

Colitis Crohn's

Martyn Dibb
Consultant Luminal Gastroenterologist
Royal Liverpool University Hospital

IBD HAS A SIGNIFICANT IMPACT ON QUALITY OF LIFE:

A large European study of people living with IBD found:



report that their lives are significantly or somewhat impacted by IBD symptoms even between flare-ups.



report making adjustments to their working life based on their IBD.



report that IBD has prevented them from pursuing an intimate relationship.



report that IBD has gotten in the way of making and keeping friends.¹²



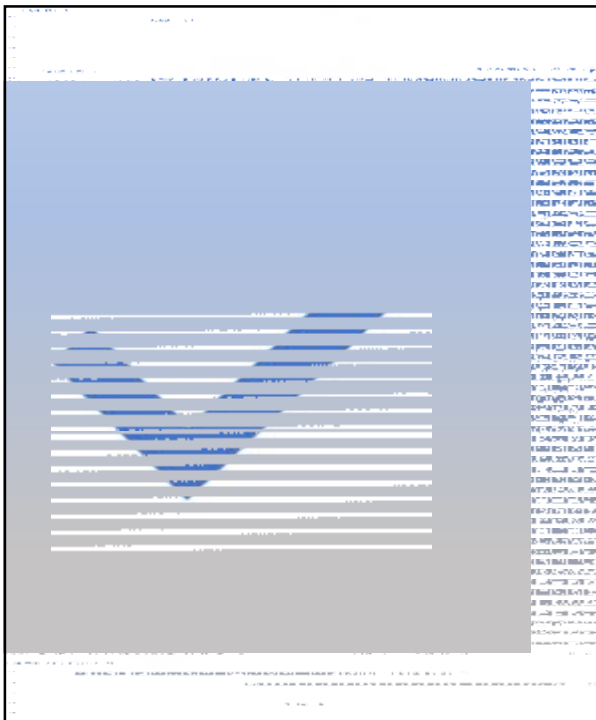
IBD has a major impact on physical and emotional wellbeing, often affecting the social interactions, family life, and the work or studies of those with the disease.¹³

Case History 1

40 year old male presents with 1/52 of loose motions 3-5x times/day 1x night. Rectal bleeding mixed with motions. No vomiting. Ex-smoker.

PMH – Hypertension. Recent hospital admission (no discharge summary).

O/E Examination Abdominal soft non-tender. PR 75. Apyrexial.



Case History 1

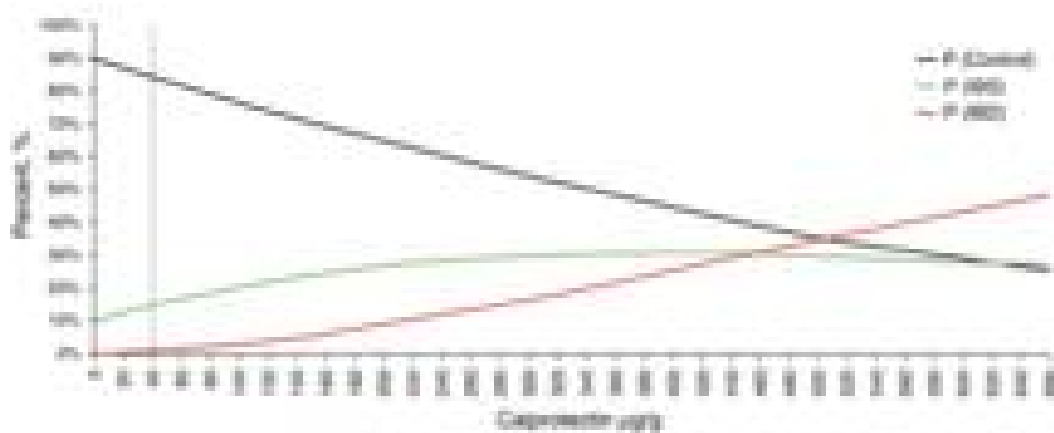
- What are the next steps?
 - A. Bloods
 - B. Faecal Calprotectin
 - C. Stool MC+S
 - D. Stool CDT
 - E. 2WW Colorectal referral
 - F. Urgent Gastroenterology referral

Faecal Calprotectin

- Calprotectin secreted in excess into the intestinal lumen during inflammation
- Sensitive but non-specific marker
- Recommended for use in Primary and Secondary Care.
- Available from primary care
- PoC kits available

