GI Pharmacology Summary

Drug	MOA	Uses	Side Effects	Notes
Drugs Used to Inhibit or Neutralize Gastric Acid Secretions				
Antacids	AL(OH)3 + HCl → ALCl3 + H2O 2HCl+Mg(OH)2 → MgCl2 + 2H2O	Nonprescription remedies for treatment of heartburn &dyspepsia.		Given 1 hour after a meal effectively neutralizes gastric acid for up to 2 hours.
Aluminum antacids			Constipation Interfere with absorption of many drugs	
Magnesium-antacids	have laxative action		diarrhea	ionic magnesium stimulates gastric release (acid rebound)
Magnesium trisilicate	slow-acting antacid			Combination of Magnesium & aluminum antacids are most commonly used (No diarrhea or constipation)
Calcium carbonate	2HCl + CaCO3 → CaCl2 + CO2+ H2O		with excessive chronic use, it may cause milk-alkali syndrome with elevation of serum calcium, phosphate, urea, nitrogen, creatinin & bicarbonate levels.	associated with "acid rebound"
Sodium bicarbonate	NaHCO3 + HCl → NaCl + H2O +CO2		-Highly absorbed, potentially causing metabolic alkalosis. -CO2 results in gastric distention and belching.	Should be avoided as it aggravates CHF & counteracts diuretic therapy for hypertension. -Short duration of action, followed by acid rebound.
H2-Receptor Antagonists (Cimetidine, Ranitidine, Famotidine Nizatidine)	# Inhibit 90% of nocturnal acid (depends on histamine). # Modest impact on meal-stimulated acid secretion (which is stimulated by gastrin, Ach and histamine). # Inhibit 60% of daytime, meal stimulated acid. #Inhibit 60-70% of total 24-h acid secretion.	Gastroesophageal Reflux Disease (GERD): Taken prophylactically before meals. In erosive esophagitis H2 antagonists healing is less than 50% hence PPI are preferred. Non-Ulcer Dyspepsia. Over-the-counter agents for treatment of intermittent dyspepsia not caused by peptic ulcer. Prevention of Bleeding from Stress-Related Gastritis: IV H2 antagonists are preferable over IV PPI because of their proven efficacy and lower cost. Peptic Ulcer Disease: Replaced by PPI.	Extremely safe drugs. Diarrhea, headache, fatigue, myalgias, and constipation (3%). Cimetidine may cause gynecomastia & impotence in men (antiandrogenic effects) and galactorrhea in women Drug Interactions: Cimetidine inhibits cytochrome P450 enzymes so can increase half-life of many drugs. Ranitidine binds 4-10 times less. Nizatidine and famotidine binding is negligible	Rapidly absorbed from intestine. Cimetidine, ranitidine, famotidine first-pass metabolism bioavailability 50%. Nizatidine has little first-pass metabolism. Duration of action: 6–10 hours, given twice daily. - Healing rate more than 80-90% after 6-8 wks. Not effective in the presence of H. pylori. Not effective if NSAID is continued.

