PHARMACOLOGY/THERAPEUTICS II BLOCK I HANDOUTS – 2017-18

52. **Drugs to Treat Nausea/Vomiting/Constipation - Kristopaitis**
53. **Self-Study – Principles of Clinical Toxicology – Clipstone**
54. **Anti-Parasitic Agents - Johnson**
55. **H2 Blockers, PPIs - Moorman**

Pharmacologic Palliation of Constipation & Nausea/Vomiting

Date: January 10, 2018- 8:30 AM

Reading Assignment: Katzung, Basic and Clinical Pharmacology, 13 th Ed
Chapter 62. Drugs used in the treatment of gastrointestinal diseases
Drugs used to stimulate gastrointestinal motility
Laxatives
Antiemetics

LEARNING OBJECTIVES

1. Explain the mechanisms of action, indications, and contraindications of the following classes of drugs used for the relief of constipation and prototype drugs in each class:
   - Bulk laxatives (Psyllium; Fiber)
   - Osmotic laxatives
     - Nonabsorbable sugars (Lactulose; Sorbitol)
     - Saline and magnesium laxatives (Magnesium citrate, magnesium hydroxide)
     - Polyethylene glycol
   - Stimulant laxatives (Senna; Bisacodyl)
   - Detergent laxatives (Docusate)
   - Lubricants (Glycerin suppository, mineral oil enema)
   - Enemas (Warm water; sodium phosphate)

2. Define fecal impaction

3. Explain the mechanisms of action, indications, and contraindications of the following antiemetics and know prototype drug in each class:
   - Dopamine receptor antagonists
     - Metoclopramide
     - Prochlorperazine
   - Prokinetic agent (Metoclopramide)
   - Antihistamines (Promethazine)
   - Serotonin antagonists (Odansetron)
   - Neurokinin receptor antagonist (Aprepitant)
   - Anticholinergics (Scopolamine)

4. Explain the indications for the use of
   - Benzodiazepenes (Lorazepam)
   - Corticosteroids (Dexamethasone)

   In the palliation of nausea and vomiting

Pharmacologic Palliation of Constipation & Nausea/Vomiting

I. A goal of **palliative care** is to relieve the suffering of patients.
Control of pain and other physical symptoms, as well as psychological, social and spiritual problems is paramount.

II. Pharmacologic Palliation of Constipation

A. BULKING AGENTS

Agents

- Dietary fiber (bran)
- Psyllium (Metamucil)

Mechanisms of Action

- Bulk-forming laxatives cause retention of fluid and an increase in fecal mass, resulting in stimulation of peristalsis.
- They usually have an effect within 12 to 24 hours and reach a maximum after several days

Side Effects

Flatulence

Contraindications

In debilitated patients who cannot drink adequate fluid (1.5 – 2 liters/day) could result in fecal impaction, intestinal obstruction

B. OSMOTIC LAXATIVES

These are soluble but nonabsorbable compounds that result in increased stool liquidity due to an obligate increase in fecal fluid**.**

- **Nonabsorbable sugars**

Agents

- Lactulose
- Sorbitol

Mechanism of Action

Lactulose is a synthetic disaccharide. Bacteria in the colon degrade lactulose into lactic acid, acetic acid and formic acid resulting in an increase in osmotic pressure and acidification of intestinal contents which in turn, softens the stool by promoting stool water content

Side Effects

- Bloating, cramps, flatulence
- Very sweet – may be difficult for patients to tolerate

- Can worsen dehydration by drawing body water into the bowel lumen

Saline and magnesium salt laxatives

Agents

- Magnesium citrate
- Magnesium hydroxide (Milk of Magnesia)
- Sodium Phosphate (Fleets Phospho-Soda)

Mechanism of Action

- Saline laxatives have an osmotic effect causing increased intraluminal volume that acts as a stimulus for intestinal motility.
- Laxatives that contain magnesium have been shown to release cholecystokinin that causes intraluminal accumulation of fluid and electrolytes and promotes small bowel and possibly even colonic transit.
- Rapid movement of water into distal small bowel and colon leads to high volume of liquid stool.
- High doses produce bowel evacuation in 1-3 hours.

Side Effects/Contraindications

- Contraindicated in any form of bowel obstruction
- Can produce dehydration without adequate fluid replacement
- Because the ions can be partially absorbed, laxatives containing magnesium and phosphorous are contraindicated in patients with impaired renal function
- Avoid sodium phosphate-containing formulations in patients with congestive heart failure, liver failure – severe electrolyte abnormalities can occur.
  - Phosphate nephropathy (intratubular deposition of calcium phosphate)
- Rare reports of ischemic colits with magnesium citrate and sodium phosphate thought secondary to a rapid fluid shift from the intravascular compartment to the gut lumen resulting in transient colonic hypoperfusion and ischemia

Clinical Indications

- Magnesium citrate and sodium phosphate indicated for bowel cleansing in preparing patients for surgery or the colon for x-ray or endoscopy
- Magnesium hydroxide is indicated for relief of constipation

Polyethylene Glycol

Trade names

Constipation - Miralax, GlycoLax
Bowel Cleanser - Colyte, Golytely

Mechanism of Action:

- Polyethylene glycol is an osmotic agent that causes retention of water in the stool resulting in a softer stool and more frequent bowel movements.

