Gastroenterology

Fatty liver disease

Steatosis and steatohepatitis

- Aetiology - alcohol, **metabolic syndrome**, starvation, Wilson’s, amiodarone, steroids
- **NAFLD** - commonest liver disease in West; mostly related to **metabolic syndrome**
- **NASH** and alcoholic steatohepatitis more likely to progress to cirrhosis
- Steatohepatitis - may be symptoms of fatigue, malaise, RUQ pain
- AST / ALT may be raised - ALT higher in NASH, AST higher in alcoholic steatohepatitis

Cirrhosis

- Hepatic fibrosis, nodular disorganisation, **portal hypertension**; ultimately hepatic failure
  - aetiology - alcohol, chronic hepatitis B / C, NASH, NAFLD, HHC, PBC, PSC, AIH, CCF
  - symptoms - fatigue, anorexia, nausea, weight loss, ascites, SBP, variceal haemorrhage
- **Child-Pugh** prognostic score - albumin, bilirubin, INR, ascites, encephalopathy
  - scores and life expectancy - A (5-6) 20 years, B (7-9) 15 years, C (> 9) 3 years
- Management - **zinc supplements**, cholestyramine, consider bisphosphonates
- Complications - hypersplenism, vitamin deficiency, synthetic failure, **HCC**
  - anaemia, thrombocytopenia, coagulopathy, DIC, ascites, SBP, encephalopathy

Ascites

- At least 1.5L fluid to be clinically detectable - may lead to **bacterial peritonitis**
- Aetiology - cirrhosis, GI / ovarian ca., lymphoma, CCF, nephrotic syndrome, pancreatitis
- Management - low salt, **spironolactone** 100-400mg od., **paracentesis**; TIPS if recurrent

Spontaneous bacterial peritonitis (SBP)

- Symptoms - abdominal pain, nausea, fever, tenderness, guarding, rigid abdomen (later)
- Management - **cefotaxime** / gentamicin with **metronidazole**
- Prognosis - **deteriorating renal function** suggests poor prognosis

Autoimmune liver disease

Primary biliary cirrhosis (PBC)

- Commonest - slow progressive **granulomatous** disease affecting **intra-hepatic bile ducts**
  - mostly affects middle-aged women; high identical twin concordance; strong FH element
  - asymptomatic or **fatigue**, pruritis (initially non-icteric), RUQ pain, **Sjögren’s syndrome**
  - later - hepatomegaly, **xanthelasma** (with **cholestasis** suggests PBC), **cirrhosis**
- Investigations - high ESR, **bilirubin** (marker of progression), hyperlipidaemia (high HDL)
  - antibodies - **AMA** (95% sensitive, 98% specific), IgM, ANA; also thyroid (check TFTs)
• Management - UDCA (slows progression), consider DMARDs / ciclosporin (clinical trials)
  • give antihistamines, cholestyramine (bile acid sequestrant), rifampicin for pruritis
  • liver transplant can be curative (only option if liver failure) but relapse may still occur
• Complications - malabsorption / vitamin deficiency, liver failure, RTA, hypothyroidism, HCC

Primary sclerosing cholangitis (PSC)
• Autoimmune obliterative inflammatory fibrosis of extra-hepatic bile ducts
  • mostly affects men aged < 35; 75% have underlying IBD, predominantly UC
  • asymptomatic or similar to PBC; also weight loss, fevers, sweats (not Sjögren’s)
• Investigations - p-ANCA (in 60%), IgG, IgM; bilirubin only raised in advanced disease
  • USS (rule out choledolithiasis), ERCP (diagnostic but invasive) / MRCP (preferred)
• Management difficult - liver transplant only life-prolonging treatment
  • consider sertraline for pruritis, vitamin supplements, low-dose UDCA (unproven efficacy)
  • avoid alcohol - consumption increases risk of cholangiocarcinoma
• Complications - biliary stones/infection, varices, cirrhosis, liver failure, cholangiocarcinoma

Autoimmune hepatitis (AIH)
• Very rare - hepatocellular infiltration and necrosis progressing to cirrhosis (HLA-DR3 / 4)
  • type I disease associated with ANA / ASMA (majority)
  • type II disease associated with anti-LKM-1 or anti-LC-1
• Symptoms of either acute / chronic hepatitis; cirrhosis often established at presentation
  • also nausea, fatigue, anorexia, diarrhoea, myalgia, arthralgia, amenorrhoea, pleuritis
• Investigations - IgG may be highly elevated - levels monitored to gauge response to therapy
  • liver biopsy - most important diagnostic procedure in AIH; perform early
• Management - prednisolone / azathioprine; consider budesonide (INH) if steroid intolerant
  • second-line - ciclosporin, tacrolimus, MMF (all less effective)
  • up to 20% will require liver transplantation (decompensated cirrhosis / liver failure)

