Constipation + Diarrhea - Classes of medication

Bulk-forming agents *Psyllium, polycarbophil*	Ferment in the colon → gas formation, increased osmotic load, water retention and wall stress → stimulates motility Swell in intestinal fluid → creates gel → facilitate passage
Osmotic agents *glycerin (suppository), lactulose, polyethylene glycol (PEG) 3350, magnesium citrate, sodium phosphate, magnesium hydroxide (milk of magnesia), sorbitol*	Contain poorly absorbed ions or molecules that create an osmotic gradient to retain water within the intestinal lumen – the ↑ pressure on the intestinal wall induces gastric motility Used for bowel evacuations before procedures (if high, frequent dosing) or for daily maintenance/-prevention (if low, daily dosing) BM within 30 mins (high, frequent doses) -> 3 days (low daily doses)
Stimulants *Senna/sennosides (Senokot®, Senokot-S®) Bisacodyl (Dulcolax®) Sodium picosu-lfate (Pico-Salex®) Castor oil*	Stimulate the smooth muscle to produce rhythmic contractions May be recommended if osmotic laxatives fail or not tolerated Sometimes referred to as a "rescue agent" A dose effective in one individual may cause painful cramping in the next BM within 6-12 hours (often overnight use)

Constipation + Diarrhea - Classes of medication (cont)

Stool softeners *Docusate sodium or docusate calcium*	Act as a surfactant → better mixing of aqueous and fatty substances to soften the fecal mass A preventative measure rather than a "rescue" Sometimes added to other laxatives (for the "gentle" touch) Most recent evidence suggests not better than placebo What to expect: BM in 1 - 5 days
Lubricants	Lubricates contents of GI tract and keeps water in GI tract Limited use -> after myocardial infarction or rectal surgery Mineral oil (heavy) – only one suitable for consumption Not recommended due to risk of aspiration → lipid pneumonia, binding of fat soluble vitamins/meds, and anal seepage What to expect: BM in 6-8 hours – avoid lying down or bedtime dosing

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Constipation + Diarrhea - Classes of medication (cont)

Suppositories & Enemas *Mineral oil retention enema, Phosphate enema, Tap water enemaMicrolax® Enema (sodium citrate, sodium laurel sulfoacetate)*	For acute relief or bowel prep for procedure Not for management of chronic constipation Presence of object in rectum stimulates defecation reflex This is in addition to any benefits provided by specific ingredient (i.e. glycerin – osmotic; mineral oil – lubricant) Patient should try to retain (hold in) product as long as possible (generally a few minutes) What to Expect: Cleansing of bowel within 1 hour; if no BM – call physician Not pleasant, therefore not the preferred route
Antidiarrheals	
Adsorbant agents *attapulgite (Kaopectate®, Fowler's®)*	Adsorbs fluid in intestine, reducing stool liquidity May give some relief, very safe (can use in kids)
Antimotility agents *loperamide (Imodium®), belladonna, diphenoxylate*	Opioid agonists that do not cross blood-brain barrier Dependence and tolerance with long-term use? NOPE
Antisecretory agents *bismuth subsalicylate (Pepto-Bismol®)*	Stimulates absorption of fluid and electrolytes across intestinal wall; also bactericidal (e. coli)and anti-inflammatory Not for children (related to ASA Reye's) Good option for traveller's diarrhea
Bulk-Forming agents *psyllium (Metamucil®)*	Identical mechanism as with constipation Creates "gel" using excess fluid in GI tract

Constipation + Diarrhea - Classes of medication (cont)

Loperamide (Imodium®)	Slows intestinal motility by stimulating opioid receptor, which reduces fecal volume and increases viscosity Very high first-pass effect and poor penetration of blood-brain barrier No dependence or tolerance with long-term use Also useful for radio- or chemo-induced diarrhea

