# IBD/ CROHN'S Cheat Sheet

by MJC3 via cheatography.com/212269/cs/46133/

## Treatment – Ulcerative Colitis

| | |
|---|---|
| **Mild-Moderate disease** | 5-Aminosalicylates (suppository or enema possibly combined with oral aminosalicylates) If unable to tolerate aminosalicylates: Steroids (topical corticosteroid or oral prednisolone) |
| **Resistant Disease** | Immunosuppressants (eg Azathioprine, Mercaptopurine) Anti-TNF monoclonal Ab (Infliximab, Adalimumab) |
| **Severe colitis** | Intravenous corticosteroids Ciclosporin Infliximab (5 mg/kg infused over 2 hours at 2 and 6 week intervals) (Assuming 3 doses, average cost per patient = £5,035) Surgery |

## Therapeutic Pyramid for Active UC

| | |
|---|---|
| **Mild:** | Topical Steroids: Aminosalicylates |
| **Moderate:** | Infliximab, Systemic Corticosteroids, Oral steroids |
| **Severe:** | Surgery, Ciclosporine, Infliximab |

## IBD and Cancer

Increased risk of colorectal cancer (CRC) in UC and Crohn's colitis
20-30% risk at 30 years from diagnosis
Regular surveillance colonoscopy performed from 8-10 years post-diagnosis
5-ASAs are protective

Risk of CRC particularly high in patients with UC + Primary Sclerosing Cholangitis
PSC also carries a high risk of cholangiocarcinoma

## Ciclosporin

Calcineurin inhibitor
Prevents clonal expansion of T cell subsets
Rapid onset of action

Used as salvage therapy for severe UC not responding to IV steroids
Usually introduced on day 3 of steroids
IV 2mg/kg/day
Responders converted to oral Ciclosporin for 3-6 months and switched to Azathioprine/6-MP (Ciclosporin not used long-term)

Requires regular monitoring of Drug levels/Full blood count/-Renal function/Blood pressure

## Immunosuppressants

| | |
|---|---|
| **Indicated for severe or refractory IBD** | Thiopurines. Methotrexate. Ciclosporin. |

## Immunosuppressants (cont)

| | |
|---|---|
| **BSG guidelines advise use in following situations** | Severe relapse or frequently relapsing disease. 2 or more steroid course required within 12 months. Relapse below 15mg prednisolone. Relapse within 6 weeks of stopping steroids. |

## Pathology of UC

| | |
|---|---|
| Idiopathic chronic inflammatory disorder of the colonic mucosa, with the potential for extraintestinal inflammation. | The disease extends proximally from the anal verge in an uninterrupted pattern to involve all or part of the colon |

## Diagnosis of IBD

| | |
|---|---|
| **Endoscopy and biopsy** | Flexible sigmoidoscopy or Colonoscopy |
| **Radiology** | Contrast enhanced ultrasound, Barium studies, CT, MRI, Capsule endoscopy |

Exclude infection

Blood tests helpful but not diagnostic

## UC vs CD

| | UC | CD |
|---|---|---|
| SKIN | Erythema nodosum Pyoderma gangrenosum | Erythema nodosum Pyoderma gangrenosum |
| EYE | Iritis Episcleritis (inflammation of the episclera : white of the eye) | Iritis Episcleritis |
| KIDNEY | Calculi (kidney stones) Pyelonephritis (inflammation of the kidney due to bacterial infection) | Calculi pyelonephritis |
| LIVER | Sclerosing cholangitis (inflammation of bile ducts: impeding bile flow) | Systemic amyloidosis (deposition of amyloid proteins) |

## UC vs CD (cont)

| | | |
|---|---|---|
| JOINTS | Serone-gative polyarthritis (blood test –ve for rheumatoid factor protein and cyclic-citru-linated peptide) | Serone gative polyar-thritis |

## Aetiology

| | |
|---|---|
| **Inappr-opriate immune response** | Increased pro-in-flammatory cytokines eg **TNF-α, IL-1β, IL-6** |
| **Breakdown in tolerance to gut microbial load** | Altered gut flora. Defects in mucosal immunity. |
| **Combin-ation of factors** | Enviromental factors. Triggered by particular bacterial pathogen. |
| | Genetic – increased risk in twins/other relative |
| | Diet |
| | Smoking |

