

**IBD :- a new era of diagnostics and therapy**

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**Aims**

- ▶ To understand the aetiology of IBD
- ▶ To understand the impact that IBD has on patients
- ▶ Diagnostics - Faecal Calprotectin
- ▶ Therapeutics - The rise of the biologic
- ▶ Referral Pathways

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**CAUSE OF IBD IS UNKNOWN,**  
but thought to be a combination of genetic predisposition, environmental triggers, and an impaired immune system.

IBD affects people of any age and diagnosis is most common in early adulthood and before.

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**Symptoms**  
 Persistent Diarrhea  
 Abdominal Pain  
 Fever  
 Weight Loss  
 Delayed growth in children<sup>9</sup>

**Treatment**  
 Medications  
 Surgery  
 Nutritional supplementation  
 Or a combination of these options<sup>10,11</sup>

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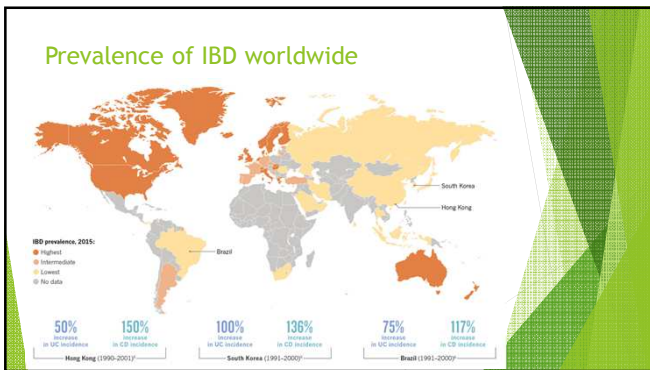
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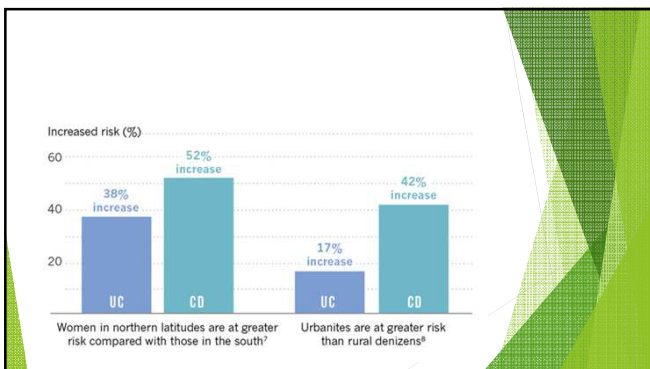
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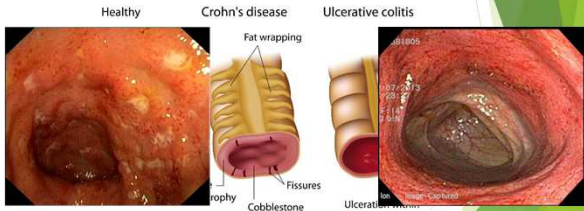
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## Inflammatory Bowel Disease




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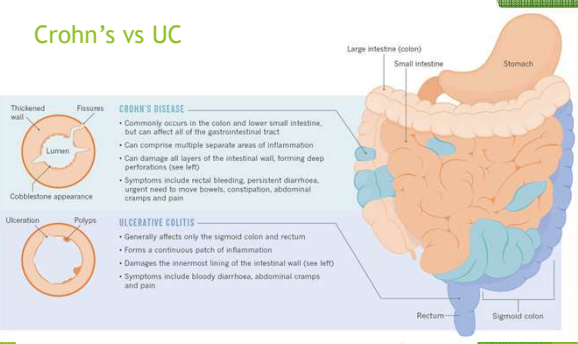
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## Crohn's vs UC