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Proton Pump Inhibitors (PPIs): **Lipophilic weak bases absorbed in small intestine and delivered to parietal cell through the blood.**	Drug is protonated and "trapped" in acidic canaliculi. Concentrated more than 1000-fold in the parietal cells. Converted to the active form which covalently binds the H+/K+ ATPase enzyme and inactivates it.	Gastroesophageal Reflux (GERD): The most effective agents in all forms of GERD Nonulcer Dyspepsia: Modest activity.10 - 20% more beneficial than a placebo. Stress- Related Gastritis: Oral immediate-release omeprazole administered by nasogastric tube. For patients without a nasoenteric tube, IV H2-blockers are preferred because of their proven efficacy. Gastric acid hypersecretory states, including Zollinger-Ellison syndrome: Usually high doses of omeprazole are used. Peptic Ulcer Disease: They heal more than 90% of cases within 4-6 weeks. **Pylori - associated ulcers**: PPI eradicate H. pylori by direct antimicrobial activity and by lowering MIC of the antibiotics. **NSAID-associated ulcers:** Healing despite continued NSAID use. Also used to prevent ulcer of NSAIDs. Rebleeding peptic ulcer: Oral or IV. High pH may enhance coagulation and platelet aggregation.	Well tolerated. May cause headache, diarrhea, abdominal pain, nausea & dizziness Reduction of cyanocobalamin (vitamin B12) absorption. Increased risk of GI and pulmonary infection. Increased serum gastrin levels causes: Chronic inflammation in gastric body, Atrophic gastritis and intestinal metaplasia. Drug Interactions: May affect absorption of drugs due to decreased gastric acidity like digoxin and ketoconazole.	Among the most widely prescribed drugs worldwide due to their outstanding efficacy and safety. Have short half-lives but effect lasts for 24 hours. At least 18 hours are required for synthesis of new pump molecules. Inhibit both fasting & meal-stimulated secretion (90-98% of 24-hour secretion). The full acid-inhibiting potential is reached in 3 to4 days. Treatment for PUD: Triple Therapy: PPI twice daily + Clarithromycin 500 mg twice daily +Amoxicillin 1gm twice daily, OR, Metronidazole 500mg twice daily.
Omeprazole Lansoprazole Esomeprazole (Nexium)				available as capsules of enteric-coated granules. -Omeprazole is taken Orally -Lansoprazole and Esmeprazole Orally & IV
Rabeprazole Pantoprazole				are tablets with a pH-sensitive coating. Prodrugs released in the intestine (Destroyed by acid). -Rabeprazole(Orally) -Pantoprazole(Orally & IV)
Immediate-Release Omeprazole				contains sodium bicarbonate to protect the drug from acid degradation results in rapid response.

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Mucosal Protective Agents	1-Both mucus and epithelial cell-cell tight junctions restrict back diffusion of acid and pepsin. 2-Epithelial bicarbonate secretion. 3-Blood flow carries bicarbonate. 4- injured epithelium are repaired by restitution 5-Mucosal prostaglandins stimulates mucus and bicarbonate secretion and mucosal blood flow.			
Sucralfate	The negatively charged sucrose sulfate binds to positively charged proteins in the base of ulcers or erosion, forming a physical barrier that restricts further caustic damage and stimulates mucosal prostaglandin and bicarbonate secretion.	1g four times daily on an empty stomach (through a nasogastric tube) reduces the incidence of upper GI bleeding in critically ill patients hospitalized in the intensive care unit and Prevention of stress-related bleeding because acid inhibitory therapies may increase the risk of nosocomial pneumonia (an infection of the lungs that occurs during a hospital stay).	Not absorbed, so no systemic adverse effects. Constipation (2%) due to the aluminum salt. Caution in renal insufficiency. Drug Interactions: Sucralfate may bind to other medications, impairing their absorption.	A salt of sucrose complexed to sulfated aluminum hydroxide. In the stomach, It breaks down into sucrose sulfate (strongly negatively charged) and an aluminum salt. Acts for 6 hours. Less than 3% of intact drug and aluminum is absorbed.
Prostaglandin Analogs (Misoprostol)	1-Stimulates mucus & bicarbonate secretion. 2- Enhances mucosal blood flow. 3- Acts on parietal cells, reducing histamine-stimulated cAMP production and causing modest acid inhibition. 4- Stimulates intestinal electrolyte & fluid secretion, 5-Increase intestinal motility 6- Uterine contractions.	Prevention of NSAID-induced ulcers in high-risk patients. Not widely used for this purpose because of: a- side effects. b. need for multiple daily dosing. c. PPI may be as effective and better tolerated. d.Cyclooxygenase2-selective NSAIDs are an option for such patients.	Diarrhea and cramping abdominal pain (10–20%). it should not be used during pregnancy No significant drug interactions.	A methyl analog of PGE1. Half-life is less than 30 min Administered 3-4 times daily.
Colloidal Bismuth Compounds: Bismuth subcitrate Bismuth subsalicylate.	Reduce the gastric HCL secretion. Help in eradication of H. pylori. Stimulates the PGE secretion. Reduce pepsin secretion. Decrease H+ ion back diffusion.	Widely used for the nonspecific treatment of dyspepsia and acute diarrhea. Has direct antimicrobial activity against H pylori and used as second-line therapy for the eradication of H pylori infection. **PPI with**	Blackening of the stool and the tongue. Prolonged usage may rarely lead to bismuth toxicity, resulting in encephalopathy.	-Bismuth is minimally absorbed from GIT (< 1%). -A mucosal protective agent, provides coat on the ulcer. -Bismuth subsalicylate reduces stool frequency and liquidity in acute infectious diarrhea, due to salicylate inhibition of intestinal prostaglandin

