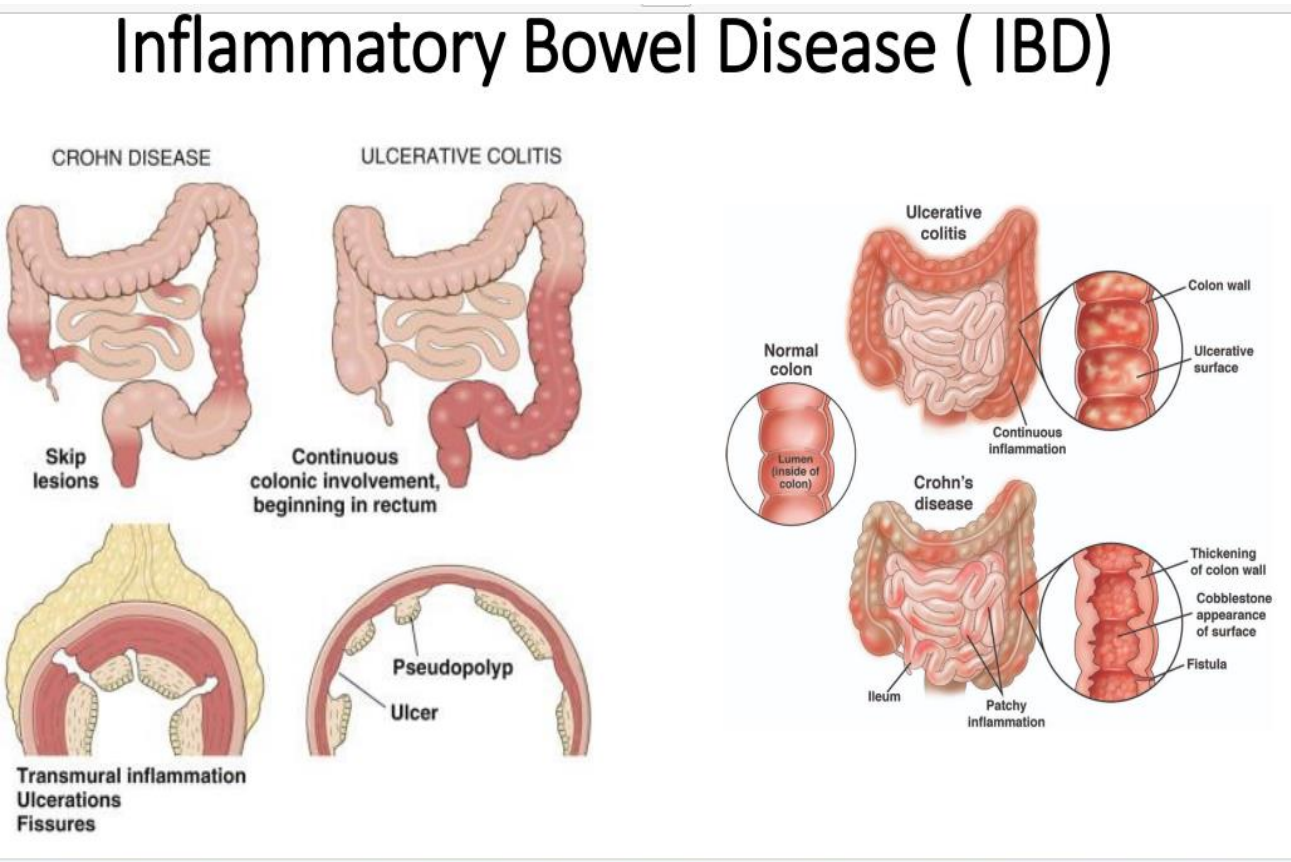
GI pharma

Inflammatory bowel disease summary



IBD signs and symptoms(very similar to bacterial gastroenteritis)→ Chronic intermittent diarrhea, rectal bleeding(hematochezia), Mucous in stool, constitutional symptoms.

