GASTROINTESTINAL, HEPATOBILIARY AND PANCREATIC DISEASE

CONTENTS

GI CLINICAL ASPECTS

- **Dysphagia** can occur high up in the throat/pharynx, or low down in the oesophagus.
  - Neurological cause → difficulty with liquids.
  - Local disease → difficulty with solids.
  - Chronic disease → strictures.
  - Must exclude oesophageal carcinoma.
  - Rare causes = achalasia, systemic sclerosis or globus hystericus (psychological Δ)

- **Heartburn** – caused by reflux oesophagitis, but present in pregnancy (from ↓ in oesophageal sphincter tone.
  - A rare cause = oesophageal candidiasis
  - PC = ill-defined burning behind sternum.
  - Worsened by stooping or lying flat.

- **Dyspepsia** (indigestion) – epigastric discomfort starts a few hours after a meal
  - Relieved by eating.
  - Causes: gastritis, gastric ulcer, duodenal ulcer.

- **Vomiting** – central vomiting centre is in the medulla, close to the CTZ.
  - Inputs from:
    - Vestibular apparatus
    - Central connections (e.g. olfactory)
    - Vagal afferents from GI-tract.
  - 3 phases:
    - nausea, ↑ autonomic activity (e.g. sweating, salivation, pallor)
    - retching + closure of glottis + ↓ respiration
    - relaxation of oesophageal & cardiac sphincters + contraction of abdominal wall muscles → expulsion of gastric contents.
  - Always consider: GI disease (food poisoning), drugs and systemic/neurological problems.
  - Patient may be haemodynamically or electrolytically compromised by ↑ fluid loss or ↓ intake.

- **Haematemesis** – check for shock (bradycardia from vagal stimulation)
  - NSAIDs?
  - Mallory-Weiss tear = violent retching followed by vomiting fresh blood?
  - Portal hypertension, oesophageal varices?
  - Alcohol?
  - Bleeding diathesis (e.g. clotting, fibrin degradation, platelets)
  - PC = a coffee ground vomitus.

- **Melaena** – passage of black, offensive, tarry stool, indicating a high GI-bleed.

- **Faecal Incontinence:**
  - *Neurogenic* – patients passes a formed stool without adequate warning.
    - Often linked with eating (gastro-colic reflex)
    - Cerebrovascular or degenerative neurological aetiology.
    - R_x = codeine (↑ constipation) and regular enemas.
  - *Overflow* – constipation, followed by leakage of faeculent material from a full bowel.
    - R_x = regular enemas, laxatives and treat cause.
    - Soft faeces → stimulant used (senna)
    - Hard faeces → roughage, bulking agent (fibrogel), and softeners (co-danthrusate)

- **Rectal bleeding:**
  - Haemorroids
  - Rectal carcinoma
  - Rectal/colonic polyps
  - Diverticulitis
  - Ischaemic colitis + angiodysplasia
  - Infective diarrhoeas
  - Ulcerative colitis + Crohn's disease
  - Melaena (beware iron tablets, bismuth salts and antibiotics)

- **Jaundice** – becomes clinically detectable at double the upper limit of the normal plasma bilirubin levels (30-40 μmol/l)
  - Infective cause? Transfusion? Travel?
  - Obstructive:
    - Dark urine and pale stool.
    - Palpable gall bladder with jaundice → pancreatic carcinoma (Courvoisier's sign)
  - Gall stone blockage is *equally* common as malignant blockages in the elderly.
  - May signify a decompensated chronic liver disease?
  - Pruritis → long standing 1° biliary cirrhosis.

- **Weight loss & anorexia** – always weigh patient as a baseline.
  - Inadequate intake – depression?
  - Malabsorption – coeliac's disease?
  - Disturbed metabolism – thyrotoxicosis?
  - Malignancy – GI or remote disease?
  - Systemic disease – TB?

THE OESOPHAGUS

MOTILITY DISORDERS

- The normal oesophagus – circular and longitudinal muscles. (striated → smooth)
  - Lower pharyngeal muscles = upper sphincter.
  - Lower sphincter prevents gastric reflux.
  - Swallowing initiates a 1° peristaltic wave
    - Upper sphincter relaxes, and a coordinated wave of contraction propels food down.
    - Cardio-oesophageal sphincter relaxes to allow bolus into stomach.
    - A 2° peristaltic wave then cleans the oesophagus of food remnants.

- **Achalasia** – degeneration of ganglionic cells, causing loss of coordination of peristalsis and relaxation of lower sphincter.
  - Progressive dysphagia and heartburn from regurgitation.
  - Can cause recurrent aspiration pneumonia.
  - Barium swallow shows a mega-oesophagus.

- **Oesophageal spasm** – in elderly
  - Mimics angina.
  - Barium swallow shows a corkscrew oesophagus.
  - R_x = nitrates and calcium antagonists (to relax smooth muscle)

- **Δ Motility** – systemic sclerosis or diabetes mellitus with autonomic neuropathy.

- Major symptoms of oesophageal disease = *dysphagia, heartburn* & *painful swallowing*
  candidiasis & HSV

HIATUS HERNIA & OESOPHAGITIS

- Hiatus hernia
  - Sliding (common), caused by reflux.
    - Worsened in obesity. Hormonal Δ in pregnancy can precipitate heartburn.
  - Rolling (rare)

- Reflux oesophagitis
  - Hormonal Δ in pregnancy
  - Can present with Haematemesis and anaemia

- Investigations:
  - Endoscopy (with therapeutic dilatation of strictures)
  - FBC
  - Barium swallow

- Management:
  - Symptom relief with *Gaviscon*, and no tight clothing or excessive bending.
  - ↓ acid production to promote healing:
    - *Cimetidine/Ranitidine* (H_2 antagonist, 50% effective)
    - *Omeprazole* (PPI, >90% effective)
  - promote gastric emptying by ↓ cardio-oesophageal tone:
    - *Domperidone* (peripheral dopamine antagonist)
    - *Cisapride* (prokinetic)

- Complications:
  - Strictures – cause dysphagia, ↓ nutrition and aspiration pneumonia.
    - Must use endoscopy to exclude malignancy. Also allows therapeutic dilatation.
  - Metaplasia – a change from a stratified squamous epithelium to a columnar epithelium (= premaligant Barrett's Oesophagus).

OESOPHAGEAL CARCINOMA

- Most occur in the middle and lower third of oesophagus, and are squamous cell carcinomas.
- They are more common in elderly patients between 60-70 years old.
- Associated with smoking and heavy alcohol intake.
- Barrett's oesophagus is a pre-malignant stage for adenocarcinoma.

- Symptoms:
  - Retrosternal pain (from local infiltration)
  - Haematemesis or anaemia
  - General weight loss
  - Aphagia
  - Aspiration pneumonia becomes a greater risk
  - Cervical lymphadenopathy and hepatomegaly.

- Investigations:
  - FBC – iron deficiency anaemia
  - ↑ ALP – hepatic metastases
  - CXR – hilar node involvement.
  - Bloods – Hypoproteinaemia, ↑ plasma urea, hypernatraemia
    - in severely malnourished and water depleted patients
  - Barium swallow – irregular strictures? Ulcerated or polypoid carcinoma?
  - Endoscopy – visualisation and biopsy
  - USS – hepatic metastases?
  - CT/MRI – extent of spread?

- Management – improve nutrition and hydration.
  - Poor prognosis (<5% 5-year survival)
  - Lower oesophageal carcinoma → curative surgery
  - Upper oesophageal carcinoma → radiotherapy
  - Laser therapy, radiotherapy and stents used palliatively to preserve swallowing.
  - Alternatively a PEG (percutaneous endoscopic gastrotomy) is inserted if lumen obliterated.

THE STOMACH AND DUODENUM

- The stomach has 3 functions:
  - act as a reservoir, mixing food
  - secreting acid and pepsinogen to aid digestion
  - secreting IF for vitamin B_{12} absorption.

- Parietal cells (acid-secreting) and chief cells (pepsinogen-secreting) in upper $^2/_3$ of stomach.
- Antrum contains mucus-secreting cells, as well as G-cells (gastrin-secreting)

- Acid secretion is stimulated by release of histamine, under neural (vagal) control, as well as hormonal control:
  - stimulatory (gastrin)
  - inhibitory (VIP/somatostatin)

GASTRITIS

- PC of gastritis:
  - Dyspepsia
  - Bleeding from acute mucosal ulceration
  - An incidental finding at endoscopy.

- Acute gastritis associated with:
  - NSAID
  - heavy alcohol binging

- Chronic gastritis associated with:
  - *Helicobacter pylori* infection
  - chemical irritation (bile reflux)
  - autoimmune (antibodies directed against gastric parietal cells and IF → pernicious anaemia.

- R_x = antacids, removal of cause, as well as H_2-receptor antagonists.

PEPTIC ULCER

- Affects about 1 in 6 people in the UK. Increasing incidence with age. ♂ > ♀ (4:1)
- Associated with:
  - Smoking
  - NSAIDs
  - Hyperparathyroidism
  - Blood group O
  - *H. pylori* infection

- Pathogenesis:
  - Factors acting against the mucosal barrier (e.g. ↑ acid secretion)
  - Factors weakening the mucosal barrier
    - Δ mucus composition
    - ↓ prostaglandins
    - ↓ blood flow
    - *H. pylori* infection
  - Zollinger-Ellison tumour – a pancreatic tumour producing large quantities of gastrin.

- Symptoms = epigastric pain (a "hunger" pain)
  - Can radiate to back, if ulcer penetrates posteriorly.
  - In a duodenal or type I gastric ulcer (prepyloric/antral), pain occurs several hours after eating, can wake the patient at night, and is relieved by eating.
  - In a type II gastric ulcer (in body of stomach), epigastric pain is induced by eating.
  - Periodicity?
  - Smoking/alcohol/NSAIDs?

- Complications:
  - Perforation → peritonitis and shock
  - GI haemorrhage → haematemesis or melaena
  - Anaemia
  - Scarring of pylorus → outflow tract obstruction
    - Repeated vomiting + weight loss and severe fluid/electrolyte imbalance.

- Investigations:
  - FBC
  - U & E
  - FOB (faecal occult blood)
  - Iron status
  - Serum amylase
  - ECG (possible MI?)
  - Barium meal
  - Endoscopy + biopsy (culture for *H. pylori*)

- Medical Management:
  - Alcohol/smoking advice. Review NSAID therapy.
  - Iron supplements
  - Antacids for symptom relief.

  - **Ranitidine/Cimetidine** (H_2 antagonists)
    - Single dose to suppress nocturnal acid secretion
    - 50% efficacy at:
      - healing proven peptic ulcers
      - preventing chronic relapse
      - healing severe oesophagitis
      - prophylactic on patients taking NSAIDs.
    - Cimetidine inhibits the cytochrome P450 system, and will prolong the effects of *phenytoin, warfarin* and *theophylline*.
    - Cimetidine also has an anti-androgenic effect to cause ↓ libido and gynaecomastia.

  - **Omeprazole** (PPI)
    - >90% effective: symptom free in 2 weeks, and healed within 1 month
    - once daily dose (long half-life)
    - no major side-effects.

