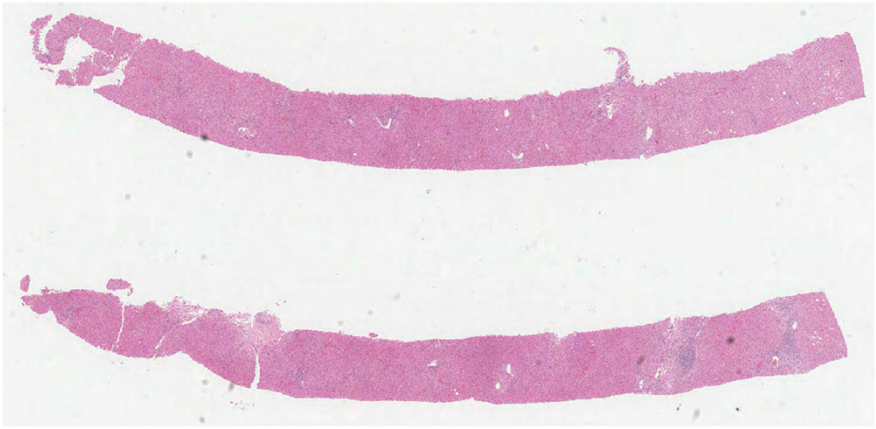
Case LS2 75M

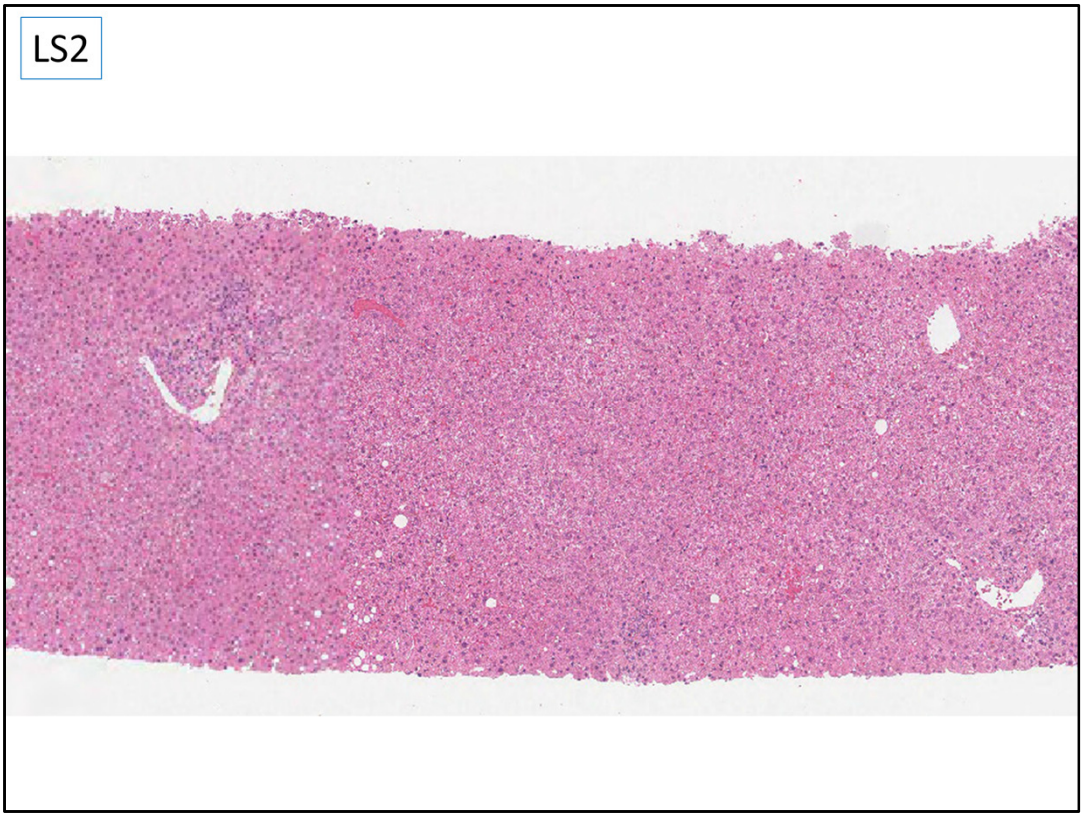
Mixed picture of abnormal LFTs - on Sodium Valproate, risk factors for NAFLD (obesity, HBP and high cholesterol), also previous biliary issues with open cholecystectomy and CBD clearance for stones.

