Overview of Medical and Surgical Management of IBD

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“A disease which varies greatly in severity and extent, not only from patient to patient but in the same individual from attack to attack”
Historical Aspects of Medical Therapy

**Early 1900s:**
- Slop diets
- Milk soured with lactic acid
- Opium
- Tincture of hamamelis
- Rectal instillations of boracic acid or kerosene

**Early to Mid 1900s:**
- DIETS: low fibre, high fibre, low fat, low carbohydrate, purified (crystalline amino acids)
- PSYCHOTHERAPY
- SULFONAMIDES: Sulfur containing antibiotics followed by sulfasalazine

**Mid to late 1900s:**
- Efficacy and more favourable safety profile of 5-ASA component alone recognized
- STEROIDS: Routine use until greater recognition of side effects, particularly with longer term use
- IMMUNOMODULATORS: 6-mercaptopurine (1960s), tacrolimus, cyclosporin, superoxide dismutase, fusidic acid

*Joseph Kirsner, Historical Original of Inflammatory Bowel Disease, Lancet 1998*
Historical Aspects of Surgical Therapy

**Ulcerative Colitis**
- **Early 1990s:** Appendectomy, caecostomy, colostomy, ileostomy
- **Mid 1900s:** Pelvic autonomic neurectomy, distal vagotomy, thymectomy, subtotal colectomy with ileo-colonic anastomosis
- **Late 1900s:** Koch's pouch, ileo-pouch anal anastomosis

**Crohn's Disease**
- **Early 1900s:** Abdominal explorations
- **Mid 1900s:** Intestinal bypass, extensive small bowel resections
- **Late 1900s:** Diverting ileostomy, strictureplasty

*Joseph Kirsner, Historical Origin of Inflammatory Bowel Disease, Lancet 1998*
Where are we now?

**Treatment Principles**

- Changes in goals of therapy
  - Treat to Target
  - Mismatch between symptoms and inflammation
  - Favourable outcomes associated with mucosal healing

Symptoms → Biomarkers → Endoscopy → Histology
### Available Medications

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Corticosteroids</strong></td>
<td>Prednisone, Hydrocortisone, Budesonide, Budesonide MMX, Topical Preparations</td>
</tr>
<tr>
<td><strong>5-Aminosalicylates</strong></td>
<td>Oral, Topical preparations (Enemas, liquid or foam, Suppositories)</td>
</tr>
<tr>
<td><strong>Immunomodulators</strong></td>
<td>Thiopurines (Azathioprine, 6-Mercaptopurine), Methotrexate, Others</td>
</tr>
<tr>
<td><strong>Biologics</strong></td>
<td>Anti-TNFs, Anti-integrins, IL-12/23</td>
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</tbody>
</table>
Where are we now?

Corticosteroids

- Hydrocortisone or Methylprednisolone
- Prednisone
- Budesonide
- Budesonide MMX
- Topical preparations
Where are we now?

5-Aminosalicylates

- Oral
- Suppositories
- Enemas
  - Foam
  - Liquid

Sulfasalazine

Oral Preparations

pH and Delayed Release

Olsalazine
Balsalazide

Enema Preparations

5-ASA

Marshall, AMJ 2000
Where are we now? Immuno-modulators

- Thiopurines
  - Azathioprine
  - 6-Mercaptopurine
- Methotrexate
- Others eg cyclosporine, tacrolimus

Warner et al, Frontline Gastroenterology, 2016
Where are we now?

Biologics

- Anti-TNFs
- Anti-integrins (vedolizumab)
- IL-12/23 (ustekinumab)

Nature Reviews Gastroenterology and Hepatology, 2017
Where are we now?

**Surgical Techniques**

- Minimally Invasive Approaches

- Ulcerative Colitis
  - Ileo-Pouch Anal Anastomosis

- Crohn’s Disease
  - Ileo-colonic resection and primary anastomosis
  - Ileostomy
  - Peri-anal disease operative approaches
Buzz Phrases

- Combination Therapy
- Therapeutic Drug Monitoring (TDM)
- Dose Escalation
- Fecal Calprotectin
- Biosimilars
- Mucosal Healing
- Post-operative Recurrence
CASES

1. Chronic Active Ulcerative Colitis
2. Severe Acute Ulcerative Colitis
3. Ileocolonic and Perianal Crohn’s Disease
Case Presentation 1: Chronic Active Ulcerative Colitis

24 year old male

- Two month history of diarrhoea, with increasing blood content of stool (~ 4 BM/day including nocturnal); no preceding travel, sick contacts or antibiotics

- Colonoscopy findings consistent with mild extensive Ulcerative Colitis

- Commenced on oral and topical 5-aminosalicylates (4g oral mesalazine and 4g mesalazine enema)

- Review 2 months later – in symptomatic and biochemical remission

- Repeat colonoscopy 4 months later demonstrating healed mucosa
Case Presentation 2: Severe Acute Ulcerative Colitis