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Colloidal Bismuth Compounds (Cont.)		**bismuth subsalicylate , tetracycline and metronidazole for 10–14 days).**		and chloride secretion. Has direct antimicrobial effects & binds enterotoxins, so useful in preventing & treating traveler's diarrhea.
Drugs Stimulating GI Motility (Pro-kinetic agents)	The enteric nervous system can independently regulate GI motility and secretion. The myenteric interneurons control: peristaltic reflex, promoting release of excitatory mediators proximally and inhibitory mediators distally. Motilin may stimulate excitatory neurons or muscle cells directly. Dopamine acts as an inhibitory neurotransmitter in the GIT, decreasing the intensity of esophageal and gastric contractions.	Potential uses: Increasing lower esophageal sphincter pressures, useful for GERD. Improving gastric emptying, helpful for gastroparesis and postsurgical gastric emptying delay. Stimulation of the small intestine useful for postoperative ileus. Enhancing colonic transit, useful in the treatment of constipation.		1-Gut distention stimulates 5-HT release from EC cells. 2-Stimulation of 5-HT3 receptors on the extrinsic afferent nerves, stimulate nausea, vomiting, or abdominal pain. 3- 5-HT also stimulates 5-HT1P receptors of the intrinsic primary afferent nerves (IPANs) which activate the enteric neurons responsible for peristaltic and secretory reflex activity. 4- Stimulation of 5-HT4 receptors (5-HT4R) on presynaptic terminals of IPANs enhances release of ACh & calcitonin gene related peptide (CGRP), promoting reflex activity.
Cholinomimetic Agents				
Bethanechol	Stimulates muscarinic M3 receptors on muscle cells and at myenteric plexus synapses .	**Was** used for the treatment of GERD and gastroparesis.		
Neostigmine	AchE inhibitor enhances gastric, small intestine, and colonic emptying.	IV neostigmine used for the treatment of acute large bowel distention (acute colonic pseudo-obstruction).	Administration of 2 mg results in prompt colonic evacuation of flatus and feces. Cholinergic effects include excessive salivation, nausea, vomiting, diarrhea, and bradycardia.	
Laxatives				Intermittent constipation is best prevented with: #a high-fiber diet. #adequate fluid intake.# responding to nature's Call.# Regular exercise.
Bulk-Forming Laxatives	Indigestible, hydrophilic colloids that absorb water, forming a bulky, emollient gel that distends the colon and promotes peristalsis.		Bacterial digestion of plant fibers within the colon may lead to increased bloating and flatus.	Effective within 1-3 days. Common preparations include natural plant products (psyllium, methylcellulose, bran) and synthetic fibers (polycarbophil).

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Dopamine D2-receptor antagonists. Metoclopramide & Domperidone	These agents block D2 receptors causing :-increase esophageal peristaltic amplitude. -increase lower esophageal sphincter pressure.-enhance gastric emptying.-have no effect on small intestine or colonic motility. Also block dopamine D2 receptors in the chemoreceptor trigger zone of the medulla (area postrema), resulting in potent anti nausea and antiemetic actions.	Gastroesophageal Reflux Disease Not effective with erosive esophagitis. Not superior to antisecretory agents. Used mainly in combination with antisecretory agents in patients with refractory heartburn. Impaired Gastric Emptying (Gastroparesis) widely used in post surgical and diabetic gastroparesis. Nonulcer Dyspepsia Prevention of Vomiting. Postpartum Lactation Stimulation. Domperidone is used to promote postpartum lactation.	Metclopromide crosses BBB so can cause: Restlessness, drowsiness, insomnia, anxiety, agitation, extrapyramidal symptoms (dystonia, akathisia, parkinsonian features) and tardive dyskinesia. Domperidone does not cross the BBB, so does not cause CNS effects. **Both drugs can elevate serum prolactin levels causing galactorrhea, gynecomastia, impotence and menstrual disorders**.	Dopamine acts as an inhibitory neurotransmitter in the GIT, decreasing the intensity of esophageal & gastric contractions.
Stool Surfactant Agents (Softeners)				
Docusate	Detergents or surfactants that act as stool-wetting and stool-softening agents, allowing the mixing of water, lipids, and fecal matter. Alters intestinal permeability and increases net water and electrolyte secretions in the intestine.	Used in symptomatic treatment of constipation & in painful anorectal conditions such as hemorrhoids and anal fissures.		Orally: Softening of feces within 1-3 days. Rectally: effective within 5 to 20 minutes.
Glycerin suppository	works by irritating the lining of the intestine and increasing the amount of fluid, making it easier for stools to pass.			
Lubricant/ Emollient	Causing lubrication of the stool & make it slippery, so that it slides through the intestine more easily. It is not absorbed and increase the bulk of the intestinal contents as it reduces the water absorption			Site of Action: Colon. Onset of Action: 6 - 8 hours.
Liquid paraffin		Used to prevent and treat fecal impaction.	Aspiration can result in a severe lipid pneumonitis. Long-term use can impair absorption of fat-soluble vitamins.	-Not recommended for regular use. - Can slip out of anal sphincter and causes embarrassment.