## Aetiology (cont)

| | |
|---|---|
| **Genetics** | 47 loci associated with UC (and counting) |

Smoking (May prevent UC and may cause CD)

## Histopathology of UC

**Superficial diffuse inflammation in the lamina propria affecting the colon only**

| | |
|---|---|
| **Chara cter-istics** | Continuous from the rectum up to the caecum |
| | Crypt abscesses, goblet cell depletion and crypt distortion |
| | Can affect the distal few cm of small bowel – 'backwash ileitis' |
| | Non-smokers |

## Histopathology of UC (cont)

| | |
|---|---|
| **The most intense inflam-mation begins :** | the lower right in the sigmoid colon and extends upward and around to the ascending colon. At the lower left is the ileocecal valve with a portion of terminal ileum that is not involved. |
| **Repeated ulceration and healing cycles result in:** | Granulation tissue resembling polyps |

## Anti-TNFs adverse effects

Infections
Steroids/Immunosuppressa-nts/Anti-TNF all increase risk of infection
Two or more therapies in combination increases risk 15 fold
Active infection/abscesses must be excluded before commencing anti-TNF treatment
Patients should be screened for exposure to TB (CXR/Tuberculin skin test)

Malignancy
Increased risk of lymphoma (but overall risk still v low)

Heart failure
Anti-TNFs contraindicated in severe heart failure

## Ciclosporin – side effects

Tremor
Paraesthesia
Malaise
Headache
Abnormal liver function tests
Hirsutism
Gingival hyperplasia

## Thiopurines

| | | |
|---|---|---|
| **Side effects** | Nausea | Advise patients to take it at night |
| | Allergic reaction | Fever/-Rash/A-rthralgia |
| | Myelosuppression | |
| | Hepatotoxicity | |
| | Pancreatitis | |
| **Monitoring** | FBC/LFT every 2 weeks for first 2 months, Then every 4-8 weeks up to ~6/12, Then every 3/12 | |

Azathioprine (Aza)
Mercaptopurine (6-MP)
Purine antimetabolites inhibiting DNA synthesis
Aza is metabolised to 6-MP
**Doses** mg/kg/day
6-MP 0.75-1mg/kg/day

## Treatment – Crohn's

| | |
|---|---|
| **Initial diagnosis if mild to moderate:** | 5-ASA's less effective but may have a chemoprotective effect against cancer risk. Glucocorticosteroids |
| **Severe active Crohn's (including fistulising Crohn's)** | Immunosuppressants Azathioprine, Mercaptopurine, Methotrexate Anti-TNF therapy (Infliximab) (sever active Crohn's) |
| **For perianal Crohn's:** | Antibiotics (Metronidazole, Ciprofloxacin) – |

Smoking cessation
Nutritional Support
Surgey
Emotional support: possible delayed growth and onset of puberty in young people
Possibility of requiring surgery

## Distribution of Crohn's disease

| | |
|---|---|
| **Small Bowel** | 80% of cases small bowel involved. Majority distal ileum. 1/3 exclusively ileitis. |
| **Ileo-colonic** | 50% have ileocolitis |
| **Colonic** | 20% colonic disease only |

## Distribution of Crohn's disease (cont)

| | |
|---|---|
| **Anus** | 33% have anal disease. Other (gastroduodenal, oesophageal, oral). Rare. |

## Treatment

UC and Crohn's are lifelong relapsing-remitting conditions

Treatment is not curative but aims to suppress inflammation and thereby maintain normal gut structure and function

## Corticosteroids

| | |
|---|---|
| **Oral** | Prednisolone (eg 40mg od, 8 week reducing course). Budesonide (lower systemic effects). Beclomethasone (Clipper). Used for moderate flares of UC/Crohn's. |
| **Intravenous:** | For severe UC or Crohn's Hydrocortisone (eg 100mg qds) |
| **Topical** | Steroid Suppositories/Enemas (eg Predsol supps, Predfoam enemas). Less effective than topical 5-ASA but can be used in combination. |

## Corticosteroids (cont)

| | |
|---|---|
| **Side effects:** | Skin thinning. Osteoporosis. Osteonecrosis Easy bruising. Cushing's syndrome (moon face, acne, hirsutism, striae). Cataracts. Diabetes. Hypertension. Psychosis. |

Corticosteroids are very effective at inducing remission They are not a long-term maintenance therapy because of the effect on cortisol levels on the hypothalamus and anterior pituitary.