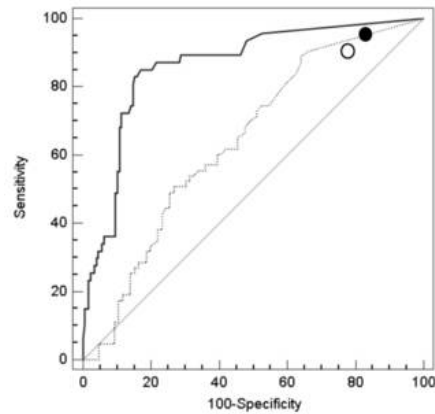
1. NICE Technology appraisal. Oct 2013. DG11

Calprotectin levels and Diagnosis



Menees et al. Am J Gastroenterol 2015; 110:444–454

Calprotectin Levels and Findings at colonoscopy



Colonoscopy
AUC of 0.863
Sens 72.3%
Spec 88.7%
(57.4% vs. 7.4%, $P < 0.001$).

Burri et al. BMC Gastroenterology 2014, 14:57

Calprotectin and histological remission

Table 4. Evolution of clinical, endoscopic, and biomarker outcomes over 52 weeks, according to histological activity.

Outcomes	Week 8		Week 30		Week 52	
	Gebios ≤ 3.0	Gebios > 3.0	Gebios ≤ 3.0	Gebios > 3.0	Gebios ≤ 3.0	Gebios > 3.0
N	3	17	6	14	7	13
Clinical remission, n [%]	2 [67]	6 [35]	3 [50]	4 [29]	3 [43]	3 [23]
Agreement, %	65		75		63	
Clinical response, n [%]	3 [100]	11 [65]	6 [100]	10 [71]	7 [100]	11 [85]
Agreement, %	43		80		43	
Mucosal healing, n [%]	3 [100]	6 [35]	6 [100]	3 [21]	6 [86]	3 [23]
Agreement, %	70		78		70	
Calprotectin levels [µg/g], median [IQR]	25.0 [6.2-37.6]	242.4 [154.8-455.6]	63.8 [31.4-83.3]	622.8 [303.8-1019.4]	27.3 [22.4-105.6]	195.7 [64.8-439.0]
p-Value		0.017		0.032		0.029
Calprotectin remission, n [%]	3 [100]	4 [24]	3 [50]	2 [14]	4 [57]	4 [31]
Agreement, %	80		85		65	
Lactoferrin levels [µg/g], median [IQR]	6.8 [5.7-7.3]	73.1 [31.0-182.4]	6.9 [2.1-93.2]	86.3 [22.8-211.0]	1.3 [0.2-26.0]	106.7 [27.7-181.8]
p-Value	0.013		0.187		0.024	
Lactoferrin remission, n [%]	2 [67]	1 [6]	3 [50]	2 [14]	3 [43]	2 [15]
Agreement, %	90		75		80	
CRP levels [mg/l], median [IQR]	2.90 [0.40-63.00]	1.70 [0.38-6.13]	0.95 [0.30-2.90]	2.83 [0.80-4.60]	1.90 [0.40-4.30]	2.90 [1.30-3.60]
p-Value	0.447		0.245		0.791	
CRP remission, n [%]	2 [67]	9 [54]	3 [50]	10 [71]	4 [57]	7 [54]
Agreement, %	47		43		50	

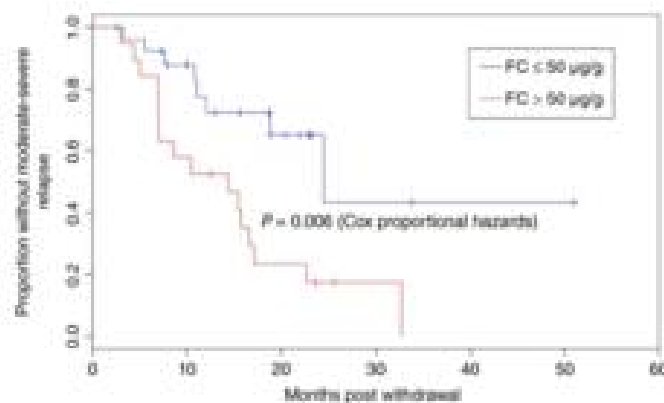
Data are expressed as numbers and percentages or median and interquartile range [IQR]. Mann-Whitney test was used to compare subgroups regarding calprotectin, lactoferrin and C-reactive protein [CRP] levels. Statistical significance was set at $p < 0.05$. Gebios ≤ 3.0 corresponds to histological remission. Clinical remission defined as Mayo score of 2 points or lower, with no individual subscore exceeding 1 point. Clinical response defined as reduction in the Mayo score ≥ 3 points and a decrease of at least 30% from the baseline score, accompanied by a decrease of at least 1 point in the rectal bleeding subscore or an absolute rectal bleeding score of 0 or 1. Mucosal healing defined as Mayo endoscopic subscore ≤ 1. Calprotectin remission defined as levels < 100 µg/g. Lactoferrin remission defined as levels < 7.25 µg/g. CRP remission defined as levels < 3.0 mg/l.