Surgical team working up for incisional hernia repair - but noted ongoing abnormal LFTs.
MRCP ?? PSC. Biopsy - ? NASH/?DILI or PSC.

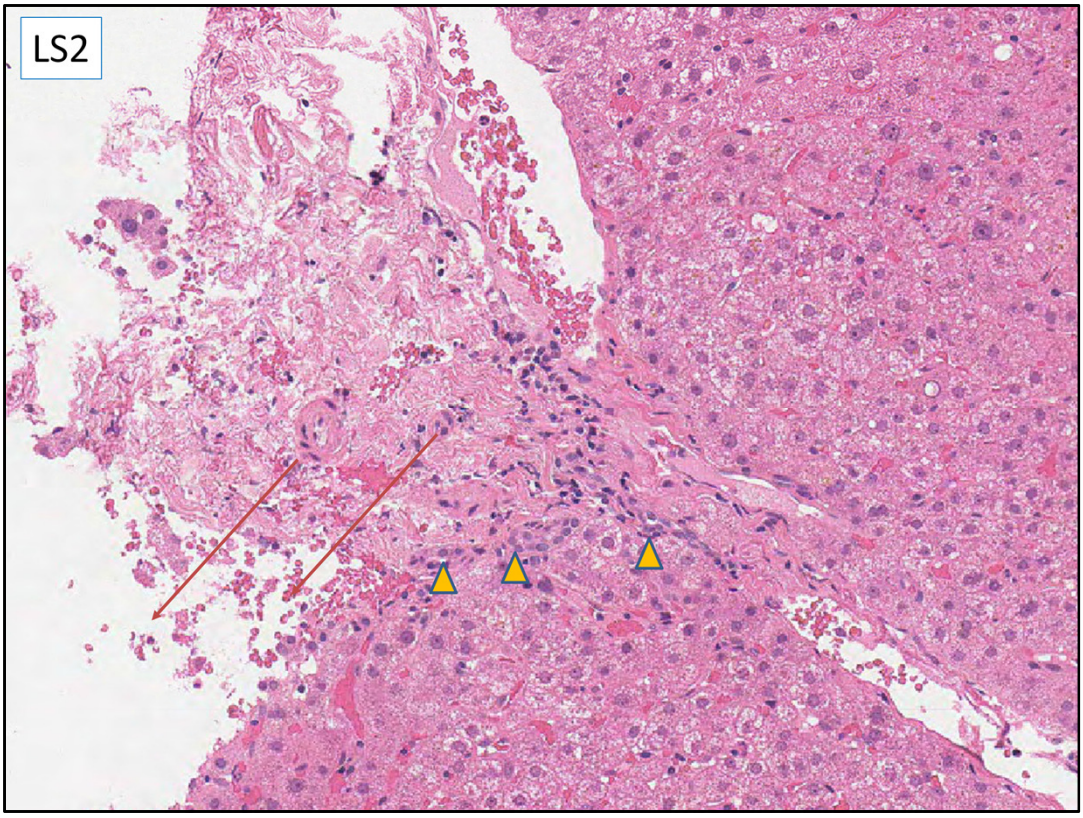