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Osmotic Laxatives	Soluble but non-absorbable compounds that result in increased stool liquidity due to an increase in fecal fluid.			
Magnesium hydroxide (milk of magnesia)			Large doses of magnesium citrate & sodium phosphate cause purgation: rapid bowel evacuation within 1-3 h. This might cause volume depletion.	Not used for prolonged periods in renal insufficiency due to the risk of hypermagnesemia.
Lactulose	Disaccharide, not absorbed causing retention of water through osmosis leading to softer, easier to pass stool.	Drug of choice in hepatic encephalopathy to trap NH3. Lactulose is converted into lactic acid, which decreases the luminal pH. So, NH3 is trapped and prevented from absorption.	in the colon, it is fermented by the gut flora producing osmotic metabolites causing **severe flatus and cramps**.	
Balanced Polyethylene Glycol	It is a laxative solution that increases the amount of water in the intestinal tract to stimulate bowel movements.	used to clean the bowel before colonoscopy, a barium x-ray or other intestinal procedures. For colonic cleansing, it is ingested rapidly (4L over 2-4 h). For chronic constipation, PEG powder is mixed with water or juice.		Safe solution: no intravascular fluid or electrolyte shifts. Does not cause cramps or flatus. PEG is an inert, non-absorbable, cosmetically active sugar. It also contains Sodium sulfate, bicarbonate and potassium chloride to replace electrolytes that are passed from the body in the stool
Stimulant Laxatives	Direct stimulation of the enteric nervous system and colonic electrolyte and fluid secretion.			
Anthraquinone Derivatives: Aloe, senna, and cascara			Chronic use leads to a brown pigmentation of the colon known as "**melanosis coli.**"	Occur naturally in plants. Poorly absorbed & after hydrolysis in the colon, produce a bowel movement in 6–12h when given orally and within 2h rectally.
Bisacodyl		Tablet and suppository for treatment of acute and chronic constipation		induces bowel movement within 6–10 h orally and 30–60 minutes rectally. Safe for acute and long-term use
Phenolphthalein			Removed from the market owing to concerns about possible cardiac toxicity.	
Castor Oil	Hydrolyzed in upper intestine into Ricinoleic acid	**Was** used as purgative to clean the colon before procedures.		-Ricinoleic acid is a local irritant.

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Opioid Receptor Antagonists	Block **peripheral** (μ) mu opioid receptors without central analgesic effects.			Do not cross the BBB.
Methylnaltrexone		Used for opioid - induced constipation in patients with advanced illness not responding to other agents.		SC injection every 2 days.
Alvimopan		Short-term use for postoperative ileus in hospitalized patients.		Given within 5 hours before surgery and twice daily after surgery until bowel function has recovered, but for no more than 7 days, because of possible **cardiovascular toxicity**. -Used Orally
Antidiarrheal Agents				
Loperamide	Opioid Agonists: Increase colonic transit time and fecal water absorption & decrease mass colonic movements		- Does not cross brain-blood-barrier so no analgesic or addiction potential.	
Diphenoxylate	Opioid Agonists: Increase colonic transit time and fecal water absorption & decrease mass colonic movements		Higher doses have CNS effects. Can cause dependence.	-Not analgesic in standard doses -Commercial preparations contain small amounts of atropine Lomotil, Diphenoxylate and Atropine which contribute to the antidiarrheal action.
Cholestyramine Colestipol Colesevelam	They bind bile salts and decrease diarrhea caused by excess fecal bile acids.		-Can cause bloating, flatulence, constipation and fecal impaction. -Cholestyramine and colestipol reduce absorption of drugs and fat, but Colesevelam does not.	Malabsorption of bile salts cause diarrhea. (Crohn's disease or after surgical resection).
Octreotide	Synthetic octapeptide with actions similar to somatostatin	- Inhibition of endocrine tumor effect (Carcinoid and VIPoma) - Diarrhea due to vagotomy or dumping syndrome or short bowel syndrome and AIDS. - To stimulate motility in small bowel bacterial overgrowth or intestinal pseudo-obstruction secondary to scleroderma	- Impaired pancreatic secretion may cause steatorrhea which can lead to fat-soluble vitamin deficiency. -Nausea, abdominal pain, flatulence, and diarrhea. -Formation of sludge or gallstones, because of inhibition of gallbladder contractility and fat absorption.	

