and full test information, including CPT codes and specimen collection instructions.

