

# Self–assessment/CPD answers

Below, you can find the answers to the self-assessment questions published in this chapter.

## Answers

### Liver and biliary disease in infancy

#### Question 1

**Correct answer: D.** Babies with cholestasis often have vitamin ADEK deficiency with a high risk of developing intracranial haemorrhage secondary to vitamin K deficiency, which can be easily corrected by parenteral vitamin K. The other tests listed are important but less urgent than the vitamin K level

#### Question 2

**Correct answer: E.** Alagille's syndrome is a genetic, multi-systemic condition typically presenting with facial dysmorphic features, cholestasis and failure to thrive. The other conditions listed are not associated with these features

### Liver and biliary disease in childhood

#### Question 1

**Correct answer: D.** Acute fulminant hepatitis (from type A, B, E or seronegative hepatitis) presents with a short clinical history, usually after a prodromal illness. Hepatomegaly is an early feature. As the child is both sleepy and irritable, he is probably encephalopathic, which is characteristic of fulminant hepatitis. Children with hepatitis C and non-alcoholic fatty liver disease are asymptomatic and do not present in this way. Those with chronic neonatal liver disease will have a long history of illness, be malnourished and have splenomegaly

#### Question 2

**Correct answer: E.** It is important to diagnose the cause of the bleeding and treat her as soon as she is stable enough to undergo endoscopy. As she has a past history of neonatal liver disease, a small liver and an enlarged spleen, she is likely to have cirrhosis and portal hypertension and is bleeding from oesophageal varices. At 11 years of age, it should be possible to carry out band ligation and then to start terlipressin or somatostatin with omeprazole.

### Liver disease in pregnancy

#### Question 1

**Correct answer: D.** This lady's symptoms and blood profile are in keeping with gallstone disease. It is prudent to exclude viral infections but note gallstones often cause a transaminase rise in young patients. The patient is now asymptomatic with no evidence of sepsis so discharge home is safe (A) with a safety net of advice to return if the pain recurs or fever develops. Early hepatology specialist (B) input is advisable but should not delay a preliminary work-up. MR scanning (C) is deemed safe in pregnancy, but should follow a preliminary

work-up and risk–benefit analysis in a patient who is otherwise well. Although it is reasonable to contact the obstetric team (E), a pregnancy-related explanation is unlikely at 22 weeks in a singleton pregnancy. The patient's viral screen was negative and liver function tests returned to normal values within 2 weeks. Abdominal pain symptoms were controlled with a low fat diet and an HPB surgical review was arranged for the post-partum period to discuss cholecystectomy.

#### Question 2

**Correct answer: C.** Although presenting before the third trimester, this woman fulfils the Swansea criteria for acute fatty liver of pregnancy and has developed significant liver dysfunction. Administration of dexamethasone to aid fetal lung maturity is a priority, along with timely delivery and supportive care. Note that pregnancy-related liver disease can present earlier in pregnancies with multiple babies than in singleton pregnancies. The alanine aminotransferase concentration is disproportionately low for the degree of liver dysfunction to be explained by a viral aetiology (A). Intra-hepatic cholangitis of pregnancy (B) does not cause an early rise in bilirubin, ascites or thrombocytopenia, and itch can be otherwise explained by iron deficiency. Doppler ultrasonography has a highly sensitivity and effectively excludes a diagnosis of portal vein thrombosis (D). Haemolysis, elevated liver enzymes and low platelets (E) is a reasonable differential diagnosis, but multidisciplinary discussion around safe delivery of the babies needs to be a priority, alongside any further work-up.

#### Question 3

**Correct answer: B.** Although there is a higher risk than in the general maternity population, particularly when there have been recent flares, successful pregnancies can occur even with poor compliance with medication (A). Endoscopy (C) is useful as a low platelet count and splenomegaly suggest portal hypertension, but there is a window to optimize her disease before pregnancy that should be addressed first. Reduction of immunosuppression (D, E) before pregnancy should only be contemplated where there is good immune control and functional reserve – as the liver function tests are abnormal at baseline and there are signs of portal hypertension, it is more critical to encourage the woman, with the support of the obstetric team, to take her medication.

### Primary sclerosing cholangitis

#### Question 1

**Correct answer: C.** Although all the other diagnoses are possible, the combination of worsening cholestasis, weight

loss and elevated CA19-9 is strongly suggestive of the development of a cholangiocarcinoma

#### Question 2

**Correct answer:** E. Irritable bowel syndrome (A) is possible but in this clinical scenario colonic carcinoma is the most likely cause of his symptoms.

#### Question 3

**Correct answer is C.** The prevalence of small duct primary sclerosing cholangitis is higher in females, and in patients with Crohn's colitis.

