Acute Hepatitis

Acute hepatitis is a rapid-onset liver inflammation, often from viral, toxic, or ischemic causes, requiring prompt diagnosis and management. This document provides a comprehensive overview for advanced practice providers (APPs) in a hospital setting.

Definition and Epidemiology

- **Definition:** Acute hepatitis is defined as liver inflammation with an onset of less than 6 months, characterized by elevated liver enzymes (ALT/AST >5 times the upper limit of normal [ULN]), often accompanied by jaundice, coagulopathy, or encephalopathy in severe cases. It can progress to acute liver failure (ALF) if untreated.
- **Prevalence:**
  - **Viral Hepatitis:** Globally, ~1.5 million new cases of HAV and HBV occur annually, with HAV being more common in developing regions (WHO, 2023). HCV affects ~71 million people chronically, with acute cases often linked to IV drug use.
  - **Alcoholic Hepatitis:** Occurs in 5-10% of heavy drinkers (EtOH >60 g/day for men, >40 g/day for women), with higher rates in hospitalized patients.
  - **Drug-Induced:** Acetaminophen is the leading cause of ALF in the U.S., accounting for ~50% of ALF cases (UpToDate, 2025).
- **Risk Factors:**
  - IV drug use (HCV), unprotected sex (HBV), travel to endemic areas (HAV), alcohol use, medications (acetaminophen, isoniazid), occupational exposure (leptospirosis, Q fever), and pregnancy (AFLP, HELLP).
- **Social Determinants:** Poor sanitation (HAV, HEV), lack of vaccination (HBV), and limited access to healthcare increase risk.
- **Demographics:**
  - **HAV/HEV:** More common in children and young adults in endemic areas.
  - **HBV/HCV:** Peak incidence in ages 20-40, often linked to high-risk behaviors.
  - **Alcoholic Hepatitis:** Typically ages 40-60, with a male predominance.

Pathophysiology

- **Mechanisms:** Hepatocyte injury from various etiologies (viral, toxic, ischemic) leads to inflammation and necrosis, impairing liver function.
  - **Viral:** Viruses (e.g., HAV, HBV) cause direct cytopathic effects or immune-mediated damage (e.g., HBV triggers cytotoxic T-cell responses).

    - **Toxic:** Acetaminophen overdose depletes glutathione, leading to oxidative stress and hepatocyte necrosis. Alcohol causes steatosis and inflammation via acetaldehyde toxicity.
    - **Ischemic:** Hypoperfusion (e.g., shock liver) causes hypoxic injury, with rapid AST/ALT elevation (>1000 U/L).
- **Effects on Liver Function and Body:**
    - **Jaundice:** Impaired bilirubin conjugation/excretion → ↑ Total bilirubin (>3 mg/dL).
    - **Coagulopathy:** ↓ Synthesis of clotting factors (e.g., II, VII, IX, X) → ↑ INR (>1.5).
- **Encephalopathy and Cerebral Edema:** In severe cases (e.g., ALF), the liver fails to detoxify ammonia via the urea cycle, leading to hyperammonemia. Ammonia crosses the blood-brain barrier and is taken up by astrocytes, where it combines with glutamate to form glutamine (via glutamine synthetase). This increases intracellular osmolarity in astrocytes, causing them to swell, which contributes to cerebral edema. Additional mechanisms include:
    - **Systemic Inflammation:** Cytokine storm (e.g., IL-1, IL-6, TNF-α) in ALF exacerbates brain swelling.
    - **Impaired Cerebral Autoregulation:** Loss of cerebral blood flow control increases intracranial pressure (ICP).
    - **Blood-Brain Barrier Dysfunction:** Allows toxins (e.g., ammonia, inflammatory mediators) to enter the brain.
    - Cerebral edema is a leading cause of death in ALF, often causing herniation and brainstem compression, especially in grade III-IV encephalopathy.
- **Key Pathway:** Hepatocyte damage → Cytokine release → Inflammatory cascade → Impaired liver function → Systemic complications (e.g., cerebral edema, multi-organ failure).