General approach to treatment: Remission then maintenance of remission (less side effect therapy because no cure)

- **Resolution of acute inflammatory processes**
- Resolution of complications (e.g. fistulae and abscesses)
- Alleviation of extraintestinal manifestations
- **Maintenance of remission**

Aminosalicylates	Corticosteroid	Biologics	Immunomodulators
• Aminosalicylic acids (5-ASA) are chemically related to **aspirin.** • Control inflammatory process • For both **induction and maintenance of remission**. • **First line** for mild to moderate **ulcerative colitis (UC)** not as effective for **Crohn's disease.** **Why? Because Crohn's disease inflammation involves much deeper layers of colon.** **The charged 5-ASA can't penetrate these layers.** • **Azo compounds(oral formulation include: Balsalazide, Olsalazine, sulfasalazine) are pro- drug** that are cleaved by colonic bacteria to:- 1. **Mesalamine=5ASA** (responsible for efficacy) 2. **Sulphapyridine** (mainly responsible for its adverse effect). • Mesalamine can be given as **single molecule enclosed within enteric coat or semipermeable coat membrane** (oral and rectal formulation)→ Less sides effects. Mainstay of therapy in **UC**	• Anti-inflammatory effect. • For **inducing remission(UC and CD).** **Why can't be used for maintenance? Because of systemic adverse effects.** • Oral: **budesonide** (delayed or extended release), **hydrocortisone, prednisolone and methylprednisolone** • Intravenous : hydrocortisone, and methylprednisolone . • Rectal: budesonide (foam or suppository), hydrocortisone(enema or foam).	1. TNF-α inhibitors 2. α-4 integrin inhibitors 3. IL-2/23 inhibitor (ustekinumab). • Increase risk of infection: evaluate for tuberculosis TNF-α inhibitors: **Adalimumab, certolizumab, Golimumab and infliximab.** • For **induction and maintenance of remission in IBD:** • **CD: First line in moderate and severe cases** • UC: **2nd line for who failed 5-ASA or unresponsive or dependent on corticosteroid.** • **loss of response because of Development of antidrug antibody** α-4 integrin inhibitors: • **Vedolizumab** • For **refractory UC and CD** • Side effects: headache, arthralgia, nausea , fatigue and musculoskeletal pain. • IL-2/23 inhibitor (ustekinumab): **For induction and maintenance of remission** in CD in **patient's refractory to or intolerant of TNF-α inhibitors.**	• For **maintenance of remission** 1.**Methotrexate(MTX) 2. Thiopurines** Methotrexate(MTX): • Structural analogue of **folic acid** • **Monotherapy for maintenance of remission in CD but not for UC** • **Sides effects:** headache, nausea , vomiting and Rash. **Improved with folic acid.** Thiopurines: • **6-mercaptopurine (6-MP)and azathioprine.** • For **maintenance of remission in CD and UC** • **Limited use due to its toxicity: bone marrow suppression and hepatotoxicity.** • Needs monitoring: **complete blood count and liver function test are required to monitor toxicity**

• Absorption of Aminosalicylates:-

- **Increases** with severe disease - **Decreases** with **decreasing pH**

• **Coadministration of PPIs or H2 receptor antagonist increases mesalamine absorption** (high Ph increases mesalamine absorption).

However. **this is not favorable** as **increasing mesalamine absorption results in premature release of mesalamine before reaching the site of action.**

• So, **it should be avoided or switch to another 5-ASA that are non-pH dependent** as **Olsalazine**