  - **Misoprostol** (a PG-E_2 analogue) - ↓ gastrin and acid secretion, and ↑ mucosal healing
    - Major side-effect is diarrhoea.

  - **Sucralftate** (aluminium hydroxide and sucrose complex) – promotes the mucosal barrier. Main side-effect is constipation.

- *H. pylori* eradication:
  - triple therapy = Colloidal Bismuth + Ampicillin/tetracycline + Metronidazole
  - dual therapy = Omeprazole + Amoxycillin.
  - Re-endescope patients after 6 weeks, because of ↑ risk of malignancy (gastric carcinoma and lymphoma)

❖ Surgical management:
- If medical management fails, or if complications apparent.
- Duodenal ulcer → highly selective vagotomy.
- Gastric ulcer → Billroth I gastrectomy
- Perforation → closure and biopsy
- Haemorrhage → endoscopic sclerotherapy, undersewing blood vessels ± vagotomy.
- Pyloric stenosis → gastroenterostomy ± truncal vagotomy.

ACUTE GI BLEEDING

❖ Presents with haematemesis, coffee ground vomiting or melaena.
❖ Mortality increases with age (>65), hypotension and pre-existing melaena.

❖ Causes:
- Varices – 5%
- Reflux oesophagitis – 5%
- Mallory-Weiss tear – 5%
- Gastric ulcer – 15%
- Gastric carcinoma - <5%
- Gastritis – 15%
- Duodenal ulcer / Duodenitis – 45%
- Small bowel – <5%

❖ Surgical team should be informed, if patient admitted. Endoscopy on next list.
❖ If Hb < 10 g/dl, a transfusion should be started.
- One unit of blood will raise the plasma Hb by 1g/dl.
- Monitor renal function.
- Give iron therapy.

GASTRIC TUMOURS

❖ Most gastric tumours are malignant adenocarcinomas.
- <5% are lymphomas and have a better prognosis.

❖ Leiomyoma is a less common benign smooth muscle tumour.

❖ **Adenocarcinoma** – more common in ♂, and associated with chronic atrophic gastritis and pernicious anaemia.
- Commonly arise in the antrum, and can cause outlet obstruction.
- Can be diffusely infiltrative → producing *linitis plastica*.
- Late symptomology of: epigastric pain, anorexia and weight loss.
  - Epigastric mass
  - Often bleed, and result in an iron-deficiency anaemia or a brisk haematemesis.
  - Enlarged Virchow's node
  - Ascites
  - Hepatomegaly
- Non-metaplastic manifestations:
  - Thrombophlebitis migrans
  - Thrombo-embolic disease
- Investigations: endoscopy, biopsy, FBC, LFTs and CXR. USS and CT for staging.
- Management is mainly a palliative mucosal/submucosal resection
- Prognosis = 10% 5-year survival.

THE SMALL INTESTINE

NORMAL FUNCTION

- Motility – peristalsis is controlled by the enteric NS and gut hormones.
  - Disruption can lead to stasis, ileus or bacterial growth.
  - TCAs can have an anticholinergic effect resulting in constipation.
  - Always ask about current medications of a patient with a Δ in bowel habits.

- Secretions and breakdown:
  - High bicarbonate concentration raises pH.
    - A fistula can cause ↑ loss of fluid and a metabolic acidosis.
  - Fluid produces a semi-liquid to aid digestion, and 8 litres need to be reabsorbed.
    - Interference results in watery diarrhoea.
  - Bile salts emulsify fats into micelles, and pancreatic lipase allows breakdown.
    - Lack of lipase results in steatorrhoea.
  - Proteolytic enzymes digest protein → pancreatic disease can lead to malnutrition.
  - Pancreatic amylase and oligo/di-saccharidases break down carbohydrates.

- Absorption – turnover of epithelial cells from crypts to tips of villi, is about 3-4 days.
  - Accounts for the sensitivity of the gut mucosa to anti-mitotic drugs and radiotherapy.
  - Glucose absorption is linked to a sodium cotransporter.
  - Upper jejunum ← calcium, iron and folic acid.
  - Terminal ileum ← vitamin B_{12} and bile salts.

- Gut associates lymphoid tissue (GALT) is scattered throughout the GI-system or localised in Peyer's patches. Secretory IgA is an important element in defence.

COELIAC'S DISEASE

- A gluten sensitive enteropathy, where α-gliadin is the main antigenic component.
- An association with HLA-B8 and DRW3.
- Peaks in young children, and in the 30-40 year olds.

- Pathology is:
  - Villous atrophy
  - Mucosal thickening
  - Chronic inflammatory cell infiltrate (predominately T-lymphocytes).
  - Tends to be more severe in proximal small bowel, and less severe in the terminal ileum.

- Symptoms include: diarrhoea, abdominal distension, nutritional deficiencies, weight loss and oedema.
  - Associated with *dermatitis herpeteformis* (an intensely pruritic, vesicular skin eruption).

- Investigations:
  - Weigh patient.
  - FBC – folate and B_{12} deficiencies can lead to a dimorphic (micro- & macrocytic) anaemia. (B_{12} deficiencies are less common as terminal ileum tends to be spared.)
  - Biochemistry – hypoproteinaemia and hypoalbuminaemia.
  - Tests for malabsorption are not accurate enough for diagnostic value.
  - Jejunal biopsy reveals villous atrophy.

- Management – gluten free diet (or a low gluten diet for young people).
  - Dietary supplements and regular monitoring. Small risk of lymphoma.

BLIND LOOP / BACTERIAL OVERGROWTH

- Malabsorption caused by bacterial growth is unlikely in the duodenum, on account of its high acidity.
  - Bacterial counts increase along the length of the jejunum, with a faecal pattern in the terminal ileum.

- Δ in structural integrity or ↓ motility can allow bacteria to multiply:
  - Surgery creating blind loops
  - Multiple diverticula
  - Autonomic neuropathy (diabetes) or systemic sclerosis → Δ motility.
  - *Achlorhydria* (a lack of HCl) allows colonisation of the upper small intestine.

- Effects of bacteria:
  - Mucosal damage
  - Cleaving conjugated bile salts → disturbs fat absorption
  - Metabolises B_{12} and impairs its binding to IF. (Folate may be produced, so blood levels are normal)

- Main features are: malabsorption, steatorrhoea, diarrhoea, and mild vitamin B_{12} deficiency.

- Investigations:
  - **^{14}C-glycocholate breath test** – labelled bile salts are given orally.
    - Bacterial deconjugation releases ^{14}C-glycine, which is measured by its breakdown and elimination as $^{14}CO_2$ in the small intestine.
    - In healthy people this will occur in the distal intestine, and is therefore delayed.
    - Therefore look for an *early* $^{14}CO_2$ peak.
  - **Hydrogen breath test** – oral lactulose is degraded by bacteria, releasing hydrogen.
    - In affected patients, this occurs in the small intestine instead of the large intestine.
    - Look for an early peak in expired hydrogen.

- Management – restore normal bowel function and motility.
  - Broad spectrum antibiotic (e.g. cefuroxine and metronidazole, tetracycline)

SHORT BOWEL SYNDOME

- A loss of a considerable length of bowel.
- The remaining functional bowel is insufficient for digestion and absorption.
- Commonest cause is surgical resection (e.g. following Crohn's), and bowel infarction.

- Symptoms - global malnutrition, ↓ B_{12} absorption & ↓ enterohepatic circulation of bile salts.

- R_x – dietary adjustment/supplementation, or parenteral nutrition at a specialist unit.

FOOD POISONING

- Any disease of an infectious or toxic nature, proven/likely to be caused by consumption of food or water.
- UK incidence = 75,000 cases per year. 10% acquired abroad.
- Poor food handling and faeco-oral contamination are the common causes.
- Clinically distinguished into either a predominantly vomiting or diarrhoeal illness.
- Fever, nausea and vomiting are common initial features, even if the illness becomes primarily diarrhoea over the next 48 hours.
  - Always follow history of symptoms for 24 hours.
  - Unlikely for vomiting to last more than 48 hours after an intestinal infection.

Vomiting Illnesses

- Major causes of food poisoning induced vomiting:
  - Rotavirus, calcivirus and Norwalk viruses.
  - *Bacillus cereus* toxin
  - *Staphylococcus aureus* toxin

- Symptoms:
  - Doubled over the toilet and vomiting, or lying prostrate in bed.
  - Upper abdominal cramping, but soft abdomen
  - ↓ grade fever
  - sinus tachycardia
  - 1 or 2 loose stools (especially if viral)

- Investigations: suspected food, vomitus, and stool cultures, toxicology & viral screen.

- Management – admit for i.v. fluid replacement if vomiting severe, or unclear diagnosis.
  - Encourage rehydration (water, thin soup)
  - Ask for review, if episode is not resolved within 24 hours.

Diarrhoeal Illnesses

- **Toxins** – self-limiting diarrhoea for up to 24 hours.
  - *B. cereus* found in cooked, stored rice.
  - *C. perfringens* found in contaminated meat.

- ***Salmonella sp.*** – 90% community acquired, 10% acquired abroad.
  - 12-48 hour incubation.
  - Invasive and often fatal in the elderly and immunocompromised.

- ***Shigella sp.*** – *S. sonnei* is commonest in the UK.
  - *S. dysenteriae, S. flexneri,* and *S. boydii* are usually imported.
  - Organisms can survive on fomites (e.g. door and toilet flush handles)
  - Commonly transmitted by children in schools and by insects.

- ***Campylobacter sp.*** – associated with milk and poultry products.
  - Incubation is 2-5 days.
  - Causes more abdominal pain than other intestinal infections.
  - Invasive in immunosuppressed/compromised patients.

- **Traveller's diarrhoea** – watery, non-bloody stool.
  - No fever.
  - Self-limiting diarrhoea over 1-5 days.
  - Enteropathogenic *E. coli* and other strains.
  - If blood or fever present, then more likely to be an invasive agent (e.g. *Salmonella*)

- **Haemorrhagic colitis** – *E. coli 0157* (also causes haemolytic uraemic syndrome)
  - Associated with beef and beef burgers
  - Sudden onset, ↑ bloody diarrhoea
  - No fever
  - 40% mortality in the elderly.

- ***Clostridium difficile*** – causes antibiotic associated diarrhoea.
  - A necrotic membrane can overly the colonic mucosa → pseudomembranous colitis

- *Clostridium* spores acquired from other patients.
- Spores germinate in gut, when flora has been decimated by antibiotic action
- Toxin produced, causes watery diarrhoea without blood.
- Ileus and toxic dilatation occasionally occurs.

❖ **Cholera** – caused by *Vibrio cholerae*
- Severe watery diarrhoea, leading to hypovolaemic shock within 12 hours.
- Need 30-40 litres of fluid replacement within first 24 hours.

❖ **Viral diarrhoea** – Rotavirus infections can affect adults.
- No blood or white cells in stool.
- Virus can be spread by fomites.

❖ ***Entamoeba histolytica*** – commonly causes asymptomatic cyst passage and acute amoebic dysentery.
- Less commonly associated with chronic non-dysenteric colitis, amoeboma and amoebic liver abscess.
- Blood, mucus and white cells present in stool
- Patient is otherwise not particularly ill
- Beware mistaking for Ulcerative Colitis, and prescribing steroids with fatal consequences.
- R_x = metronidazole & diloxanide furoate.