Magro et al. JCC 2016:1-10

Calprotectin Predicts....

- IBD Relapse (Theede et al, Inflamm Bowel Dis 2016, May;22:5. 1042-8)
- Endoscopic severity in UC (Kawashima et al, BMC gastro, 2016. 16;47.)
- Histological response in UC (Theede et al, Inflamm Bowel Dis 2016, May;22:5. 1042-8)
- Pouchitis (Pronio et al, Rev Esp Enferm Dig, 2016, 108;4:190-195)
- Quality of Life in IBD patients (Gauss et al, 2016. Medicine. Apr;95(16):e3477)

Calprotectin and Relapse after Crohn's Surgery



UK Anti-TNF withdrawal study group APT, 2016;Feb 19.

Calprotectin can be abnormal in...

- GI Infections
- NSAID'S (Rendek Z et al, Scand J Gastroenterol 2016. 51;1:28-32.)
- Previous Surgery (Boerlage TC et al, Obes Surg. 2016 May 23)
- PPI Use (M Cohen BJGP June 2016)
- Coeliac Disease (Capone et al, WJG 2014. 14:20:611-620)
- UGI Cancers (Vincent Z et al, Ann Clin Biochem 2015; 52:660-4)

Faecal Calprotectin in Primary Care



Turvill et al, Primary health care R+D, 2016.

Case History 1



Bloods



CRP 98 Alb 42 WCC 12 Hb 135



Calprotectin >2100



Stool MC+S – Campylobacter



Next actions?

Antibiotics

Admit to Hospital

Case History 1

Represents 6 weeks later

Ongoing diarrhoea
>6day, nocturnal symptoms

Frank Bleeding on most occasions

PR 93bpm, Apyrexial

No guarding

Stool Culture negative

What next?

- Repeat bloods / Calprotectin
- Admit
- 2WW referral
- Urgent Gastro referral

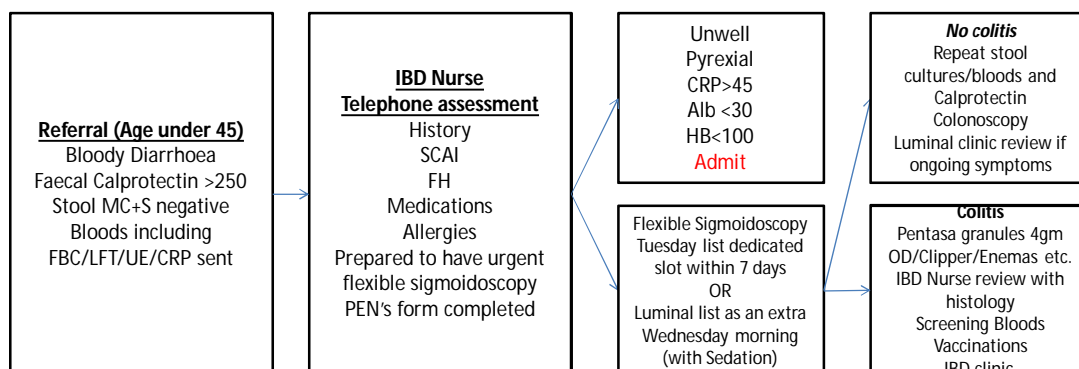
Ulcerative Colitis – When to admit

Truelove and Witt's Criteria	Severe
Bloody Stools per day	>6
Pulse	>90
Temperature	>37.8 degrees
Hb	<10.5gm/dl
CRP	>30

Non-response to oral prednisolone or treatment escalation

Truelove SC, Witts LJ. Cortisone in ulcerative colitis: preliminary report on a therapeutic trial. Br Med J. 1954;2:375–378.