Adverse effects:-

• **Sulfasalazine:-**

Folate administration is recommended as sulfasalazine inhibits folate absorption→anemia!!
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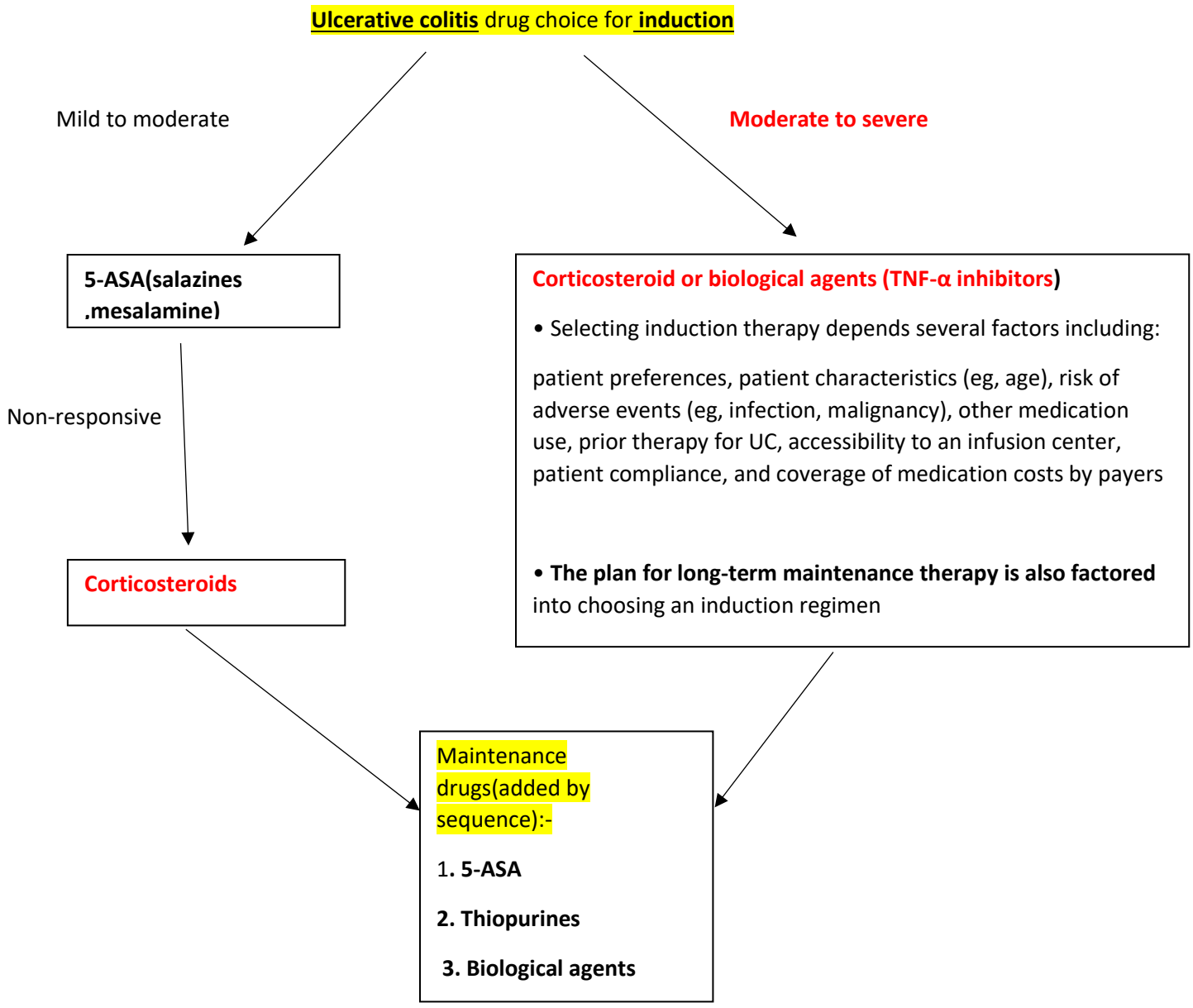
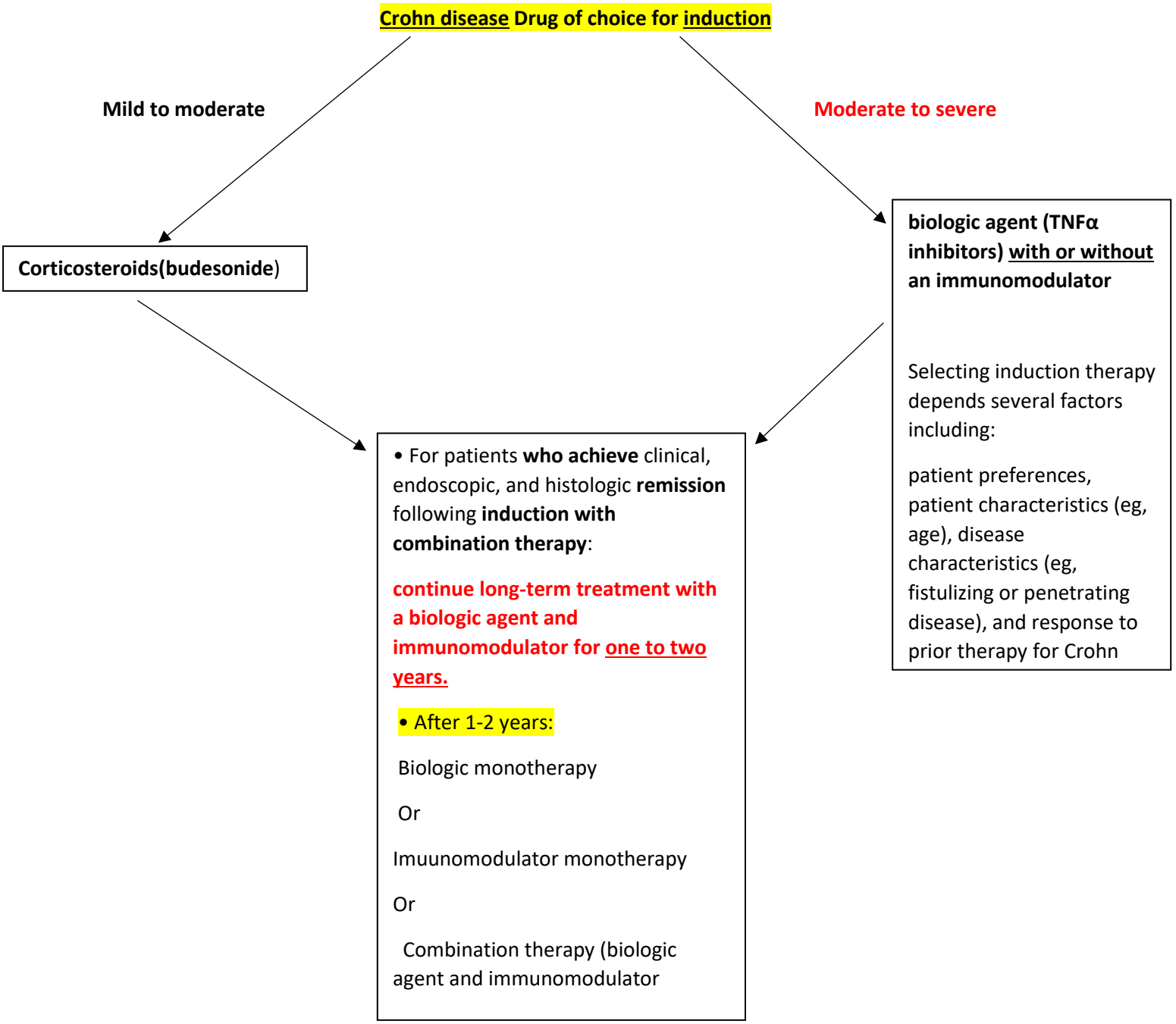
• headache, nausea and fatigue.

• **Reversible male infertility**

•. **Serious reactions**: **hemolytic anemia , nephritis, pneumonitis,**

fever, rash, Steven-Johnson syndrome. Mesalamine: • Well tolerated • Headache, dyspepsia • Rarely : acute interstitial nephrites			




Crohn disease Drug of choice for induction
Mild to moderate
Moderate to severe
Corticosteroids(budesonide)
biologic agent (TNFα inhibitors) with or without an immunomodulator
Selecting induction therapy depends several factors including:
patient preferences, patient characteristics (eg, age), disease characteristics (eg, fistulizing or penetrating disease), and response to prior therapy for Crohn
• For patients who achieve clinical, endoscopic, and histologic remission following induction with combination therapy:
continue long-term treatment with a biologic agent and immunomodulator for one to two years.
• After 1-2 years:
Biologic monotherapy
Or
Imuunomodulator monotherapy
Or
Combination therapy (biologic agent and immunomodulator