## Inflammatory Bowel Disease (IBD)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Crohn’s Disease</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease involvement</strong></td>
<td>Mostly small intestine</td>
<td>Mostly large intestine</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>Not beneficial</td>
<td>May be beneficial</td>
</tr>
<tr>
<td><strong>Appendectomy</strong></td>
<td>May increase risk</td>
<td>May prevent</td>
</tr>
<tr>
<td><strong>Visual presentation</strong></td>
<td>Thickened, fatty, edematous, cobblestone, like fried eggs</td>
<td>Diffuse erythema, friability of mucosa, topical, red, fragile</td>
</tr>
<tr>
<td><strong>Microscopic distribution</strong></td>
<td>Often focal</td>
<td>Always diffuse</td>
</tr>
<tr>
<td><strong>Depth of inflammation</strong></td>
<td>Transmural</td>
<td>Mucosal</td>
</tr>
<tr>
<td><strong>Fistulae</strong></td>
<td>Often present</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Strictures</strong></td>
<td>Often present</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Diarrhea</strong></td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Recurrence post-surgery</strong></td>
<td>Not cured</td>
<td>Cured</td>
</tr>
</tbody>
</table>

### Acute disease

- **Mild** &lt;4 BM ± blood
- **Moderate** ≥4 BM ± blood
- **Severe** &gt;6 BM + blood
- **Fulminant** &gt;10 BM + continuous bleeding

### Extraintestinal Manifestations (EIM)

- Symptoms/diseases that result from IBD that present outside the intestines
- ≥1 EIM is observed in about 20-40% of IBD patients
- Ocular, pulmonary, cardiovascular, dermatological, renal, neurologic, hepatobiliary, oral, muscoskeletal
- Treating IBD → treats EIM
- Bone disease manifestations: osteoporosis
  - DEXA scores: Z score &lt;-2 if &lt;50y/o, T score &lt;-2.5 if ≥50y/o
  - Risk factors: older age, female, Caucasian/Asian, family history, small bone structure, low Ca & Vit D intake, smoking, alcohol
  - IBD risk factors: corticosteroid therapy, active GI inflammation, Vit D deficiency, Ca malabsorption

### Nutritional deficiencies

- Due to ↓dietary intake (↓desire to eat), disease GIT, or resected bowel
- Malabsorption of vitamins & minerals
  - Duodenum: Fe
  - Jejunum: Ca, folate, Fe, Phos, Zn
  - Ileum: fat soluble vitamins (ADEK), Vit B12
  - Terminal ileum: Vit B12

### Treatment

#### Treatment Overview

<table>
<thead>
<tr>
<th>5-ASA</th>
<th>Corticosteroids</th>
<th>Immunomodulators</th>
<th>Antibiotics</th>
<th>Biologicals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
<td>Mild to mod Maintenance</td>
<td>Active disease Induce remission</td>
<td>Steroid sparing Maintenance</td>
<td>Suspected infections, abscess, fistulas</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>Slow</td>
<td>Quick</td>
<td>Slow</td>
<td></td>
</tr>
<tr>
<td><strong>Agents</strong></td>
<td>Sulfasalazine, Canasa, Rowasa, Colazal, Dipentum, Asacol, Lialda, Apriso, Pentasa</td>
<td>Prednisone, prednisolone, methylprednisone, budesonide, hydrocortisone</td>
<td>Azathioprine, 6-MP, methotrexate, cyclosporine, tacrolimus</td>
<td>Metronidazole, ciprofloxacin</td>
</tr>
</tbody>
</table>
5-ASA | aminosalicylic acids

- **MOA:** anti-inflammatory + immunosuppressive actions
  - Anti-inflammatory: (−)COX, LOX, platelet activation factor synthesis
  - Immunosuppression: (+)adenosine release → impairs leukocyte function & activation; ↓ cytokine synthesis