Urgent Colitis Pathway

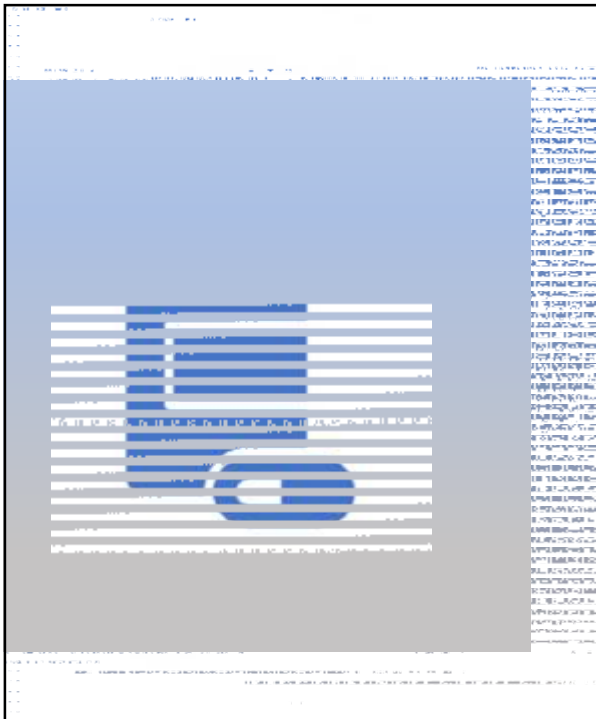


Case History 2

- 25 yr old male with Ulcerative colitis (left-sided) on Friday pm.
 - Normally on Pentasa 2gm daily
 - Had Clipper with good effect previously
 - Diarrhoea 3-5x/day
 - Blood most occasions
 - Apyrexial/PR 60
 - No weight loss
 - CRP 9 Alb 45 Hb 130 WCC 8
 - Calprotectin 225
 - Stool MC+S negative

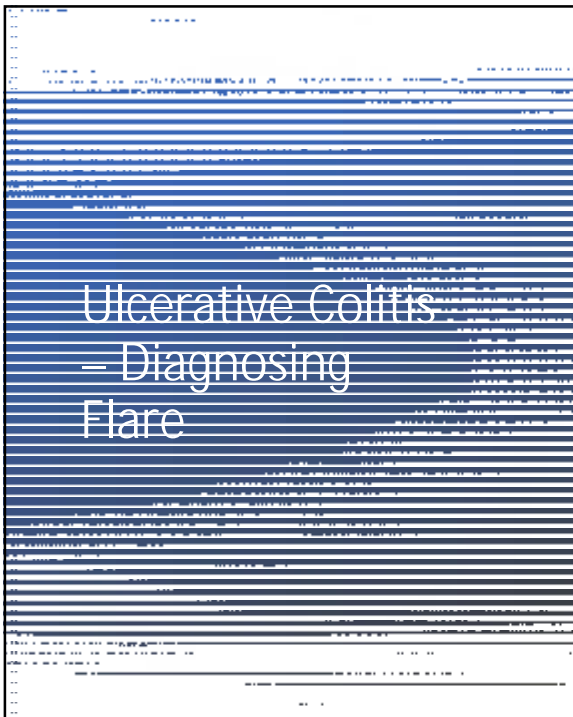
Case History 2

- What do you do?
 - Prednisolone 30mg OD for 5/7
 - Double Pentasa
 - Add Mesalazine enema
 - Add Steroid Enema
 - Oral Beclomethasone
 - Contact IBD nurse team



Case History 2

- What can you safely do?
 - ~~Prednisolone 30mg OD for 5/7~~
 - Double Pentasa (upto 4gm daily) – 4.8gm for asacol/octasa
 - Add Mesalazine enema
 - Add Steroid Enema
 - Oral Beclomethasone 28/7
 - Contact IBD nurse team



Simple Colitis Activity Index

- General well-being
- Daytime Bowel Frequency (0-3, 4-6, 7-9, >9)
- Nocturnal Bowel Frequency (0, 1-3, 4-6)
- Urgency
- Blood
- Extracolonic features (Erythema nodosum, pyoderma, arthritis)