- It appears to have no effect on active absorption or secretion of glucose or electrolytes
- No significant intravascular fluid or electrolyte shifts occur

Side Effects
Minimal

Clinical Indications
- Large volume (ie 4 liters) ingested rapidly causes rapid evacuation for bowel cleansing before endoscopy
- Smaller daily doses can be used for constipation.

C. STIMULANT LAXATIVES

Agents:
- Senna
- Bisacodyl (Dulcolax)

Mechanism of Action:
- Bisacodyl is a contact laxative that acts on the large intestine to produce strong but brief peristaltic movements. This agent stimulates sensory nerve endings to produce parasympathetic reflexes that results in peristalsis of the colon. Local axon reflexes and segmental reflexes are stimulated, which produces widespread peristalsis of the colon.
- Senna undergoes conversion to active metabolites in the colon that stimulate the myenteric plexus and induce net fluid secretion.
- Response in 6-12 up to 24 hours.

Side Effects
- Electrolyte abnormalities depending on volume of stool
- Senna - Melanosis coli – brown pigmentation of the colon
  - Lipofuscin laden macrophages
  - No clinical sequela

Clinical Indication
Relief of constipation

D. DETERGENT LAXATIVES

Agent
Docusate (Colace)

Mechanism of Action

- Docusate is an anionic surfactant that is believed to increase the penetration of fluid into the stool by emulsifying feces, water, and fat
- Soft feces = easier passage
- Minimal effect on peristalsis
- Initial response in 1-3 days

Clinical Indications

Docusate is used to soften or prevent the formation of hard stools.

E. LUBRICANTS

Agents

- Glycerin suppository/enema
- Mineral oil enema

Mechanism of Action

- Due to its osmotic effect, glycerin softens, lubricates, and facilitates the elimination of inspissated feces. By serving as a bowel irritant it may also stimulate rectal contractions.
- Mineral oil helps soften (by coating fecal material with mineral oil) and lubricate hard stools, easing their passage without irritating the mucosa.
- Lubricants may stimulate a response within 30 minutes.

Side effects/contraindications

Mineral oil should **never be administered orally** to debilitated patients - inhalation/aspirationof the oil can lead to lipoid pneumonitis**.**

Clinical Indications

Usually reserved for treatment of fecal impaction

F. LARGE VOLUME ENEMAS

Agents

Sodium phosphate enema (Fleet's enema)
Tap water

Mechanism of Action

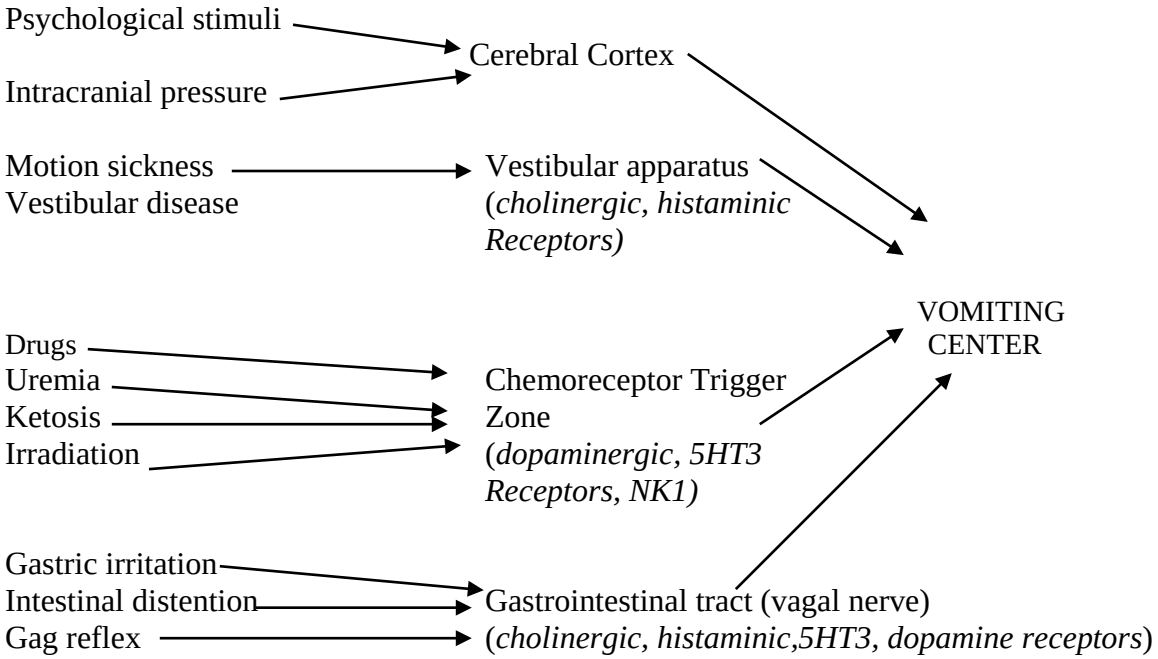
Soften stool by increasing water content
Distend distal colon inducing peristalsis