- **Site of action**

<table>
<thead>
<tr>
<th>Site of action</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectum only</td>
<td>Canasa suppository</td>
</tr>
<tr>
<td>Rectum + sigmoid colon</td>
<td>Rowasa enema</td>
</tr>
<tr>
<td>Colon only</td>
<td>Sulfasalazine, Colazal, Dipentum</td>
</tr>
<tr>
<td>Colon + terminal ileum</td>
<td>Asacol, Lialda</td>
</tr>
<tr>
<td>Colon + terminal ileum + jejunum/ileum</td>
<td>Apriso</td>
</tr>
<tr>
<td>Colon + terminal ileum + small intestine</td>
<td>Pentasa</td>
</tr>
</tbody>
</table>

- **Comparing 5-ASA agents**

<table>
<thead>
<tr>
<th></th>
<th>Azulfidine</th>
<th>Canasa</th>
<th>Rowasa</th>
<th>Colazal</th>
<th>Dipentum</th>
<th>Asacol</th>
<th>Lialda</th>
<th>Apriso</th>
<th>Pentasa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic</td>
<td>sulfasalazine</td>
<td>mesalamine</td>
<td>mesalamine</td>
<td>balsalazide</td>
<td>olsalazine</td>
<td>mesalamine</td>
<td>mesalamine</td>
<td>mesalamine</td>
<td>mesalamine</td>
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<tr>
<td>Induce remission</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>Maintenance of remission</td>
<td></td>
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<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Taper down: mild−mod</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Dosage form</td>
<td>Suppository</td>
<td>Enema</td>
<td>Prodrug of mesalamine</td>
<td>Coating requires pH ≥7</td>
<td>Delayed &amp; ER in MMX system, requires pH ≥7</td>
<td>Gelatin coated capsules, pH&gt;6, ER Intellicor system</td>
<td>Micro-spheres</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Counseling points</td>
<td>Evacuate bowel 1st</td>
<td>Bedtime, lay on left side, ≥8hrs</td>
<td></td>
<td></td>
<td></td>
<td>QD</td>
<td>QD</td>
<td></td>
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</tr>
</tbody>
</table>

- **Adverse effects**
  - **Common SE among all 5-ASA:** headache, nausea, rash, interstitial nephritis, pericarditis, pancreatitis, hepatitis, paradoxical exacerbation of colitis
  - **Sulfasalazine SE**
    - Dose related reactions: nausea, dyspepsia, headache, fatigue, dizziness
      - Dependent on metabolism status (slow acetylators) & dosage (seen if >4g/day)
      - Due to sulfapyridine component of sulfasalazine
    - Hypersensitivity reactions: rash (SJS), fever, arthralgias, hepatic dysfunction, hematological toxicity
      - Due to sulfa component of sulfasalazine
      - Avoid sulfasalazine if patient has sulfa allergies or if on other sulfonamides
    - Male infertility: reversible after 3 months of discontinuing sulfasalazine
    - Discoloration: urine → orange, soft contact lens & tears → yellow
    - Other: vomiting, dyspepsia, anorexia, folate malabsorption, connective tissue disease
  - **Balsalazide, olsalazine, mesalamine SE**
    - Hair loss, pneumonitis, secretory diarrhea (olsalazine)

**Corticosteroids**

- **Indication:** induce remission of active IBD
- **MOA:** unknown, suppresses immune system, (−)cytokines, (−)prostaglandins, ↓ margination of monocytes & neutrophils
- **Agents:** prednisone, prednisolone, methylprednisone, budesonide, hydrocortisone
- **Dosing**

<table>
<thead>
<tr>
<th>Severe/active IBD</th>
<th>Mild to moderate IBD</th>
<th>Taper down</th>
</tr>
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<tbody>
<tr>
<td>40-60mg IV prednisone equivalents/day</td>
<td>40mg PO prednisone equivalents/day</td>
<td>1. Dose by 5mg per week to 20mg 2. Then ↓ dose by 2.5mg per week or every other week</td>
</tr>
</tbody>
</table>
Minimizing bone loss
- Use lowest possible dose of steroids
- Lifestyle modifications: smoking cessation, ↓alcohol intake, ↑weight bearing exercises
- Supplemental Ca + VitD
  - <50 y/o → Ca 1000mg qd
  - >50 y/o → Ca 1500mg qd
  - Vit D 400-800 IU qd
- Steroid-sparing medications: azathioprine or 6-MP

