

# Splenomegaly (enlarged spleen)

- An abnormal increase in size and weight of the spleen but irrespective of function
- Massive splenomegaly: chronic myeloid leukaemia, visceral leishmaniasis, myelofibrosis
- Causes of splenomegaly:
  - Inflammation
  - Infections:
    - Viruses: EBV, CMV, Hepatitis, measles, HIV
    - Bacteria – TB, typhoid, brucella, treponaemes
    - Fungi: histoplasma
    - Metazoa: hydatid disease
    - Protozoa: leishmania, malaria, toxoplasmosis
  - Sarcoidosis
  - SLE
  - Rheumatoid arthritis
  - Amyloidosis
  - Storage diseases
  - Congestion: secondary to cirrhosis of liver or splenic/portal vein thrombosis, right sided heart failure, Budd-Chiari syndrome
  - Congenital: hereditary haemolytic anaemias, polycystic disease
  - Neoplasia: lymphoma and leukaemia
  - Myeloproliferative disorders: myelofibrosis, polycythaemia vera
  - Iatrogenic: antibiotics

## Hypersplenism

- Abnormal function related to size.
- Inappropriate removal of red/white cells and platelets
- Normal marrow production of blood components
- Reversal of these changes after removal

## Leukaemia vs Lymphoma

Leukaemia is a cancer of the blood forming cells which begins in the bone marrow. They can spread into the bloodstream and to other parts of the body. They can be either lymphoid or myeloid in origin.

Lymphoma is a cancer of the lymphatic system, including the lymph nodes, spleen, and thymus. The cancer cells are atypical lymphocytes.

## Goitre

- Can be diffuse or affect a specific lobe
- Nodular, multinodular, smooth appearance
- Can be associated with retrosternal extension, hoarseness of voice, pressure on airway (indications for surgical intervention).
- **Hashimotos thyroiditis** – presents with symptoms of hypothyroidism. Autoimmune condition – antibodies to thyroglobulin and thyroid peroxidase. Destruction of the thyroid gland – extensive infiltration of lymphocytes with formation of germinal centres.
- **De Quervain thyroiditis** – triggered by viral infection. Multinucleate giant cells seen (granulomatous thyroiditis). Inflammation usually transient and resolves within 2-6 weeks.
- **Riedel thyroiditis** – rare – extensive fibrosis involving thyroid and contiguous neck structures. Mimics thyroid carcinoma (firm fixed thyroid.)
- **Graves disease** – ophthalmopathy, pre-tibial myxoedema, hyperthyroidism. Autoimmune condition – antibodies to the TSH receptors. The antibodies occupy the receptor and therefore cause hyperthyroidism. Macroscopic: diffuse symmetrical enlargement of the gland, deep red coloured parenchyma. Microscopic: hyperplasia and hypertrophy of gland, scalloping of colloid, lymphocytes.

## Abdominal aortic aneurysm (AAA)

- Localised abnormal dilation of a blood vessel (or heart) that can be either congenital or acquired.
- True aneurysm – involves attenuated but intact arterial wall
- False aneurysm – defect in vascular wall leading to extravascular haematoma freely communicating with intravascular space
- Dissection – blood enters through a defect in the arterial wall and tunnels between its layers.
- Saccular – outpouching involving only a portion of the wall.
- Fusiform – diffuse and circumferential
- Can form due to poor intrinsic quality of vascular wall connective tissue, balance of collagen degradation and synthesis altered by inflammation and proteases, weakened vascular wall through loss of smooth muscle cells.
- Two most important causes of aortic aneurysms are hypertension and atherosclerosis
- Mycotic aneurysms – caused by infection, through a septic embolus, extension of suppurative process or circulating organisms directly infecting the wall.
- AAA – more frequently seen in men and smokers, rarely occur before age 50.
- Macroscopic: wall of aneurysm is thin, lumen filled with layered an unorganised thrombus. Usually found infrarenally. Can be up to 15cm in diameter.
- Inflammatory AAA – 5 - 10% of all aneurysms, raised inflammatory markers. Localised immune response to the presence of the aneurysm.
- Complications: thrombosis, embolism, pressure effects, rupture, ischaemia.
- Risk of rupture: 11% per year if 5-6cm. 25% per year for aneurysms >6cm. Expand by 0.2-0.3cm per year, but 20% expand more rapidly.

