PATHOLOGY OF THE ACUTE ABDOMEN
Dr A. Barbour, Discipline of Pathology. Copyright University of Adelaide 2008

ISCHAEMIC BOWEL DISEASE
- The celiac, superior and inferior mesenteric and internal iliac arteries provide blood to the stomach and intestines. There are various interconnections between these vessels.
- Small bowel tends to be involved more commonly than large bowel
- Transmural infarction tends to result from compromise of the major blood vessels (arterial or venous), whereas mucosal +/- submucosal infarction results from hypoperfusion (acute (e.g. in shock) or chronic (e.g. due to atherosclerotic narrowing))
- Arterial occlusion is predominantly a disease of the elderly and acute occlusions resulting in transmural infarction have a high mortality.

Transmural ischaemia/infarction
- Major vascular compromise
  - Arterial e.g. embolic, atherosclerosis + thrombosis, vasculitis
  - Venous e.g. volvulus, intussusception, strangulation related to hernia or adhesions, venous thrombosis
- Haemorrhagic (‘dusky’), oedematous wall, mucosal sloughing, serosal exudate. Haemorrhagic from venous congestion and haemorrhage in venous obstruction and from collateral bleeding in arterial obstruction.
- Histologically: necrosis, initially mucosal, then extending to involve muscularis propria, acute inflammation, vasodilation, haemorrhage
- Lumen often contains blood
- Clinically: abdominal pain, variable tenderness (may only develop later), nausea, vomiting, maybe bloody diarrhoea
- Complications:
  - Perforation from necrosis
  - Septicaemia: infarcted mucosa allows bacteria to penetrate bowel wall and enter blood stream

Chronic ischaemia
- Mucosal inflammation and ulceration, ultimately submucosal fibrosis +/- stricture
- Clinically: variable intermittent abdominal pain, often after a meal, diarrhoea, weight loss, pseudo-obstruction
- May mimic inflammatory bowel disease

BOWEL OBSTRUCTION
- Bowel obstruction can be partial or complete, simple (i.e, non-strangulated) or strangulated.
- Causes: hernias, adhesions, intussusception, volvulus, neoplasms, inflammatory strictures (e.g. Crohn’s disease, scarring following diverticulitis). Rarer causes include gallstones, worms, bezoars, congenital narrowings, Hirschsprung’s disease, meconium ileus.
- Causes of pseudo-obstruction (due to impaired motility without physical narrowing of the lumen) include paralytic ileus (from peritonitis), acute or chronic ischaemia, infarction, neuromuscular problems
- In cases of obstruction with compression and/or twisting of the vascular supply (hernias, adhesions, intussusception, volvulus) vascular compromise, initially venous, and later arterial, develops leading to bowel ischemia and infarction and potentially further morbidity and mortality. Such strangulated obstructions are surgical emergencies.
- Clinically: symptoms depend on level
  - Abdominal discomfort/pain, maybe colicky, vomiting with high obstructions
  - Colicky abdominal pain, abdominal distension (excess gas and fluid in intestine), constipation with low obstructions, though vomiting (may be feculent) may occur later
- Complications of obstruction:
  - Dehydration -> hypovolaemia: net secretion of fluid into the intestinal lumen is enhanced due to substances released from bacteria in the static luminal contents. Vomiting accentuates the fluid and electrolyte deficits.
  - Infarction: many pathologies that cause obstruction can also lead to strangulation with ultimate infarction of the bowel e.g. herniation, intussusception, adhesions, volvulus. Strangulation develops from compression and twisting of vessels in the wall and mesentery. Impaired venous drainage -> congestion and haemorrhage, ultimately arterial compromise also develops. When infarction develops, previously colicky pain from obstruction may become continuous and abdominal tenderness and fever may appear. Bacteria may enter the blood stream via infarcted mucosa, leading to septicaemia. Infarcted bowel wall may perforate, leading to acute peritonitis and septic shock.
  - Progressive distension proximal to the obstructive lesion may lead to impaired blood flow within the distended bowel wall but this rarely leads to necrosis of the wall and perforation. When it does occur, it is mainly with colonic obstruction if decompression through the ileocecal valve does not occur.
Hernias
- Portions of bowel protrude into outpouchings of peritoneum. Bowel may become trapped (incarcerated) -> obstruction and strangulation
- Examples: inguinal, femoral, umbilical hernias, abdominal wall weakening due to surgical scars

Adhesions
- Surgical handling and dust from surgical gloves leads to acute inflammation of serosal surfaces including that covering the bowel. The predominantly fibrinous exudate on the inflamed serosa heals by organization resulting in fine bands of fibrous tissue forming between abdominal organs. Adhesions may also develop in other conditions that cause inflammation within the peritoneal cavity e.g. with endometriosis
- Viscera may become twisted, trapped -> obstruction and strangulation