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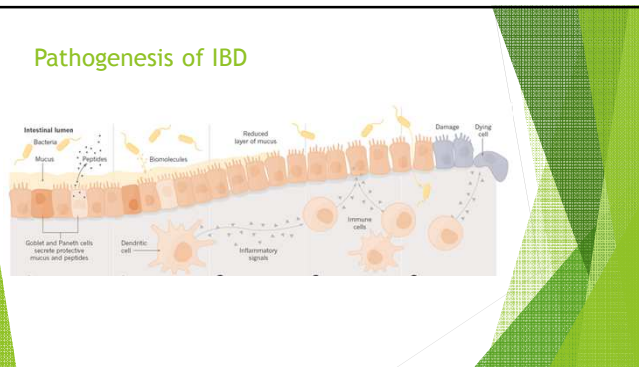
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## Pathogenesis of IBD




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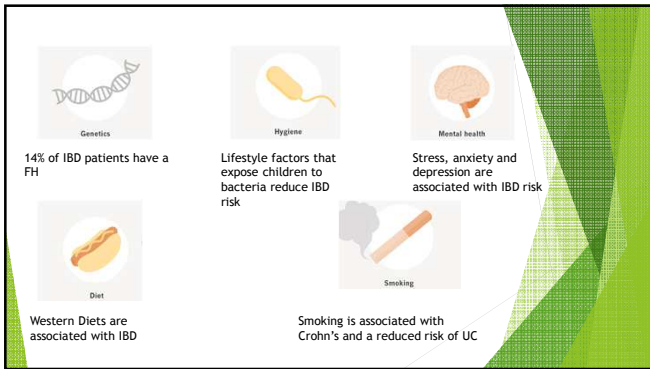
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**Genetics**  
14% of IBD patients have a FH

**Hygiene**  
Lifestyle factors that expose children to bacteria reduce IBD risk

**Mental health**  
Stress, anxiety and depression are associated with IBD risk

**Diet**  
Western Diets are associated with IBD

**Smoking**  
Smoking is associated with Crohn's and a reduced risk of UC

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### IBD significantly impacts Quality of Life

- ▶ 40% report making adjustments to their working life based on IBD
- ▶ 35% report that IBD has prevented them pursuing an intimate relationship
- ▶ 26% report that IBD has gotten in the way of making and keeping friends

Lovell, et al. IBD and health related quality of life - Deciphering the IBD experience. 2014. IBD Europe

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### IBD and Quality of Life

A large European study of people living with IBD found:

- 48%** report that their lives are significantly or somewhat impacted by IBD symptoms even between flare-ups.
- 40%** report making adjustments to their working life based on their IBD.
- 35%** report that IBD has prevented them from pursuing an intimate relationship.
- 26%** report that IBD has gotten in the way of making and keeping friends.<sup>12</sup>

Lovell, et al. IBD and health related quality of life - Deciphering the IBD experience. 2014. IBD Europe

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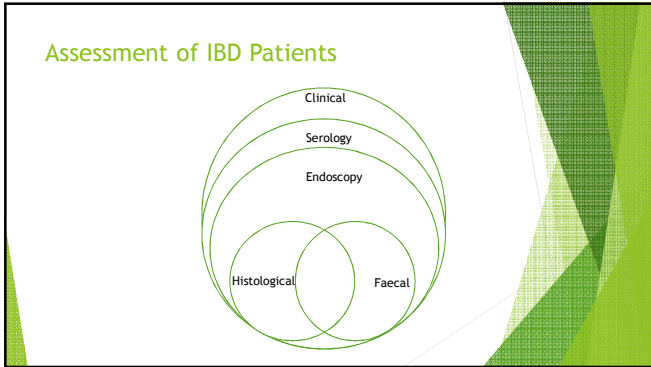
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### Faecal Calprotectin

- ▶ Calprotectin secreted in excess into the intestinal lumen during inflammation
- ▶ Sensitive but non-specific marker
- ▶ Recommended for use in Primary and Secondary Care. <sup>1</sup>
- ▶ Available from primary care
- ▶ PoC kits available

