IBD | Inflammatory Bowel Disease

	Cz | Crohn's Disease	UC | Ulcerative Colitis
Disease involvement	Mostly small intestine	Mostly large intestine
Smoking	Not beneficial	May be beneficial
Appendectomy	May increase risk	May prevent
Visual presentation	Thickened, fatty, edematous, cobblestone, like fried eggs	Diffuse erythema, friability of mucosa, topical, red, fragile
Microscopic distribution	Often focal	Always diffuse
Depth of inflammation	Transmural	Mucosal
Fistulae	Often present	Absent
Strictures	Often present	Absent
Diarrhea	Common	Common
Recurrence post-surgery	Not cured	Cured

Acute disease

Mild	<4 BM ± blood
Moderate	≥4 BM ± blood
Severe	>6 BM + blood
Fulminant	>10 BM + continuous bleeding

EIM | Extraintestinal Manifestations

- 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 <-2 if <50y/o, T score <-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					
	5-ASA	**Corticosteroids**	**Immunomodulators**	**Antibiotics**	**Biologicals**
Indications	Mild to mod Maintenance	Active disease Induce remission	Steroid sparing Maintenance	Suspected infections, abscess, fistulas	Mod to severe Failed other options
Onset	Slow	Quick	Slow		
Agents	Sulfasalazine, Canasa, Rowasa, Colazal, Dipentum, Asacol, Lialda, Apriso, Pentasa	Prednisone, prednisolone, methylprednisone, budesonide, hydrocortisone	Azathioprine, 6-MP, methotrexate, cyclosporine, tacrolimus	Metronidazole, ciprofloxacin	Infliximab, adalimumab, certolizumab, natalizumab

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**

Rectum only	Canasa suppository
Rectum + sigmoid colon	Rowasa enema
Colon only	Sulfasalazine, Colazal, Dipentum
Colon + terminal ileum	Asacol, Lialda
Colon + terminal ileum + jejunum/ileum	Apriso
Colon + terminal ileum + small intestine	Pentasa

- **Comparing 5-ASA agents**

	Azulfidine	Canasa	Rowasa	Colazal	Dipentum	Asacol	Lialda	Apriso	Pentasa
Generic	sulfasalazine	mesalamine	mesalamine	balsalazide	olsalazine	mesalamine	mesalamine	mesalamine	mesalamine
Induce remission							√		√
Maintenance of remission					√ (for pts intolerant to sulfasalazine)	√	√	√	
Tx mild–mod	√	√	√	√		√	√		√
Dosage form		Suppository	Enema	Prodrug of mesalamine		Coating requires pH ≥7	Delayed & ER in MMX system, requires pH ≥7	Gelatin coated capsules, ph>6, ER Intellicor system	Micro-spheres
Counseling points		Evacuate bowel 1st	Bedtime, lay on left side, ≥8hrs				QD	QD	

- **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**

Severe/active IBD	Mild to moderate IBD	Taper down
40-60mg IV prednisone equivalents/day	40mg PO prednisone equivalents/day	1. ↓Dose by 5mg per week to 20mg 2. Then ↓dose by 2.5mg per week or every other week

- **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