## Ciclosporin & Tacrolimus (FK506)

| | |
|---|---|
| **Ciclosporin** | Inhibits dephosphorylation of nuclear factor of activated T cells (NFATc) |
| **Tacrolimus (FK506)** | Binds to FK-506 binding protein (FKBP). Calcineurin inhibitor. |
| **Both prevent** | interleukin 2 release and clonal expansion of T cell subsets |

## Differential Diagnosis of UC

| | |
|---|---|
| **Crohn's Colitis** | |
| **Infective colitis:** | *E.coli* |
| | *Campylobacter* |
| | *Salmonella* |
| | *Yersinia* |
| | *Amoebic Dysentery* |
| **Ischaemic Colitis** | |
| **Pseudomembranous Colitis* | Clostridium difficile infection |

## Anti-TNF Therapy

Tumour Necrosis Factor α
Inflammatory cytokine involved in pathogenesis of Crohn's (and UC)
You tube TNF McAB Therapy
Monoclonal anti-TNF antibodies
Infliximab –
Route: IV
Licensed for Refractory Crohn's or UC/Fistulating Crohn's
Also used for severe UC

Adalimumab (Humira)
Subcutaneous
Licensed for refractory Crohn's

## Pathology of Crohns Disease

| | |
|---|---|
| **Idiopathic chronic inflammatory disorder of the full thickness of the intestine** | Most commonly the ileum and the colon, with the potential to involve the gastrointestinal tract at any level from the mouth to the anus and perianal region. |

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## Pathology of Crohns Disease (cont)

| | |
|---|---|
| **Typically there is patchy disease in the gastro-intestinal tract** | with intervening areas of normal mucosa “Skip lesions” |
| **Transmural inflam-mation with lymphoid aggregates** | (clusters of lymphoid cells-include T-cells, B-cells and NK cells.) |
| **Non caseating granulomas (60% cases)** | Caseating “turning to cheese” |

**Skip Leisons**

| | |
|---|---|
| **Strictures and fistula formation* | In Crohn’s, strictures make the bowel too tight, and fistulas create unnatural pathways—both are serious complications. |

**Perianal disease**

**Can affect any part of the GI tract**

**Smokers**

## Treatments Summary

**Crohn’s & Ulcerative Colitis**

Salicylates

5-Amino salicylic acid (5-ASA); mesalamine (Asacol)

Steroids (glucocorticoids): Methylprednisolone (Medrol)

Immunosuppressants: Azathi-oprine & mercaptopurine

## Treatments Summary (cont)

Ciclosporin A (Sandimmun or Neoral) Tacrolimus (FK-506, Fujimycin) (Prograf, Advagraf, Protopic)

**NOVEL TREATMENTS**

Nicotine: useful in UC?
LTB4 antagonists eg zileuton.
Fish oils, eicosopentanoic acid diverts LT production towards LTB5 production.
IL1 receptor antagonists (UC).
Short Chain fatty acids.
CuZnSOD and desferrioxamine (Peroxyl scavenger).

## Epidemiology

| Crohn's disease | Ulcerative Colitis |
|---|---|
| Incidence 8-10/100,000 in UK Prevalence ~150 per 100,000 (1 in 660 people) | Incidence 15/100,000 in UK Prevalence 200 per 100,000 (1 in 500 people) |

Peak age at diagnosis 20-40, second smaller peak aged ~60

## 5-ASAs

| | |
|---|---|
| **5 Aminos alicylic acid (Mesal-azine)** | Moderate inflam-matory cells and cytokine release from epithelial cells. Mechanism not fully understood but involves inhibition of cyclooxygenase and prostanoid formation and N-acetyl-5-ASA through PPAR gamma (Peroxisome Proliferator Alpha Receptor gamma) |