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Octreotide (Cont.)		- It inhibits pancreatic secretion, so used in patients with pancreatic fistula - treatment of pituitary tumors - Sometimes used in gastrointestinal bleeding	-Hyper or hypoglycemia due to hormonal imbalance. -Hypothyroidism. -Bradycardia.	
Drugs Used for Treatment of Irritable Bowel Syndrome (IBS)				
Dicyclomine Hyoscyamine	Block muscarinic receptors in the enteric plexus and on smooth muscle.	Treatment of Irritable Bowel Syndrome	-Low doses cause minimal autonomic effects. Higher doses cause anticholinergic effects, including dry mouth, visual disturbances, urinary retention, and constipation. For these reasons, antispasmodics are infrequently used.	- Antispasmodics (Anticholinergics) - Their efficacy for relief of abdominal symptoms has never been convincingly demonstrated.
Alosetron	Potent & selective antagonist of the 5-HT3 receptor.	-Restricted to women with severe diarrhea-predominant IBS not responding to conventional therapies.		- Antispasmodic (Anticholinergic) -Rapidly absorbed, half-life of 1.5h but has a much longer duration of effect -Its efficacy in men has not been established.
Prucalopride	High-affinity 5-HT4 agonist	- Used for the treatment of chronic constipation in women.	- No cardiovascular toxicity	-Antispasmodic (Anticholinergic)
Lubiprostone	PG analog stimulates type 2 chloride channel (ClC-2) in the small intestine & this increases liquid secretion in the intestine which stimulates intestinal motility & bowel movement within 24 hours of taking one dose.	- Used in the treatment of chronic constipation.	- Should be avoided in women of child-bearing age. -Nausea (30%) due to delayed gastric emptying	- Approved for the treatment of women with IBS with predominant constipation. Its efficacy for men with IBS is unproven.
Antiemetic Agents				
Ondansetron Granisetron	Serotonin 5-HT3 antagonists (Block central 5-HT3 and peripheral (main effect).	-Prevention of acute chemotherapy-induced nausea and emesis and postoperative nausea and vomiting	Headache, dizziness, and constipation.	-Prevent emesis due to vagal stimulation and chemotherapy. Other emetic stimuli such as motion sickness are poorly controlled. -Their efficacy is enhanced by combination therapy with dexamethasone and NK1-receptor antagonist.
Aprepitant	-Block central NK1receptors in the area postrema	-Used in combination with 5-HT3-receptor antagonists and corticosteroids for the prevention of acute and		