Adverse effects of medication for the GI tract

Bulk-forming Agents	flatulence, bloating are common
Osmotic Agents	nausea, abdominal bloating, cramping, diarrhea, flatulence, skin rashes/hives
Stimulants	: bloating, abdominal discomfort, flatulence, diarrhea Highest incidence of cramping/pain (due to muscle contractions) Caution: Avoid in pregnancy if possible (do not stimulate!) Avoid if sensitive to electrolyte or fluid abnormalities
Stool softeners	bloating, abdominal discomfort, flatulence
Lubricants	allergic reactions, anal seepage, alteration of vitamins/minerals/drugs
Suppositories & Enemas	discomfort, bloating, cramping, allergic reactions
Loperamide (Imodium®)	cramping, discomfort, skin rash, dry mouth; Possible CNS usually only if compromised BBB = drowsiness, dizziness, confusion (rare)
Dimenhydrinate (Gravol®)	drowsiness + anticholinergic effects
Doxylamine + Pyridoxine (Diclectin®)	drowsiness, fatigue

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Adverse effects of medication for the GI tract (cont)

Domperidone	headache, menstrual irregularities, dry mouth, diarrhea, abdominal discomfort
Ondansetron (Zofran®)	headache, dizziness, drowsiness, constipation, diarrhea (all rare)
H2-Antagonists	headache, dizziness, drowsiness Difficult to differentiate between heartburn symptoms and some adverse effects (nausea, vomiting, constipation, diarrhea) Very rare – reduction in RBC, WBC, and platelets; bradycardia, allergic reactions Because of reduction in acidity, it can potentially interact with absorption of drugs or vitamins (like B12) that need an acidic environment to absorb Separate as much as possible, while also understanding that we want prolonged reduction in acidity
Proton Pump Inhibitors (PPIs)	very well tolerated; limited to headache, diarrhea, flatulence, nausea, abdominal pain Long-term (years): decrease in bone mineral density + others via post-marketing surveillance

Adverse effects of medication for the GI tract (cont)

Sucralfate	constipation or diarrhea, nausea, headache, indigestion, dry mouth Bezoars have been reported in people treated with sucralfate (most had comorbidities that contributed such as low gastric motility) May increase blood glucose due to high carbohydrate content
Antacids	Calcium – constipating Magnesium & aluminum – diarrhea, and can make stool a whiter colour
Misoprostol	headache, abdominal cramps, diarrhea, vaginal bleeding, uterine cramping
Aminosalicylates *5-ASA (Asacol®)*	nausea, diarrhea, abdominal pain, headache, rash, rhinitis, photosensitivity Meds are well tolerated; can be difficult to discern adverse effects from condition
Immunosuppressants *Methotrexate (MTX)*	ulcerative stomatitis, leukopenia, nausea, abdominal distress, malaise, fatigue, chills & fever, dizziness, decreased resistance to infection
Pancreatin (Creon®)	Rare - nausea, vomiting, diarrhea
Local anesthetics (dibucaine, pramoxine)	Use > 7 days: possible CNS effects (restlessness, excitement, nervousness, paresthesias, dizziness, tinnitus, blurred vision, nausea and vomiting, muscle twitching and tremors, convulsions) and cardiovascular effects (hypotension, bradycardia)
Corticosteroids (hydrocortisone)	Use > 14 days, mucosal atrophy

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Nausea, & Vomiting - Classes of medication

Dimenhydrinate (Gravol®)	An antihistamine (with anticholinergic activity){{nl{{ Only effective for nausea & vomiting caused by motion sickness (vestibular apparatus) Used for all types of nausea (like a virus…..) inappropriately (sedation may provide benefit)
Doxylamine + Pyridoxine (Diclectin®)	Prescription product specifically for nausea and vomiting during pregnancy Mechanism of action largely unknown Doxylamine = antihistamine; pyridoxine = vitamin B6 Safe for baby Used when concerned about proper nutrition Effect ~ 8 hours after dose
Domperidone	Mechanism of action: a peripheral dopamine antagonist, that blocks dopamine receptors in the GI tract; also has pro-kinetic properties, which increases peristalsis to improve gastric emptying rates Also stimulates release of prolactin – used to enhance milk production while breastfeeding (see Module 8) Primary use: antiemetic for multiple GI conditions, prevention of nausea & vomiting with concurrent medications (chemo), enhance milk production, GERD