Coeliac disease
• Autoimmune inflammation triggered by gluten (wheat, rye, barley); HLA-DQ2 / 8
• Symptoms - anaemia, abdominal discomfort, diarrhoea, mouth ulcers, angular stomatitis
  • gluten ataxia - cerebellar signs with peripheral neuropathy (reversible with GFD)
• Associations - subfertility, miscarriage, low birthweight, dermatitis herpetiformis
• Investigations - anti-tTGA / anti-endomysial antibodies; undetectable after 6m GFD
  • in equivocal cases - negative HLA-DQ2 / 8 makes coeliac disease very unlikely
• Management - gluten-free diet (GFD); consider vaccinations, bisphosphonate
  • dietician referral; gluten-free food available on NHS prescription
• Complications - osteoporosis, malnutrition (e.g. vit. D), hyposplenism, lactose intolerance
  • conflicting evidence on increased risk of small bowel lymphoma
Gastroenteritis

- Mostly viral - **norovirus** commonest; also **Campylobacter, E. coli, Salmonella, Shigella**
  - bacterial cases (dysentery) and food poisoning are **notifiable diseases**
- Risks - poor hygiene / sanitation, immunocompromise, **PPI overuse**, bad food
- Consider treatment with **loperamide** - but not if high pyrexia, blood / mucous in stools

Gastro-oesophageal reflux disease (GORD)

- Risks - high intra-abdominal pressure, smoking, alcohol, coffee, obesity, hiatus hernia
  - may be a cause of chronic cough; **H. pylori** infection is **not** related to GORD
- **Alarm symptoms** - dysphagia, weight loss, anaemia, vomiting, age > 55, FH, melaena
- Most common is endoscopy-negative GORD; **Savary-Miller** grading:
  - grade 1 - one fold demonstrating erosions (exudative / erythematous)
  - grade 2 - multiple folds affected, confluent erosions
  - grade 3 - multiple circumferential erosions
  - grade 4 - ulcers, stenosis or shortening
  - grade 5 - squamocolumnar metaplasia (**Barrett's oesophagus**)
- Management - **PPI** for 1-2 months; continue only while symptomatic, lowest tolerated dose
  - **aspirin** and NSAIDs may be **protective** against oesophageal cancer

Peptic ulcer disease (PUD)

- Duodenal (more common) or gastric ulcers - **H. pylori** associated with majority of both
  - other causes - **NSAIDs** (inc. aspirin), smoking, alcohol, steroids, stress, bile reflux
- Symptoms - **epigastric pain** (classically: eating relieves duodenal but exacerbates gastric)
  - also night waking, nausea, belching, bloating; GORD is a separate entity
- Investigations - FBC (iron-deficiency), **H. pylori** testing (stool / breath test - see below)
- Management (NSAID-induced) - **PPI** for 2 months e.g. 20mg omeprazole od.

*Helicobacter pylori*

- Gram-negative spiral bacillus - mostly **vacA-positive or cagA-positive** (higher risk)
- Investigations - 13C-urea breath test / stool antigen test; serology less reliable
- Management - 20mg omeprazole, 1g amoxicillin, 500mg clarithromycin - all tds. for 1 week
  - if penicillin-allergic - substitute amoxicillin for 400mg metronidazole (250mg clarithro.)
  - if gastric **MALT** (NH) lymphoma - 2 week eradication therapy
- Complications - **GI bleed**, perforation (peritonitis), **gastric ca.** (6-fold increased risk)
Haemochromatosis (HHC)

- **Autosomal recessive** disease affecting HFE gene (often C282Y mutation; chromosome 6)
  - variable penetrance; causes hepcidin deficiency causing **increased GI iron absorption**
- Symptoms (late) - **fatigue, arthropathy**, abdominal pain, **erectile dysfunction**, CVD
- Investigations - **fasting transferrin** / **serum ferritin**; HFE genetics if high transferrin
- Management - venesection (500ml weekly), hepatitis A/B vaccination
- Complications - DM, cirrhosis (and HCC), amenorrhoea, cardiomyopathy, arrhythmias, neuropsychiatric problems, hypothyroidism, adrenal insufficiency, pseudo-gout

Hepatic failure

- Characterised by ascites, jaundice, **encephalopathy**, haemorrhagic diathesis
  - aetiology - poisoning (**alcohol**, paracetamol), hepatitis, EBV, CMV, HCC, Wilson’s, AIH
  - complications - renal failure, SBP, cerebral oedema, haemorrhage (inc. retroperitoneal)
  - treat haemorrhagic diathesis with vitamin K, FFP, platelets
- **Encephalopathy** - may be asterixis, fetor hepaticus, hyperventilation, hypothermia
  - serum **ammonia** raised - give lactulose; consider neomycin, flumazenil (in cirrhosis)
  - grade 1 - mild confusion, depression, irritability, sleep disturbance / cycle inversion
  - grade 2 - lethargy, gross mental deficits, personality change, inappropriate behaviour
  - grade 3 - severe confusion, somnolence, amnesia, raging fits, incomprehensible speech
  - grade 4 - coma