## **Ischaemic bowel**

- Obstruction of blood supply.
- Chronic, progressive hypoperfusion vs acute compromise – can lead to infarction of large lengths of bowel.
- Can range from mucosal infarction, mural infarction, transmural infarction.
- Causes: atherosclerosis, AAA, hypercoagulable states, oral contraceptives, embolisation of cardiac vegetations or aortic atheroma.
- Hypoperfusion – cardiac failure, shock, dehydration, systemic vasculitides
- Macroscopic: continuous/segmental and patchy, haemorrhagic and ulcerated mucosa, oedematous and thickened wall. Intensely congested, dusky colour. Serositis. Linear demarcation between affected and non-affected bowel.
- Microscopic – atrophy and sloughing of the epithelium. Chronic ischaemia – fibrous scarring.

## **Renal carcinoma**

- 6<sup>th</sup> and 7<sup>th</sup> decades
- 2:1 male preponderance
- Smokers have double the incidence
- Obesity, hypertension, unopposed oestrogen therapy, exposure to asbestos, petroleum products, heavy metals, end stage renal disease, cystic disease, tuberous sclerosis
- Most cases are sporadic although familial variants account for 4%
- VHL (Von Hippel-Lindau) gene implicated in development of both familial and sporadic clear cell carcinomas
- **Clear cell carcinoma** – 70-80% of renal carcinomas. 95% are sporadic
- Loss of sequences on short arm of chromosome 3 – harbours the VHL gene
- Characterised microscopically by cells with abundant clear cytoplasm.
- **Papillary carcinoma** – 10 -15%. Papillary growth pattern
- Associated with MET mutations
- **Chromophobe carcinoma** – 5%. Cells show prominent cell membranes and pale eosinophilic cytoplasm. Excellent prognosis, but can look very similar to oncocytoma.
- Macroscopic appearance clear cell carcinoma – bright yellow-grey-white spherical masses of variable size. Yellow colour – lipid component. Necrosis and haemorrhagic foci can be seen. Renal vein invasion can be seen.
- Benign neoplasms: renal papillary adenoma, angiomyolipoma, oncocytoma

## **Torsion of testicle**

- Twisting of the spermatic cord
- Obstructs venous drainage of testicle
- Can lead to infarction – urological emergency
- Neonatal torsion – can occur in utero or shortly after birth
- Arteries remain patent – leads to vascular engorgement and haemorrhagic infarction
- 6 hour window for treatment

## **Horseshoe kidney**

- Fusion of the upper poles (10%)
- Fusion of the lower poles (90%)
- Horseshoe-shaped structure – continuous across the midline anterior to the great vessels
- Found in 1 in 500-1000 autopsies

## Osteosarcoma

- Affects children and young adults – 10-25 years
- Patients with Paget's disease are at a slightly increased risk
- Tumour of primitive mesenchymal bone forming cell
- Risk factors: radiation, rapid bone growth, genetic predisposition, Li-Fraumeni syndrome, pre-existing bone disease
- Cancer cells produce osteoid matrix or mineralised bone
- Lifting of periosteum due to laying down of reactive bone – Codman triangle
- Most commonly – arises in metaphysis of long bones
- Bulky tumours – grey/white, areas of haemorrhage and cystic degeneration
- Formation of bone by the tumour cells is diagnostic



## Myocardial infarction

- Coronary artery atheromatous plaque – acute change – haemorrhage, erosion, ulceration, rupture, fissuring
- Exposure of subendothelial collagen – clotting cascade activated
- Vasospasm initiated by the mediators released from platelets
- Thrombus can completely occlude the lumen
- Ischaemia of the myocardium
- 0-4 hours after infarct – no gross features
- 4-24 hours – dark mottling
- 1-3 days – mottling with yellow-tan infarct at the centre
- 3-7 days – hyperaemic border surrounding the yellow-tan infarct
- 2-8 weeks – grey-white scar progressive from border towards core of infarct
- >2 months – scar complete