❖ ***Giardia lamblia*** – protozoan infection acquired abroad.
- 3-5 bulky stools a day
- pale stool
- griping abdominal pain + wind.
- ↓ weight
- Cysts appear in stool intermittently, making diagnosis by culture difficult.
- R_x = metronidazole (10% relapse rate)
- Other protozoa can cause diarrhoea. Most are acquired abroad with the exception of *Cryptosporidium* (← associated with visits to UK farms). R_x depends on the individual protozoa involved.

1. Travelled abroad? *traveller's diarrhoea, amoebic or Shigella dysentery, protozoal causes*
2. Been in a hospital or nursing home recently? *C. difficile or Salmonella*
3. Receiving or just finished a course of oral antibiotics? *C. difficile*
4. Is the diarrhoea frankly bloody? *Shigella, amoebic dysentery or ulcerative colitis*
5. Blood in the stool? *E. Coli, Salmonella, Campylobacter, Shigella, and inflammatory bowel disease*
6. Occult blood in the stool? *No → traveller's diarrhoea, cholera, C. difficile, viral and protozoal*
7. Diarrhoeal episode > 1 week? *Non-infectious causes, Giardiasis, Salmonella, immunodeficiency*
8. Abdominal pain and tenesmus? *Related to colon involvement in Campylobacter, Salmonella and Shigella infections.*
9. Grumbling mild abdominal pain with chronic diarrhoea? *Giardiasis*

❖ Physical signs – sodium and water depletion
- Fever ← *Salmonella, Shigella, Campylobacter and C. Difficile.*
- Dehydration if severe diarrhoea (>10 stools/day), or severe vomiting.

- Abdominal distension → colon dilatation → *Salmonella, Campylobacter and C. Difficile.*
- Sepsis → fever, tachycardia, renal impairment,
  - Caused by invasive strains of *Salmonella.*
  - Patients develop acute renal failure and shock, and may die within 3-4 days.

❖ Investigations:
- Standard culture (*Salmonella, Shigella or Campylobacter spp.*)
- Bloody stool → culture for *E. Coli 0157*
- Viral diarrhoea (no blood) → request virology
- –ve FOB and recent travel → ova, cysts and parasites screen
- +ve FOB and recent travel → "hot stool" (direct observation for amoebae), as well as standard & *E. coli* cultures.
- ↑ WCC in bacterial diarrhoea
- U & E to monitor i.v. therapy
- Stool WCC
- Blood cultures if patient admitted (even if afebrile)
- AXR – if abdomen distended, or an alternative/surgical diagnosis suspected.
- If stool cultures –ve, and diarrhoea continues → sigmoidoscopy and rectal biopsy to diagnose inflammatory bowel disease.

❖ Management:
- Fluid replacement (3-4 litres saline daily)
  - Potassium replacement
  - Avoid milk because of temporary lactase deficiency
- Antidiarrhoeal remedies:
  - Loperamide for patients with traveller's diarrhoea without systemic signs.
    - Only use loperamide for a maximum of 2 days.
    - Do not give to elderly, children, and patients with bloody or severe diarrhoea, as it may lead to toxic dilatation of the colon.
- Antimicrobial therapy:
  - Until pathogen is identified give oral or i.v. ciprofloxacin to:
    - Immunocompromised
    - Very ill patients (↑ fever, dehydrated, renal impairment)
    - Patients > 60 years
  - Generally the quinalones will shorten diarrhoea by 24 hours, except for *Salmonella.*

ORGANISM / SYNDROME	PATIENTS TO BE TREATED	R_x
Salmonella / Campylobacter	Ill, immunocompromised, elderly	Ciprofloxacin
Shigella	All	Ciprofloxacin, cotrimoxazole
E. Coli 0157	None	---
Traveller's diarrhoea	p.r.n.	Ciprofloxacin & loperamide
Clostridium difficile	All	Metronidazole, vancomycin
Cholera	All	Tetracycline, metronidazole
Viral	None	---
Entamoeba histolytica	All	Metronidazole & diloxanide furoate
Giardia lamblia	All	Metronidazole, tinidazole
Cryptosporidium parvum	None	---

- Report all patients with food poisoning (± diarrhoea) to the Public Health Authorities.

TUMOURS

- Resected appendices may contain small carcinoid tumours.
  - Derived from neuroendocrine cells.

- **Carcinoid syndrome** – rare
  - Ileal carcinoid tumour with extensive liver metastases
  - Produces large amounts of 5-hydroxytryptamine and other active substances.
  - Symptoms:
    - upper body flushing
    - secretory diarrhoea
    - ↓ weight
    - wheezing
    - fibrosis of tricuspid and mitral valves may occur
    - ↑ urinary excretion of 5-hydroxyindole acetic acid (metabolite of 5-HT)
  - Palliative R_x = 5-HT antagonists
    - occasional surgical resection/embolisation of metastases.

INFLAMMATORY BOWEL DISEASE

[Refer to Crohn's Disease*]*

THE LARGE INTESTINE

NORMAL STRUCTURE AND FUNCTION

- The colon begins at the caecum, and consists of ascending, transverse, descending and sigmoid sections.
  - There are two smooth muscle layers in the colon wall:
    - Inner circular layer, forming haustra.
    - Outer, incomplete longitudinal layer, forming taenia coli.
  - Colonic mucosa is flat, lacking any crypts, but containing many goblet cells.

- Superior mesenteric artery supplies the colon up to the splenic flexure, while the inferior mesenteric artery supplies the descending and sigmoid colon.
  - The splenic flexure and sigmoid colon are sites more at risk of ischaemic colitis.

- The function of the colon is to reduce the water content of the faeces from 2 litres/day to 150 ml/day.

- Defaecation – the passage of faeces into the rectum produces the desire to defaecate.
  - Internal anal sphincter and puborectalis muscle relax, decreasing the acute angle between the rectum and anus.
  - Voluntary relaxation of the external anal sphincter, and contraction of the abdominal muscles allows defaecation to proceed.

DIVERTICULAR DISEASE

- Diverticula are outpouchings of the colon through the muscle layer, usually at the point of entry of small arteries through the submucosa.
  - Can occur anywhere within the colon, but most common in the sigmoid colon.
  - Produced by the ↑ intraluminal pressures forcing the mucosa through weakened areas of the colon wall.

- Diverticulosis = painless and symptomless presence of diverticula.
- Diverticular Disease = presence of diverticula with mild symptoms, but no acute problem.
- Diverticulitis = implies the presence of inflammation or infection within diverticula.

- ♂:♀ = 1 to 1½. Prevalence increases with age (50% of people >60 years).

- Clinical features of painful diverticulosis:
  - LIF pain
  - Constipation
  - Diarrhoea
  - PR bleed

- Clinical features of diverticulitis:
  - Malaise
  - Fever
  - LIF pain and tenderness
  - Palpable abdominal mass/distension?

- Complications:
  - Haemorrhage → anaemia (differentiate from angiodysplasia and colonic carcinoma)
  - Stasis abscess → infection
  - Perforating abscess → peritonitis, fever and leucocytosis
  - Post-inflammatory stricture → colicky pain from obstruction
  - Enterovesicular fistula → cystitis and pneumaturia
  - Enterovaginal fistula → faecal discharge PV
  - Enteroenteral fistula (to small intestine) → diarrhoea

- Investigations
  - *diverticulosis* – barium enema or colonoscopy
  - *diverticulitis* – FBC, WCC, U & E, CXR
  - *perforation* – plain AXR and erect CXR
  - *obstruction* – gastrograffin or dilute barium enema
  - *fistula* – MSU, cystoscopy, colonoscopy
  - *haemorrhage* – colonoscopy, selective angiography.

- Management:
  - Diverticulosis – high fibre diet and reassurance.
  - Acute diverticulitis –
    - i.v. fluids
    - pain relief
    - i.v. Cefuroxime (vs. coliforms) + Metronidazole (vs. *Bacteroides sp.*)
    - inform surgical team.
  - Surgery:
    - Resection and 1° anastomosis (without peritonitis)
    - Hartmann's procedure (peritonitis)
    - Resection, 1° anastomosis and defunctioning proximal colostomy (fistula)

IRRITABLE BOWEL SYNDROME

- Clinical presentation – long history
  - Stress and psychological Δ.
  - Episodic symptomology
  - Abdominal pain (commonly LIF, can be periumbilical or RUQ)
  - Alternating diarrhoea and constipation
  - Tenesmus and incomplete emptying
  - Ribbon-like or pellet-like stools
  - Mucus in stool
  - No abnormal findings o/e other than tenderness.

- Investigate patients:
  - With recent travel abroad
  - Onset of symptoms at an age >40 years
  - With a recent Δ in symptoms
  - Other symptoms not associated with IBS (e.g. PR bleeding or ↓ weight)

- Management:
  - Most patients will respond to placebo
  - Treat psychological problems, such as depression
  - High fibre diet, although many patients worsen with addition of bran
  - Antispasmodics (e.g. mebeverine or peppermint oil)

BENIGN TUMOURS (POLYPS)

- *Metaplastic* – small, regenerative, no malignant potential.

- *Haematomatous* – seen in **Peutz-Jeugher** syndrome (autosomal dominant)
  - Oral mucocutaneous pigmentation
  - Extensive haematomas in the small (and large) bowel
  - No malignant potential

- *Adenomas* – malignant potential, increases with size
  - Tubular
  - Villous – diarrhoea and potassium loss.
  - Multiple adenomas seen rarely in the autosomal dominant **polyposis coli**
  - Most are asymptomatic and are found incidentally
  - Can cause a PR-bleed, and chronic iron-deficiency anaemia.

- Management – removal and sent for histological analysis
  - Removal by snaring or diathermy via colonoscopy
  - Repeated surveillance
  - R_x for polyposis coli = pancolectomy with ileoanal anastomosis.

MALIGNANT TUMOURS

- Colorectal adenocarcinoma is the 2nd most common cause of cancer death in the UK.