### IgG4-related disease

#### Question 1

**Correct answer:** B. Autoimmune pancreatitis type 1 (AIP) and immunoglobulin (Ig)4-related sclerosing cholangitis (IgG4-SC) are the pancreatic and biliary manifestations of IgG4-related disease (IgG4-RD). IgG4-RD is typically corticosteroid-responsive. A biopsy should be done to confirm clinical suspicions and rule out malignancy. Oral prednisolone therapy is the optimal first-line therapy. Biliary stenting is indicated in patients with obstructive jaundice caused by common bile duct strictures, to ensure adequate bile flow and prevent biliary sepsis; however, early administration of corticosteroids will reduce the pancreatic mass effect and relieve biliary obstruction quickly (in days to weeks). Biliary stenting (E) can be reserved for patients with biliary sepsis or for where corticosteroid treatment will be delayed because malignancy is suspected. Rituximab (D) is third-line therapy for patients with IgG4-RD who have relapsed or developed severe adverse effects on corticosteroids, usually after a trial of a second-line immunomodulator. Supportive management (A) is not an option in a patient who is jaundiced with 'urgent' disease and multiorgan involvement, given the risk of biliary complications, progressive organ dysfunction and related morbidity. Surgical resection (C) may be an option for localized pancreatic malignancy, which is not the case here, but is not appropriate for either multiorgan IgG4-RD or single organ autoimmune pancreatitis.

#### Question 2

**Correct answer:** B. The expansion of clonally restricted CD4 + cytotoxic T cells (SLAMF7+) in the circulation and infiltrating tissue affected in patients with IgG4-related disease is believed to be central to its pathogenesis (B), producing a number of pro-fibrotic cytokines and interacting with B cells (antigen-driven). Both B cells and plasmablasts are prominent in the circulation and tissue in IgG4-RD (E). T follicular helper cells (C) provide help to B cells, and Tfh-2 cells are prominent in the blood and IL4-producing CXCR5 producing cells are prominent in germinal centres in affected organs of IgG4-RD. T regulatory cells (A) producing IL10 and transforming growth factor- $\beta$  are found to be elevated in the blood and tissue in IgG4-RD, unlike in many other autoimmune diseases. Whilst T helper 2 cytokines are often seen in

those IgG4-RD patients with atopic disease, T helper 1 cells are not a feature of the disease. B cell depletion leads to profound clinical responses as well as a decline in plasmablasts and CD4 + cytotoxic T lymphocytes.

### Haemochromatosis

#### Question 1

**Correct answer:** C. This is a pragmatic approach to the pre-symptomatic individual as it prevents iron accumulation and offers benefits to other patients. Venesection (B) is not required as the ferritin is normal. Observation (A) is a reasonable alternative with treatment if the ferritin rises above normal. Avoidance of iron-rich foods (D) should be advised. Liver assessment (E) is not required here.

#### Question 2

**Correct answer:** D. This patient is not likely to have any success with venesection (B), and blood donation (C) is even stricter in its criteria. The patient requires treatment (A) and should not be discharged (E). He has symptomatic iron loading so treatment should be attempted. Deferasirox is an oral iron chelator which has shown to be effective in phase 2 trials and has been used by clinicians when venesection is not possible – this treatment could be attempted in this scenario.

#### Question 3

**Correct answer:** B. Liver ultrasound is required as part of the investigation here before anything else. It is likely to show evidence of fatty liver. FibroScan (E) and/or biopsy (C) can be indicated after this, but ultrasonography should be undertaken first. Weight loss (D) may ultimately improve serum ferritin concentrations, and blood donation could be considered; significant iron loading is, however, unlikely and venesection (A) is not likely to be of particular clinical benefit. Serum ferritin and alanine transaminase (ALT) are often raised in the context of fatty liver and the compound heterozygote state rarely leads to end organ damage due to iron overload.

### Complications of cholestasis

#### Question 1

**Correct answer:** A. Rifampicin is the second-line anti-pruritus treatment of choice for cholestasis in most centres (naltrexone is an alternative option but has issues related to tolerability). The maximum dose of rifampicin in this indication is 600 mg daily, but it should be started at 150 mg per day and liver function tests checked at 4 weeks because of potential hepatotoxicity. It can then be cautiously increased to a maximum of 600 mg as needed. Antihistamines (B) typically do not work in cholestatic itch but can be sedative so should be avoided. Transplantation (C) is effective for controlling pruritus but should only be considered when patients have failed all medical options (this patient has only failed first-line therapy). Ursodeoxycholic acid (UDCA). Naltrexone (D) would be a reasonable treatment to consider but in current guidelines it is recommended for use after

rifampicin has been tried. The reason for this is that tolerability can be a challenge with an opiate-withdrawal type reaction being very common in patients. (E) at the optimal dose of 12–16 mg/kg improves itch a little in patients with mild itch but has no impact on severe itch, and increasing the dose is of no value. Occasional patients with primary biliary cirrhosis get a paradoxical itch with UDCA (i.e. UDCA causes or worsens itch rather than improving it).