Intussusception
- Segment of bowel becomes telescoped into distal segment -> obstruction and strangulation
- Typically from an underlying pathologic lesion in adults, but not in children

Volvulus
- Twisting of bowel loop about mesentery -> obstruction and strangulation

DIVERTICULOSIS
- Multiple small herniations of mucosa and submucosa (pseudodiverticula) through muscularis propria of large bowel
- In sigmoid colon and extending for variable distance proximally
- ?due to increased intraluminal pressure related to low fibre diet, constipation and straining. Most common in Western populations
- Common: reportedly in > 50% of people over 70 yrs
- Middle-aged and elderly
- Most asymptomatic
- Complications
  - Acute inflammation (diverticulitis). Possibly related to faecolith formation
    - Causing left lower abdominal pain and tenderness, fever, constipation or diarrhoea
    - Acute inflammation and necrosis ->
      - Local perforation -> local abscess formation
      - Free perforation with generalised acute peritonitis (less common)
      - Fistula formation
  - Acute severe or recurrent bleeding
  - Recurrent inflammation -> scarring and stricture and partial bowel obstruction

ACUTE APPENDICITIS
Typically in adolescents and young adults
Pathogenesis
- In many cases unknown
- Some apparently related to obstruction e.g. faecolith, lymphoid hyperplasia
- While acute appendicitis is often said to result from obstruction, in many cases a cause of obstruction is not found and the majority are not distended. While ischaemia in obstructed appendices could play a role in the pathogenesis, it is not said to be infarcted. Microscopically, the first abnormality is focal acute inflammation in the mucosa, often distally. Inflammation then spreads from the mucosa through the wall. The stages in acute appendicitis are referred to as: early focal, acute suppurative, gangrenous and perforated.

Morphology
- Suppurative acute inflammation commences in mucosa then becomes transmural
- Mucosal ulceration
- May progress to gangrene (transmural necrosis) and rupture
- Macroscopically: swollen, hyperaemic appendix with fibrinous/fibrinosuppurative serosal exudate (once inflammation has become transmural)

Clinically
- Classically initially periumbilical abdominal pain (visceral), subsequently right lower abdominal pain and tenderness (related to inflammation of parietal peritoneum overlying appendix)
- Variable anorexia, nausea, vomiting, malaise
- Mild fever, tachycardia

Complications
- Perforation (high risk): Neutrophils are numerous (suppurative inflammation) in an established acute appendicitis and release of lysosomal contents during phagocytosis and on death of neutrophils -> necrosis. Secondary bacterial infection from bacteria entering the wall following mucosal damage, and impaired blood flow within the inflamed wall may contribute to necrosis. Once necrosis is transmural (especially once the muscularis propria/externa becomes necrotic) the wall is extremely weak and can perforate ->
  - Generalized peritonitis and sepsicaemia or
  - Local abscess formation, later developing surrounding fibrosis and adhesions
- Ascending phlebitis -> liver abscesses

Treatment: remove surgically before perforation if possible
CHOLELITHIASIS/GALLSTONES
Very common in developed countries
Cholesterol, pigmented and mixed stones
Majority develop in the gallbladder but occasionally may form in the bile ducts

Cholesterol stones
Predominantly composed of cholesterol
Commonest type in developed countries
Single or multiple generally pale stones
Some may contain variable amounts of calcium carbonate and bilirubin to give them a darker colour, and 10-20% contain sufficient calcium carbonate to make them radio-opaque, whereas most are radiolucent
Pathogenesis is multifactorial
- Supersaturation of bile by cholesterol, which cannot all be maintained in solution by available bile salts and lecithin
- Gallbladder hypomotility
- Excess of factors that promote nucleation e.g. mucin, or deficiency of factors that inhibit nucleation
- Cholesterol comes out of solution and crystallizes, crystals become trapped in mucus (-> biliary sludge) enabling growth
Risk factors
- Increased hepatic secretion of cholesterol
  - Increasing age
  - Oestrogen i.e. in females, OCP use and pregnancy
  - Obesity, diet/high blood cholesterol
  - Familial/genetic
  - Certain ethnic groups
  - Certain drugs
  - Other
- Decreased secretion of bile salts e.g. impaired enterohepatic circulation
- Gallbladder hypomotility e.g. in pregnancy