Also HVG, rhodanine



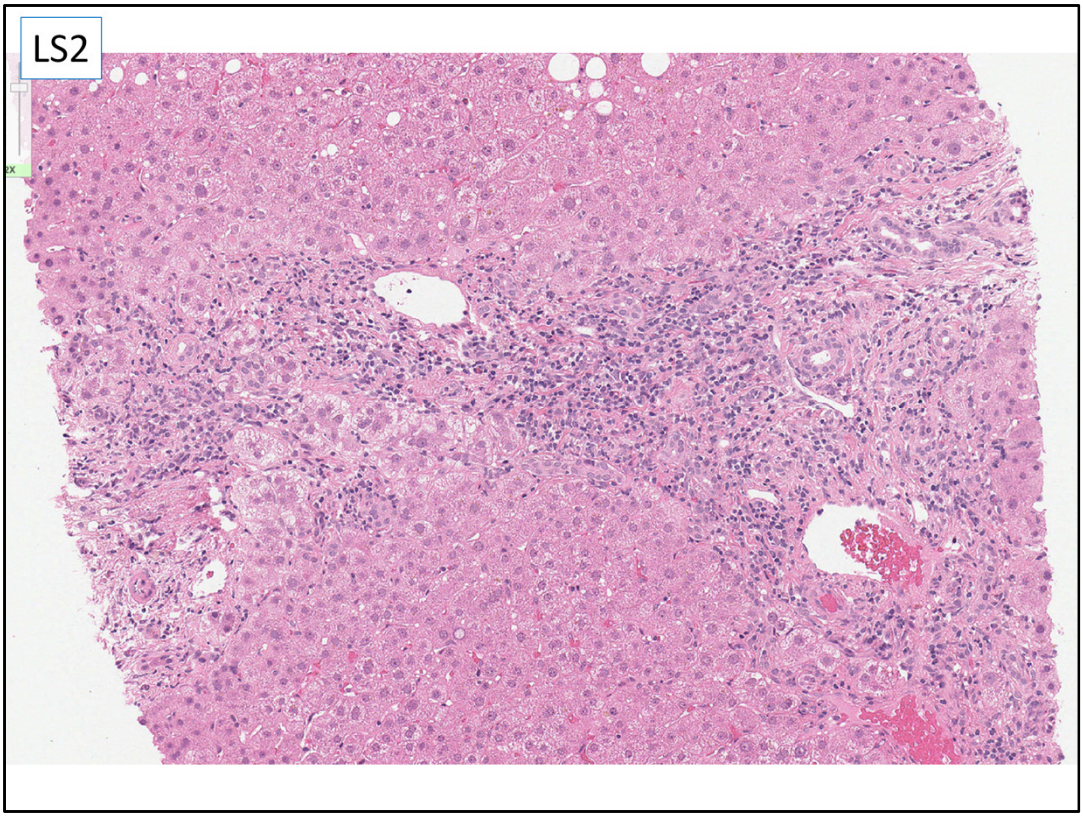
Expansion of some of the portal tracts, together with chronic inflammation is apparent at low magnification