#### Question 2

**Correct answer: B.** Fatigue is an important symptom in primary biliary cholangitis (PBC) (A) (more so than in other cholestatic diseases). It typically gets progressively worse as the day goes on, so a good coping approach is to focus key activities early in the morning. Patient ‘ownership’ of the problem is key. It is important that patients do not compensate for fatigue by withdrawing from normal daily activities (such as work) as social isolation can result, compounding the quality-of-life impairment (C). Fatigue in PBC typically has both peripheral and central (or brain-based) components so central fatigue (including the sense of ‘brain fog’ that is frequently described by patients. Although depression (E) can complicate fatigue in PBC, it is usually reactive to the limitations that patients perceive in relation to living a normal life; depression is only very rarely the cause of fatigue. In some PBC patients with severe central fatigue, sleep disturbance, in particular daytime somnolence, can be prominent. This can be a major contributor to problems at work (it is not uncommon to hear of patients falling asleep at their computer). If this is the case, formal sleep assessment and appropriate sleep intervention is useful. Occasional patients with profound daytime somnolence resistant to other approaches benefit from modafinil therapy (D), but it is not a treatment for fatigue.

#### Question 3

**Correct answer: B.** Osteoporosis can complicate chronic cholestasis and is important to consider in all patients. Proactive management has markedly reduced fracture rates. A traumatic fracture as has occurred here does not suggest osteoporosis but should remind clinicians that all patients with cholestasis should be routinely assessed. The assessment and management is, however, no different from that seen in other non-cholestatic settings. Non-cholestatic risk factors are important. Smoking is key. Exercise (C) is protective rather than harmful. As the body mass index is normal, weight loss (D) would in fact increase the risk of osteoporosis. Bisphosphonates (E) may be appropriate (as may calcium and vitamin supplements) but only after formal assessment. Although the absolute risk of osteoporosis is higher in women than men, the relative risk (i.e. the additional risk that comes from cholestasis) is greater in men.

### Management of portal hypertension, Budd–Chiari syndrome and portal vein thrombosis

#### Question 1

**Correct answer: E.** The patient clearly needs resuscitation, aiming for a systolic blood pressure of 90 mmHg, but

conservative blood transfusion policy is now standard practice, aiming for a haemoglobin of 70–80 g/litre so blood is not needed at this stage. The other options are appropriate after resuscitation. Antibiotics (A) significantly improve survival. Urgent endoscopy (B) is recommended in all cases of suspected variceal bleeding, and haemostasis can be achieved in >90% of patients. Vasoactive therapy with either octreotide (D) or terlipressin is recommended and improves both haemostasis and early mortality.

#### Question 2

**Correct answer: E.** A combination of a non-selective  $\beta$ -blocker (propranolol or carvedilol) and a variceal eradication programme with repeat banding is recommended first-line treatment for secondary prophylaxis, rather than using either approach alone (A, B). Nitrates (C) are not recommended. A transjugular intrahepatic portosystemic shunt (D) is used for secondary prophylaxis in some situations but is not considered first-line treatment and is only available in specialist centres.

#### Question 3

**Correct answer: D.** The patient’s presentation is consistent with acute Budd–Chiari syndrome. Doppler ultrasound (US) is the recommended initial imaging to diagnose hepatic vein occlusion. MRI (A), CT (B) and US (C) are also used but would not be considered first-line investigations. A positron emission tomography-computed tomography scan (E) would not be used to diagnose Budd–Chiari syndrome.

### Diagnosis and management of ascites and hepatorenal syndrome (acute kidney injury) in cirrhosis

#### Question 1

**Correct answer: D.** This man is gravely ill with spontaneous bacterial peritonitis (SBP) and, according to evidence-based UK and international guidance, needs immediate antibiotic treatment and albumin fluid resuscitation rather than crystalloid or another type of colloid

#### Question 2

**Correct answer: A.** This man is extremely unwell and ideally requires HDU. Terlipressin is a potent vasoconstrictor which reverses mesenteric vasodilation in advanced cirrhosis thereby improving renal blood flow. Albumin has been shown to be the most effective plasma volume expander in patients with cirrhosis. Serum creatinine will improve in most patients treated with terlipressin and albumin. Imaging (D) is required but he needs medical care immediately and radiological contrast may worsen his renal function. Diuretics (C) should be avoided whilst his creatinine is elevated. He has only been in hospital for 24 hours and one should get the culture data before discussing changing antibiotic treatment (E) empirically.