## **Left ventricular hypertrophy**

- Increased mechanical work of the heart
- Secondary to pressure or volume overload – hypertension or aortic stenosis
- Myocytes increase in size – hypertrophy
- Results in an increased size and weight of the heart
- Can lead to the development of heart failure
- Decreased cardiac output and tissue perfusion, and pooling of blood in the venous capacitance system (results in pulmonary/peripheral oedema or both)
- Macro: concentric thickened myocardium
- Histologically: increased cell and nuclear size

## Lung cancer

- 2 thirds are inoperable irrespective of type
- Small cell carcinoma – surgical intervention is inappropriate – often metastasised by the time of diagnosis
- Small cell carcinoma – 14% of lung tumours. Poor prognosis. Most frequently associated with smoking. Often located at the hilum. More frequently seen in men. Can be associated with paraneoplastic syndromes
- Adenocarcinoma – most frequent (38%). Peripheral location within the lung. More frequently seen in women. Need to distinguish from metastatic adenocarcinoma.
- Squamous cell carcinoma – 28% of tumours – associated with smoking (metaplastic change of the respiratory epithelium.) Paraneoplastic syndrome – parathyroid related peptide. Usually large on presentation.
- Risk factors: smoking, asbestos, arsenic, ionising radiation, vaporised metals.
- Molecular pathology – many mutations now identified linked to the development – EGFR, KRAS etc. Used as targets from therapies.
- 15% 5 year survival.

# Tuberculosis infection

- Mycobacterium tuberculosis var. hominis
- Also, mycobacterium tuberculosis var. bovis
- Lung is the commonest site of involvement
- However, tonsils with cervical lymph node involvement can also occur – scrofula
- Terminal ileum – caused by ingesting infected milk
- After initial infection, a Ghon focus forms, normally at the periphery of the lung. If the lymphatics become involved with consequent enlargement of the hilar lymph nodes, it is known as the primary complex. If it also enters the blood stream it can cause military TB, meningitis, bone and joint TB, renal TB.
- Macro: inflamed and fibrotic lung tissue, areas of cavitation.
- Histologically: characterised by caseating granulomas. Ziel-Nielsen stain to look for acid-fast bacilli.

# Pneumonia

- Bronchopneumonia and lobar pneumonia
- Bronchopneumonia – patchy consolidation of lung
- Consolidation of a large portion of a lobe or the entire lobe is lobar pneumonia
- But....patterns can overlap
- The same organisms may produce either pattern – depends on patient susceptibility
- Lobar pneumonia – congestion (heavy, boggy and red in colour due to vascular engorgement), red hepatisation (neutrophils, red cells and fibrin fill alveolar spaces), grey hepatisation (disintegration of red cells, persistence of fibrinosuppurative exudate), resolution (exudate is broken down by enzymatic digestion, produces debris which is resorbed or ingested by macrophages.)
- Bronchopneumonia – consolidated areas of acute suppurative inflammation. Most often multilobar – frequently basal due to the tendency of secretions to gravitate to lower lobes.
- Complications – abscess formation, empyema, bacteraemic dissemination

# Chronic Obstructive Pulmonary Disease

- Chronic bronchitis and emphysema
- Most patients have features of both
- Risk factor: smoking
- Causes an increased anaesthetic and surgical operative risk (and prolonged recovery)
- 4<sup>th</sup> leading cause of morbidity and mortality in US
- Emphysema – irreversible enlargement of airspaces distal to the terminal bronchiole
- Destruction of the walls
- Centriacinar emphysema – most common variant and commonly seen in smokers
- Panacinar emphysema – seen in alpha 1 antitrypsin deficiency
- Chronic bronchitis – goblet cell hyperplasia, inflammatory infiltrates, thickening of the wall

