Approach to Abnormal Liver Tests

ABDOMINAL

29–33

KEY DECISION RULE

Healthy ALT upper limit (ACG)[1]

U/L in men and 19–25 U/L in women; assess any ALT above this

Abnormal ALT, AST, ALP or bilirubin on routine or acute testing

→ Repeat tests; history: alcohol, drugs, supplements, metabolic and viral risk[1,2]

→ R = (ALT/ULN) ÷ (ALP/ULN); bilirubin, INR, albumin, platelets[1,12]

→ **Liver failure, cholangitis or overdose?**

Yes →

Emergency: admit; hepatology, GI or toxicology

- ALF: INR ≥1.5 + confusion, no cirrhosis[3,12]
- Possible acetaminophen excess[5]
- Fever, RUQ pain, jaundice[11]
- Drug + ALT >3×, bilirubin >2× ULN (Hy's law)[2]
- Shock, hypoglycemia, ↑lactate[3]
- Pregnancy: HELLP, acute fatty liver[12]

→ **NAC if acetaminophen risk or early ALF; ALF: ICU, transplant[3,4,5]**

If not: which pattern?

	Hepatocellular, mild R >5, <5× ULN	**Hepatocellular, marked** R >5, ≥5× ULN	**Cholestatic or mixed** R <5	**Isolated bilirubin** enzymes normal
CAUSES	• MASLD; alcohol-related disease • Drugs, herbal supplements[2] • HBV, HCV, iron overload, Wilson, autoimmune	• **Acetaminophen toxicity** • **Ischemia, HSV, Budd-Chiari, Wilson** • Acute hepatitis A, B, E; drugs; autoimmune	• **Cholangitis** • Stone; pancreatic or biliary cancer • PBC, PSC, drugs, infiltration	• Gilbert syndrome • Hemolysis; hematoma resorption • Direct: sepsis, TPN, drugs; Dubin-Johnson[1]
CLUES	• Obesity, diabetes, dyslipidemia[7] • AST:ALT ≥2:1 suggests alcohol[1,12] • AST ≫ ALT, high CK: muscle, not liver[12]	• Overdose, or repeated excess + alcohol[5] • ALT:LDH <1.5: ischemia, acetaminophen[6] • HSV: fever, anicteric; pregnant, immunosupp.[3,12]	• Fever, RUQ pain, jaundice: Charcot[11] • Painless jaundice, weight loss: cancer • Itch, middle-aged woman: PBC; IBD: PSC[1,10]	• Indirect; rises with fasting, illness[1] • Anemia, high LDH, low haptoglobin
WORKUP	• HBsAg, anti-HBc, HCV Ab; iron studies[1] • ANA, anti-smooth muscle, IgG; ceruloplasmin[1] • Ultrasound; FIB-4 ≥1.3 → elastography[7]	• Acetaminophen level even if no history[5] • HAV IgM, HBsAg, anti-HBc IgM, HSV PCR[3] • Doppler ultrasound; trend INR, glucose[3]	• High GGT confirms liver source of ALP[1] • Ultrasound: dilated ducts → MRCP/ERCP[1] • Normal ducts: AMA (PBC); MRCP (PSC)[1,10]	• Fractionate: direct vs indirect[1] • CBC, smear, reticulocytes, haptoglobin • Direct: ultrasound, as for cholestasis[1]
MANAGE	• Stop alcohol and culprit drugs[2] • MASLD: weight loss, treat metabolic risk[7] • HBV, HCV: refer for antivirals[8,9]	• NAC now if acetaminophen possible[5] • Stop the drug; autoimmune: steroids[2,12] • Suspect HSV: empiric IV acyclovir[3]	• Cholangitis: antibiotics, then drainage[11] • Stones: ERCP, then cholecystectomy[12] • PBC: ursodiol 13–15 mg/kg/d[10]	• Gilbert: reassure; no further tests[1] • Hemolysis: find and treat the cause

Stethopedia
stethopedia.ca/approach/abnormal-liver-tests

Evidence [1] Kwo 2017, Am J Gastroenterol [2] Chalasani 2021, Am J Gastroenterol [3] Shingina 2023, Am J Gastroenterol [4] Lee 2009, Gastroenterology [5] Dart 2023, JAMA Netw Open [6] Cassidy 1994, J Clin Gastroenterol [7] Rinella 2023, Hepatology [8] Osiowy 2025, Can Liver J [9] Bhattacharya 2023, Clin Infect Dis [10] Lindor 2019, Hepatology [11] Miura 2018, J Hepatobiliary Pancreat Sci [12] Manual 2024–25, pp. 84–87