## 5-ASAs (cont)

| | |
|---|---|
| **Uses - UC** | Maintainence of remission – mainstay of long-term treatment for UC. Treatment of mild-moderate flares. Chemoprotective effect against colorectal cancer. |
| **Uses – Crohn’s** | Limited effectiveness compared to UC. Limited effectiveness in active Crohn’s or maintaining remisson. May reduce risk of relapse after surgery. |

## 5-ASAs (cont)

| | |
|---|---|
| **Side Effects:** | Diarrhoea! Nausea. Headache Rash (rarely Stevens-J-ohnson syndrome). Nephrotoxicity (Inter-stitial nephritis & Nephrotic syndrome). Agranulocytosis (low white blood cell count). Pancreatitis. |

**Oral**

pH dependent resin (Asacol, Salofalk, Mesren)
Time-controlled (Pentasa)
Multimatrix pH dependent delivery (Mezavant)
Carrier molecules split by colonic bacterial enzymes (Sulfasalazine, Olsalazine, Balsalazide

**Dose**

1.6-4.8g/per day
Single daily dosing seems as effective as traditional bd/tds

**Topical**

Suppositories - Proctitis
Foam or Liquid enemas - Distal colitis (rectum and sigmoid)
Check FBC/Renal function annually

## UC vs CD

| Ulcerative colitis | Crohn's disease |
|---|---|
| Affects the colon only | Affects any part of the GI tract |
| Male:F-emale 1:1 | Male: Female 1:2 |

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## UC vs CD (cont)

| | |
|---|---|
| Bloody diarrhoea<br>Abdominal pain | Abdominal pain<br>Weight loss<br>Perianal disease<br>Bloody diarrhoea |
| Continuous, always begins in rectum | Skip lesions |
| No strictures | Stricture and fistula formation with perianal disease |
| Mucosal inflammation<br>Diffuse inflammation in the lamina propria<br>Patchy ulceration with crypt abscesses, goblet cell depletion and crypt distortion | Transmural inflammation throughout bowel wall, lymphoid aggregates and non-necrotising granulomas. Can develop fissuring ulcers, crypt abscesses, goblet cell depletion and crypt distortion |
| Terminal ileum in 10% cases | Often affects the terminal ileum (80%) Any part of alimentary tract can be affected |
| No fistulas | Fistulas |

## Clinical Presentation – Crohn's

| | |
|---|---|
| **Typical Features:** | Abdominal Pain. Diarrhoea. Weight loss. Anorexia. |

Obstruction secondary to strictures
Abscesses, Fistulae
Depends on portion of GI tract involved

## Histopathology Crohn's Disease of Ileum

Inflammatory cells (the bluish infiltrates) extend from mucosa through submucosa and muscularis.

On the serosal surface inflammatory cells appear as nodular infiltrates with pale granulomatous centres.

## Clinical Presentation of UC

**'Bloody diarrhoea' and passage of mucus**

**Urgency**

**Abdominal Discomfort (pain unusual)**

**Usually insidious onset**

Can be severe with systemic upset, fever
Requires hospitalisation
May need urgent surgery

## UC AND CROHNS

| Ulcerative Colitis | Crohn's Disease |
|---|---|
| Only affects colon | Affects mouth to anus |
| No fissures, horizontal ulcers | Deep ulcers & fissures |

## UC AND CROHNS (cont)

| | |
|---|---|
| Malignant change common | Malignant change rare |
| Fistulae less common | 10% have fistulae |
| 25% have anal involvement | 60% have anal involvement |
| Muscular shortening of the colon | Fibrous shortening |
| No skip lessons | Skip lesions |
| No fat or vitamin malabsorption | Fat & vitamin malabsorption |
| No granulomas (collection of macrophages) | Granulomas in 50% |
| Mild lymphoid reaction | Marked lymphoid reaction (increased WBC) |
| Mild fibrosis | Fibrosis |
| Mild Serositis | Serositis (inflammation, serous membranes) |
| Raised ANCA (antineutrophil cytoplasmic antibodies. Autoantibodies directed against own neutrophils.) | ANCA normal |
| More common in non-smokers or ex smokers | Increased incidence in smokers |