- Risk factors include:
  - Inflammatory bowel disease (ulcerative colitis and Crohn's)
  - Adenomas
  - Polyposis Coli (rarely)
  - ↑ fat, and ↓ fibre diet
  - ↑ faecal bile salts
  - ↓ selenium
  - ↑ anaerobic bacterial count in the faeces
  - ↓ vitamins A, C and E
  - genetic susceptibility from abnormal p53 function, and alleleic loss of chromosome 18q
    - *p53 prevents entry into S-phase of replication, until genetic material is checked and repaired.*
  - *Li Fraumeni* syndrome – early development of a wide range of cancers

- Pathology – adenocarcinomas can be annular (apple-core), ulcerative or polypoid (cauliflower) in appearance
  - Majority located in the rectum or sigmoid colon
  - Spread is by lymphatic, haematogenous and peritoneal routes
  - 75% of lesions are within 60 cm of anal margin
  - 3% are synchronous (i.e. a 2nd lesion is found at the same time)
  - 3% are metachronous (i.e. 2nd lesion is found later)

- Duke's Staging based on histology:
  - **A** – involves mucosa or submucosa only (95% 5yr survival)
  - **B_1** – tumour penetrates muscle wall, but not serosa (50% 5yr survival)
  - **B_2** - tumour penetrates muscle wall and serosa
  - **C_1** – muscle wall + lymph node involvement (25% 5yr survival)
  - **C_2** – serosa + lymph nodes
  - **D** – distant metastases including liver (↓ ↓ ↓ 5yr survival)

- Caecal carcinoma (15%) and hepatic flexure carcinoma (5%)
  - Anaemia (bleeding)
  - ↓ weight
  - RIF mass
  - ? small bowel obstruction
  - R_x = right hemicolectomy

- Splenic flexure carcinoma (10%) and sigmoidal carcinoma (20%)
  - Δ bowel habits (constipation and diarrhoea)
    - Annular nature causes bowel obstruction in 33% of cases → constipation
    - Faecal liquefaction, mucosal inflammation and ↑ mucus secretion above the obstruction → diarrhoea
  - PR-bleed
  - R_x = left hemicolectomy (elective), or Hartmann's procedure (emergency)

- Rectal carcinoma (50%)
  - Δ bowel habit
  - Fresh PR-bleed +mucus
  - Tenesmus (caused by prolapse of tumour at rectosigmoidal junction into rectum)
  - Palpable mass on *per rectal* examination
  - R_x = low anterior resection (elective), or abdomino-perineal resection with colostomy (emergency)

- Investigations:
  - Digital PR-exam
  - FBC, U & E
  - LFTs (↑ alkaline phosphatase if liver metastases present)
  - FOB
  - Sigmoidoscopy/colonoscopy + biopsy
  - Double contrast barium enema ← "apple-core lesion" or polyps
  - CEA (carcinoembryonic antigen) – raised in chronic disease.

- Management:
  - Elective or emergency surgery
  - Surgery with adjuvant chemotherapy for Duke's C (5-fluoururacil and levamisole)

  - Pre-operative radiotherapy reduces risk of local recurrence, but can impair bowel function in 33% of patients.

  - Total mesorectal excision for rectal carcinoma, with coloanal anastomosis and a temporary defunctioning stoma to protect anastomosis.
    - May prevent local recurrence.

CROHN'S DISEASE

- Can affect the GI tract anywhere from mouth to anus, though it has a particular tendency to involve the terminal ileum.
  - Patchy skip lesions, affecting all the layers of the bowel → thickening and matting
  - Deep fissure and ulcers in the mucosa → cobblestone appearance
  - Aphthous ulceration is an early feature
  - ↑ inflammatory cells and lymphoid hyperplasia
  - non-caseating granulomata

- Risk factors:
  - ↑ American Jews, ↓ Blacks
  - young adults
  - 10-15% have an affected 1st degree relative
  - HLA-B27 individuals often have the complication of Ankylosing Spondylitis.
  - Autoimmune problems (would explain immune complexes causing uveitis and arthritis)
  - Infection by cell-wall deficient mycobacteria?

- Main symptoms:
  - RIF abdominal pain caused by peritoneal involvement or bowel obstruction
    - Local tenderness and guarding
    - Colicky
    - Nausea, vomiting and borygmi (burping) associated with pain
  - Diarrhoea and steatorrhoea
  - ↓ weight (anorexia or malabsorption)
  - ↓ sodium, potassium, calcium, and magnesium
  - low grade fever
  - oedematous skin tags in anal region
  - perianal abscesses and fistulae

- Malabsorption of:
  - Fat from ↓ surface area, and ↓ bile salt re-uptake from terminal ileum →steatorrhoea
  - Vitamin B_{12} from loss of IF receptors in terminal ileum → anaemia
  - Vitamin D from interruption of entero-hepatic recirculation of bile
  - Protein from loss through an ulcerated mucosa
  - Carbohydrates from loss of enzymes of brush border

- Extra-intestinal manifestations:
  - *Hepatic*:
    - Fatty Δ
    - Cirrhosis
    - Pericholangitis
    - Abscess
    - Biliary carcinoma
    - Sclerosing cholangitis
  - Gall Stones
  - *Renal* – urolithiasis, pyelonephritis, cystitis
  - *Skin* – erythema nodosum, pyoderma gangrenosum
  - Aphthous stomatitis
  - Finger clubbing
  - *Occular* – uveitis, episcleritis, conjunctivitis
  - *Arthritic* – ankylosing spondylitis, sero-negative arthritis
  - Thrombus and embolism

- Investigations:
  - FBC – normochromic normocytic anaemias
    - Iron and folate deficiencies?
    - Megaloblastic anaemias uncommon despite ↓ B_{12}
  - Raised ESR, CRP, WCC, plasma viscosity and acute phase proteins (e.g. ferritin)
  - Albumin and total protein – hypoalbuminaemia is common
  - LFTs – hepatobiliary involvement
  - Blood and stool cultures – amoebic or bacillary dysentery
    - Administration of steroids is disastrous in these cases
  - AXR – fluid levels from bowel obstruction

  - Barium follow through – "rose thorn" ulceration
    - Thickening
    - Narrowing ("string-like") strictures
    - Fistulae

  - ERCP, sigmoidoscopy or colonoscopy – biopsy for a non-caseating granuloma
  - Indium-labelled white cell scan – for areas of active disease

- Medical management:
  - Diet
    - ↑ protein, energy.
    - ↓ fat, milk
    - mineral supplements (A,D,E,K)
    - plasma/blood transfusions
    - enteral feeding by NG-tube?

  - Diarrhoea – *diphenoxylate*, *loperamide (c/i in patients with gall stones)*, *codeine* or *prednisolone*
    - Corticosteroids can be given orally or by enema.
    - Side effects include osteoporosis, skin atrophy and cataracts

  - 5-aminosalicylic (5-ASA) drugs
    - induce remission and prevent relapse
    - *Sulphasalazine* consists of sulphapyrdine bound to 5-ASA by an azo-bond.
      - Bond is broken down in large intestine, allowing the unabsorbed 5-ASA to exert its anti-inflammatory effect.
      - Side-effects caused by sulphonamide component include: anorexia, vomiting, haemolysis, and agranulocytosis.
    - *Mesalazine* – resin (enteric) coated 5-ASA. pH dependent release of active 5-ASA into ileum and colon.
    - *Olsalazine* – two molecules of 5-ASA joined by an azo-bond, that is cleaved by intestinal bacteria

  - *Azothiaprine* (immunosuppressives) if steroids and NSAIDs fail.
  - *Metronidazole* – versus fistulae and perianal disease

- Surgical management = multiple resections of strictures, abscesses, fistulae and perforations.
  - Indications for surgery are:
    - Failure of medical therapy, with severe ill health
    - Persistent obstruction or fistulae
    - Acute perforation / appendicitis
    - Chronic peri-rectal infection
    - Failure to thrive in adolescence
    - Malignancy
  - ↑ relapse in this multi-centric disease results in repeated surgery
    - Side-effect is short-bowel syndrome, where total parenteral nutrition is required.

ULCERATIVE COLITIS

- Confined to the mucosa and submucosa of the large bowel.
  - Hyperaemic mucosa with thin walls → reddened, and bleeds readily
  - Widespread ulceration with preservation of adjacent mucosa, which takes on a pseudo-polypous appearance.
  - Inflammatory cell infiltrate found in lamina propria
  - Crypt abscesses
  - ↓ goblet cells

- Symptoms:
  - Diarrhoea mixed with blood/mucus/pus (seen on PR-exam)
  - ↓ weight, abdominal distension/tenderness
  - proctitis with diarrhoea, urgency and tenesmus
  - fever & tachycardia, dehydration, and electrolyte imbalance
  - hypoalbuminaemia, anaemia and ↑ ESR

- possible toxic dilatation of colon → always admit an acute attack

❖ Extra-intestinal effects:
- *Joints* – seronegative arthritis, ankylosing spondylitis
- *Eye* – uveitis, iritis, scleritis, conjunctivitis
- *Skin* – erythema nodosum, pyoderma gangrenosum
- *Liver* – pericholangitis, fatty Δ, chronic active hepatitis, 1° biliary cirrhosis, gall stones
- *Blood* – thromboembolic disease

❖ Site of ulcerative colitis:
- 15% total colitis
- 25% left sided colitis
- 30% distal colitis
- 30% proctitis

❖ Complications:
- Toxic dilatation → perforation
- Hypokalaemia
- Hypoalbuminaemia
- Acute haemorrhage → anaemia
- Stricture
- Dysplasia → carcinoma

❖ Histological comparison:

HISTOPATHOLOGICAL FEATURES	ULCERATIVE COLITIS	CROHN'S DISEASE
Inflammatory process	Superficial and continuous	Transmural and patchy
Granulomas	Infrequent	Majority
Crypt abscesses	Frequent	Some
Goblet cells	Depleted	Preserved

❖ Investigations:
- FBC – iron deficiency anaemia
- Colonoscopy with biopsy – inflamed friable mucosa, bleeds to touch
- Plain AXR – check for toxic dilatation of colon
- Erect CXR – air under diaphragm if perforated
- Barium enema - ↓ haustrations, dilatation and superficial ulceration
- Blood and stool cultures to rule out amoebic/bacillary dysentery

❖ Medical management:
- ↑ fibre diet
- antidiarrhoeal agents (e.g. codeine phosphate)
- ↑ dose oral prednisolone, or rectal hydrocortisone
- 5-ASAs for mild attacks, and maintenance therapy
- immunosuppressives (azothiaprine) occasionally

❖ Surgical management:
- Panproctocolectomy with ileostomy
- Colectomy with preservation of anal sphincter and creation of an ileal (J-shaped) pouch.

- Indications:
  - Failure or severe side-effects of medical therapy
  - High risk of developing carcinoma (>10 years chronicity)
  - Acute megacolon, perforation, or life-threatening bleeding

OTHER INFLAMMATORY BOWEL DISEASE

❖ **Non-specific colitis**
- Local sigmoproctitis with diarrhoea
- Non-specific appearance on sigmoidoscopy, and biopsy
- Exclude any infective causes

- R_x = steroid enemas

- **Ischaemic Colitis**
  - In elderly people, particularly around the splenic flexure
  - Bloody diarrhoea + abdominal pain
  - Barium enema shows "thumb printing" indentations on bowel wall
  - Symptoms may resolve spontaneously
  - R_x = maintain fluid balance and analgesia

- **Radiation Colitis**
  - 2° to therapy directed against a pelvic tumour
  - Bloody diarrhoea + tenesmus + abdominal pain
  - Can lead to ulceration and stricture formation
  - R_x = local steroids

BLEEDING FROM THE LOWER GI TRACT

- **Occult** – usually from the proximal colon and small bowel
  - Meckel's diverticulum
  - Intersusseption
  - Infarction/ischaemia of small bowel
  - Caecal carcinoma
  - Angiodysplasia (arteriovenous malformations)

- **Blood mixed with stool**
  - Left sided colonic tumour and polyps
  - Inflammatory bowel disease (ulcerative/ischaemic/radiation colitis)
  - Diverticular disease
  - Infective colitis
  - Angiodysplasia

- **Fresh blood in small amounts** – usually from rectum and anus
  - Rectal carcinoma
  - Proctitis
  - Solitary rectal ulcer
  - Perianal Crohn's disease
  - Anal carcinoma
  - Fissure *in ano*
  - Haemorroids

- **Severe bleeding** (rare)
  - Diverticular disease
  - Ischaemic colitis
  - Haemorroids

THE LIVER

NORMAL FUNCTION AND ANATOMY

- The liver lies directly below the right diaphragm, with its left lobe lying beneath the heart and left diaphragm.
  - A hepatic inflammation/abscesses may lead to pulmonary or pericardial diseases, because of their close proximity.