Pigment stones
Mainly composed of calcium bilirubinate, generally multiple
About 50% radio-opaque
Relatively more common in developing countries
Risk factors and pathogenesis:
- Chronic haemolysis -> excess bilirubin in bile
- Biliary tract infection -> excessive deconjugation of bilirubin in bile
- Other
Complications/effects of gallstones
- Asymptomatic: most
- Biliary colic: transient steady, rather than colicky, pain/discomfort caused by transient obstruction of the cystic duct
- Cholesterosis: fine yellow streaks in mucosa related to presence of lipid filled macrophages in lamina propria. No clinical significance
- Chronic cholecystitis: variable fibrosis, muscle hypertrophy, chronic inflammation and development of pouches of epithelium extending into the wall associated with gallstones leading to thickening and sometimes calcification of the gallbladder wall. Clinical features are probably related to the presence of stones rather than the chronic inflammation
- Acute cholecystitis: see later
- Common bile duct obstruction -> obstructive jaundice +/- bacterial cholangitis
- Mucocele of gallbladder: chronic impaction of a stone in the cystic duct may lead to the development of a mucocele or hydrops of the gallbladder: continued secretion of mucus by the lining epithelial cells and absorption of bile pigment results in the accumulation of clear mucinous fluid with distension of the obstructed gallbladder
- Adenocarcinoma of gall bladder: uncommon but gallstones appear to predispose
- Acute pancreatitis: see later
- Internal biliary fistulas: inflammatory adhesions may form between the gallbladder and adjacent structures e.g. duodenum or colon, which when associated with necrosis can lead to the formation of a cholecystenteric fistula. Such fistulae may arise insidiously.

ACUTE CHOLECYSTITIS
Calcus
- >90% of cases
- Gallstone obstructs neck of gallbladder or cystic duct
Acalculous
- Related to infection, severe trauma, burns, major surgery, shock, vasculitis
- Possibly related to ischaemia
Acute calculus cholecystitis
Pathogenesis uncertain but obstruction of the cystic duct or gallbladder neck by stone is present in most. Obstruction -> biliary stasis with alteration of bile constituents by epithelium -> chemical damage to wall -> inflammation. Ischaemia caused by distension and contraction of the gallbladder may contribute. Secondary bacterial infection may occur.
Macroscopically: thickened congested wall, often haemorrhagic, mucosal ulceration
Histologically: neutrophil infiltrate, ulceration, oedema and haemorrhage +/- necrosis. With time – proliferation of fibroblasts (organization) and scarring.

Outcomes
- Spontaneous organization with supportive treatment: most cases. The gallbladder in acute cholecystitis does not become gangrenous and perforate as readily or as early as an appendix in acute appendicitis so there is generally not as much urgency to remove it. Some cases are removed later electively.
- Empyema: pus filled gallbladder
- Gangrenous cholecystitis (necrosis from release of lysosomal contents of neutrophils +/- impaired blood flow within the inflamed wall +/- secondary bacterial infection (ascending from the GIT)) can -> perforation -> generalised acute peritonitis or localised pericholecystic abscess. Adhesions and necrosis can lead -> cholecystenteric fistula

MECKELS DIVERTICULUM
- In approx. 2% of population
- Failure of complete regression of vitelline (omphalomesenteric) duct
- Antimesenteric border distal ileum
- Lined by small intestinal type mucosa, sometimes with areas of gastric or colonic epithelium or pancreatic tissue
- Most asymptomatic
- Complications: usually in children
  - Peptic ulceration with bleeding or perforation
  - Acute inflammation with symptoms resembling acute appendicitis
  - Bowel obstruction from intussusception or twisting around a persistent fibrous band between the diverticulum and the umbilicus

PERFORATION OF A HOLLOW VISCUS WITH SECONDARY BACTERIAL ACUTE PERITONITIS
Perforation of a hollow viscus leads to spillage of its contents (e.g. faeces, bile) into the peritoneal cavity. Gastric juice and bile initially cause a chemical peritonitis but ultimately secondary infection develops. Infection is usually by multiple different organisms and reflects the flora of the involved organ. A variety of aerobic (e.g. E. coli, enterococci, Klebsiella sp.) and anaerobic (e.g. Bacteroides fragilis) organisms, mostly gram negative, cause infection following perforation of the distal small intestine and large intestine. A fibrinosuppurative exudate and serosal vasocongestion develop. Occasionally spilled contents may remain localised by the omentum or mesenteries and viscera to form an abscess. Generalised peritonitis causes abdominal pain, tenderness, guarding, rigidity, fever, tachycardia and ultimately signs of shock. There may be abdominal distension and decreased bowel sounds reflecting paralytic ileus.

Large amounts of bacterial cell wall components, including endotoxins (lipopolysaccharides) on gram negatives, often associated with bacterial invasion of the blood stream, initiate a cascade of events with systemic release of cytokines (e.g. TNF-alpha, IL1, IL6, platelet activating factor) and vasoactive mediators (e.g. nitric oxide) from macrophages, neutrophils, mast cells, platelets and endothelial cells, resulting in widespread vasodilatation, endothelial injury and increased vascular permeability -> shock, progressing to organ dysfunction, and in some cases DIC and/or ARDS.