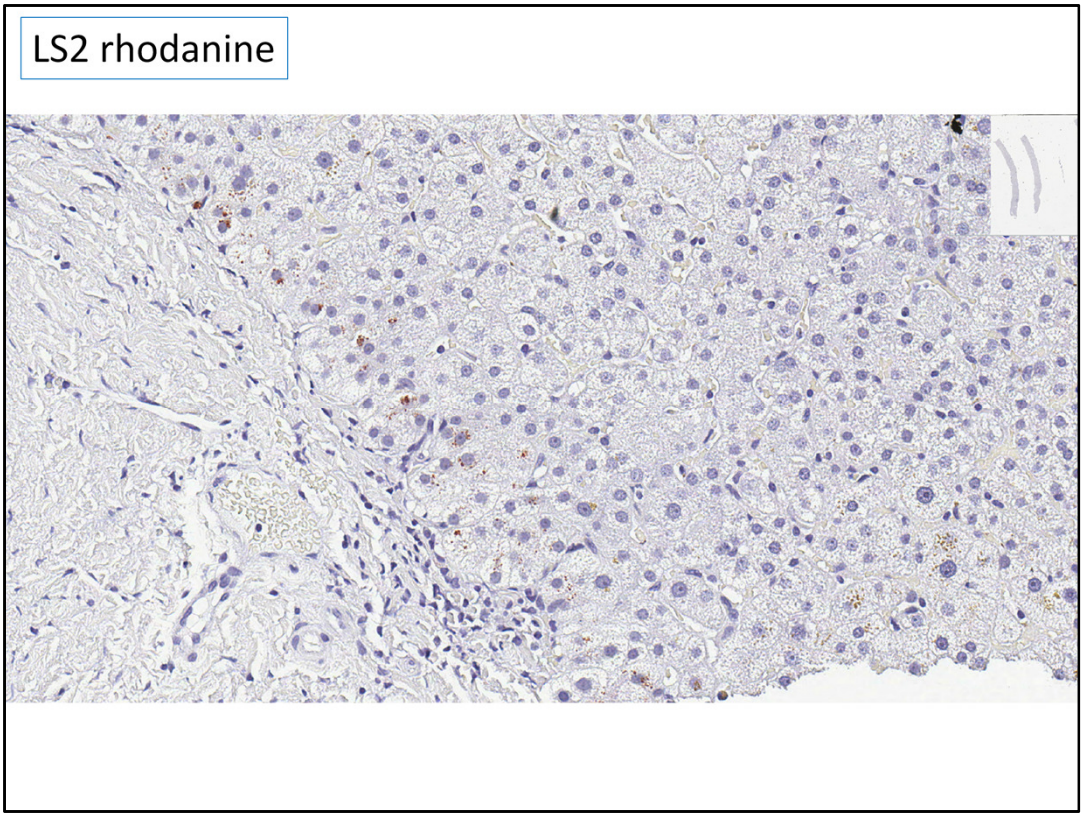
There is minimal steatosis present in the parenchyma.



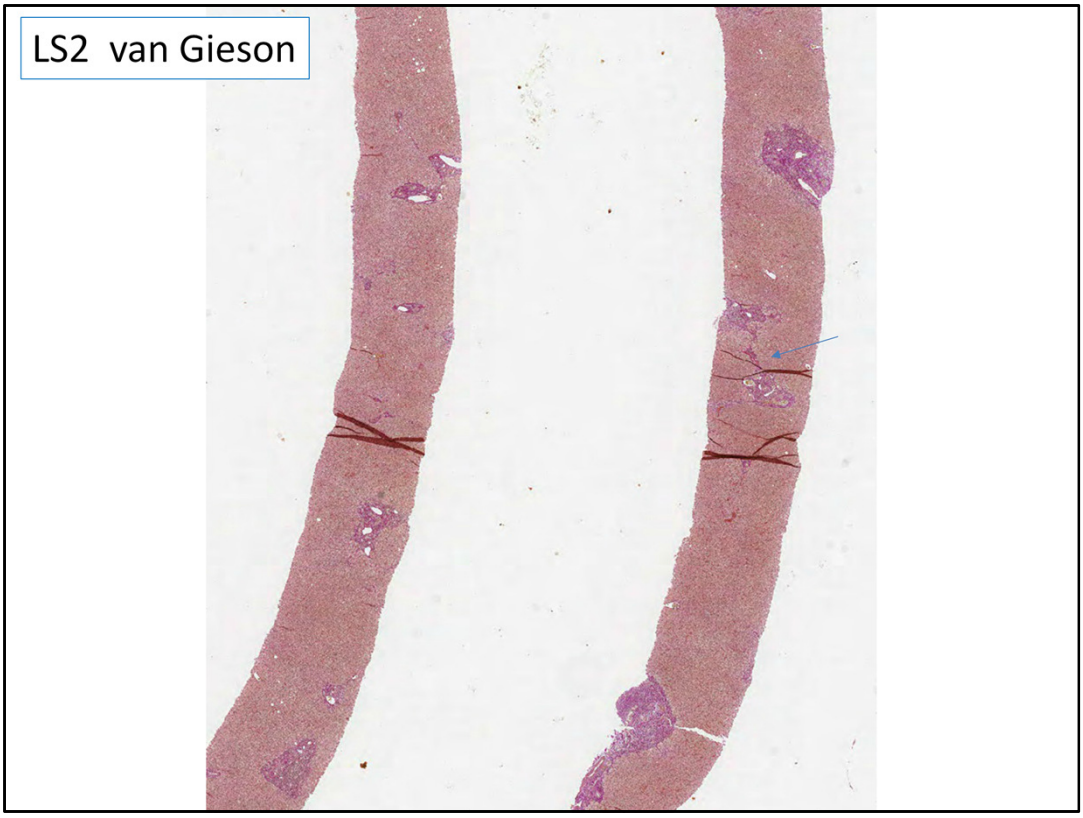
A portal area with fibrosis, unaccompanied hepatic artery branches (arrows). Slight prominence of marginal ductules (arrow heads)