Nausea, & Vomiting - Classes of medication (cont)

Ondansetron (Zofran®)	Mechanism of action: serotonin receptor antagonist in chemoreceptor trigger zone and along GI tract (CTZ) Primary use: chemotherapy induced nausea & vomiting Occasionally used in severe nausea & vomiting in pregnancy (concerned about baby nutrition)

PUD + GERD - classes of medication

H2-Antagonists *-tidine*	Blocks H2 receptors which prevents acid secretion; reduces the volume and acidity of secretions allowing a lesion to heal Can take up to 3 months to heal a lesion Cimetidine was first drug lots of significant drug interactions via CYP450 enzymes and significant adverse effects (gynecomastia) not widely used anymore but still available
Ranitidine (Zantac®), famotidine, nizatidine	Most effective if taken regularly (every day) to consistently reduce acid and allow lesion to heal Can also be used as needed (PRN) for heartburn by anyone Very safe, Smoking decreases the effectiveness of H2-antagonists (encourage smoking cessation)

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PUD + GERD - classes of medication (cont)

Proton pump inhibitors (PPIs) *-prazole*	Proton pumps = cells that are present in the lining of the stomach; their job is to 'pump' protons (H+) into the stomach for acid secretion PPIs inhibit this, preventing acid secretion, creating a less acidic environment for a lesion to heal ↓ acidity more than H2-antagonists (more effective) Also very safe; recently OTC A longer duration of action than H2-antagonists = less frequent dosing
Omeprazole, esomeprazole, lansoprazole, pantoprazole, rabeprazole	Have a longer onset of action than H2-antagonists (don't work as quickly) – would not be effective to use PRN (as needed) for heartburn
Sucralfate	A cytoprotective agent that adheres to and then protects ulcerated gastric or duodenal mucosa Product also contains aluminum, which lowers acidity of gastric contents

PUD + GERD - classes of medication (cont)

Antibiotics	Must be specific for h. pylori – breath tests confirm presence We attempt to completely eradicate the bacteria, due to extremely high rate of recurrence Eradication of h. pylori allows ulcers to heal more rapidly and remain in remission longer, often permanently Otherwise, organism may survive for life We always give at least 2 antibiotics to: Increase effectiveness of therapy Reduce chance of resistance Also give with H2-antagonist or a PPI to allow for healing
amoxicillin, clarithromycin, metronidazole, tetracycline	Specific for h. pylori As with all antibiotic therapy, complete course must be finished – at least 1 week
Antacids	Neutralize acid that is already present – do NOT have an effect on future acid secretion – supportive role only Most appropriately used as needed (PRN) Very safe and can be used for long periods of time (years) with few consequences – Tums® are also used as a calcium supplement! – but long term use for recurring heartburn indicates underlying problem Can interfere with absorption of many medications – separate by 2 hours

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PUD + GERD - classes of medication (cont)

Misoprostol *Arthrotec® = diclofenac + misoprostol*	A mucosal protective agent, occasionally used to prevent GI adverse effects of long-term NSAID use A synthetic prostaglandin E analogue, increasing mucous production ALSO used for medically-induced abortions, and to evacuate uterus after miscarriage DO NOT USE FOR PREGNANT PATIENTS

