IBD/ CROHN'S Cheat Sheet

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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)

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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

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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 Abdominal pain	Abdominal pain Weight loss Perianal disease Bloody diarrhoea
Continuous, always begins in rectum	Skip lesions
No strictures	Stricture and fistula formation with perianal disease
Mucosal inflammation Diffuse inflammation in the lamina propria 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

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