Causes of Acute Hepatitis

Category	Causes	Notes
Viral	-HAV: Fecal-oral, travel. -HBV: Blood, sexual. -HCV: IV drug use. -HEV: Waterborne, pregnancy. -Adenovirus: Esp. in kids, immunocompromised. -HIV: Acute seroconversion, opportunistic infections. -HSV: Fulminant hepatitis, high mortality. -EBV, CMV: Mononucleosis.	HAV: Self-limited; HBV/HCV: May become chronic. HSV: Rare, often fatal without treatment.

Category	Causes	Notes
Toxic	-Alcohol: >60 g/day (alcoholic hepatitis). -Acetaminophen: >4 g/day (or less with alcohol). -Herbal: Kava, comfrey, black cohosh. -Drugs: Isoniazid, chemotherapy (see table). -Toxins: Carbon tetrachloride, sea anemone sting, aflatoxin (contaminated grains). - Mushroom Poisoning: Amanita phalloides (amatoxin).	Acetaminophen: Most common drug cause; ↑ INR. Mushrooms: Severe necrosis, ALF risk. Aflatoxin: Tropical regions, carcinogenic.
Ischemic	-Shock Liver: Hypotension (sepsis, MI). -Heat Stroke: Hyperthermia → Liver ischemia. - Trauma: Direct liver injury, hemorrhage.	AST/ALT >1000 U/L; resolves with perfusion. Heat stroke: Often with rhabdomyolysis.
Immune	-Autoimmune Hepatitis (AIH): Anti-smooth muscle Ab. -Hemophagocytic Lymphohistiocytosis (HLH): Triggered by infections (EBV, CMV), malignancy. -DRESS Syndrome: Drug reaction (e.g., allopurinol).	HLH: Hyperferritinemia, cytopenias; high mortality. DRESS: Rash, eosinophilia, multi-organ involvement.
Vascular	-Sinusoidal Obstructive Syndrome (SOS): Chemotherapy, stem cell transplant. -Budd-Chiari: Hepatic vein thrombosis. -Portal Vein Thrombosis: Hypercoagulable states.	SOS: Sinusoidal damage, ascites. Budd-Chiari: Ascites, hepatomegaly.
Metabolic	-Wilson's Disease: Copper overload. -Alpha-1 Antitrypsin Deficiency: Abnormal protein accumulation. -Reye's Syndrome: Aspirin use in kids, viral illness. -Glycogen Storage Diseases (e.g., GSD Type I): Metabolic stress.	Wilson's: Low ceruloplasmin, Kayser-Fleischer rings. Reye's: Encephalopathy, microvesicular steatosis.
Malignancy	-Metastases: Breast, lung, colon. -Lymphoma: Infiltration, HLH risk. -Hepatocellular Carcinoma: Rare in acute setting.	Often cholestatic pattern, hepatomegaly. Lymphoma: May present with fever, night sweats.
Endocrine	-Adrenal Crisis: Cortisol deficiency → Hypotension, stress. -Anorexia: Starvation → Hepatic stress, ↓ glycogen. -Thyroid Storm: Hypermetabolic state →Liver injury.	Adrenal Crisis: Rare, linked to severe stress. Thyroid Storm: Rare, associated with Graves' disease.
Infectious	-Sepsis: Indirect injury, cytokine storm. -Leptospirosis: Zoonotic, water exposure. -Q Fever: Coxiella burnetii, livestock exposure. -Malaria: Plasmodium spp., esp. falciparum.	Leptospirosis: Jaundice, renal failure (Weil's disease). Q Fever: Granulomas on biopsy. Malaria: Hemolysis, hepatic involvement.

Category	Causes	Notes
Obstetric	-Acute Fatty Liver of Pregnancy (AFLP): 3rd trimester. -HELLP Syndrome: Hemolysis, elevated LFTs, low platelets.	AFLP/HELLP: ↑ risk of liver failure, maternal/fetal mortality.
Other	-Celiac Disease: Transaminitis, gluten-related. -Sarcoidosis: Granulomatous hepatitis.	Celiac: Associated with gluten exposure, may resolve with diet. Sarcoidosis: Non-caseating granulomas.