- 32 year old male
  - 1 year history of extensive UC
    - Preceding this current presentation he had been asymptomatic on 4g Oral Mesalazine daily
  - Over preceding 2 months, increasing stool frequency and reduced consistency, with progressive blood within stool
  - Reviewed in Clinic – commencement of prednisone 40mg daily given severity of symptoms (in addition to exclusion of infective cause)
  - Phone review 2 weeks later prompted arrangements for urgent colonoscopy given no improvement
  - Colonoscopy – severe, extensive colitis (CRP 40, Hb 110, Alb 32)
Acute Severe Ulcerative Colitis

- **MANAGEMENT**
  - Admission with multidisciplinary input
    - Medical, surgical, IBD nurse, pharmacist, dietician
  - Stool Chart
  - Avoidance of anti-diarrhoeals/opiates
  - Intravenous steroids e.g. 100mg hydrocortisone q8 hourly
  - VTE prophylaxis
  - Reassessment
    - Minimal improvement by Day 3
  - Infliximab
    - Ongoing symptoms and no improvement in CRP
  - Decision made to proceed with **sub-total colectomy**
Ileo-pouch anal anastomosis: Staged Procedure
Case Presentation 3: Ileocolonic and Peri-anal Crohn’s Disease

- 32 year old female
  - 10 year history of Crohn’s disease – extent of intestinal involvement unknown; history of peri-anal abscess
  - Restaging: colonoscopy demonstrating patchy colonic and ileal (~15cm) involvement of moderate severity; MRI pelvis – actively draining complex fistulous tract with 1.5cm collection
  - Urgent colorectal surgical review – examination under anesthesia and placement of Seton
  - Follow-up for medical therapy
    - Commencement of infliximab and azathioprine
    - Review 3 and 6 months later
      - No further peri-anal drainage
      - Improvement of luminal symptoms

Gesce et al, GUT, 2014
Special Populations

Pregnancy

Elderly
<table>
<thead>
<tr>
<th>Medical Therapy</th>
<th>Potential Adverse Effects</th>
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</table>
| Aminosalicylates| Interstitial Nephritis  
|                 | Hypersensitivity Reaction (Sulfur)                            |
| Corticosteroids | Early:  
|                 | - acne, moon face, oedema, striae  
|                 | - Sleep and mood disturbance  
|                 | - Glucose intolerance  
|                 | - Dyspepsia  
|                 | Prolonged Use:  
|                 | - Cataracts  
|                 | - Osteoporosis  
|                 | - Osteonecrosis of femoral head  
|                 | - Myopathy  
|                 | - Susceptibility to infection                                |
| Thiopurines     | Myelosuppression  
|                 | Pancreatitis  
|                 | Infection  
| Methotrexate    | Gastro-intestinal  
|                 | Hepatotoxicity  
|                 | Renal toxicity  
|                 | Teratogenic  
|                 | Pneumonitis                                                |
| Anti-TNFs       | Infusion Reactions  
|                 | Dermatological  
|                 | Lupus-like syndrome  
|                 | Demyelination                                               |
|                 | Infection – common; opportunistic*  
|                 | Melanoma  
|                 | Lymphoma*                                                   |
| Anti-integrin   | Low risk of serious infections  
|                 | Mild nasopharyngitis                                        |
|                 | Few infusion reactions                                      |
|                 | No malignancy signal                                        |
| IL 12/23        | Low risk of serious infections  
|                 | No malignancy signal                                        |
Medication Safety

Corticosteroids
- Minimisation of exposure

Thiopurines
- TPMT testing
- Metabolite Testing
- Haematologic Monitoring
- Skin Protection

Methotrexate
- Haematologic and Hepatic Monitoring
- Folic Acid

Anti-TNF
- TB screening
- Hepatitis B status assessment
Future Therapies

- Additional Biologics
- Small Molecules
- Faecal Microbial Transplantation
- Nutritional Therapies
- Mesenchymal Stem Cells
Health Maintenance
Smoking Cessation
Nutrition
Psychological Health
Bone health
Vaccinations
Cancer Surveillance
- Colonoscopy (CRC)
- Skin
- Mammography
- Pap smears
Summary

- Individualized Approach
- Targeted Therapy
- Minimization of Risk
- Health Maintenance
- Multi-disciplinary Approach
Medical Therapies

• Ulcerative Colitis:
  • 5-aminosalicylates
  • Corticosteroids (sparingly)
  • Biologics (Anti-TNFs; Vedolizumab)
  • Clinical Trials

• Crohn’s Disease:
  • Corticosteroids (sparingly)
  • Immunomodulators
  • Biologics (Anti-TNFs; Vedolizumab; Ustekinumab)
  • Clinical Trials

Surgical Therapies

• Ulcerative Colitis
  • Pouch Creation

• Crohn’s Disease
  • Fistula Management
  • Limited/Extensive Resection
  • Stricturoplasty
  • Ileostomy