An expanded portal area with fibrosis, scattered chronic inflammatory cells, and increased ducts and ductules (on right). The pale periportal hepatocytes (left) are likely due to accumulation of bile salts.



Rhodanine stain shows brown granules of copper within the periportal hepatocytes. This is an indication of chronic biliary disease. Copper is excreted into bile, together with bile salts, by the periportal hepatocytes. If a bile duct is damaged or destroyed, these accumulate in the periportal hepatocytes, and after a few months can be demonstrated by rhodanine (stains copper) or Shikata orcein (stains copper associated protein). This is referred to as 'cholate stasis' – cholate refers to the bile salts. This should not be confused with accumulation of bile pigment, bilirubinostasis, which is seen in the canaliculi between hepatocytes in other conditions, such as acute large duct obstruction.



Low magnification of van Gieson stain – variable portal fibrosis, with a focus of early portal to portal bridging fibrosis (arrow).

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A	Fatty liver disease
B	Drug induced liver disease
C	Biliary disease (PSC or large duct obstruction/stone)
D	Chronic hepatitis
E	cirrhosis

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Correct answer: C. The portal tract features and presence of periportal copper are characteristic of chronic biliary disease.

The clinical information raised a number of possible causes for the abnormal liver function tests, and the pathologist is being asked to identify the most likely cause. The portal tracts do show features of chronic biliary disease – these can be quite subtle, and the presence of copper/copper associated protein is particularly useful in confirming a morphological impression of biliary disease. The biopsy may show non-specific features of chronic biliary disease (as here) or suggest a specific disease – ductopenia (bile duct loss, seen as hepatic arteries without an accompanying duct) with periductal fibrosis or fibro-obliterative scars in primary sclerosing cholangitis (PSC); bile duct granulomas and interface hepatitis in primary biliary cholangitis (PBC).

Comments on other options:
Fatty liver disease – there is minimal steatosis present here but not sufficient for a diagnosis of non-alcoholic fatty liver disease (NAFLD) which requires macrovesicular steatosis in >5% hepatocytes.

Drug induced liver disease – the history is of sodium valproate – which may cause acute and chronic hepatitis but not chronic biliary disease. Chronic biliary disease would be a rare pattern of drug induced liver injury, whereas there is a history of choledocholithiasis to accound for the changes here.

Chronic hepatitis – as a generic term for any chronic liver inflammation with fibrosis – is

best avoided as it can be clinically misleading (does the pathologist mean autoimmune hepatitis?). If the only abnormality in a biopsy is non-specific portal fibrosis and inflammation, it is better to write that as the diagnosis, rather than 'chronic hepatitis'. Sometimes, small biopsies may just show these non-specific features without an indication of the aetiology, but nevertheless biopsy evidence of the presence of chronic liver disease needing further assessment can be clinically useful.

Cirrhosis – not present here. There is at most focal portal to portal bridging fibrosis. Cirrhosis requires a diffuse transformation of liver architecture to one of parenchymal nodules separated and surrounded by fibrous tissue. Macronodular cirrhosis (nodules >3mm) can be difficult to recognise in small narrow biopsies, but in this case there is plenty of tissue to allow good assessment of the architecture.