Common Drugs Causing Acute Hepatitis

Drug	Mechanism	Notes
Acetaminophen	Hepatocyte necrosis (dose-dependent)	>4 g/day; ↑ risk with alcohol; leading cause of ALF.
Isoniazid	Idiosyncratic, metabolite toxicity	TB treatment; monitor LFTs monthly; risk ↑ with age.
Amoxicillin-Clavulanate	Cholestatic injury	Common antibiotic cause; onset 1-4 weeks post-exposure.
Statins	Idiosyncratic, hepatocyte injury	Rare; e.g., atorvastatin; usually mild, reversible.
Chemotherapy	Direct toxicity, SOS risk	E.g., cyclophosphamide, busulfan; high risk in stem cell transplants.
Phenytoin	Hypersensitivity reaction	Rash, eosinophilia possible; DRESS risk; monitor LFTs.
Ketoconazole	Hepatocyte injury	Antifungal; risk of severe injury; avoid in liver disease.
Nitrofurantoin	Idiosyncratic, chronic use	UTI treatment; can mimic AIH; risk with prolonged use.
Allopurinol	Hypersensitivity, DRESS	Gout treatment; rash, eosinophilia; severe in renal impairment.
Methotrexate	Direct toxicity, fibrosis risk	Psoriasis, RA; dose-dependent injury; risk ↑ with alcohol.
Valproic Acid	Mitochondrial toxicity	Antiepileptic; risk in kids, metabolic disorders; ↑ ammonia.
Azathioprine	Idiosyncratic, cholestatic	Immunosuppressant; used in AIH but can paradoxically cause injury.

Clinical Presentation

- **Symptoms:**
  - **Early:** Fatigue, malaise, nausea, vomiting, anorexia (esp. in anorexia nervosa, HLH), fever (leptospirosis, Q fever, brucellosis).

    - **Liver-Specific:** Jaundice, dark urine (↑ conjugated bilirubin), pale stools, right upper quadrant (RUQ) pain (liver capsule stretch).
    - **Severe:** Confusion, disorientation (encephalopathy), bleeding (coagulopathy).
- **Physical Exam:**
    - **General:** Icterus (scleral, skin), fever (infectious causes), weight loss (malignancy).
    - **Liver:** Hepatomegaly, RUQ tenderness, splenomegaly (HLH, leukemia).
    - **Neurologic:** Asterixis, altered mental status (encephalopathy), seizures (Reye's syndrome, severe ALF).
    - **Other Signs:** Rash/eosinophilia (DRESS), spider angiomas/ascites (if underlying cirrhosis), Kayser-Fleischer rings (Wilson's disease).
- **Substance Use:**
    - **Alcohol:** Alcoholic hepatitis (Maddrey's Discriminant Function [MDF] >32 → Severe).
    - **IV Drug Use:** HCV risk, often with needle-sharing history.
- **Red Flags:** INR >1.5, encephalopathy (any grade), bilirubin >20 mg/dL, or signs of cerebral edema (e.g., headache, vomiting, papilledema) indicate risk of ALF.

Diagnostic Workup

- **Labs:**
    - **Liver Function Tests (LFTs):**
    - ALT/AST >5x ULN (viral: ALT > AST; alcohol: AST:ALT >2:1; ischemic: >1000 U/L).
    - **Bilirubin:** Total >3 mg/dL (conjugated if liver injury).
    - **Alkaline Phosphatase (ALP):** ↑ in cholestatic injury (e.g., DRESS, SOS).
    - **Coagulation:** INR >1.5 (synthetic dysfunction).
    - **Viral Serologies:** HAV IgM, HBsAg, anti-HCV, HEV IgM, HIV (acute seroconversion), HSV PCR, adenovirus PCR, EBV/CMV IgM.
    - **Infectious:** Leptospira IgM, Coxiella serology (Q fever), malaria smear, Brucella serology, syphilis (RPR/VDRL).
    - **Metabolic/Immune:** Ceruloplasmin (Wilson's), ferritin (>1000 ng/mL in HLH), ANA/anti-smooth muscle Ab (AIH), anti-tissue transglutaminase (celiac).
    - **Toxins:** Acetaminophen level, EtOH level, drug screen (if suspected).
    - **Encephalopathy:** Ammonia (↑ in ALF, correlates poorly with encephalopathy severity but confirms hyperammonemia).
- **Imaging:**
    - **Ultrasound (US) Abdomen:** Hepatomegaly, rule out Budd-Chiari (hepatic vein thrombosis), SOS, or portal vein thrombosis; Doppler for vascular flow.