## Appendicitis

- Most cases idiopathic
- Other causes – enterobius vermicularis, tropical parasites, foreign material. Infection (viral/bacterial/amoebiasis/schistosomes), inflammation (UC, Crohns), ischaemia, neoplasia (caecum, appendix, pseudomyxoma, carcinoid)
- Serositis can be caused by other conditions located nearby to the appendix – diverticular disease, endometriosis, salpingitis
- Subserosal vessels congested, erythematous surface, haemorrhagic ulceration, gangrenous necrosis, perforation.
- Microscopic – neutrophilic infiltrate

## Gastric/peptic ulceration

- Uncommon cause of perforation thanks to advent of PPI medications
- Begins as an erosion (superficial breach of mucosa) – progresses to ulceration
- 350,000 new cases per year in the US
- Aetiology: Helicobacter pylori, NSAID use, alcohol, smoking, Zollinger-Ellison syndrome
- H. pylori – near universal association with duodenal ulcers, and in 90% of gastric ulcers not related to NSAID use.
- H. pylori – produces urease which protects against acid. Also produces proteases which break down glycoproteins in gastric mucosa, and phospholipase which damages epithelial cells.
- Macro: 90% of them are <4cm, clean base, surrounded by erythematous mucosa, may be blood vessels present in the base.
- Location: duodenum: stomach – 4:1



## **Gallbladder – cholecystitis**

- Acute and chronic phases
- Chronic – characterised by a thickened and fibrotic wall
- Erosion of mucosal surface
- Cholesterosis can be present – yellow granules scattered over surface of mucosa
- Perforation can occur in severe forms (gangrenous appendicitis)
- Microscopic: thickened fibromuscular wall, with erosion of mucosa (loss of normal folded epithelium)
- Obstruction of duct by gallstone is a common cause
- Empyema can form

## Pancreatitis

- Pathogenesis – aetiology affecting duct system, the acinar cells, the blood supply.
- Destruction of exocrine cells – release of pancreatic lytic enzymes which leads to more of the pancreas being destroyed
- Oedema, haemorrhage, secondary peritonitis and systemic release of inflammatory mediators can occur
- Complications: abscess formation, pseudocyst formation, haemorrhagic pancreatitis, duodenal obstruction
- Assessment: Glasgow score, Ranson Criteria, APACHE III
- Aetiology: Gallstones, Ethanol, Trauma, Steroids, Mumps, Autoimmune, Scorpion stings, Hyperlipidaemia/hypercalcaemia, ERCP, Drugs
- Chronic – repeated episodes of acute – more of the pancreas replaced by fibrous/scar tissue – function deteriorates

## Colonic Polyps

- **Tubular adenoma:** 90% occur in the colon, 50% are single
- Usually < 1cm in size and pedunculated. Risk of adenocarcinoma is related to size – higher risk if 6-10mm or larger. Darker in colour than the normal mucosa.
- **Villous adenoma** – less frequent than tubular adenoma. Commonly found in rectum/rectosigmoid. Higher change of malignancy – 40% risk if sessile and >4cm
- Soft, papillary villous projections, large base with no stalk.
- **Hyperplastic polyp** – 90% of all polyps. Often in rectosigmoid. Previously thought to have no/minimal malignant potential.
- Right sided – associated with cancers that show microsatellite instability.
- Macro: small, sessile and often located on top of mucosal folds. Same colour as surrounding normal mucosa.

## Colorectal carcinoma

- Most frequently seen in the rectum, followed by the sigmoid
- Right sided tumours – more frequently have a polypoid architecture
- Left sided tumours – annular and constrictive
- Most frequently classified as moderately to well differentiated adenocarcinoma
- Risk factors – adenomas, ulcerative colitis, family history, Peutz-Jeghers, ethnicity (whites more than blacks, and Jews more than Mormons), smoking, alcohol
- Screening: faecal occult blood test
- FAP autosomal dominant inheritance and accounts for 2% of colorectal carcinomas, APC gene abnormality on chromosome 5.
- HNPCC – autosomal dominant, 5% of cases, mutation in DNA mismatch repair genes
- Li-Fraumeni syndrome includes colorectal carcinoma as one of the features
- Sporadic type: Adenoma – carcinoma sequence, chromosomal instability (85%), microsatellite instability 15%
- Staging: Duke's and TNM
- Comment on differentiation, plane of excision, relationship to non-peritonealised margin, vascular invasion, lymph node involvement, and completeness of excision.

