RECOMMENDATIONS SECTION O

1. We recommend routine consideration of the possibility of drug-induced autoimmune-like hepatitis (DI-ALH) and prompt cessation of any suspected precipitant. *Grade of evidence: low. Strength of recommendation: strong.*

2. We recommend performing a liver biopsy if there is not prompt resolution of liver injury on withdrawal of the suspected precipitant. *Grade of evidence: low. Strength of recommendation: strong.*

3. For DI-AILH, we recommend starting prednisolone (0.5 mg/kg/day or up to 40 mg/day, as for idiopathic AIH), if there is either (a) jaundice, (b) advanced fibrosis on liver biopsy or (c) failure of serum transaminases to fall substantially within a week of stopping the suspected precipitant. Patients with liver failure should be discussed with a transplant centre. *Grade of evidence: low. Strength of recommendation: strong.*

4. We recommend that (a) prednisolone be tapered as for standard AIH, until serum transaminases (and IgG, if elevated) have fallen to normal, and then be phased out gradually, (b) patients then be monitored by serial serum transaminases. In the event of hepatitis relapse, subsequent management is that of standard AIH, with prednisolone and a steroid-sparing agent. *Grade of evidence: low. strength of recommendation: weak.*

5. Features of chronicity (such as advanced fibrosis on biopsy) also make it less likely that the drug is the sole cause. We recommend treating such patients as if they have standard AIH. Always consider seeking an expert clinical opinion. *Grade of evidence: low. Strength of recommendation: weak.*

SECTION P. COVID-19 AND AIH[431]

COVID-19 might involve the liver,[431] and cause abnormal liver tests.[432] In patients with AIH, COVID-19 might cause a 'flare' in serum transaminase,[433] which is usually mild, but in cirrhotic patients might result in acute on chronic liver failure.[431]

COVID-19 might be more severe in patients taking immunosuppressive drugs, including rituximab,[434] high-dose steroids, thiopurines, and (possibly) mycophenolate and tacrolimus.[435] However, other surveys[436] do not support this Thus some, although not all, guidelines suggest modest reduction of immunosuppression dose.[437 438] NICE guidance recommends[439 440] specific antiviral treatment within 5–7 days of symptoms in patients with cirrhosis, and in those taking immunosuppressive drugs.

Several cases have been reported of AIH developing shortly after COVID-19.[19 20] However many are probably coincidental.

Patients with AIH should receive COVID vaccination. About half, especially those taking steroids or mycophenolate, had impaired cellular and humoral responses to two doses of COVID vaccine; however, a third dose then achieved an adequate humoral (though not cellular) response.[441] Despite this, COVID-19 infection in AIH is less severe in vaccinated patients.[442]

Several cases of an acute AIH-like illness have been reported within 4 weeks of COVID-19 vaccination, including both the viral vector (Oxford and Janssen) and mRNA (Pfizer and Moderna) variants.[443–445] AIH is usually, mild and responds to corticosteroids, but a few cases have been fatal or have required liver transplantation. Incidence of post-vaccine liver injury[446] is low: 4 per 10 000, and some cases are probably coincidental. However, AIH following COVID vaccination rarely causes advanced fibrosis, and rarely relapses after steroids are stopped. In some reports,[444 447] liver injury developed twice after repeated exposure to the same vaccine, although not after re-exposure to a different vaccine. These features suggest a causative role for the vaccine in some cases.

Box 3 Proposed standards for diagnosis and management of autoimmune hepatitis.

(A) Patients within 10 years of diagnosis

1. Documented exclusion of viral cause: at diagnosis.
   For acute icteric presentation: (HAV, HBV, HCV, HEV, EBV, CMV, HIV)
   For indolent presentations (HBV, HCV, HIV)
   2. Diagnostic liver biopsy: performance, or documented reason for not performing.
   3. Documentation of biopsy discussion at clinical-pathological meeting.
   4. Time between initial raised serum ALT and starting steroid treatment <18 weeks, and <4 weeks, if jaundiced (peak bilirubin >60 mmol/L).
   5. Initial prednisolone dose ≤40 mg or 0.5 mg/kg/day 6. Steroid-sparing agent introduced within 4 weeks of starting steroid in patients with compensated liver disease and serum bilirubin <100 mmol/L.

Tests performed to assess achieved:

   8. Documented fracture risk assessment (FRAX score or DEXA) within 3 months of starting steroids.
   9. Documented encouragement of annual eye examination if age >60 and on steroids for >12 months.
   10. Steroids stopped within 12 months of starting or documented reason for continuing.

(B) All patients

11. Patients on thiopurines or mycophenolate: full blood count documented ≥3 times over past 365 days.
   12. Patients on azathioprine of mycophenolate for >3 years: documented discussion about pros and cons of stopping.
   13. Non-invasive fibrosis imaging assessment performed at least once over past 3 years

RECOMMENDATIONS SECTION P

1. We recommend that patients with AIH with cirrhosis/or those receiving immunosuppressive treatment who develop COVID-19 infection, be considered for appropriate antiviral therapy. *Grade of evidence: high. Strength of recommendation: strong.*

2. We recommend that steroid therapy usually be continued during COVID-19 infection. The decision to withhold steroid-sparing agents should be individualised, based on infection severity. *Grade of evidence: low. Strength of recommendation: weak.*

CONCLUSION

In these guidelines, we have described what we think are the best strategies for managing patients with AIH, based on current knowledge. In box 3 we propose diagnostic and management standards, against which services could be audited. Organisation of services for AIH in the UK and elsewhere could potentially be improved, and in box 4, we make proposals for this. Finally, our understanding of AIH and its management remains incomplete, and so, in box 5, we propose some priorities for clinical research.