- Arterial supply:
  - Hepatic artery – a branch of the celiac axis
  - Portal vein – formed by the union of the splenic and mesenteric vein
    - The portal veins drain most of the blood from the GI tract

- The venous drainage of the liver pass via numerous hepatic veins to the inferior vena cava.

- The liver has five distinct functions:
  - Houses the major excretory pathways for a number of large molecules, producing bilirubin, urea and others.
  - Synthesises a number of important specialised proteins, including albumin and all the clotting factors.
  - Maintains stable levels of amino acids and glucose in the blood.
  - Supplies bile salts and bicarbonate to aid in digestion.
  - Detoxifies many potential toxins, drugs and metabolites.

- Major hepatic dysfunction leads to metabolic derangement and bleeding.

SYMPTOMS OF LIVER DISEASE

- Anorexia
- Fatigue
- Nausea and vomiting
- Jaundice
- Bleeding (especially from the nose or GI tract)
- Encephalopathy

SIGNS OF LIVER DISEASE

- Jaundice
- Hepatomegaly (or ↓ size in hyperacute hepatic failure)
- Right hypochondrial tenderness
- Fever (sometimes)

INVESTIGATIONS

- Albumin, clotting, urea and glucose → measures synthetic function
- Bilirubin, ALP, other hepatic enzymes → measures liver damage or excretory function

- LFTs – cholestatic (↑ ALP) or hepatocellular (↑ ALT, AST, GGT) disease
  - There are 5 differentials that need to be considered in a very ill patients with abnormal LFTs:
    - Cholestasis caused by sepsis
    - Ischaemic hepatitis
    - Acute hepatitis C
    - Total parenteral nutrition (TPN) hepatitis
    - Drug induced hepatitis (including halothane)

- USS – quick, inexpensive and non-invasive.
  - Identifies gall stones (90% sensitive), and the diameter of the common bile duct
  - Assess size of liver and spleen
  - Detect liver/splenic abscesses (90% sensitive)
  - Detect sub-pleural fluid
  - Targeting liver biopsy

- CT scan – looks at liver texture.
  - Identifies small abscesses, and fluid/pus collections
  - Visualises the pancreas and para-aortic nodes

- Biopsy – diagnoses chronic hepatitis
  - Stages lymphomas and diagnoses tumours.

ACUTE LIVER DISEASE

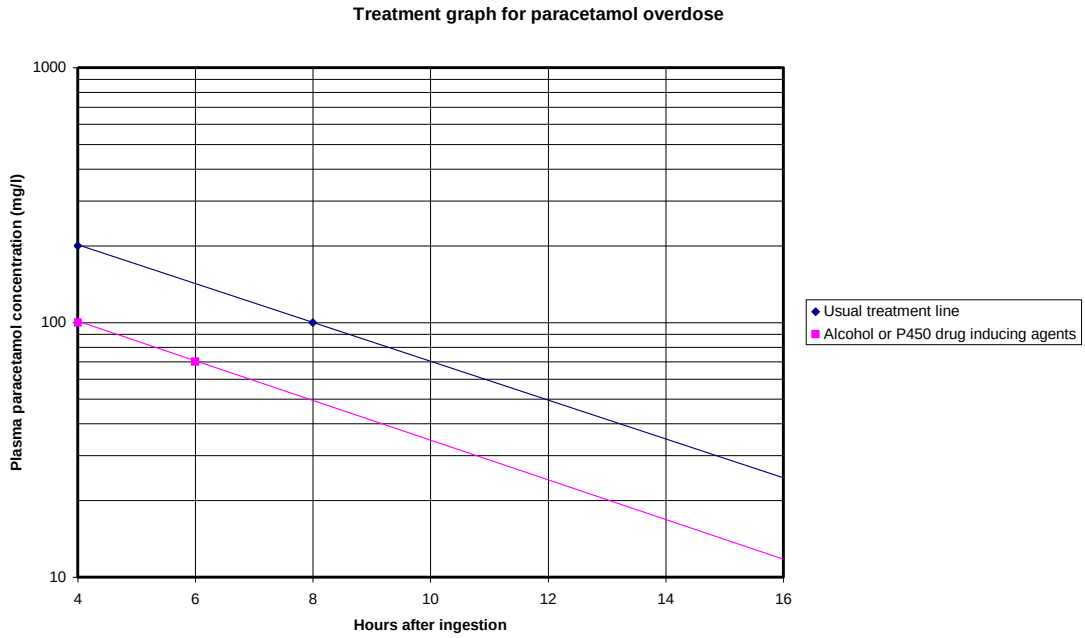
PARACETAMOL POISONING

- Most cases of overdose are intentional suicide attempts.
- Excessive doses of paracetamol will overwhelm the normal hepatic detoxification pathway, and shunt metabolism along another route that allows a toxic metabolite to accumulate.
  - Causes liver failure/damage, and occasionally renal failure.
  - Few symptoms are presented, and this history may not be forthcoming.

- Investigations:
  - Serum paracetamol and aspirin levels
  - LFTs, Prothrombin time, Glucose
  - Creatinine, U & E
  - Interval between taking the overdose and presentation
  - Patient is an alcoholic, or taking P450 inducing drugs (e.g. carbamazepine, phenytoin, rifampicin)?

- Management:
  - If <4hrs and >15 tablets (7.5g) → gastric washout
  - Otherwise, administration of i.v. actylcysteine
    - ↑ available amounts of glutathione to counteract the toxic metabolite of paracetamol
  - If presentation is >16 hours, then serum paracetamol is not a good guide to the need to treat. Instead base decision on:
    - Amount of paracetamol consumed
    - Serial INR
    - Liver enzymes (AST)

  - Patients who develop hepatic failure should be considered for transplantation.



HEPATOTOXICITY OF OTHER DRUGS

- Early warning signs:
  - Fatigue
  - Anorexia
  - RUQ abdominal tenderness
- Late features:
  - Jaundice
  - Abnormal LFTs
  - Hepatic fibrosis
  - Chronic hepatitis
  - Cirrhosis
  - Neoplasia
    - Adenoma/haemangioma
    - Carcinoma/haemangiosarcoma
  - Hepatic vascular damage
    - Sinusoidal dilatation
    - Budd-Chiari, veno-occlusive
- Hepatotoxins that cause enzyme induction:
  - Alcohol
  - Barbiturates
  - Carbamazepine
  - Diphenylhydantoin
  - Griseofulvin
  - Primidone
  - Rifampicin
- Hepatotoxins that cause enzyme inhibition:
  - Cimetidine
  - Isoniazid
  - Ketoconazol
  - Propoxyphene

GILBERT'S SYNDROME

- A benign inherited disorder that causes jaundice with no other abnormal LFTs
- Patient has a partial inability to conjugate bilirubin
  - Results in unconjugated hyperbilirubinaemia
  - Especially during infection, and following operations/fasting.
- Must exclude haemolytic jaundice from the differential diagnosis
  - Look for any anaemia and increased reticulocytosis.

WILSON'S DISEASE

- Normal copper metabolism – absorbed from the stomach and small intestine
  - Stored in the liver
  - Incorporated into *caeruloplasmin* and secreted into the blood
  - Biliary excretion
- An autosomal recessive disease – failure to excrete copper into bile
  - 95% have abnormal caeruloplasmin levels
  - ↑ Copper has a toxic effect on:
    - liver
    - basal ganglia
    - brain
    - eyes
    - kidney
    - skeleton
- Symptoms – onset between ages 5-30
  - Hepatic disease in early life, with neurological dementia in adolescence.
  - Haemolysis, renal tubular damage, and osteoporosis (rare)
  - Diagnostic *Kayser-Fleischer rings* = green-brown discolouration
  - Hepatic consequences = acute hepatitis or chronic persistent hepatitis
  - Neurological sequelae = tremor, choreoathetosis, dystonia, parkinsonism, dementia.
- Investigations – (↓) serum caeruloplasmin in patient *and siblings*.
- R_x = *D*-**penicillamine** (1-4 g/day, a copper binding agent)
  - Continue for life (even during pregnancy), and monitor body copper levels.

BUDD-CHIARI SYNDROME

- Uncommon obstruction of larger hepatic veins or IVC.
  - 1° proliferative polycythaemia, or paroxysmal nocturnal haemorrhage
  - Antithrombin III, protein C or protein S deficiencies
  - Pregnancy
  - Liver, kidney or adrenal tumours
  - IVC stenosis or congenital venous webs
  - *50% unknown cause*

- Causes hepatic congestion and back pressure in centrilobular areas.
  - Resulting in fibrosis and cirrhosis

- Symptoms:
  - Upper abdominal pain
  - Ascites
  - Tender hepatomegaly
  - Peripheral oedema (if IVC occulusion)
  - Cirrhosis and portal hypertension

- Investigations – hepatic venography and USS
  - Showing ↓ hepatic flow and reversed portal flow
  - Ascitic fluid protein > 25 g/litre.

- Management:
  - if recent thrombosis suspected → streptokinase, heparin and oral anticoagulation
  - otherwise R_x ascites:
    - ↓ sodium (40-20 mmol/day)
    - Spironolactone (100-400 mg/day, *beware gynaecomastia*)
    - Paracentesis (3-5 l/day, with *haemagel* colloid to support circulation)
    - Le Veen Shunt = a long tube connecting peritoneal fluid to internal jugular vein
    - Porta-systemic shunt?
    - Stenting of IVC stenosis?

- Poor prognosis (especially if sudden onset)
  - 33% to 66% die within 1 year
  - ↓ ↓ ↓ 5 year survival.

ALCOHOLIC HEPATITIS

- An acute illness associated with acute/chronic alcohol abuse

- Symptoms:
  - Deep jaundice
  - RUQ abdominal pain
  - Tender hepatomegaly
  - Fever
  - ↑ WCC
  - Prolonged prothrombin time
  - Spider naevi and palmar erythema (without cirrhosis)
  - Abnormal LFTs

- Investigations:
  - LFTs
  - Coagulation tests
  - FBC
  - Ultrasound – to exclude carcinoma
  - Blood cultures – to exclude infection

- Differential diagnosis:
  - Extrahepatic obstructive jaundice (e.g. gall stones or pancreatic carcinoma)
  - Liver abscess (bacterial or amoebic)
  - Cholangitis

- Management:
  - Fluid and nutritional support
  - Abstinence from alcohol
  - Invasive procedures may lead to early death
  - Mortality is 30-60%

BACTERIAL LIVER ABSCESS

- More common in Western worlds, and in elderly people.