#### Question 3

**Correct answer: A.** He is at high risk of subsequent spontaneous bacterial peritonitis and this risk is significantly

reduced with longterm secondary antibiotic treatment. He must not drink alcohol again and if successful in his abstinence, he may find his ascites fully resolves after 6 months. He should reduce his salt intake (B) but excessive restriction is rarely possible. His diuretic dose (C) will need to be tailored according to response, blood tests and urine sodium levels rather than set at a defined level. Current UK guidelines are that patients need to be abstinent for 6 months prior to liver transplantation – referral would be too early (D). Fluid restriction (E) is ineffective at ascitic control and may lead to further renal impairment.

### Hepatic encephalopathy

#### Question 1

**Correct answer: C.** The priority here is to identify and treat the precipitating factor for the encephalopathy. An infection screen including sending blood, urine and ascites (including leucocyte count) for culture, and a chest X-ray, should be the priority. Care is supportive with a low threshold for commencing broad-spectrum antibiotics. Patients with cirrhosis are often hyponatraemic, and 5% dextrose (A) is best avoided. Patients with cirrhosis should never be placed on a low-protein diet (D); they are sarcopenic. There could be a risk of aspiration with oral lactulose (B), but if the patient can swallow, this might be beneficial. CT of the brain (E) would be indicated if he had a reduced conscious level or focal neurology.

#### Question 2

**Correct answer: A.** This man has good history to support the development of minimal/low grade hepatic encephalopathy (HE). He has impairment of his higher executive function and should not be driving. A neuropsychological test battery (E) is likely to support this diagnosis but is time-consuming and best undertaken by those who are expert at testing. Referral to the dementia service (D) is not indicated. Ammonia level (B) is a poor discriminator of minimal HE and if normal does not rule this out. Although commencing lactulose (C) might improve minimal HE symptoms, there is no strong evidence base to support its efficacy.

#### Question 3

**Correct answer: E.** This patient has a poor prognosis and should be referred for liver transplantation as a priority. Rifaximin (a non-absorbable antibiotic; B) should be commenced alongside lactulose on discharge as per National Institute for Health and Care Excellence guidance, but there is still a high risk of developing recurrence. There is no evidence to support oral LOLA (D) here. Stopping immunosuppressants (C) could risk a hepatitis flare. Contrast CT (A) would be helpful in looking for a large spontaneous shunt but this is not the most important next step.

### Acute liver failure: updates in pathogenesis and management

#### Question 1

**Correct answer: C.** Coagulopathy is a diagnostic feature of acute liver failure.

#### Question 2

**Correct answer: D.** The patient has clearly deteriorated despite supportive therapy as evidenced by an increase in prothrombin time and also lactate of 4mmol/litre, which are markers of poor prognosis.

#### Question 3

**Correct answer: E.** Dilation of the pupils with poor reaction to light in a patient with acute liver failure is a sign of cerebral herniation due to increased intracranial pressure. In these patients, a liver transplant is unlikely to result in neurological recovery.

### Liver transplantation

#### Question 1

**Correct answer: B.** UKELD is best prognostic score currently available to predict mortality at 1 year in patients with chronic liver disease. The Child–Pugh score (A) is a good prognostic score for chronic liver disease but not as accurate at predicting 1-year mortality as UKELD. MELD (C) is a good prognostic score for chronic liver disease but not as accurate at predicting 1-year mortality as UKELD. The King's Acute Liver failure score (D) is a prognostic score for patients with acute liver failure. The Milan criteria (E) is a prognostic score for patients with hepatocellular carcinoma.

#### Question 2

**Correct answer: B.** INR is a very useful test in predicting prognosis from acute liver failure.

The amount of paracetamol ingested (A) is not of use in predicting prognosis from acute liver failure. A low serum potassium (C) is not associated with poor prognosis in acute liver failure. A low serum phosphate (D) can indicate a good prognosis in acute liver failure. A high lactate is associated with a poor prognosis.

#### Question 3

**Correct answer: A.** tacrolimus is associated with nephrotoxicity. The immunosuppressant sirolimus is associated with poor wound healing (B). The immunosuppressant MMF is associated with diarrhoea and gastrointestinal upset (C). Tacrolimus has not been associated with teratogenicity (D) and patients are advised to continue during pregnancy. Tacrolimus (E) is not associated with neutropenia however azathioprine is.