Bloods (U+E/LFT/CRP/FBC) – key results (low Hb, Alb under 30, CRP >45)

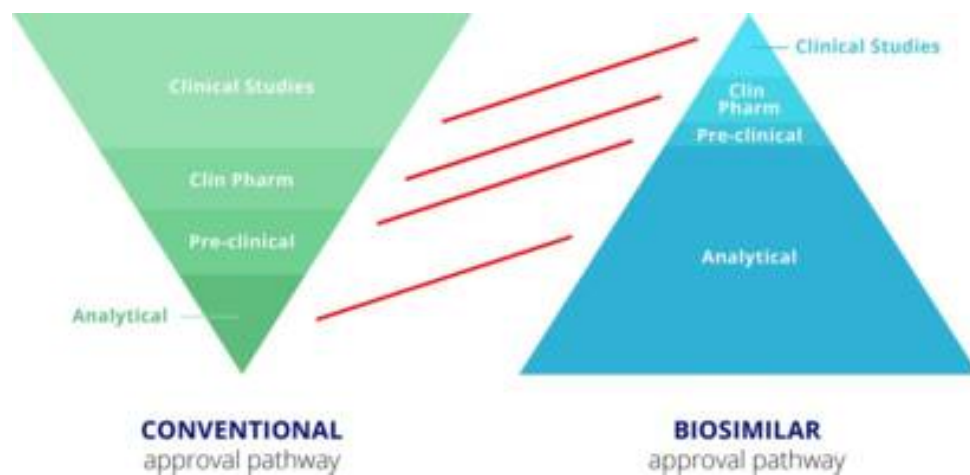
Faecal Calprotectin (greater >250)

Exclude infection (MC+S/CDT)

IBD Drugs and Prices

	Est Annual Cost	
Prednisolone	-	Steroid
Beclomethasone	-	Steroid
Mesalazine (Pentasa 2gm OD)	£100-430	5ASA
Methotrexate	£36	Antimetabolite
Azathioprine	£80	Thiopurine
6 Mercaptopurine	£1600	Thiopurine
Infliximab	£10,584	Anti-TNF
Biosimilar Infliximab	£3000-4000	Anti-TNF
Golimumab	£9155	Anti-TNF
Adalimumab	£9528	Anti-TNF
Biosimilar Adalimumab	£4000-5000	Anti-TNF
Vedolizumab	£16,913	Anti-Integrin
Ustekinumab	£10,735	Anti-IL23
Tofenacinib	?£10000	JAK inhibitor

Biosimiliars



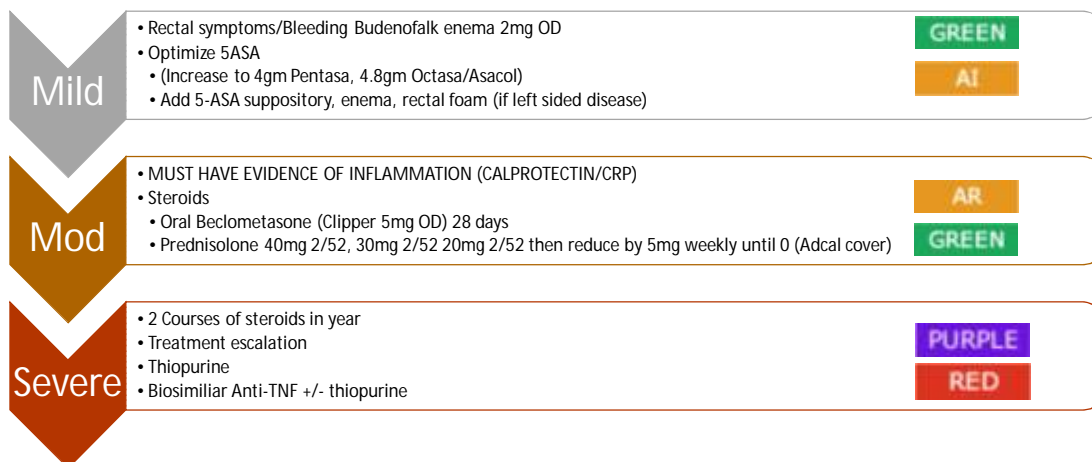
IBD Helpline numbers

Royal Liverpool University Hospital
IBDnurses@rlbuht.nhs.uk
 Belle/Dan – 0151 7062659