Complications following surgical treatment of the peritonitis include deep wound infections and residual intra-abdominal infection.

Causes of perforation include acute appendicitis, peptic ulceration, acute diverticulitis, acute gastric ulceration, acute cholecystitis, Crohn's disease, bowel malignancies, bowel infarction.

ACUTE PANCREATITIS
Inappropriate activation of pancreatic enzymes within the pancreas -> variable, sometimes severe, acute inflammation, oedema and necrosis of the pancreas. In severe cases bleeding occurs within the pancreas and surrounding tissues: acute haemorrhagic pancreatitis. Fat necrosis develops within and around the pancreas and fatty acids combine with calcium salts -> focal calcification and sometimes hypocalcaemia. Fat necrosis may be widespread throughout the abdominal cavity.

Risk factors
- 80% associated with either gallstones or alcohol.
- Gallstones: obstruction of ampulla of Vater and pancreatic duct by stone
- Alcohol
  - ?pathogenesis ?via metabolic injury
  - Often underlying chronic pancreatitis
- Miscellaneous: other cases associated with e.g. hypercalcaemia, hyperlipidaemia, certain drugs, certain infections, genetic predisposition, trauma, shock
- Idiopathic

Clinically
Typically severe abdominal pain that is referred to the back. Often nausea, vomiting +/- shock.
Elevated serum amylase and lipase

Complications include
- Full-blown acute pancreatitis is a medical emergency – enzymes and cytokines released into circulation -> activation of systemic inflammatory response with further liberation of inflammatory cytokines and vasoactive agents -> vasodilatation, increased vascular permeability -> shock +/- disseminated intravascular coagulation and acute respiratory distress syndrome
- Pancreatic abscess from infection of the necrotic pancreas
- Pancreatic pseudocyst: persistent localised collections of necrotic debris that become surrounded by fibrous tissue
• Bowel obstruction from surrounding oedema
• Gastrointestinal, intraperitoneal or retroperitoneal bleeding (uncommon)
• Hypocalcemia
• Pancreatic ascites

INFLAMMATORY BOWEL DISEASE
• Group of chronic systemic inflammatory diseases predominantly involving the gastrointestinal tract (GIT): Crohn’s disease and ulcerative colitis and some ‘indeterminate’ forms.
• Disease tends to run a relapsing and remitting course, with exacerbations followed by disease free intervals. Some patients experience continually active disease. Occasional patients may only experience one episode. Attacks may have an insidious or acute onset. Attacks may last days, weeks or even months.
• Patients may also develop a number of extra-intestinal manifestations
• May develop at any age but onset often in young adults
• Cause unknown ?autoimmune. Share features with other autoimmune diseases: increased incidence in first degree relatives and association with certain MHC class 2 alleles. Unknown trigger (?microbial) induces an aberrant and destructive immune response.
• Most common in developed societies.

Crohn’s disease
Involvement of the terminal ileum is common, but may affect any part of the GIT

Morphology
Macro:
• ‘Skip’ lesions (areas of abnormality with normal bowel in between)
• Thickening of the wall
• Mucosal ulceration, including fissuring ulceration
• Cobblestone appearance of the mucosa
• Serosal vasocongestion when active

Micro:
• Patchy transmural chronic inflammation, predominantly lymphoid with germinal centres, and eventually scarring
• Non-necrotizing granulomas common
• Acute inflammation, oedema and mucosal ulceration when active

Clinically
• Intermittent attacks: diarrhoea, fever, crampy abdominal pain
• Often perianal fissures
• Weight loss
• Extra-intestinal manifestations e.g. arthritides, characteristic skin rashes, eye inflammation

Complications
• Anaemia (from blood loss or malabsorption of iron or vitamin B12 or folate)
• Malabsorption of specific nutrients/vitamins
• Bowel perforation
• Fistulas to other organs
• Bowel obstruction
• Carcinoma

Ulcerative colitis
Involves colon only, always affects rectum and extends proximally to variable extent in different patients

Morphology
Macro:
• No skip lesions
• Reddened ulcerated mucosa
• Regenerating mucosal pseudo-polyps
• No or minimal thickening of the wall
• Eventual mucosal atrophy

Micro:
• Acute and chronic inflammation of the mucosa, sometimes superficial submucosa
• Superficial ulceration
• No granulomas

Clinically
• Intermittent attacks: bloody, often mucoid diarrhoea, crampy abdominal pain, fever
• Weight loss
• Extra-intestinal manifestations e.g. arthritides, skin rashes, eye inflammation, sclerosing cholangitis

Complications
• Anaemia (from blood loss)
• Dehydration
• Toxic megacolon -> perforation
• Carcinoma, more common than with Crohn’s