Hyperlipidaemia

- High **total cholesterol**, high **LDL**, high **triglycerides**; dyslipidaemia includes low HDL
  - aetiology - familial, **obesity**, alcohol, **hypothyroidism**, steroids / Cushing’s, DM, thiazides
  - 1% IHD risk increase per 1% LDL increase; 2% IHD risk reduction per 1% HDL increase
- **Metabolic syndrome** - **obesity**, dyslipidaemia (high TG, low HDL), **HTN**, IFG / DM
  - thought to be all related to **insulin resistance**; of dubious use as a concept
  - Ideally TChol < 5, TG (fasting) < 4.5, LDL < 3, HDL > 1.2; but do not chase targets
- **Statin** therapy if history of IHD, TIA / stroke, PVD, DM, FH; or 10-year CVD risk > **20%**
  - simvastatin 40mg no. (‘fire and forget’ in primary prevention; 80mg if severe / MI)
  - side-effects - fatigue, headache, indigestion; rarely hepatotoxicity (LFTs < 3x normal OK)
  - **rhabdomyolysis** - after 6m; risk increased by hypothyroidism, **CYP450 inhibitors**
  - **Fibrates** if isolated high TG, or gemfibrozil for men if statin not tolerated (**not** with statin)

Familial hypercholesterolaemia (FH)

- Associations - premature arcus senilis (white/grey corneal ring), tendon xanthomata
- **Simon Broom criteria** - definite diagnosis if TChol > 7.5, LDL > 5, tendon xanthomata
  - FH is **LDL**-predominant; FCH is mixed LDL / TG hyperlipidaemia
- Management - statins; consider **ezetimibe** if not tolerated
Inflammatory bowel disease (IBD)

- **Management** (same principles for both Crohn’s / UC):
  - *topical agents* - **suppositories** for distal disease, liquid or **foam enemas** for proximal
  - induction of remission:
    - mild - topical **mesalazine** (proctosigmoiditis); add oral mesalazine if required
    - moderate - oral **prednisolone**; in proximal Crohn’s oral **budesonide** (fewer s/e)
    - severe - IV **hydrocortisone**; in UC short-course IV **ciclosporin** / **infliximab**
    - **secondary** maintenance therapy (in steroid-dependent or refractory disease):
      - **azathioprine**; then consider **methotrexate**; then **adalimumab** / **infliximab**
      - **cholestyramine** for diarrhoea; **loperamide** only in stable disease (risk of toxic megacolon)

**Crohn’s disease**

- Features - transmural ‘cobblestone’ colon, *skip lesions*, *granulomas*, ‘rose-thorn’ ulcers
  - any part of GI tract ‘from mouth to anus’; most commonly **terminal ileum**
  - more often affects girls aged 15-30; *smoking* major risk / exacerbating factor
- Symptoms - **diarrhoea** (mucous > blood), weight loss, abdominal pain, malaise, anorexia
  - also **mouth ulcers**, *perianal lesions* (skin tags, abscesses, fistulae)
  - extra-intestinal - clubbing, erythema nodosum / pyoderma gangrenosum, conjunctivitis, **ankylosing spondylitis**, steatosis, PSC, osteomalacia, granulomata, **renal stones**
- Investigations - ASCA, high CRP in active disease, stool culture, **ileocolonoscopy**
- Treatment (maintenance) - **smoking cessation**, metronidazole if fistulating, PPI if gastric
  - 80% require **surgery** (conservative resections) for symptomatic relief over lifetime
- Complications - **fistulae, strictures** (obstruction / perforation), osteoporosis, anaemia, **CRC**

**Ulcerative colitis (UC)**

- Features - ‘Margherita’ colon, **pseudopolyps**, thin ulcers, *crypt abscess*, goblet depletion
  - higher incidence amongst Ashkenazi Jews; **appendicectomy** may be protective
  - **distal disease** (proctitis, sigmoiditis, left-sided colitis), **extensive colitis** (up to hepatic flexure, 40% of patients), **pancolitis** (20%); incompetent ileocaecal valve in 10%
- Symptoms - **bloody diarrhoea**, weight loss, abdominal pain, **tenesmus**, urgency
  - also mouth ulcers, erythema nodosum / pyoderma gangrenosum, episcleritis, AS, **PSC**
  - mild - < 4 stools/day; moderate - 4-6 stools, systemic upset; severe - > 6 stools, fever
  - NSAIDs may trigger acute flare-up
- Investigations - **p-ANCA**, magnesium (low), albumin (low), sigmoidoscopy / colonoscopy
- Treatment (maintenance) - **mesalazine** (topical or oral)
  - if severe episode - consider **ciclosporin** PO for 3-6 months
  - surgery - if stable ileal pouch-anal anastomosis (IPAA); if acute **subtotal colectomy**
  - **leucaphoresis** undergoing specialist trials / research for improving remission
- Complications - **CRC, toxic megacolon** (treat with IV ciclosporin), osteoporosis
Irritable bowel syndrome (IBS)

