Ulcerative Colitis

Definition of ulcerative colitis

- An autoimmune chronic inflammatory disease of the colon and rectum, with a relapsing-remitting pattern

Epidemiology of ulcerative colitis

- Incidence about 10 per 100,00 per year
- Prevalence is about 1 per 1000
- Slightly more prevalent in men
- More prevalent in northern hemisphere western countries

Causes and risk factors for ulcerative colitis

- Thought to be a combination of environmental and genetic triggers
- Monozygotic twin concordance rate of 10%
- Smoking is protective (unlike Crohn's)

Presentations of ulcerative colitis

- **Gastrointestinal**
  - Bloody diarrhoea (maybe with mucus)
  - Lower abdominal discomfort
  - Abdominal tenderness
  - Palpable masses
  - Abdominal distension (can be indicative of toxic megacolon)
  - Urgency and frequency of stools (especially in acute attacks)
  - Tenesmus
- **Systemic**
  - Malaise, lethargy, anorexia
- **Extra-intestinal manifestations:**
  - Erythema nodosum
  - Uveitis/episcleritis
  - Arthropathy
  - Pyoderma granulosum
  - Primary sclerosing cholangitis (75% of PSC is seen in UC patients)
- NB. In an acute attack the patient may be pale, febrile, dehydrated, tachycardic and hypotensive

Differential diagnosis of ulcerative colitis

- Infectious diarrhoea
  - Shigella, Salmonella, Campylobacter, E.coli, amoebae, Clostridium difficile
- Crohn's disease
- Ischaemic colitis
- Radiation enteritis
- Chemical colitis
- CMV colitis
- GI malignancy
- Coeliac disease

- Irritable bowel syndrome

Pathology of ulcerative colitis

- **Macroscopic pathology**
  - Inflammation extends proximally from the rectum (unlike Crohn's, where the inflammation can be anywhere)
  - Hence inflammation can be classified as proctitis (limited to rectum), left-sided colitis (extending to sigmoid and descending colon), or pan-colitis (when entire colon involved)
  - Mucosa is reddened, inflamed, and bleeds easily.
  - Extensive ulceration, with islands of normal mucosa
- **Microscopic pathology**
  - Superficial inflammation of mucosa (unlike Crohn's, which is full-thickness)
  - Chronic inflammatory cell infiltrate in lamina propria (part of mucosa just under epithelium)
  - Crypt abcesses
  - Goblet (mucus-making) cell depletion

Acute management of ulcerative colitis

- This is a medical emergency and patients with severe colitis should be admitted, ideally onto a gastrointestinal ward.

http://www.bsg.org.uk/images/stories/docs/clinical/guidelines/ibd/ibd_2011.pdf

- Calculate severity according to **Truelove and Witts'** criteria:
  - More than 6 bloody stools per day (often nocturnal) and at least one of:
    - Temp >37.8 on 2 out of 4 days
    - Hb <10.5
    - ESR >30
    - Pulse >90
    - Colon dilated >5.5cm
- Immediate investigations
  - Bloods
    - FBC, U&E, LFT, CRP, ESR, coagulation, G&S
    - B12, folate, iron studies
    - Amylase and beta-HCG
    - Consider TPMT levels (see below)
  - Cultures
    - Blood culture
    - Stool culture
  - Imaging
    - AXR: Check for megacolon: >5.5 cm dilated.
    - USS and CT
- Supportive management
  - IV fluids (replace deficit followed by maintenance fluids)
  - Thromboprophylaxis (e.g. prophylactic LMWH)
  - Stool chart
  - Weigh daily
  - Assess nutritional status: if deplete then enteral feeding is preferable
  - No role for being NBM and can increase lactose intolerance
- Flexible sigmoidoscopy

- Should be undertaken within 72 hours (ideally 24h) to obtain diagnostic biopsy and to exclude CMV colitis.

- **Treatment**
  - Steroids
    - 60mg po Prednisolone or 400mg iv hydrocortisone (100mg four times daily) for up to five days
    - There is no benefit in steroid therapy beyond 10 days.
  - Avoid antibiotics unless clear evidence of infection
  - Surgery
    - If any evidence of toxic megacolon (dilatation >5.5cm or caecum >9cm) then consider urgent colectomy depending on the clinical state of the patient.
    - A stool frequency >8/day or CRP >45 at 3 days predicts the need for colectomy in about 85% of cases.
    - Consider rescue therapy or colectomy if no improvement or deterioration at day three
- Rescue therapy
  - Ciclosporin (2mg/kg/day)
    - Check magnesium, cholesterol and creatinine
    - Watch out for toxicity
    - Following remission, continue oral ciclosporin for 3-6 months
  - Infliximab
    - Check LFT, Hep B/C, HIV, varicella, TB (CXR or consider ELIZA)
      - No evidence for Hep C reactivation
    - Ensure vaccinations up to date (but no live vaccines)
    - Used as a bridge to further immunosuppressive drugs and not to maintain remission as evidence is limited.
  - If no response to rescue therapy is seen within 4-7 days then colectomy is recommended.

Further management of ulcerative colitis and maintenance of remission

- **Recommendations**
  - Long term maintenance therapy is recommended for most patients, especially those with extensive or left-sided disease or those with proctitis who relapse more than once per year
- **Medical maintenance for UC**
  - Patients should receive maintenance therapy with aminosalicylates, azathioprine or mercaptopurine
  - NICE does not recommend long-term use of anti-TNF therapy
  - Oral mesalazine 1.2-2.4g daily should be first-line
  - Topical mesalazine +/- oral can be used in patients with distal disease
  - Azathioprine 2-2.5mg/kg/day or mercaptopurine are the first-line agents for steroid-dependent disease
    - Long-term treatment with steroids is not acceptable
  - All patients should have thiopurine methyltransferase levels (TPMT) measured before starting thiopurines (metcaptopurine and azathioprine) to avoid fatal administration to those with no or low TPMT levels.
  - Methotrexate can be considered in patients who do not respond to above treatments
- **Surgery**
  - Indications
    - Severe attacks which don't respond to medical treatment or toxic megacolon (>5.5cm on AXR, thin-walled, thumb-printing, gas in bowel wall)
    - If toxic dilatation and no response to steroids over 24 hours, go straight to colectomy as perforation rates >30%

        - Poorly-controlled disease
        - Recurrent acute-on-chronic disease
        - Presence of dysplasia or carcinoma
    - Subtotal colectomy with ileostomy, with the option of returning later for a re-anastomosis and ileo-anal pouch formation.
    - Colectomy may also be considered in chronic disease due to poor response to medication, excessive steroid requirements or risk of cancer.

Complications of ulcerative colitis

- Acute
    - Toxic megacolon
        - Mortality approximately 20%
- Primary sclerosing cholangitis
- Colorectal carcinoma
    - Risk increased 10-20 times once patients have had UC for 20 years
    - 5-asa treatment seems to reduce risk
    - Start screening colonoscopy at 10 years, then repeat at 1,3,or 5-year intervals depending on risk
    - Mucosal dysplasia on rectal biopsy is associated with cancer elsewhere in the bowel.
- Pouchitis after colectomy (with relapsing-remitting course)
- Osteoporosis from steroid therapy
    - Bisphosphonates to over 65s on steroids
    - DEXA, then bisphosphonates if T<1.5 if not over 65

Prognosis of ulcerative colitis

- With treatment, mortality only slightly more than normal population and that is mostly in the first two years after diagnosis
- 10% need colectomy in first year, 14% will have colectomy at 20 years
- 50% will relapse in any one year
- 90% get back to normal employment after 1 year