- Aetiology:
  - Infection from biliary tree or portal drainage area
  - Local spread (e.g. from a subphrenic abscess)
  - Haematogenous spread from other sites (e.g. lungs)
  - Trauma
  - Cryptogenic (20-30%)

- Risk factors:
  - elderly
  - diabetes
  - alcoholism
  - corticosteroid therapy
  - malignancy
  - immune deficiency

- Symptoms:
  - ↓ grade fever
  - ↑ WCC and ↑ ESR
  - tender hepatomegaly (sometimes)
  - right sided pleural effusion/crackles
  - Ascites
  - Splenomegaly
  - Mental confusion
  - Jaundice and abnormal LFTs (uncommon)

- Management: (overall mortality is 10-15%)
  - Polymicrobial – anaerobes, *Strep. milleri*, and gram negative bacilli
  - Blood cultures positive in only 50%, and will not reveal complete flora
    - Perform a percutaneous aspiration to optimise antibiotic therapy.
    - Remove as much pus as possible (by percutaneous drainage if a large abscess)
  - **Penicillin/Ampicillin**
  - **Metronidazole**
  - An antibiotic vs. gram negative bacteria:
    - **Clindamycin**, **gentamicin** (aminoglycoside), **tetracyclines**, or **chloramphenicol**

AMOEBIC LIVER ABSCESS

- Typically a recent history of travel (within prior few months) to an endemic area for *Entamoeba histolytica*.

- Clinical presentation:
  - Acute fever
  - RUQ abdominal pain <10 days
  - Right shoulder, epigastric or pleuritic pain
  - Tender hepatomegaly (50%)
  - Crackles at right lung base

- Jaundice is uncommon, and signifies either a severe disease or (more likely) an alternative diagnosis.

- Investigations:
  - Aspiration of abscess, and culture
  - USS of liver – reveals 1-3 abscesses
  - Antibody test to *E. histolytica* (95%)
  - ↑ ESR
  - ↑ ALP, and possibly a ↑ transaminases
  - CXR – elevation of right diaphragm ± pleural effusion
  - Stools are negative for *E. histolytica*

- R_x = **Metronidazole**, ↑ dose for 10 days
  - It can take 4-7 days for the fever to resolve.

LEPTOSPIROSIS (WEIL'S DISEASE)

- Water exposure

- Signs
  - Cough
  - Fever
  - Bleeding tendency

- Investigations:
  - Renal impairment
  - Proteinuria
  - ↑ WCC
  - moderately elevated LFTs

GLANDULAR FEVER

- Typically affects teenagers and early 20s

- Signs:
  - Non-tender lymphadenopathy
  - Sore throat
  - Fever

- Investigations:
  - Atypical lymphocytes on blood film
  - Positive Monospot and Paul Bunnell test
  - EBV screen

HYATID CYST OF LIVER

- Residence in Wales or developing world
- Occasional hepatomegaly, otherwise no signs.
- Investigations:
  - Normal LFTs
  - Normal WCC
  - Scan reveals a cyst with septae ± calcified rim

TOXOPLASMOSA GONDII

COXIELLA BURNETII

HEPATITIS A

- Acute self-limiting hepatitis, common across the world except in northern Europe and USA.
- Typically presents in children.
- Caused by ↑ infections picornovirus (an enterovirus)
- Transmission – faecal/oral route

- Risk factors include:
  - Recent travel
  - ↓ sanitation
  - eating shell-fish (e.g. oysters)

- Incubation = 3-6 weeks, with virus excreted in faeces 2-3 weeks before onset of symptoms

- Symptoms:
  - Malaise and weakness
  - Followed by anorexia
  - Nausea and vomiting?
  - Vague, dull RUQ pain
  - Jaundice and dark urine (occurs after the other symptoms)
    - Heralds recovery within 2-3 weeks
  - Most patients remain tired/debilitated for some weeks
    - (supra-tentorial) post-hepatitis syndrome?

- Investigations:
  - 100-fold ↑ AST /ALT, but only 4-fold ↑ ALP
  - 20-fold ↑ bilirubin
  - normal or ↓ WCC
  - normal ESR (and plasma viscosity)
  - prolonged INR (monitor along with LFTs to assess progress)
  - normal renal function

- Management:
  - Bed rest, and nutritional maintenance
  - Admit patients with an INR>2
  - 1 in 2000 will develop fulminant hepatic failure → refer to transplant unit
  - Ban alcohol temporarily
  - No chronic carrier state.

- Prevention:
  - **Havrix** (an inactivated virus vaccine)
  - **Anti-HAV serum globulin** for immediate protection after exposure.

HEPATITIS B

- A hepadnavirus (only affecting humans), that can lead to hepatic carcinoma.
- Incubation = 4-20 weeks
- Patient remains infectious as long as HB_sAg is present in the blood
- Blood, saliva, sexual and vertical transmission
- Quite common in institutions for the mentally handicapped

- Symptoms: (*recovery within 3-6 weeks*)
  - Malaise, fever and muscle weakness
  - Followed by anorexia
  - Diarrhoea, nausea and vomiting?
  - Vague, dull RUQ pain
  - Arthritis or rash (cf. serum-sickness syndrome)
  - Jaundice and dark urine
  - Distaste for cigarettes

- Investigations
  - LFT pattern similar to Hepatitis A
  - Prolonged INR
  - Normal ESR & WCC
  - HB_sAg – acute hepatitis B carrier?
  - Anti-HB_s – prior hepatitis B, or immunisation?
  - Anti-HB_c IgM – recent acute hepatitis B?
  - Anti-HB_c IgG – hepatitis B infection in the past?
  - HB_eAg – acute hepatitis B or highly infectious carrier?
  - Anti-HB_e – prior hepatitis B, but not highly infectious?

- Management:
  - Monitor patients to assess whether they have become chronic carriers
  - If symptomology is very severe (e.g. jaundice), they are less likely to become carriers
  - Silent (**anicteric**) hepatitis B is more likely to result in a chronic carrier state
  - If patients remain HB_eAg positive, they are "super carriers" and highly infectious.

- Prevention:
  - **Engerix** = a recombinant hepatitis B vaccine, containing HB_sAg (95% effective)
  - **i.m. anti-HB_s hyperimmune serum globulin** within 24 hours of exposure.

HEPATITIS C

- RNA flavivirus that can lead to chronic hepatitis or hepatic carcinoma.
- Highly infectious – transmission via blood and saliva. (10% vertical transmission)
- Incubation = 2-26 weeks ; **no vaccine**

- Symptoms:
  - Malaise, fever and muscle weakness
  - Followed by anorexia
  - Diarrhoea, nausea and vomiting?
  - Vague, dull RUQ pain
  - Arthritis or rash (cf. serum-sickness syndrome)
  - Distaste for cigarettes
  - Infrequent jaundice

- Investigations:
  - LFT pattern similar to Hepatitis A
  - Prolonged INR
  - Normal ESR & WCC
  - Hepatitis C antibodies requested, if patient is negative for hepatitis A & B

- Management:
  - Bed rest and nutritional support.
  - Patient may develop acute liver failure, and must follow up to assess chronic carrier state.
  - If positive hepatitis C RNA in circulation → manage as if they have chronic hepatitis.

- Acute hepatitis C – 20% recovery
  - 80% develop chronic hepatitis C.
    - 10% of these will progress onto cirrhosis
      - a further 10-15% of these will develop hepatocellular carcinoma.

HEPATITIS D

- Incomplete RNA virus, usually requires hepatitis B for replication
  - Will simultaneously infect a patient with hepatitis B
  - Or will super-infect a chronic hepatitis B carrier

- Endemic to Mediterranean, Africa and South America
- Incubation = 6-9 weeks
- Blood/sexual transmission
- Prevented by **Engerix** (the hepatitis B vaccine)

HEPATITIS E

- An RNA virus
- Incubation = 4-20 weeks
- Faecal/oral transmission
- Endemic to areas of ↓ sanitation
- No vaccine available

OTHER CAUSES OF VIRAL HEPATITIS

- Cytomegalovirus (CMV)
- Epstein-Barr Virus (EBV)
- Yellow Fever
- Herpes Simplex Virus (HSV)

ACUTE LIVER FAILURE

- UK causes:
  - Paracetamol overdose (55%)
  - Non-A, non-B hepatitis (20%)
  - Hepatitis B (10%)
  - Other causes (10%)
  - Hepatitis A (5%)

- Clinical presentation:
  - **Jaundice** – period between jaundice and encephalopathy determines outcome:
    - 0-7 days → *hyperacute liver failure* (35% survival without transplant)
    - 8-28 days → *acute liver failure* (7% survival without transplant)
    - >28 days → *subacute liver failure* (15% survival without transplant)
  - **Encephalopathy:**
    - Consciousness varies from drowsy to unresponsive to pain
    - Liver flap
    - Hepatic foetor (sweet smelling breath)
    - Grossly impaired spatial awareness
    - Cannot draw a 5-pointed star, or put numbers on a clock face.
  - Cerebral oedema
  - Coagulopathy
  - Oliguric renal failure
  - Hypoxaemia
  - Hypoglycaemia
  - Susceptibility to infection

- Investigations:
  - LFTs - ↑ transaminases and bilirubin
  - ABGs – respiratory alkalosis caused by hyperventilation
  - Prolonged INR
  - ↓ blood glucose
  - ↑ serum creatinine
  - blood cultures – to exclude gram-negative sepsis and cholangitis from differential.

- **Cerebral Oedema**:
  - Results from loss of cell membrane integrity and alteration in the permeability of the blood-brain barrier
  - ↑ intracranial pressure → ↓ perfusion, ischaemia and herniation of brainstem.
  - Clinical symptoms:
    - Systemic hypertension
    - Bradycardia
    - ↑ muscle tone → decerebrate posture and Δ pupillary reflexes
  - R_x = keep supine, mannitol (20%)

- **Coagulopathy**:
  - Caused by reduced synthesis of clotting factors
  - R_x = fresh frozen plasma (FFP) ; Vitamin K of limited use.

- **Oliguric Renal Failure**:
  - 50% develop this hepatorenal syndrome
  - toxic effect of paracetamol overdose or other toxins
  - poisoning by Leptospirosis

- **Hypoxaemia**:
  - R_x = ventilation and ↑ O_2
  - *prostacyclin* improves peripheral oxygen delivery

- **Hypoglycaemia**:
  - A defect in gluconeogenesis, as well as ↑ levels of insulin
  - Monitor blood glucose, and give 10% glucose
    - Beware hypokalaemia induced by this.

- **Infection**:
  - Bacterial and candidal infections common, because of impaired cell-mediated immunity and neutrophil function.
  - R_x = frequent blood cultures and appropriate antimicrobial/antifungal therapy.

CHRONIC LIVER DISEASE

CAUSES OF CHRONIC HEPATITIS

- **α_1-Antitrypsin deficiency**
  - Uncommon hereditary problem
  - Abnormal or absent production of the enzyme → cannot be exported from the liver
  - Leads to enzyme accumulation and chronic liver disease (usually in childhood)
  - Systemic deficiency of α_1-antitrypsin causes emphysema
  - Since it is an acute phase protein, tests for deficiency can only be made during periods no infection/inflammation
  - No treatment, but smoking should be avoided.