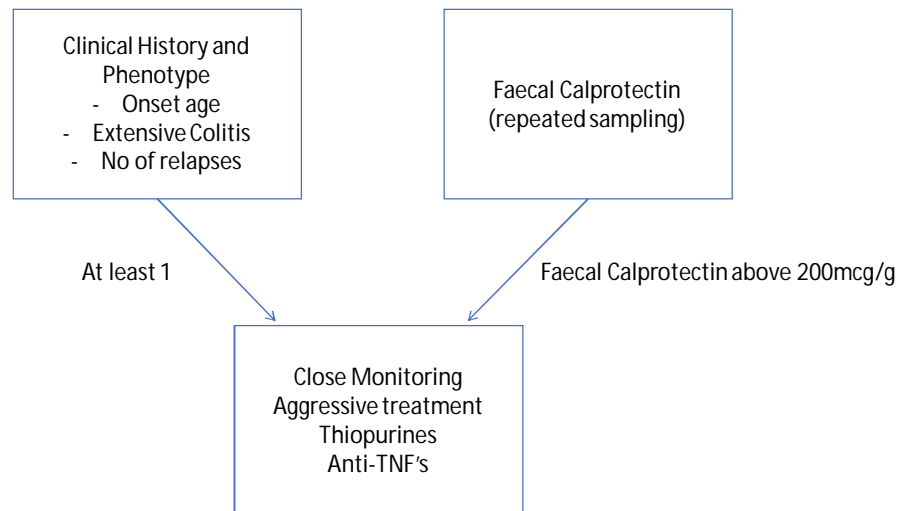
Aintree
 Andrew – 0151 5294801

Whiston & St. Helens
 Hayley – 0151 4787776

Ulcerative Colitis (histologically diagnosed)



Predicting Relapse in UC patients



Case History 2

Patients symptoms settle with treatment

Further flare in symptoms leads to initiation of Thiopurine

Handed over for shared care after stabilization


Ongoing infrequent mild symptoms and comes in for his Azathioprine


What monitoring is useful?


Review of IBD in GP


- U+E – Refer renal if >20% above baseline
- FBC – Neutropenia
- LFT's
- Ferritin (annually)
- Flu and Pneumococcus vaccines
- Cervical screening for female patients on immunomodulators


Case History 3


 54yr old woman with Crohn's Disease


 Annual FU from local hospital, not on treatment


 Previous surgery

 Presents with 6kg weight loss, nausea, significant diarrhea (no bleeding)

 Evidence of previous Perianal disease. No current abscess/fistulae.

 Stool samples negative

 CRP 15, Alb 35, Hb 109, WCC 8.7

 Calprotectin 209

Case History 3

What Investigations are next?

- USS abdominal
- Flexible Sigmoidoscopy
- Colonoscopy
- MR SB
- CT abdomen

What can you give her whilst waiting for the hospital?

- Prednisolone 30mg OD 5/7
- Budesonide 9mg OD 28/7
- Ensures plus (not juice preparations)
- Pentasa/5ASA

Case History 3

What Investigations are next?

- ~~USS abdominal~~
- ~~Flexible Sigmoidoscopy~~
- Colonoscopy
- MR SB
- ~~CT abdomen~~ (unless abscess suspected)

What can you give her whilst waiting for the hospital?

- ~~Prednisolone 30mg OD 5/7~~
- Budesonide 9mg OD 28/7
- Ensures plus (not juice preparations)
- ~~Pentasa/5ASA~~