- **CT/MRI:** For malignancy (e.g., metastases, HCC), vascular causes, or trauma (e.g., liver laceration).

- **Other Tests:**
  - **Liver Biopsy:** Indicated if cause unclear (e.g., AIH, HLH, sarcoidosis; granulomas in Q fever, brucellosis).
  - **ICP Monitoring:** In ALF with grade III-IV encephalopathy (suspected cerebral edema).
  - **Genetic Testing:** If metabolic disease suspected (e.g., Wilson's, alpha-1 antitrypsin deficiency).
- **Key Tips:**
  - Viral serologies first; acetaminophen level in all (even if not reported).
  - Ferritin >1000 ng/mL → Suspect HLH; order bone marrow biopsy if cytopenias present.
  - Consider zoonotic infections (leptospirosis, Q fever, brucellosis) in patients with occupational exposure (e.g., farmers, veterinarians).

Management Flowsheet: Acute Hepatitis

- **Identify Cause:**
  - **Viral:** Serologies (HAV IgM, HBsAg, HSV PCR).
  - **Toxic:** Acetaminophen level, EtOH history, drug exposure (e.g., methotrexate).
  - **Ischemic:** History of hypotension, trauma, heat stroke.
  - **Infectious:** Leptospira IgM, Q fever serology, malaria smear, Brucella serology.
- **Supportive Care:**
  - **Hydration:** IV fluids (LR if dehydrated, cautious if volume overloaded).
  - **Nutrition:** High-calorie diet, 1.5 g/kg protein (unless encephalopathy).
  - **Nausea:** Ondansetron 4 mg IV q8h.
- **Specific Therapy:**
  - **Acetaminophen:** N-acetylcysteine (NAC) 150 mg/kg IV over 1h, then 50 mg/kg over 4h.
  - **HBV:** Tenofovir 300 mg daily (如果是急性重症).
  - **HSV:** Acyclovir 10 mg/kg IV q8h.
  - **Alcoholic:** Prednisolone 40 mg daily (MDF >32). (contraindications: infection, GIB)
  - **HLH:** Dexamethasone, etoposide (HLH-94 protocol).
  - **Leptospirosis:** Doxycycline 100 mg IV BID.
- **Monitor:**
  - LFTs, INR, bilirubin q12-24h.

- **Encephalopathy:** Neuro checks, ammonia; monitor for cerebral edema (e.g., CT head if grade III-IV).
- **Consult:** GI/hepatology if INR >1.5, encephalopathy (consider transplant).

Treatment

- **General Principles:** Identify and treat the underlying cause, provide supportive care, and monitor for progression to acute liver failure (ALF).
- **Supportive Care:**
  - **Hydration:** IV fluids to maintain euvolemia; avoid overhydration to prevent worsening cerebral edema in ALF. Cautious if patient appears volume overloaded (peripheral edema, ascites)
  - **Nutrition:** 1.5 g/kg protein (reduce to 0.5 g/kg if encephalopathy present), high-calorie diet (30-40 kcal/kg/day) to support liver regeneration.
  - **Nausea/Vomiting:** Ondansetron 4 mg IV q8h or metoclopramide 10 mg IV q6h.
  - **Avoid Hepatotoxins:** Discontinue alcohol, acetaminophen, herbals, and offending drugs (e.g., allopurinol, nitrofurantoin, methotrexate).
- **Specific Therapy:**
  - **Acetaminophen Overdose/Mushroom Poisoning:** N-acetylcysteine (NAC) 150 mg/kg IV over 1h, then 50 mg/kg over 4h, followed by 100 mg/kg over 16h (total 72h protocol); effective even in late presentation.
  - **HBV (Severe/Fulminant):** Tenofovir 300 mg daily or entecavir 0.5 mg daily; consider lamivudine 100 mg daily if unavailable.
  - **HSV Hepatitis:** Acyclovir 10 mg/kg IV q8h (urgent; mortality >50% if untreated); continue until clinical improvement.
  - **Alcoholic Hepatitis:** Prednisolone 40 mg daily x 28 days (MDF >32, no infection); assess response with Lille score at day 7 (score >0.45 → Poor response, consider transplant). Contraindications: Infection/GIB
  - **Autoimmune Hepatitis (AIH):** Prednisone 40-60 mg daily + azathioprine 1-2 mg/kg/day (if no contraindications); taper prednisone after remission.
  - **Wilson's Disease:** Penicillamine 250 mg QID (chelator); zinc acetate 50 mg TID (maintenance); triage to transplant if ALF.
  - **Hemophagocytic Lymphohistiocytosis (HLH):** Dexamethasone 10 mg/m² daily +etoposide 150 mg/m² (HLH-94 protocol); treat underlying trigger (e.g., EBV).
  - **Adrenal Crisis:** Hydrocortisone 100 mg IV q6h + IV fluids (NS 1L bolus); treat precipitant (e.g., infection).
  - **Leptospirosis:** Doxycycline 100 mg IV BID or penicillin G 1.5 million units IV q6h x 7 days.