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Aprepitant (Cont.)		delayed nausea and vomiting from chemotherapy.		
Dronabinol, Nabilone	Mechanisms for these effects are not understood.	-Used for chemotherapy-induced vomiting.	Euphoria, dysphoria, sedation, hallucinations, dry mouth, and increased appetite.	-Cannabinoids (Psychoactive agents)
Prochlorperazine Promethazine Droperidol	Antiemetics due to blocking dopamine and muscarinic receptors.		-Sedative effects due to antihistamine activity.	-Antipsychotic drugs
Lorazepam Diazepam		-Reduce anticipatory vomiting caused by anxiety		-Benzodiazepines
Di-phenhydramine, Dimenhydrinate	-H1 Antihistamines & Anticholinergic Drugs	-Particularly useful in motion sickness.	-May cause dizziness, sedation, confusion, dry mouth, cycloplegia, and urinary retention.	-Have significant anticholinergic properties.
Meclizine	-H1 Antihistamine & Anticholinergic Drug	-Used for the prevention of motion sickness and the treatment of vertigo due to labyrinth dysfunction.	- May cause dizziness, sedation, confusion, dry mouth, cycloplegia, and urinary retention.	- Minimal anticholinergic properties and less sedating.
Hyoscine (scopolamine)	-H1 Antihistamines & Anticholinergic Drugs	-Particularly useful in motion sickness.	-May cause dizziness, sedation, confusion, dry mouth, cycloplegia, and urinary retention.	-Very high incidence of anticholinergic effects. It is better tolerated as a transdermal patch.
Drugs Used to Treat Inflammatory Bowel Disease				
5-aminosalicylic acid (5-ASA)	-Inhibition of cytokine, prostaglandin and leukotriene synthesis. - Free radical scavenging - Immunosuppressive activity (inhibits both T-cell proliferation and subsequent activation and differentiation) -Impairment of white cell adhesion and function.	-Treatment of inflammatory bowel disease - first-line agents for treatment of mild to moderate active ulcerative colitis. -Their efficacy in Crohn's disease is unproven, although used as first-line therapy for mild to moderate disease involving the colon or distal ileum.	-Due to systemic absorption: especially in slow acetylators: Nausea, headache, arthralgia, myalgia, bone marrow suppression, and malaise. -Also allergic reactions, oligospermia, and folate deficiency.	--Aminosalicylates work topically (not systemically) in areas of diseased gastrointestinal mucosa. -Up to 80% of unformulated 5-ASA is absorbed from the small intestine and does not reach the distal small bowel or colon. -A number of formulations deliver 5-ASA to various distal segments of the small bowel or the colon.
Azo Compounds (Sulfasalazine, Balsalazide, Olsalazine)	-Bind to 5-ASA (5-ASA bound by an azo (N=N) bond) → azo structure -In the terminal ileum and colon, resident bacteria cleave the azo bond by an azoreductase enzyme, releasing 5-ASA.	-Deliver 5-ASA to various distal segments of the small bowel or the colon.		-The azo structure markedly reduces absorption of the parent drug from the small intestine.
Pentasa	Timed-release microgranules	-Release 5-ASA throughout the small intestine		Mesalamine Compound
Asacol		- Deliver 5-ASA to various distal segments of the small bowel or the colon.		- 5-ASA coated in a pH-sensitive resin that dissolves at the pH of the distal ileum and proximal colon

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Enema (Rowasa) Suppositories (Canasa)		- Deliver 5-ASA to various distal segments of the small bowel or the colon.		
Glucocorticoids (Prednisolone, Hydrocortisone, Budesonide)	-Inhibit production of inflammatory cytokines and chemokines. -Reduce expression of inflammatory cell adhesion molecules. - inhibit gene transcription of nitric oxide synthase, phospholipase A2, cyclooxygenase-2, and NF- B.	-Treatment of inflammatory bowel disease (Moderate to severe active IBD. Not useful for maintenance)		-Prednisolone: Orally or IV. -Hydrocortisone: Rectally for rectal and sigmoid involvement. -Budesonide: A controlled-release oral formulation ,releases the drug in the distal ileum and colon for ileal and proximal colon involvement.
Azathioprim, 6-Mercaotopurine	-Immunosuppressants. Inhibit purine nucleotide metabolism and DNA synthesis and repair, resulting in inhibition of cell division and proliferation and may promote T-lymphocyte apoptosis.	-Onset delayed for 17 weeks. -Used in induction and maintenance of remission. -Allow dose reduction or elimination of steroids.	Nausea, vomiting, bone marrow suppression, hepatic toxicity and allergic reactions(fever, rash, pancreatitis, diarrhea and hepatitis).	-Antimetabolites (Purine analogs; which produce thioguanine nucleotides (Active form). *Allopurinol increases levels of the drugs.
Methotrexate	-Inhibition of dihydrofolate reductase enzyme which is important in the synthesis of thymidine and purines. -At high doses, it inhibits cellular proliferation. -At low doses used in IBD, it interferes with the inflammatory actions of interleukin-1, stimulates adenosine release, apoptosis and death of activated T lymphocytes.	-Antimetabolite, Used in cancer chemotherapy, rheumatoid arthritis and psoriasis. -Induction and maintenance of remissions of Crohn's Disease.	-At high doses, can cause: bone marrow depression, megaloblastic anemia, alopecia and mucositis. Renal insufficiency may increase risk of hepatic accumulation and toxicity.	- Side effects counteracted by folate supplementation.
Infliximab	- binds to both soluble & transmembrane forms of TNF- α and inhibits their ability to bind to TNF receptors and may cause lysis of these cells.	- Used in moderate to severe Crohn's disease. Also used in acute and chronic treatment of patients with for refractory ulcerative colitis	-Acute: fever, chills, urticaria, or even anaphylaxis -Delayed : serum sickness–like reactions may develop after infliximab infusion, but lupus-like syndrome occurs only rarely. - Therapy is associated with increased incidence of respiratory infections; reactivation of TB. -Contraindicated in severe congestive heart failure.	- A chimeric immunoglobulin (25% mouse, 75% human) - Given by IV infusion. -Half life 8-10 days with persistence of antibodies in plasma for 8-12 weeks. - Response might be lost due to development of antibodies to infliximab. - Antibodies to infliximab can decrease its clinical efficacy