IBD, IBS, pancreatitis + Hemorrhoids - Meds

Inflammatory Bowel Disease (IBD)	key treatment includes anti-inflammatories + also an auto-immune component
Aminosalicylates *5-aminosalicylic acid (5-ASA), sulfasalazine, mesalamine*	Anti-inflammatories (a GI topical effect) Inhibit production of inflammatory mediators prostaglandins and leukotrienes For mild symptoms, would not treat an exacer-bation Used to lengthen times between exacerbations Can be given orally (formulated for minimal systemic absorption) or rectally (if lesions are more present in lower tract) – all work topically
Corticosteroids	Useful because of both anti-inflammatory and immunosuppressant activity Auto-immune & inflammatory components to IBD Used to treat exacerbations to send disease into remission Short term therapy, at high doses (pulse therapy) To minimize adverse effects

IBD, IBS, pancreatitis + Hemorrhoids - Meds (cont)

Budesonide (Entocort®)	A unique corticosteroid used specifically for IBD Encapsulated to avoid significant absorption in stomach or duodenum, then released slowly in lower tract In direct (topical) contact with lesions (ulcers) Any absorption that does occur is almost entirely removed by first-pass metabolism Avoids most long-term corticosteroid adverse effects (would still monitor)
Immuno-suppr-essants *Methotrexate, azathioprine, mercaptopurine*	Suppresses auto-immune component of disease only For more severe disease, where aminosalicylates are not enough to prevent exacerbations Takes ~3 months for onset of action Can increase time between exacerbations
Methotrexate (MTX)	Folate antagonist, interfering with DNA synthesis, repair, and cellular replication – most active against rapidly dividing cells Used in many auto-immune diseases (rheum-atoid arthritis, IBD) Due to the mechanism of action, we must replace folic acid that is being inhibited
Biologics	
Infliximab (Remicade®)	tumour necrosis factor (TNF)-α inhibitor (a cell signaling protein involved in inflammation and immune response)
Adalimumab (Humira®)	also TNF-inhibitor

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IBD, IBS, pancreatitis + Hemorrhoids - Meds (cont)

Irritable Bowel Syndrome	Abdominal pain or discomfort with altered bowel habits which occur over a period of at least 3 months “Altered bowel habits” = bloating, cramping, mucous in stool, constipation, diarrhea
Antispasmodics *dicyclomine & hyoscine*	reduce muscle spasms of GI tract by blocking muscarinic receptors (anticholinergic effects!)
Calcium channel blockers (CCB) *pinaverium*	very specific for GI smooth muscle, reduces muscle contractions by inhibiting calcium influx (hypotension!)
Opioid agonists *loperamide*	doesn’t cross blood-brain barrier; trimebutine – also has anti-serotonin activity
Antidepressants *TCAs & SSRIs*	address neurological connection (serotonin receptors in CNS and GI) and overlap of neurological conditions with IBS ~55% patients given TCA or SSRI saw benefit compared to ~35% placebo
Osmotics & stool softeners	used for prevention or as needed
Pancreatitis	Acute or chronic inflammation of the pancreas (very painful) Usually caused by gallstones, heavy alcohol use, or cystic fibrosis (CF)
Pancreatin (Creon®)	Enzymes are not absorbed Capsules formulated to release in duodenum

IBD, IBS, pancreatitis + Hemorrhoids - Meds (cont)

Hemorrhoids	Commonly seen with constipation, diarrhea, pregnancy, advancing age and possibly physical exertion Symptom relief only – no meds are curative Products can provide short-term relief of pain, burning, itch, discomfort and irritation while swelling subsides and healing occurs
Local anesthetics *dibucaine, pramoxine*	to relieve pain Safe if < 7 days of continued use
Corticosteroids *hydrocortisone*	to reduce itch and inflammation Safe if < 14 days of continued use
Astringents *hamamelis*	dries out skin to relieve burning, itching, and pain
Anti-infectives *framycetin*	if concerned about infection
Protectants *glycerin, petrolatum*	to provide barrier for healing
Vasoconstrictors *phenylephrine*	to relieve inflammation and limit bleeding; short term only

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