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

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.
Prevalence of IBD worldwide

Symptoms
- Persistent Diarrhea
- Abdominal Pain
- Fever
- Weight Loss
- Delayed growth

Treatment
- Medications
- Surgery
- Nutritional supplementation
- Or a combination of these options

Increased risk (%)

Women in northern latitudes are at greater risk compared with those in the south.

Urbanites are at greater risk than rural denizens.
14% of IBD patients have a FH

Lifestyle factors that expose children to bacteria reduce IBD risk

Stress, anxiety and depression are associated with IBD risk

Western Diets are associated with IBD

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

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

IBD and Quality of Life

A large European study of people living with IBD found:

- 48% report making adjustments to their working life based on 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
Assessment of IBD Patients

Clinical Serology Endoscopy Histological Faecal

- Faecal 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
- NICE kits available

1. NICE Technology appraisal. Oct 2013. DG11

Calprotectin Levels and Findings at colonoscopy

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

Calprotectin and cut-off ranges

<table>
<thead>
<tr>
<th>Calprotectin Level (mg/g)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50 mcg/g</td>
<td>97.3</td>
<td>94.3</td>
<td>91.1</td>
<td>91.9</td>
</tr>
<tr>
<td>50-100 mcg/g</td>
<td>95.3</td>
<td>89.0</td>
<td>84.2</td>
<td>93.0</td>
</tr>
<tr>
<td>100-200 mcg/g</td>
<td>89.1</td>
<td>84.6</td>
<td>74.3</td>
<td>91.2</td>
</tr>
</tbody>
</table>

*1. Localized IBD; 2. Extensive IBD; 3. Repeated sampling; 4. Positive predictive value; NPV, negative 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%.

Predicting Relapse in UC patients

- Clinical History and Phenotype
  - Onset age
  - Extensive Colitis
  - No of relapses
- Faecal Calprotectin (repeated sampling)
  - Close Monitoring
  - Aggressive Treatment
  - Anti-TNF's

At least 1 Faecal Calprotectin above 200mcg/g
Calprotectin and histological remission

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 (Gaass et al., 2016. Medicine. Apr;95(16):e3477)

Predicting Relapse in Crohn’s patients

- Clinical History and Phenotype
  - Onset age
  - Extensive Disease
  - Perianal Involvement
  - Steroids at diagnosis
  - No of surgeries
- Faecal Calprotectin (repeated sampling)
  - CRP
- Close Monitoring
  - Aggressive treatment
  - Thiopurines
  - Anti-TNF’s

At least 1

Faecal Calprotectin above 250mcg/g
CRP>10
Calprotectin and Relapse after Crohn’s Surgery

Calprotectin and cancer

Calprotectin can be abnormal in...

- NSAID’s (Rendek Z et al, Scand J Gastroenterol 2016. 51;1:28-32)
- Previous Surgery disentage TC et al, (Surg 2016. May 23)
- PPI Use de Coler B.GP 2014)
- Coeliac Disease (Capone et al, WJG 2014. 14;20:611-620)
Faecal Calprotectin in Primary Care

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

- Calprotectin for monitoring of Infectious Diarrhoea
  - Stool MC+S positive Calprotectin at baseline
  - Ongoing Symptoms (and normal CRP)
  - Calprotectin 4-6 weeks later
  - <100 treat as post-infectious IBS
  - 100-250 repeat in 4 weeks
  - >250 refer to Gastroenterology

- Urgent IBD referral pathway - RLUH
  - Age under 50
  - Bloody Diarrhoea
  - Faecal Calprotectin >250
  - Stool MC+S/CDT negative
  - Bloods (UE, LFT, FBC, CRP, tTg)

- Telephone Assessment
  - IBD
  - 5ASA
  - Steroids
  - Urgent IBD
  - Urgent Colonoscopy
  - If Severe as per T+W criteria

- Trial:
  - Budesonide
  - Urgent IBD
  - Unclear
  - Repeat Calpro
  - CT Abdo or VCE if still

Fax: 0151 7065832
20TH CENTURY
- Steroids
- Surgery
- 5-ASA
- Aspirin

21st Century
- Step treatment pathways
- Biologics (with drug and antibody monitoring)
- Thiopurines (with metabolite monitoring)
- Therapeutic endoscopy
- Biomarkers
- Minimally invasive surgery

IBD Medications

IBD Drugs and Prices

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisolone</td>
<td>£1-20</td>
<td>Steroid</td>
</tr>
<tr>
<td>Beclometasone</td>
<td>£20</td>
<td>Steroid</td>
</tr>
<tr>
<td>Mesalazine</td>
<td>£100-430</td>
<td>5ASA</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>£36</td>
<td>Antimetabolite</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>£80</td>
<td>Thiopurine</td>
</tr>
<tr>
<td>6-Mercaptopurine</td>
<td>£1000</td>
<td>Thiopurine</td>
</tr>
<tr>
<td>Infliximab</td>
<td>£10,584</td>
<td>Anti-TNF</td>
</tr>
<tr>
<td>Biosimilar Infliximab</td>
<td>£6800</td>
<td>Anti-TNF</td>
</tr>
<tr>
<td>Golimumab</td>
<td>£9155</td>
<td>Anti-TNF</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>£9528</td>
<td>Anti-TNF</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>£14,913</td>
<td>Anti-Integrin</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>£10,735</td>
<td>Anti-IL23</td>
</tr>
</tbody>
</table>
Treatments POST diagnosis

Ulcerative Colitis
- Salofalk Granules 3gm (Left sided) or Pentasa Granules 5gm (Pancolitis)
- 5-ASA enema (foam or liquid) for Left sided disease
g- 5-ASA suppository for proctitis
- Rectal Steroids
- Cliperon 5mg
- Prednisolone for severe

Crohn’s
- 5-asa for colonic disease
- Budesonide for ileal disease
- Antibiotics
- Enteral Nutrition

Clipper 5mg

Prednisolone for severe

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

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
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 appendicitis. 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

- Toolkit - Optimise referrals, pathway, flare management, cancer surveillance
- Curriculum, educational resources, workshops, podcasts and Twitter chat

We need your help
- Practice audit of journey to diagnosis, GP reference group