## **Crohn disease**

- Inflammatory bowel disease
- Peaks in 20's and also 50's-60's
- Associated with smoking
- Can affect anywhere from mouth to anus
- Transmural granulomatous inflammation
- Macro: mesenteric fat wraps around the bowel, thickened bowel wall (oedema/fibrosis/inflammation.) Skip lesions. Sharp demarcation with normal bowel.

## Ulcerative colitis

- Closely related to Crohn's
- But limited to the colon and rectum
- Extraintestinal features: migratory polyarthritis, ankylosing spondylitis, uveitis, skin lesions (pyoderma gangrenosum and erythema nodosum), sacroiliitis, uveitis (overlap with Crohn's)
- 2.5-7.5% of individuals with UC also have primary sclerosing cholangitis
- Macro: extends in a continuous fashion. Termed 'pancolitis' if all of the colon involved. Distal ileum can be affected – 'backwash ileitis.' Mucosa – red, granular, broad based ulcers, pseudopolyps. Dilation – leading to toxic megacolon.
- Histologically: inflammation confined to the mucosa and superficial submucosa. Granulomas are not present.

## Subdural Haematoma

- Space between inner surface of dura mater and outer surface of arachnoid mater
- In reality – dura is composed of 2 layers. When bleeding occurs, these 2 layers separate and this is what creates the subdural space where the blood accumulates.
- Bridging veins – prone to tearing and they are the source of bleeding in subdural haematomas in most cases
- Atrophy of brain – stretch the vessels
- Infants – the bridging vessels are thin walled and therefore fragile
- Macroscopic: collection of freshly clotted blood, across surface of brain, no extension into sulci
- Underlying brain is flattened
- Haematoma can be broken down and organised
- Chronic subdural haematoma – recurrent bleeds

## **Epidural/extradural haematoma**

- Dura fused with the periosteum on the internal surface of skull
- Dural arteries (middle meningeal artery) – vulnerable to injury with temporal skull fractures
- Arterial pressure of bleeding – dura separates from inner surface of skull
- Clinically, characterised by lucid interval
- Can expand rapidly



## Subarachnoid haemorrhage

- Most frequent cause – rupture of saccular/ berry aneurysm
- Can also occur as a result of extension of traumatic haematoma/intracerebral haemorrhage
- Atherosclerotic, mycotic, traumatic, dissecting aneurysms can also form
- Saccular aneurysms – 2% of the population!!
- Found near major branch points in anterior circulation
- Multiple aneurysms can be found
- Aneurysm structure – lack smooth muscle and intimal elastic lamina – developmental disorder
- Increased incidence with polycystic kidney disease, Ehlers-Danos syndrome, neurofibromatosis type 1, Marfan syndrome
- Smoking and hypertension also risk factors

# Meningioma

- Benign tumours of adults
- Usually attached to the dura
- Arise from meningotheelial cells of the arachnoid
- Prior radiation therapy – risk factor
- Associated with loss of chromosome 22
- Rounded masses – compress underlying brain but separate from it
- Necrosis and haemorrhage usually absent
- Slow growing tumours
- Vague symptoms
- 3:2 female predominance

## **Brain Tumour - Glioma**

- Most common group of brain tumours
- Astrocytomas, oligodendrogliomas
- Arise from progenitor cells that differentiate down one of the cell lineages
- Characteristic age distributions and clinical course and anatomic locations
- Mass effects from tumours (herniation, effacement of sulci, compression of ventricles etc.)

## **Meningitis**

- Inflammatory condition
- Affects leptomeninges and CSF within subarachnoid space
- Usually caused by an infection
- Bacterial and viral forms
- Macroscopic: exudate within the leptomeninges across surface of brain, meningeal vessels are engorged.
- Abundant neutrophils identified microscopically