Diagnosing UC vs Crohn's

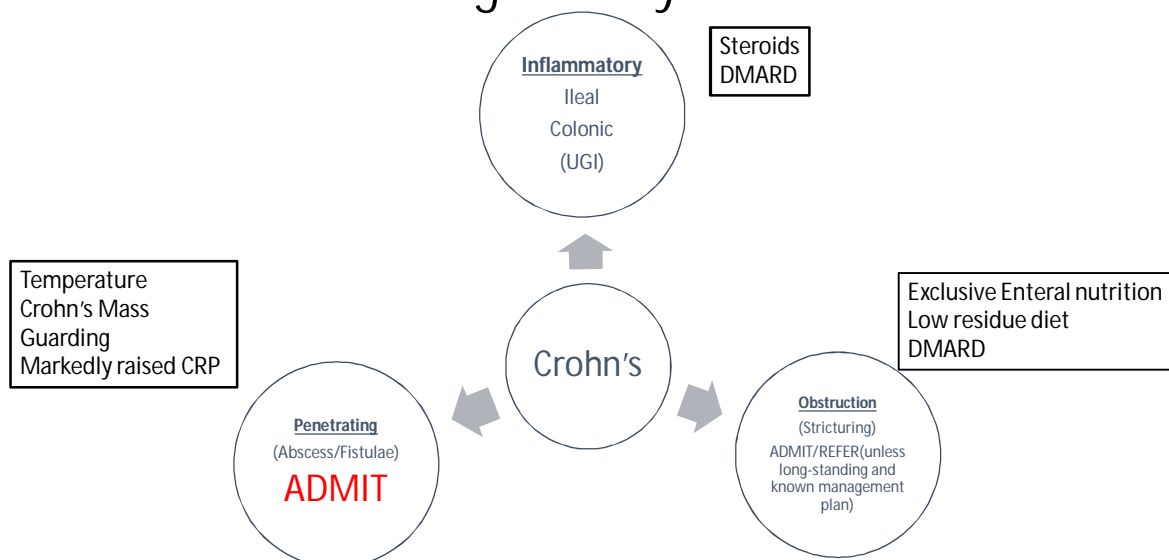
UC

- Rectal bleeding
- Endoscopy
 - Rectal involvement (apart from PSC/Therapy)
 - Histology (Goblet cell depletion, Cryptitis/Atrophy)

Crohn's

- Symptoms
- Raised inflammatory markers
- Evidence of GI inflammation on endoscopy/Radiology
 - Skip lesions
 - Ideally compatible histology
- Chronicity

Crohn's – assessing activity



Crohn's Poor Prognostic Markers for surgery

Young onset

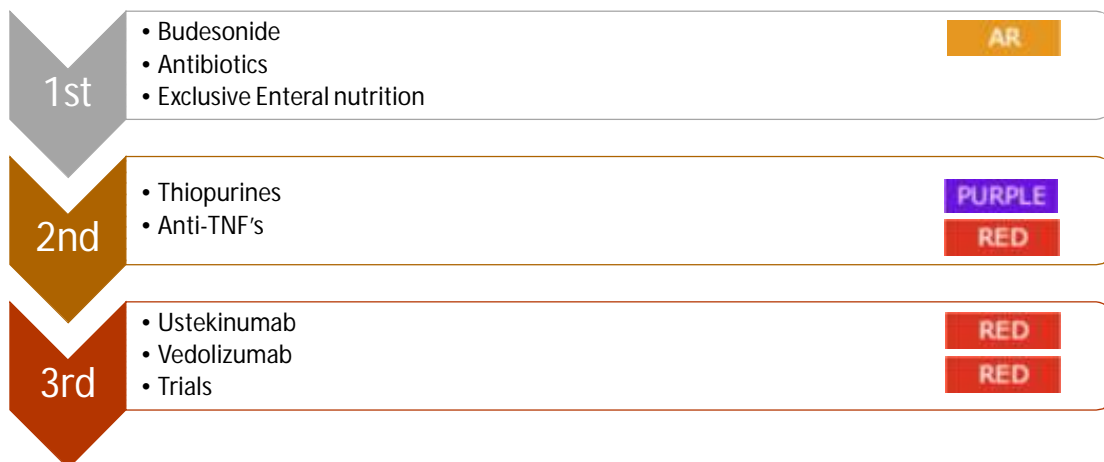
Male

Penetrating disease (fistulae/Abscess)

Smoking

Perianal disease

Crohn's Disease – Treatments



Microscopic Colitis

- Persistent watery diarrhoea
- 2 forms
 - Collagenous and Lymphocytic Collitis
 - Can be associated with drugs and coeliac
 - Diagnosed on histology only
- Mainstay of treatment – Loperamide/Budesonide at dose needed to control symptoms.



Top Tips

Always exclude infection in a flare

Calprotectin useful in diagnosis, flare and for prognosticating

Escalating 5ASA and rectal treatments safe/effective in UC

Steroids good for managing flares (but use a modern one to minimize S/E and preserve BMD)

Annual vaccinations of IBD patients

Early contact with IBD team in Crohn's and non-responsive UC