- **Haemochromatosis**
  - Autosomal recessive condition leading to ↑ iron absorption from the gut, and ↑ deposition in tissue
  - Clinical manifestations:
    - Diabetes mellitus
    - Bronzed appearance
    - Symmetrical arthritis (knees, MCP joints)
    - Gynaecomastia
    - Hypogonadism
    - Hepatomegaly → cirrhosis → hepatoma

- **Wilson's Disease**
  - Autosomal recessive defect in copper excretion from hepatic lysosomes into the bile
  - ↑ copper tissue deposition in the liver, brain and kidneys
  - ↓ caeruloplasmin levels in the blood
  - ↑ free copper in the blood, and urine
  - Can present as an acute fulminant hepatic failure initially, but leads to chronic liver disease in childhood or young adulthood
  - Symptoms:
    - Acute haemolysis
    - Renal tubular acidosis
    - Extrapyramidal neurological features
    - R_x = *D*-penicillamine
- **Autoimmune chronic hepatitis**
  - Young/middle-aged ♀
  - Associated with other autoimmune conditions:
    - ulcerative colitis
    - pericarditis
    - thyroiditis
    - migrating arthritis
    - fibrosing alveolitis
  - Diagnosis by abnormal LFTs and a positive antinuclear & anti-smooth muscle antibodies
  - Insidious onset → rapid cirrhosis
  - R_x = immunosuppressive therapy

- **1° Biliary cirrhosis**
  - A chronic obstructive cholangitis seen in middle-aged ♀
  - Symptoms – jaundice + pruritis
  - Investigations
    - abnormal LFTs (cholestasis pattern)
    - ↑ anti-mitochondrial antibodies
    - ↑ serum IgM
  - No proven treatment; can lead to cirrhosis

- **Granulomatous hepatitis**
  - Caused by around 30 infectious and non-infectious diseases:
    - TB and sarcoidosis (classic)
    - Tropical parasitic diseases (e.g. schistosomiasis)
    - Q-fever
    - Chronic fungal disease (e.g. histoplasmosis)
  - 10% of normal people have hepatic granulomata → granulomatous hepatitis implies hepatic dysfunction in addition to the presence of granulomata on biopsy
  - Can sometimes cause pyrexia of unknown origin (PUO)
  - R_x directed towards the underlying cause.

- **Alcoholism:**
  - Fatty Δ
  - Mallory's hyaline bodies
  - Central zonal type of liver damage

CHRONIC HEPATITIS

- Graded histologically:
  - *Minimal* and *mild* – restricted to portal tracts
  - *Moderate* – damage to the border between lobules, including bile duct proliferation
  - *Severe* – extensive inflammatory cell infiltrate and fibrosis

- Clinical presentation:
  - Abnormal LFTs
  - Hepatomegaly
  - Markers of active hepatitis B or hepatitis C infection?
  - Fatigue
  - Fever

CAUSE	SEROLOGICAL TEST
Hepatitis B	HB_sAg
Hepatitis C	Anti-HCV, or PCR for HCV
Haemochromatosis	Serum iron, and iron-binding capacity
α_1-Antitrypsin deficiency	Serum levels of AAT (when no inflammation)
Wilson's disease	Copper and caeruloplasmin levels
Chronic hepatitis of unknown origin	*None*
1° biliary cirrhosis	Antimitochondrial antibodies
Autoimmune chronic hepatitis	ANA, smooth muscle antibodies
Alcoholic liver disease	Blood alcohol?
Granulomatous hepatitis	γ-globulins for Q-fever or schistosomiasis?

- **Liver Biopsy:**
  - Risk of bleeding. Mortality is 1 in 2000.
  - Mortality rises in:
    - Abnormal clotting times
    - Cirrhosis
    - Abnormal platelet function

  - Procedure:
    - Seek written consent
    - Recent drugs? (Aspirin, NSAIDs)
    - Spider naevi, oesophageal varices or radiological reports suggesting cirrhosis?
    - Measure clotting time and platelet count
    - Group and save blood for cross-match
    - 4 hours rest before biopsy is performed, to observe any bleeding problems

  - Following biopsy:
    - Pain in right lower chest, or right shoulder.
    - If ↑ pulse or look increasingly unwell, summon SHO or registrar, and cross-match for 4 units of whole blood.

  - May need to repeat after 6-12 months to monitor efficacy of treatment.

- Management:
  - Hepatitis B and hepatitis C → α-interferon (30% response rate)
  - Automimmune hepatitis and 1° biliary cirrhosis → immunosuppressive therapy
  - Wilson's disease → copper chelation with *D*-penicillamine
  - Abstinence from alcohol
  - Progressive deterioration in young people may indicate the need for transplantation.

CIRRHOSIS OF THE LIVER

- Hepatic cirrhosis is the end-stage for many chronic inflammatory processes of the liver
- Most common cause is alcohol abuse
  - But any of the above causes of chronic hepatitis may also lead to cirrhosis

- Histologically characterised by fibrosis and regenerating nodules.

- Clinical features:
  - Spider naevi on the face or upper trunk (>5)
  - Palmar erythema
  - Dupuytren's contracture
  - Gynaecomastia and testicular atrophy
  - ↓ grade PUO

  - *Portal hypertension* (from opening up of porta-systemic anastomosis as a result ↑ resistance to drainage of the GI-system and spleen) *:*
    - Ascites
    - Oesophageal varices
    - Haemorrhoids (rectal)
    - Caput medusae (umbilical)
    - Splenomegaly (from dilated splenic vein)

  - *Hypoalbuminaemia:*
    - Leuconychia
    - Ankle oedema
    - Sacral oedema

  - Folate, iron, riboflavin or pyroxidine deficiency → glossitis/angular cheilitis

  - Prolonged bleeding (INR) → bruising/haemorrhage

  - ↓ *Immune function:*
    - subacute bacterial peritonitis
    - pneumococcal pneumonia
    - bacteraemia
    - pulmonary TB

  - Dementia

  - Korsakoff's psychosis, and Wenicke's encephalopathy (caused by alcohol or subdural haematomas)

- CAGE questionnaire for recognising alcohol abuse:
  - Have you ever felt you should **C**ut down your drinking?
  - Have you ever been **A**nnoyed by criticism of your drinking?
  - Have you ever felt **G**uilty about your drinking?
  - Do you drink in the morning (**E**ye opener)?

  - Clues to diagnosis:
    - Hypertension
    - ↑ uric acid
    - asymptomatic rib fractures on CXR

ASCITES

- Occurs with sinusoidal obstruction **within** the liver, and **not** caused by obstruction of the portal vein

- Sinusoidal portal hypertension → splanchnic arteriolar v/d → arterial hypotension → stimulation of:
  - ADH
  - renin-angiotensin-aldosterone system
  - sympathetic NS

  →→→ sodium and water retention → ↑ plasma volume

- If this compensation mechanism is sufficient to normalise circulatory haemostasis → then renin, aldosterone, ADH, and noradrenaline levels return to normal.

- In decompensated cirrhosis, circulatory haemostasis is inadequate → renin, aldosterone, noradrenaline and ADH levels remain high:
  - Causes renal v/c → hepatorenal syndrome
  - Results in continuous water and salt retention → *ascites* & dilutional hyponatraemia

- Graded R_x:
  - Sodium restricted diet (10% response)
  - Add 100-200mg spironolactone daily (additional 50% response)
  - Add 40mg Frusemide daily (additional 25% response)
    - Must monitor treatment and urine output to prevent:
      - Hypovolaemia
      - Electrolyte Δ
      - Pre-renal ARF/impairment

- Reformed alcoholics and patients with cirrhosis for other reasons may be candidates for liver transplantation.

OESOPHAGEAL VARICES

- Partially preventable by prophylactic sclerotherapy
  - done by endoscopic injection after a provisional diagnosis of hepatic cirrhosis is made

- Difficult to control bleeding varices:
  - 50% will also bleed from a second GI site (e.g. gastric/duodenal ulcers)
  - stomach varices are difficult to access
  - there may be concomitant platelet/clotting abnormalities (from the cirrhosis)

- Presence of blood in the GI tract will:
  - ↑ absorption of toxic compounds (e.g. ammonium, bilirubin)
    - diseased liver cannot metabolise these → encephalopathy
  - act as a natural laxative

- R_x:
  - ↓ portal pressure with an infusion of *somatostatin* (**octerotide**) or *vasopressin*
  - emergency sclerotherapy
  - rarely use balloon tamponade

SPONTANEOUS BACTERIAL PERITONITIS

- Passage of gut bacteria into the intestinal lymphatics and ascitic fluid
  - Occurs in 10% of ascitic patients
  - Always by gram –ve species (e.g. *E. coli*)

- Risk factors:
  - GI haemorrhage
  - ↑ serum bilirubin
  - ↓ ascitic fluid protein content (e.g. ↓ complement and immunoglobulin content)
  - prior spontaneous bacterial peritonitis

- Symptoms:
  - Abdominal pain
  - Fever
  - Rebound tenderness?

- Investigations:
  - Aspiration of ascitic fluid
  - Look for white cells, glucose and amylase
  - Gram stain and culture

- R_x = a gram negative antibiotic (e.g. **cefotaxime**)
- Mortality is 20-40%

BENIGN TUMOURS

- Adenomas and haemangiomas are very rare
- Adenomas are associated with the oral contraceptive pill and anabolic steroids
  - Present with shock (from intraperitoneal rupture and haemorrhage)

1° MALIGNANT TUMOURS

- Associated with cirrhosis and hepatitis B.
- The possibility should be considered in any patient with known chronic liver disease, or a patient with cirrhosis who is showing signs of general deterioration.

- Investigations:
  - ↑ serum α-fetoprotein (AFP)
  - USS or CT will show a usually solitary tumour
  - Biopsy if no serious clotting problems
- R_x:
  - If tumour is restricted to one lobe (rare) → resection
  - Systemic chemotherapy, or chemotherapy direct into the hepatic artery
  - Poor prognosis – few survive more than 3 months.

2° MALIGNANT TUMOURS

- Most commonly caused by metastases from the GI tract, bronchus and breast
  - It will often be the first presentation of the 1° tumour

- Symptoms:
  - General malaise
  - ↓ weight
  - Non-specific abdominal pain
  - Possible hepatomegaly (with an irregular edge)
- Diagnosis by ↑ ALP, USS or CT. A biopsy may be needed.
- Little active therapy (although some patients with breast disease may respond).

THE BILIARY SYSTEM

NORMAL STRUCTURE AND FUNCTION

- The biliary tree collects bile salts and bilirubin, which are secreted by hepatocytes, and either stores them or delivers them to the small intestine…
  - Where they aid lipid, cholesterol and phospholipid (lethicin) absorption through micelle formation.

- Bile canaliculi channel bile salts from the hepatocytes to the interlobular bile ductules within the portal canals of the liver.
  - These ductules converge into right and left hepatic ducts
  - The right and left hepatic ducts unite to form the common hepatic duct
  - Outside the liver, the cystic duct (connecting to the gall bladder) joins the common hepatic duct, to form the common bile duct
  - This runs to the medial side of the 2nd part of the duodenum, where it enters with the pancreatic duct at the Ampulla of Vater.
  - The Sphincter of Oddi prevents bile passage into the duodenum in the absence of food.