- **Q Fever:** Doxycycline 100 mg PO BID x 14 days; add hydroxychloroquine 200 mg TID if chronic.
- **Malaria:** Artesunate 2.4 mg/kg IV at 0, 12, 24h, then daily x 7 days (per WHO); follow with artemisinin-based combination therapy (ACT).
- **Brucellosis:** Doxycycline 100 mg PO BID + rifampin 600 mg daily x 6 weeks.
- **DRESS Syndrome:** Stop offending drug (e.g., allopurinol, phenytoin); prednisone 1 mg/kg/day, taper over 6-8 weeks.
- **Reye's Syndrome:** Supportive care, IV glucose (prevent hypoglycemia), monitor for cerebral edema.

- **Management of Encephalopathy and Cerebral Edema**
  - **Lactulose: 30 mL PO/NG q2-4h (titrate to 2-3 bowel movements/day) to reduce ammonia absorption.**
  - **Rifaximin: 550 mg PO BID (adjunct to lactulose) to reduce gut ammonia production.**
  - **Cerebral Edema (ALF):**
    - **Elevate head of bed to 30 degrees to reduce ICP.**
    - **Mannitol: 0.5-1 g/kg IV bolus (if ICP >20 mmHg or signs of herniation); ensure euvolemia.**
    - **Hypertonic Saline: 3% NaCl 250 mL IV over 30 min (goal serum Na 145-155 mmol/L) to reduce brain swelling.**
    - **Monitor: CT head if grade III-IV encephalopathy; ICP monitoring if available (goal ICP <20 mmHg).**
    - **Avoid: Over-sedation (e.g., benzodiazepines); maintain normocapnia (PaCO2 35-40 mmHg).**

Monitor

- **Labs:** LFTs, INR, bilirubin, creatinine q12-24h (trend improvement).
- **Neurologic:** Neuro checks q1-2h (encephalopathy grading); watch for signs of cerebral edema (e.g., Cushing's triad: hypertension, bradycardia, irregular respirations).
- **Renal Function:** Especially in leptospirosis, HELLP, AFLP (risk of AKI); consider dialysis if needed.

Substance Use Interventions

- **Alcohol Cessation:** Alcoholic hepatitis patients need counseling, referral to addiction services, and possible pharmacotherapy (e.g., naltrexone 50 mg daily).
- **IV Drug Use:** Screen for HCV, offer needle exchange programs, and refer to harm reduction services.

Key Tip INR >1.5 + encephalopathy → Triage to transplant center (ALF); early intervention critical for HSV, HLH, and cerebral edema management.

Indications for Liver Transplant

- **Acute Liver Failure (ALF):** Defined as INR >1.5 + encephalopathy (any grade) within 8 weeks of onset, without underlying chronic liver disease.

King's College Criteria (for Transplant Urgency)

- **Acetaminophen-Induced:** pH <7.3 (after fluids) OR (INR >6.5 + creatinine >3.4 mg/dL + encephalopathy grade III/IV).
- **Non-Acetaminophen:** INR >6.5 OR any 3 of: age <10 or >40, bilirubin >17.5 mg/dL, etiology (drug, indeterminate), jaundice >7 days before encephalopathy, INR >3.5.

Specific Etiologies

- Fulminant viral hepatitis (e.g., HSV, HBV, HEV in pregnancy).
- Wilson's disease with ALF (ceruloplasmin <20 mg/dL, hemolysis, Coombs-negative anemia).
- Severe alcoholic hepatitis (MDF >32, non-responsive to steroids after 7 days, Lille score >0.45).
- Mushroom poisoning (Amanita phalloides) with ALF (e.g., INR >2, encephalopathy).
- AFLP/HELLP with persistent liver failure post-delivery.
- Budd-Chiari syndrome with acute decompensation (failed thrombolysis/stenting).