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Adalimumab	- Anti-Tumor Necrosis Factor Therapy			- Fully humanized IgG antibody, given SC.
Certolizumab	- Anti-Tumor Necrosis Factor Therapy		- immunogenicity appears to be less of a problem than that associated with infliximab.	- Polyethylene glycol Fab fragment of humanized anti-TNF-α, also given SC.
Natalizumab	-An antibody against the cell adhesion molecule α 4-integrin subunit. -Prevents binding of several integrins on circulating inflammatory cells to vascular adhesion molecules	-Used for patients with moderate to severe Crohn's disease who have failed other therapies	-Acute infusion reactions & a small risk of opportunistic infections	- Anti-Tumor Necrosis Factor Therapy -Humanized IgG4 monoclonal antibody -Given by IV infusion every 4 weeks, and patients should not be on other immune suppressants to prevent the risk of progressive multifocal leukoencephalopathy (rare and usually fatal viral disease)
Pancreatic Enzyme Supplements				
Pancrelipase		-To treat pancreatic enzyme insufficiency	-Excessive doses may cause diarrhea and abdominal pain. -The high purine content of pancreas extracts may lead to hyperuricosuria and renal stones.	-Available in both non-enteric-coated (given with acid suppression therapy) & enteric-coated preparations. -Administered with each meal and snack. -In general, pancreatic enzyme supplements contain a mixture of amylase, lipase, and proteases.
Drugs Used to Treat Variceal Hemorrhage				
Somatostatin & Octreotide	-They inhibit the release of glucagon and other gut peptides that alter mesenteric blood flow.	-In patients with cirrhosis and portal hypertension, intravenous somatostatin or octreotide reduces portal blood flow and variceal pressures. -They promote initial homeostasis from bleeding esophageal varices.		-They are generally administered for 3–5 days.
Beta-Receptor-Blocking Drugs	-Beta-receptor antagonists reduce portal venous pressures via a decrease in portal venous inflow.	-Nonselective β blockers significantly reduce the rate of recurrent bleeding (Non-selective blockers such as propranolol and nadolol are more effective than β1-selective)		-The decrease is due to a decrease in cardiac output (β1 blockade) and to splanchnic vasoconstriction (β2 blockade) caused by the unopposed effect of systemic catecholamines on α receptors.
Vasopressin	-IV infusion causes splanchnic arterial vasoconstriction that leads to reduced splanchnic perfusion and lowered portal venous pressures.	-Vasopressin was commonly used to treat acute variceal hemorrhage. Because of its high adverse-effect profile, it is no longer used for this purpose.	- hypertension, myocardial ischemia or infarction, or mesenteric infarction. Nausea, abdominal cramps, and diarrhea (due to intestinal hyperactivity). vasopressin promotes	-Antidiuretic hormone -A potent arterial vasoconstrictor. -Side effects are common -Terlipressin is a vasopressin analog that have similar efficacy to vasopressin with fewer

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Vasopressin (Cont.)		-In patients with acute gastrointestinal bleeding from small bowel or large bowel vascular ectasias or diverticulosis, vasopressin may be infused—to promote vasospasm—into one of the branches of the superior or inferior mesenteric artery through an angiographically placed	retention of free water, which can lead to hyponatremia, fluid retention, and pulmonary edema.	adverse effects

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