1. NICE Technology appraisal. Oct 2013. DG11

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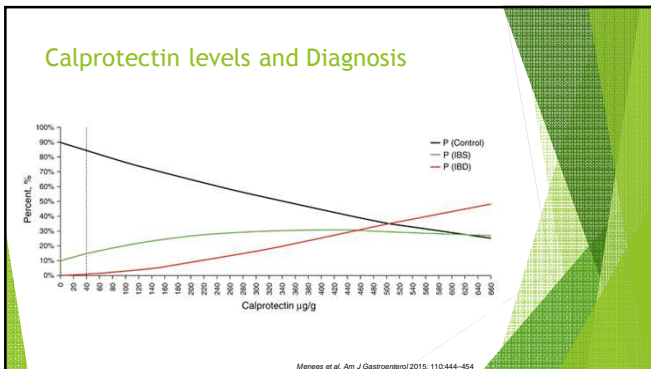
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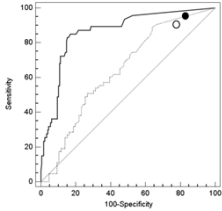
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### Calprotectin Levels and Findings at colonoscopy



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

Burni et al. BMC Gastroenterology 2014, 14:57

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### Calprotectin and cut-off ranges

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
IBS vs IBD at FC 50 µg/g	87.5	77.7	79.2	86.5
IBS vs IBD at FC 100 µg/g	97.2	76.3	75.3	97.4
IBD remission vs active at FC 50 µg/g	55.2	98.9	97.0	77.4
IBD remission vs active at FC 100 µg/g	72.4	95.6	91.3	84.3
IBD remission vs active at FC 250 µg/g	89.7	75.6	70.3	91.9

FC, faecal calprotectin; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; NPV, negative predictive value; PPV, positive predictive value.

But this PPV and NPV can only be calculated understanding the prevalence of the target condition within the population.

In most settings in the UK the prevalence of IBD is less than 1% - This would raise the NPV to nearly 100%.

Dhaliwal et al. Frontline Gastro 2015;6:14-19

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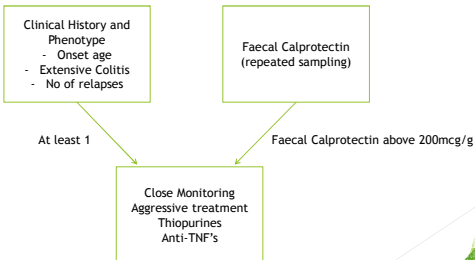
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### Predicting Relapse in UC patients




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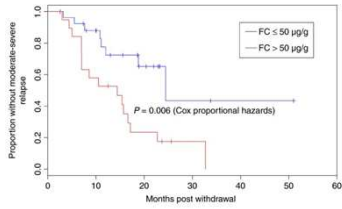
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### Calprotectin and Relapse after Crohn's Surgery



UK Anti-TNF withdrawal study group APT 2016/feb 19

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### Calprotectin and cancer

	FC, mcg/g		NPV		PPV		Sensitivity		Specificity	
	Median	IQR	Value	95% CI	Value	95% CI	Value	95% CI	Value	95% CI
Neoplasia										
Cancer	227	94.5 to 496	98.6	95.7 to 99.6	8.7	5.3 to 11.9	82.7	79.1 to 86	35.2	31.5 to 39.2
Cancer and polyps	189.5	88 to 494	97.2	93.8 to 98.9	15.6	12.4 to 18.4	91.9	82.6 to 96.7	36.4	32.5 to 40.5
Organic enteric disease	232	79 to 580	89.4	84.3 to 93	32.7	28.4 to 37.4	86.1	79.7 to 90.8	39.8	35.4 to 44.2

FC = faecal calprotectin, IQR = interquartile range, NPV = negative predictive value, PPV = positive predictive value.

Turvill et al 2016, British Journal of

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### Calprotectin can be abnormal in...