Contraindications

- Active alcohol/drug use (unless sober ≥6 months).
- Uncontrolled sepsis or multi-organ failure (irreversible).
- Irreversible brain injury (e.g., cerebral edema with herniation, confirmed by CT).
- Advanced malignancy (e.g., metastatic disease).

Key Tips

- Early transfer to a transplant center is critical if ALF criteria are met; mortality >80% without transplant in ALF.
- Consider MELD score (>25 indicates poor prognosis) for prioritization in alcoholic hepatitis.

Examples

- **1. Case 1:** Acute Viral Hepatitis (HAV)
- **Presentation:** 35 y/o M, recent travel to Mexico, presents with jaundice, nausea, fatigue, ALT 1500 U/L, AST 1200 U/L, bilirubin 5 mg/dL, HAV IgM positive.
- **Interpretation:** Acute hepatitis (HAV), self-limited in most cases.
- **Management:** Supportive care (IV fluids, ondansetron 4 mg IV q8h), monitor LFTs/INR q24h, avoid alcohol, educate on hand hygiene to prevent spread. Expected resolution in 4-8 weeks.

- **Case 2:** Alcoholic Hepatitis (Severe)
- **Presentation:** 50 y/o M, heavy drinker (100 g/day EtOH x 10 years), presents with RUQ pain, jaundice, fever, AST 300 U/L, ALT 100 U/L, bilirubin 10 mg/dL, MDF 40.
- **Interpretation:** Acute alcoholic hepatitis, severe (MDF >32).
- **Management:** Rule out infection (blood cultures, CXR), start prednisolone 40 mg daily x 28 days, assess Lille score at day 7 (if >0.45, consider transplant referral), nutrition support (1.5 g/kg protein), alcohol cessation counseling, monitor for encephalopathy and ALF.

- **Case 3:** Acetaminophen Toxicity with ALF
- **Presentation:** 30 y/o F, suicidal overdose (20 g acetaminophen), presents with nausea, vomiting, ALT 5000 U/L, INR 2.5, grade II encephalopathy, pH 7.2, creatinine 3.5 mg/dL.
- **Interpretation:** Acute hepatitis (acetaminophen), progressing to ALF (meets King's College Criteria: pH <7.3, INR >2, encephalopathy).
- **Management:** Start NAC (150 mg/kg IV over 1h, then per protocol), urgent transfer to transplant center, monitor for cerebral edema (CT head, elevate HOB 30°), mannitol 0.5 g/kg IV if ICP >20 mmHg, supportive care (IV fluids, glucose).

- **Case 4:** Leptospirosis (Weil's Disease)
- **Presentation:** 45 y/o M, farmer, presents with fever, jaundice, AKI, conjunctival suffusion, ALT 800 U/L, bilirubin 8 mg/dL, creatinine 2.8 mg/dL, Leptospira IgM positive.
- **Interpretation:** Acute hepatitis (leptospirosis), severe with renal involvement (Weil's disease).

- **Management:** Doxycycline 100 mg IV BID x 7 days, IV fluids (NS 1L bolus, then maintenance), monitor renal function (consider dialysis if AKI worsens), supportive care for liver injury (nutrition, avoid hepatotoxins).

- **Case 5:** HSV Hepatitis in Pregnancy
- **Presentation:** 28 y/o F, 32 weeks pregnant, presents with fever, RUQ pain, ALT 2000 U/L, INR 1.8, grade I encephalopathy, HSV PCR positive.
- **Interpretation:** Fulminant HSV hepatitis, high risk of ALF.
- **Management:** Acyclovir 10 mg/kg IV q8h (urgent), supportive care (IV fluids, lactulose for encephalopathy), monitor for cerebral edema (neuro checks q1h), urgent OB/GI consult (consider delivery if stable), transfer to transplant center (ALF criteria met).