- Common functional disorder - mostly affects women aged 30-40
- NICE criteria for diagnosis: 6 months of abdominal pain / bloating / bowel habit change
  - also straining, mucous, aggravated by eating, abdominal pain relieved by defecation
  - often associated with food intolerance (rarely true allergy); myriad of other symptoms
- If constipation-predominant - fibre, ispaghula husk, lactulose; avoid stimulant laxatives
- If diarrhoea-predominant - low fat, loperamide; consider low-dose TCA
- For abdominal pain - mebeverine, peppermint oil, low-dose TCA, TENS

Ménétrier’s disease

- Rare hypertrophic gastropathy with increased mucous, decreased acid, hypoproteinaemia
  - high epidermal growth factor receptor (EGFR) stimulation causing mucosal proliferation
  - on gastric biopsy - foveolar hyperplasia, cystic pit dilatation, low parietal / chief cells
- Symptoms - nausea, epigastric pain, diarrhoea, weight loss, melaena, gross oedema
- Management - PPIs, octreotide, partial gastrectomy if refractory
  - potentially related to CMV and H. pylori infection - eradicate if found
- Complications - gastric carcinoma

Portal hypertension

- Hepatic portal vein pressure > 11 mmHg - opens portosystemic anastomoses
  - prehepatic - portal or splenic vein thrombosis, tumour compression
  - hepatic - cirrhosis, chronic hepatitis, schistosomiasis, granulomas
  - posthepatic - hepatic vein obstruction (Budd-Chiari), pericarditis, CCF
- Varices - gastro-oesophageal junction, umbilicus, anorectal junction, retroperitoneum
  - if acute bleed - terlipressin, ciprofloxacin, vit. K / FFP, endoscopic band ligation
  - if band ligation unsuccessful - TIPS (stent connects portal and hepatic veins)
  - if gastric bleed - consider N-butyl-2-cyanoacrylate embolisation (risk of PE, stroke)
  - prophylaxis - beta-blockers (carvedilol), nitrates, endoscopic vein ligation (with PPI)

Whipple’s disease

- Rare multisystem disorder - intestinal lipodystrophy - weight loss, cough, intestinal fat
  - thought to be due to defective cell-mediated immunity and Tropheryma whippelii infection
  - affects middle-aged white men / sewage workers; associated with HLA-B27 (AS)
- Symptoms - polyarthralgia, abdominal pain, malabsorption, fever, chronic cough
  - also hyperpigmentation, lymphadenopathy, pericarditis, confusion, uveitis, effusion
- Diagnosis - intestinal biopsy shows periodic acid-Schiff (PAS) macrophages; also PCR
- Management - long-term antibiotics (e.g. doxycycline); fatal if untreated
Wilson’s disease

- **Autosomal recessive ATP7B mutation** (chromosome 13) causing *hepatic copper retention*
  - presents with *liver disease* in children and *neuropsychiatric illness* in young adults
  - liver features - acute hepatitis, steatosis, asymptomatic hepatomegaly
  - neuropsychiatric features - depression, *asymmetric tremor*, ataxia, clumsiness, chorea
  - other features - Kayser-Fleischer ring, **sunflower cataracts**, osteopenia, arthritis
  - Investigations - caeruloplasmin (low), **24hr urinary copper** (high), liver biopsy, MRI
  - Treatment - **penicillamine** / zinc / trientine, avoid coppery food (shellfish, chocolate, nuts)

Zollinger-Ellison syndrome

- **Gastrin**-secreting tumour - stimulates *parietal cell hyperplasia* and high acid output
  - gastrinoma usually in the duodenum, pancreas, elsewhere in abdomen
  - 25% associated with **MEN-I** (parathyroid, pituitary, pancreas tumours)
  - may also secrete ACTH leading to Cushing’s syndrome / hyperaldosteronism
  - Symptoms - **peptic ulcer disease**, diarrhoea, abdominal pain, GORD, nausea
  - Investigations - *H. pylori* (negative), endoscopy (low, large duodenal ulcer / gastric folds)
    - fasting gastrin > 1000 pg/ml highly suggestive, but often 100 - 1000 pg/ml
    - specific tests - **IV secretin** / calcium gluconate causing significant gastrin increase
  - Treatment - high-dose PPI, SC *octreotide* depot for pain / diarrhoea, **surgical resection**