Autoimmune Hepatitis

Suspect it in any unexplained hepatitis · it is one of the few causes of acute liver failure with a specific, effective treatment

Treat it *before it scars*

WHEN TO SUSPECT IT *the presentation is deceptively variable*

WHO

Predominantly women, at any age, with a **bimodal peak** in adolescence and around the fifth decade. **Ask about other autoimmune disease** in the patient and the family: thyroid disease, celiac, type 1 diabetes, vitiligo, rheumatoid arthritis.

HOW IT PRESENTS

Anything from asymptomatic transaminitis to acute liver failure. Fatigue, jaundice, arthralgia, amenorrhea. **Around a third already have cirrhosis at diagnosis**, because the indolent form goes unnoticed for years.

THE ACUTE TRAP

Acute severe autoimmune hepatitis can present as acute liver failure with negative antibodies and a normal IgG. Do not exclude it on serology alone in a patient with unexplained acute hepatitis, because it is **treatable and the window is short**.

MAKING THE DIAGNOSIS *a composite, not a single test*

Element	Detail
Pattern	**Hepatocellular**: transaminases raised well out of proportion to alkaline phosphatase. A cholestatic picture should redirect you toward PBC, PSC or an overlap
Autoantibodies	**Type 1 (the great majority of adults): ANA and anti-smooth muscle antibody. Type 2: anti-LKM1**, mainly children and young adults, often more aggressive. Anti-SLA is highly specific and identifies patients who relapse more. **Titers do not track disease activity**, so do not follow them
Raised IgG	Elevated in most cases and **genuinely useful for monitoring**, unlike the antibody titers. A normal IgG does not exclude the diagnosis, particularly in acute severe disease
Liver biopsy	**Essentially always required**, to confirm and to stage. Classic findings are **interface hepatitis with a plasma-cell-rich infiltrate**, and rosetting of hepatocytes
⚠ Exclude the mimics first	**Viral hepatitis A, B, C and E, plus EBV and CMV**, and **drug-induced liver injury**, which can be indistinguishable histologically: nitrofurantoin, minocycline, statins, infliximab and checkpoint inhibitors are recognized culprits. **In anyone under about 40, exclude Wilson disease** with ceruloplasmin, and consider alpha-1 antitrypsin deficiency and hemochromatosis

TREATMENT *steroids to induce, a steroid-sparing agent to maintain*

Phase	Detail
Induce remission	**Prednisone or prednisolone**, usually with **azathioprine** added early as the steroid-sparing agent. **Budesonide is an alternative to prednisone in non-cirrhotic patients** with fewer systemic effects, but **it should not be used in cirrhosis**, where portosystemic shunting removes its first-pass advantage and it carries a thrombosis risk
Check TPMT before azathioprine	Low thiopurine methyltransferase activity predicts **severe myelosuppression**. Check activity or genotype first, and monitor the CBC regardless. Azathioprine also takes weeks to work, which is why steroids carry the induction
Define remission properly	**Normal transaminases AND a normal IgG**, ideally with histological resolution. **Biochemical improvement alone is not remission**, and stopping there is the commonest reason patients relapse
Treat for long enough	Maintain for **at least 2 to 3 years** and for a minimum of 2 years of complete biochemical remission before considering withdrawal. **Relapse after stopping is common, well over half in most series**, and many patients need indefinite low-dose maintenance. Consider a biopsy before withdrawal
Refractory disease	Mycophenolate or a calcineurin inhibitor as second-line. **Reconsider the diagnosis and check adherence before escalating**, since both explain apparent non-response more often than true refractoriness. **Transplant** for acute liver failure or decompensated cirrhosis

ACUTE SEVERE AIH *a different clinical problem with a short decision window*

Question	Answer
How is it different?	Presents with **jaundice and coagulopathy** rather than an incidental transaminitis. **Antibodies are negative in a substantial minority and the IgG can be normal**, so the usual diagnostic scaffolding fails exactly when speed matters. Histology may show **massive or centrilobular necrosis** rather than classic interface hepatitis
Should steroids be started?	**Yes, promptly, once infection and other causes are excluded**, because this is one of very few causes of acute liver failure with a specific medical therapy. Use intravenous steroids if oral intake is unreliable
⚠ When to stop waiting	**Reassess within about 7 days.** If bilirubin and INR are not improving, **steroids have failed and continuing them adds sepsis risk while the window for transplant closes. Contact a transplant center at presentation, not after steroids fail**: the two should run in parallel
What predicts failure?	Deepening jaundice, rising INR and any **encephalopathy**. Encephalopathy in this setting means transplant assessment now, since medical rescue rates fall sharply once it appears

MONITORING & PEARLS

- **Steroid cover is part of the prescription.** Bone protection with calcium, vitamin D and a bisphosphonate where indicated, plus attention to glucose, blood pressure and cataract on prolonged therapy. Vaccinate before immunosuppression where possible, and **screen for hepatitis B before starting**, since immunosuppression can reactivate it.
- **Overlap syndromes are real.** A cholestatic ALP or a positive AMA alongside autoimmune hepatitis suggests overlap with PBC, and an abnormal MRCP suggests PSC overlap, which is particularly worth considering in a young patient with inflammatory bowel disease.
- **Once cirrhotic, surveillance does not stop when the liver enzymes normalize.** Continue **6-monthly ultrasound for hepatocellular carcinoma** and screen for varices, because immunosuppression controls inflammation but does not reverse established cirrhosis.
- **Pregnancy is usually well tolerated and often quiescent**, but **flares are common postpartum**, so plan monitoring around delivery. **Azathioprine is generally continued**, whereas mycophenolate is teratogenic and must be stopped and substituted well before conception.

References: AASLD practice guidance on the diagnosis and management of autoimmune hepatitis · EASL clinical practice guidelines on autoimmune hepatitis · International Autoimmune Hepatitis Group simplified diagnostic criteria.

Educational aid; verify against current guidance, local formulary and patient factors.