Complications

Acute

- **Acute Liver Failure (ALF):** Occurs in 1-2% of acute hepatitis cases; defined as INR >1.5 + encephalopathy within 8 weeks of onset. Leading causes include acetaminophen, HSV, and Wilson's disease.
- **Encephalopathy and Cerebral Edema:** Ammonia-driven astrocyte swelling, compounded by inflammation and impaired autoregulation, leads to cerebral edema (common in ALF). Risk of herniation and death if untreated.
- **Coagulopathy:** ↓ Clotting factors → ↑ INR, risk of bleeding (e.g., GI bleed, epistaxis). Vitamin K 10 mg IV may help if deficiency present, but often ineffective in ALF.
- **Acute Kidney Injury (AKI):** Common in leptospirosis, HELLP, AFLP, and acetaminophen toxicity (due to acute tubular necrosis).
- **Infections:** Patients with ALF are immunocompromised; risk of sepsis (e.g., gram-negative bacilli, Candida).

Long-Term

- **Chronicity:** HBV/HCV progress to chronic infection in 5-10% of acute cases, increasing risk of cirrhosis and HCC.
- **Cirrhosis:** Common in alcoholic hepatitis (if drinking continues) and chronic drug-induced injury (e.g., methotrexate, amiodarone).
- **Hepatocellular Carcinoma (HCC):** Rare in acute setting but a long-term risk with chronic HBV/HCV or hemochromatosis.

- **Fibrosis:** Chronic exposure to hepatotoxins (e.g., methotrexate, alcohol) can lead to fibrosis, even without cirrhosis.

Prognosis

Mortality

- **HAV/HEV:** <1% (rarely fulminant, except HEV in pregnancy: 20-25% mortality).
- **Alcoholic Hepatitis (MDF >32):** 30-50% at 1 month without treatment; 20-30% with steroids and abstinence.
- **ALF:** >80% mortality without transplant; 20-30% with transplant (dependent on etiology, e.g., acetaminophen has better post-transplant outcomes).
- **HSV Hepatitis:** 50-75% mortality, even with acyclovir, if untreated or delayed.
- **Leptospirosis (Weil's Disease):** 5-10% mortality with severe disease (AKI, liver failure).

Recovery

- **Viral Hepatitis (HAV, HEV):** Most resolve in 4-8 weeks with supportive care; fulminant cases rare (<1%).
- **Drug-Induced:** Resolution in 2-4 weeks if drug stopped (e.g., nitrofurantoin, allopurinol), unless ALF develops.
- **Alcoholic Hepatitis:** 50-70% 1-year survival with steroids and abstinence; poor prognosis if drinking continues.
- **Metabolic (e.g., Wilson's):** Good with early chelation (penicillamine); poor if ALF develops without transplant.

Key Factors

- Early intervention (e.g., NAC for acetaminophen, acyclovir for HSV) significantly improves outcomes.
- Absence of ALF, treatment of underlying cause (e.g., antibiotics for leptospirosis), and cessation of hepatotoxins (e.g., alcohol, methotrexate) are critical.
- Cerebral edema management (e.g., mannitol, hypertonic saline) can be lifesaving in ALF.

Key Pearls

- ALT/AST >5x ULN, bilirubin ↑ → Suspect acute hepatitis; differentiate based on history (travel, IV drug use, medications).
- Viral serologies first; acetaminophen level in all (even if not reported); consider zoonotic infections (leptospirosis, Q fever, brucellosis) in at-risk patients.

- AST:ALT >2:1 → Alcoholic hepatitis; MDF >32 → Steroids (if no infection); Lille score >0.45 at day 7 → Consider transplant.
- INR >1.5 + encephalopathy → Triage to transplant center for ALF evaluation; monitor for cerebral edema (CT head, ICP monitoring).
- Alcohol/IV drug use → Screen for HCV, counsel cessation; stop hepatotoxic drugs (e.g., methotrexate, nitrofurantoin, amiodarone).
- **Cerebral Edema in ALF:** Driven by hyperammonemia (astrocyte swelling via glutamine), inflammation, and impaired autoregulation; manage with mannitol, hypertonic saline, and neuro checks.

References

- **UpToDate:** “Acute Hepatitis” (2025).
- **AASLD Guidelines:** Alcoholic Hepatitis (2023).
- **NEJM:** “Acute Liver Failure” (Lee, 2012).
- **WHO:** “Malaria Treatment Guidelines” (2023).
- **EASL:** “Management of Acute Liver Failure” (2024).