- The gall bladder can store about 50ml of bile.

- Bile acids are synthesised from cholesterol in hepatocytes. Conjugation with taurine and glycine increases their solubility, and they form glycocholate and taurocholate salts.

- Enterohepatic recirculation (takes place several times a day):
  - secretion of bile salts into the small intestine
  - their subsequent reabsorption in the terminal ileum
  - and finally their first-pass extraction into hepatocytes and re-secretion into the biliary tract.

- Failure of bile salt absorption → colonic irritation and diarrhoea
  - Occurs in Crohn's disease, and after an ileal resection
  - R_x = **cholestyramine** (binds to bile salts)
    - Depletes the bile acid pool, and ↓ pruritis in prolonged obstructive jaundice.

- An imbalance in bile salt synthesis results in aggregation and formation of gall stones.

GALL STONES AND CHOLECYSTITIS

- More common in ♀, and prevalence rises with age.

- Risk factors:
  - Supersaturation of bile with cholesterol
  - Impaired gall bladder motility
  - Bile stasis
  - Prolonged ↑ red cell turnover (e.g. hereditary spherocytosis) → pigment stones.

- Asymptomatic presentation – most gall stones are asymptomatic, and are identified incidentally during USS.

- Symptomatic presentation:
  - Episodic RUQ pain, classically after food and lasting several hours = biliary colic
  - Severe pain radiating to the right scapula
  - ↑ risk of developing cholecystitis and pancreatitis

- Complicated presentation:
  - Acute cholecystitis and duct obstruction –
    - abscess formation
    - gall bladder perforation and peritonitis
    - mucocoele formation
  - Stasis –
    - cholangitis
    - pancreatitis
  - Chronic cholecystitis → scarred, shrunken, non-functioning gall bladder
  - Carcinoma is **rarely** a complication.

- Investigation:
  - ↑ serum bilirubin
  - ↑ ALP > ↑ ASL/ALT
  - USS (90% sensitivity) – small and thick walled
    - Common bile duct should be < 8mm width
    - Dilatation → extrahepatic obstruction
  - Murphy's Sign = *ask patient to inspire during palpation. Gall bladder moves down and nudges examiner's fingers, resulting in a sharp pain.*

- Management:
  - Non surgical (20% suitability, and ↑ recurrence)
    - Gall stone dissolution
    - Extracorporeal shock wave lithotripsy
    - Mechanical litholysis
  - Surgery – cholecystectomy
    - Remove stones and avoid recurrence.
    - Open surgery.
    - Laparoscopic surgery - ↓ pain, ↓ scarring, ↓ length of stay, and ↓ convalescence

- Common bile duct stones:
  - May pass spontaneously, or may have to be removed by ERCP
  - Present with RUQ pain, jaundice and fever (caused by ascending cholangitis)

ASCENDING CHOLANGITIS

- Infection of the biliary tree - ↑ morbidity and mortality
- A plain AXR may show gall stones (10%) or gas in the biliary tree.
  - Indicates the presence of gas forming bacteria

- Can present as an unexplained pyrexia, or gram –ve septicaemic shock.

- R_x = i.v. fluids + ↑ flow oxygen + antibiotics
  - e.g. **cefotaxime** (vs. gram –ve species) and **metronidazole** (vs. anaerobes)
  - ERCP to look for stones or strictures.

TUMOURS

- Cholangiosarcoma is rare – associated with gall stones in the elderly
- Presents with painless, obstructive jaundice
- Most tumours are inoperable
- Symptomatic relief with ERCP stent insertion to alleviate biliary obstruction
- Malignant disease is usually 2° to "head of pancreas carcinoma" or metastases from lymph nodes at the porta hepatis.

THE PANCREAS

NORMAL STRUCTURE AND FUNCTION

- Situated retroperitoneally, with the 2nd part of the duodenum wrapped around its head, and its tail overlying the spleen.
  - Exocrine secretions are drained by a branching system of ducts, all draining into the main pancreatic duct.
  - This enters the medial wall of the 2nd part of the duodenum along with the common bile duct, at the Ampulla of Vater.

- Acid in the duodenum stimulates release of *secretin* → ↑ pancreatic secretions (water, electrolytes and bicarbonate)

- Fat in the duodenum stimulates release of CCK from the pancreas:
  - Contraction of gall bladder
  - Relaxation of sphincter of Oddi
  - Promotes pancreatic enzyme secretion
  - Trophic to the pancreas

- Pancreatic enzymes are all secreted in an inactive form, to prevent autodigestion:
  - Lipase & phospholipase → fats
  - Amylase → starch
  - Chymotrypsin & trypsin → protein

- Endocrine function of the pancreas is served by the Islets of Langerhans.
  - β-cells produce insulin
  - α-cells produce glucagons
  - D-cells produce somatostatin
  - PP-cells produce pancreatic polypeptide
    - *It is very rare of specific tumours to produce excess individual hormone production.*

ACUTE PANCREATITIS

Gall stones
Ethanol
Trauma (abdominal)

Steroids
Mumps
Autoimmune
Scorpion venom
Hyperlipidaemia
ERCP / emboli
Drugs (e.g. sulphasaline)

- Caused by reflux of pancreatic enzymes resulting in autodigestion (33% idiopathic)
- Clinical presentation:
  - Severe epigastric pain, radiating to the back → patient lying still and shallow breathing
  - ↑ ↑ ↑ Vomiting
  - Pallor + Sweating
  - Hypotension
  - Profuse peripheral perfusion } → Shock
  - Tachypnoea
  - Abdominal rigidity, tenderness and guarding
  - *Grey-Turner's sign* (bruising in the flanks) & *Cullen's sign* (bruising around the umbilicus)
  - Jaundice (oedematous pancreatic head can compress common bile duct on 3rd to 4th day)
  - Loss of bowel sounds after 12-24 hours, because of ileus.

- Differential diagnosis:
  - Acute pancreatitis
  - Perforated peptic ulcer
  - Acute cholecystitis
  - Myocardial infarction

- Investigations:
  - 5-fold ↑ serum amylase (i.e. >1000 IU/ml) (lower rises occur in other disorders)
  - ↓ Albumin
  - ↓ corrected calcium
  - ↓ haemoglobin and ↑ WCC
  - ↑ Urea and creatinine (may progress to ARF)
  - ↑ Blood sugar (may need to be controlled with insulin)
  - Prolonged prothrombin time
  - ↑ fibrin degradation products (FDPs) } → disseminated intravascular coagulation
  - thrombocytopaenia
  - Blood gases – metabolic acidosis and hypoxia
  - USS – gall stones or oedematous/necrosed pancreas
  - Plain AXR – excludes a perforated viscous
    - Shows sentinel sign of pancreatitis: *a loop of distended proximal jejunum surrounding the pancreas.*

- Management:
  - Pain relief with opiates (avoid morphine as it causes spasm of the sphincter of Oddi)
  - NBM
  - i.v. fluids and antibiotics
  - regular aspiration through NG tube, since nausea and vomiting common
  - ↑ flow oxygen
    - *Pain usually subsides within a 2 days. Severe cases require admission to ITU*

- Early complications:
  - Shock
  - Disseminated intravascular coagulation (DIC)
  - Renal failure
  - Hypoxia
  - Ileus
  - Hyper/hypo glycaemia

- Late complications:
  - Pseudocyst – suspected if there is continuing pain, ileus and a smooth epigastric swelling
    - Diagnoses by USS, and may require drainage. (Some resolve spontaneously)
  - Ascites
  - Pleural effusion (↑ amylase content)
  - Abscess formation (↑ morbidity and mortality)
    - Caused by *E. coli* → R_x = cefotaxime & metronidazole, + drainage.
  - Candidaemia

CHRONIC PANCREATITIS

- Associated with heavy alcohol intake – protein plugs block the small ducts
  - Causes back pressure and damage to endocrine and exocrine cells
  - Heals by fibrosis, ductal dilatation and calcification
  - An irreversible process, that can be arrested if the patient stops drinking.

- Symptoms:
  - Chronic epigastric pain (may radiate to the back)
    - May be relieved by sitting forward
    - Can run a relapsing and remitting course, with individual episodes mimicking acute pancreatitis
  - ↓ weight (malabsorption)
  - steatorrhoea (↓ lipase secretion)
  - IDDM or NIDDM depending on degree of β-cell damage

- Differential diagnosis = chronic pancreatitis or pancreatic carcinoma

- Investigations:
  - Plain AXR – intra-gland calcification
  - USS – small, fibrotic gland, with ductal dilatation
  - ERCP – Δ normal anatomy
  - Serum amylase *normal* (except when the condition runs a relapsing course)
  - Faecal fat collection?

- Management:
  - Advise on stopping alcohol
  - Referral to a pain clinic for *narcotic analgesics*, if pain is leading to depression
  - Pancreatic enzyme supplements (reduce malabsorption)
  - H_2 antagonists – prevents a low duodenal pH from restricting residual enzyme function
  - Medium chain triglycerides – do not require digestion before absorption
  - Vitamin A, D, E & K supplements

TUMOURS

- The pancreas can give rise to a number of *rare, benign* tumours which are hormonally active:
  - VIPoma, glucagonoma, insulinoma
  - Zollinger-Ellison gastrinomas – secrete gastrin, and cause peptic ulcers.

- Risk factors for adenocarcinoma:
  - Male (♂:♀ is 2:1)
  - 50-70 years old
  - chronic pancreatitis
  - ↑ dietary fat
  - occupation exposure in chemical/metal industry

- Pathology:
  - 60% in head
  - 25% in body
  - 15% in tail
  - A ductal carcinoma – hard infiltrating growth
  - Lymphatic spread → peritoneal/regional nodes
  - Haematogenous spread → liver, lung

- Clinical features:
  - *head* – jaundice
  - *body* – malabsorption, anergia and ↓ diabetes
  - *ampullary* – cholangitis
  - can present with painless jaundice, or a "boring" epigastric/back pain
  - anorexia, lethargy and ↓ weight
  - duodenal obstruction → nausea and vomiting
  - malignant ascites
  - hepatomegaly, or an abdominal mass from nodal involvement
  - superficial/migratory thrombophlebitis

- Investigations:
  - ↑ ALP
  - fasting oral GTT (to look for diabetes)
  - USS (pancreatic mass, metastases, biliary tree distension?)
  - ERCP – fine needle aspiration cytology (FNAC)? Biopsy? Stenting?
  - Barium meal
    - Widening of duodenal loop?
    - Medial filling defect?
    - Reversed "3" sign

- Palliative management:
  - Oral methadone/morphine, or a celiac axis block
  - Enzyme and insulin supplements
  - ERCP + stenting to relieve jaundice
  - Surgical biliary or intestinal bypasses to alleviate pain
    - Cholecystojejunostomy
    - Gastroenterostomy

- Rare curative care – reserved for young and fit, with no metastases and early diagnosis.
  - *Whipple's resection* = removal of duodenum and head of pancreas.

- Prognosis:
  - 90% die within 1 year
  - 14 months with resection, 5 months if palliative
  - Peri-ampullary and Islet cell tumours have a 40% 5-year survival.