Rectal steroids
- Cortenema, Colocort
  - Hydrocortisone retention rectal suspension 100mg/60mL
  - Indication: ulcerative proctitis, ulcerative proctosigmoiditis, left-sided UC
- Cortifoam
  - Hydrocortisone acetate rectal aerosol
  - Indication: ulcerative proctitis of distal portion of the rectum
- Entocort EC
  - Budesonide: glucocorticoid as a controlled release gelatin capsule
    - ↓Systemic bioavailability → ↓SE
  - Indication: treatment of mild to moderate active Crohn’s disease involving ileum and/or ascending colon

Immunosuppressive therapy
- Agents: azathioprine, 6-MP, methotrexate, cyclosporine, tacrolimus
- Azathioprine & 6-MP
  - Uses: used for steroid-sparing effects, combined with biologics to ↓immunogenicity, not FDA approved for IBD, good for bridging since very slow onset of action
  - Adverse effects: infection, pancreatitis, bone marrow suppression, hepatotoxicity, GI disturbances, allergic reaction (fever, rash, arthralgias, myalgias), and possibly malignancy
- Methotrexate
  - Use: use for steroid-sparing effect if azathioprine or 6-MP won’t work, not FDA approved for IBD
  - Adverse effects: hepatotoxicity, bone marrow suppression, GI effects, dermatological, infections
  - Need to supplement with folic acid
- Cyclosporine & tacrolimus
  - Use: reserved for severe, treatment-refractory colitis; when all else fails
  - Adverse effects: nephrotoxicity, hypertension, paresthesias

Antibiotics
- Indications: Crohn's with abscesses or fistulas, intestinal or perianal disease, pouchitis, suspected infection
- Metronidazole
  - MOA: unknown, anti-inflammatory, immunosuppressive
  - Adverse effects: nausea, metallic taste, disulfiram reaction, peripheral neuropathy
- Ciprofloxacin
  - MOA: unknown
  - Adverse effects: vaginitis, abdominal pain, distal neuropathy, tendinopathy

Biologic agents
- Agents: infliximab, adalimumab, certolizumab, natalizumab
- MOA: (-)TNFα → ↓GI inflammation + ↓adhesion
- Adverse effects: autoimmunity, CHF, hepatotoxicity, malignancy, demyelinating disease, progressive multifocal leukoencephalopathy (PML), infection, bone marrow suppression, injection site reactions
  - Infusion-related reactions
    - Acute infusion reaction: ≤24hrs, IgE-mediated type I hypersensitivity or rate related
    - Delayed infusion reaction: ≥48hrs, serum sickness-like (type III hypersensitivity), lupus-like, viral syndrome, or IBD flare
  - Infections
    - Pneumonia, abscess, cellulitis, sepsis, herpes zoster, opportunistic infections, reactivation of chronic hep B in carriers, reactivation of latent TB
Do not administer anti-TNFα agents if active infection or latent TB

- **CHF:** related to infliximab doses >10mg/kg or in moderate to severe HF patients with doses >5mg/kg
- **Lymphoma:** rate has not exceeded the general population
  - Breast, colon, cervix, prostate, melanoma, gall bladder, squamous, basal-cell carcinoma, non-Hodgkin’s lymphomas, hepatosplenic T-cell lymphoma
- **Hematological:** leukopenia, neutropenia, thrombocytopenia, pancytopenia
- **Hepatotoxicity:** acute liver failure, jaundice, autoimmune hepatitis, reactivation of HBV
- **Neurological:** optic neuritis, seizure, CNS demyelinating disorders, multiple sclerosis, CNS manifestation of systemic vasculitis
- **Dermatological:** erythema multiforme, SJS, TEN, psoriasis
- **Natalizumab adverse effects**
  - Hypersensitivity: seen especially with natalizumab within 2hrs after starting infusion
  - Infections: ↑ risk if given with steroids or with immunosuppressants
  - Hepatotoxicity: seen 6 days after 1st dose or after multiple doses
  - PML: rare but serious opportunistic brain infection secondary to JC virus → need antibody test