- ▶ 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)

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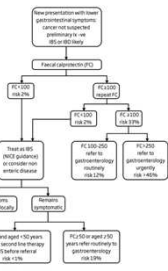
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### Faecal Calprotectin in Primary Care



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

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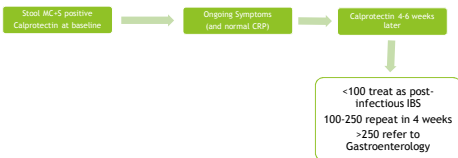
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### Calprotectin for monitoring of Infectious Diarrhoea




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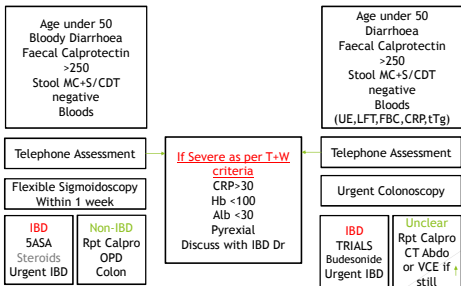
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### Urgent IBD referral pathway - RLUH




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### 20<sup>TH</sup> CENTURY

- ▶ Steroids
- ▶ Surgery
- ▶ 5-ASA
- ▶ Azathioprine

### 21<sup>st</sup> Century

- ▶ Step treatment pathways
- ▶ Biologics (with drug and antibody monitoring)
- ▶ Thiopurines (with metabolite monitoring)
- ▶ Therapeutic endoscopy
- ▶ Biomarkers
- ▶ Minimally invasive surgery

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### IBD Medications

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### IBD Drugs and Prices

	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	£6800	Anti-TNF
Golimumab	£9155	Anti-TNF
Adalimumab	£9528	Anti-TNF
Vedolizumab	£16,913	Anti-Integrin
Ustekinumab	£10,735	Anti-IL23

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### Treatments POST diagnosis

<b>Ulcerative Colitis</b>	
▶ Salofalk Granules 3gm (Left sided) or Pentasa Granules 4gm (Pancolitis)	▶ 5-asa for colonic disease
▶ 5-ASA enema (foam or liquid) for Left sided disease	▶ Budesonide for Ileal disease
▶ 5-ASA suppository for proctitis	▶ ?Antibiotics
▶ Rectal Steroids	▶ ?Enteral Nutrition
▶ Clipper 5mg	
▶ Prednisolone for severe	

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### Flaring Patient

- ▶ Nurse-led IBD help-line
  - ▶ Phone number
    - ▶ Royal Liverpool 0161 7062659
    - ▶ Aintree 0151 5294801
    - ▶ Whiston 0151 2904417
  - ▶ Prescriptions
  - ▶ Problems related to Disease modifying drugs

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### Conclusions

- ▶ Expanding availability of high cost drugs poses resource challenges
  - ▶ Drug monitoring and Biosimilars may mitigate this
- ▶ Faecal Calprotectin allows us to approach diagnosis in new ways
- ▶ Wide availability of IBD helplines
- ▶ New pathways for Urgent referrals

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**CROHN'S & COLITIS UK**

FORMER  
INFLAMMATORY  
BOWEL DISEASE  
TRUST

**RCGP Spotlight Project - Detecting and Treating IBD**  
April 2017 - March 2018

It can take more than a year for people to receive a confirmed diagnosis of IBD and many undergo emergency care in the meantime (IBD 2020)

*"My daughter was diagnosed with Crohn's at 18. She'd been ill off and on for 18 months, told she had anorexia, viruses and agoraphobia. She weighed five stone and was very poorly by the time a doctor said it could be Crohn's."*

*"I didn't know who to contact when I got sick and got different advice from the GP and the hospital."*

**Raising awareness and improving diagnosis and management of IBD**

- Clinical lead
- Toolkit - Optimal referral pathway, flare management, cancer surveillance
- Curriculum, educational resources, workshops, podcasts and Twitter chats

**We need your help**

- Practice audit of journey to diagnosis, GP reference group

crohnsandcolitis.org.uk

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