Clinical Indications

Usually reserved for treatment of fecal impaction

III. Pharmacologic Palliation of Nausea and Vomiting

A. Pathophysiology of nausea and vomiting



Chemoreceptor trigger zone is located in the area postrema outside the blood brain barrier
Vomiting Center is located in the lateral reticular formation of the medulla and coordinates the motor mechanisms of vomiting

B. Antiemetic Drugs

Dopamine receptor antagonists

Phenothiazines - **Prochlorperazine (Compazine)**
Butyrophenones - Haloperidol (Haldol)
Benzamides – Metoclopramide (Reglan)

Serotonin (5HT3) antagonists

Ondansetron (Zofran)
Granisetron (Kytril)
Dolasetron
Polansetron

Antihistamines
Promethazine (Phergan)
Diphenhydramine

Anticholinergics
Scopolamine

Corticosteroids
Dexamethasone

Benzodiazepenes
Lorazepam
Alprazolam

Cannabinoids
Dronabinol (Marinol)
Nabilone

Neurokinin (NK1) receptor antagonist
Aprepitant

B. Select Antiemetics

- **Agent -** Prochlorperazine (Compazine)

  Mechanisms of Action
  - Prochlorperazine acts centrally by inhibiting the dopamine receptors in the medullary chemoreceptor trigger zone

  Adverse Effects
  Extrapyramidal effects, dystonic reactions

  Clinical Indications
  - Opioid related nausea and vomiting
  - Moderately effective for nausea caused by various GI disorders (ie gastroenteritis)

- **Agent -** Metoclopramide (Reglan)

  Mechanism of Action
  - Antiemetic properties are due to central and peripheral dopamine receptor inhibition

- Prokinetic - Within the gastrointestinal tract activation of dopamine receptors inhibits cholinergic smooth muscle stimulation; blockade of this effect is believed to be the primary prokinetic mechanism of action of metoclopramide. Metoclopramide increases esophageal peristaltic amplitude, increase lower esophageal sphincter pressure, and enhance gastric emptying but has no effect on small intestine or colonic motility

Adverse Effects

- Extrapyramidal effects, such as dystonia, akathisia, parkinsonism, may develop due to central dopamine receptor blockade.
- Tardive dyskinesia – black box warning – risk increases with total cumulative dose. Avoid use for greater than 12 weeks
- Acute dystonic reactions, such as trismus, torticollis, facial spasms, can be treated with an anticholinergic agent (benztropine or diphenhydramine).
- Cautious use in patients with Parkinson's Disease

Clinical Indications

- Chemotherapy induced nausea and vomiting
- Vomiting due to dysmotility of the upper GI tract - gastric stasis and diabetic gastroparesis

Agent - Ondansetron (Zofran); Granisetron (Kytril)

Mechanism of Action

- Ondansetron is a competitive, highly selective antagonist of 5-hydroxytryptamine (serotonin) subtype 3 (5-HT 3) receptors. 5-HT 3 receptors are present peripherally on vagal nerve terminals and centrally in the area postrema of the brain. Cytotoxic drugs and radiation appear to damage gastrointestinal mucosa, causing the release of serotonin from the enterochromaffin cells of the gastrointestinal tract. Stimulation of 5-HT 3 receptors causes transmission of sensory signals to the vomiting center via vagal afferent fibers to induce vomiting. By binding to 5-HT 3 receptors, ondansetron blocks vomiting mediated by serotonin release.

Side Effects

Most common side effect is headache
Small but statistically significant prolongation of the QT interval

Clinical Indications

- Chemotherapy induced nausea and vomiting and its prophylaxis
- Radiation induced nausea and vomiting and its prophylaxis

- Agent – Aprepitant

Mechanism of Action

- Aprepitant inhibits the neurokinin 1 (NK_1) receptor in the chemoreceptor trigger zone

Side Effects

Fatigue, dizziness, diarrhea

Clinical indications

- Prevention of nausea/vomiting from highly emetogenic chemotherapy
  Augments activity of 5-HT3 receptor antagonist + glucocorticoids

- **Agent -** Promethazine (Phenergan)

Mechanism of Action

Antiemetic effects come from its H(1) receptor blocking properties.

Adverse Effects

Sedation

Clinical Indications

Promethazine is effective in the active and prophylactic treatment of motion sickness

- **Agent** Scopolamine

Mechanism of Action

Pure anticholinergic agent

Adverse Effects

- *Dry mouth (xerostomia)
- Acute narrow angle glaucoma (contraindicated in patients with known glaucoma)
- Urinary retention
- Confusion

Clinical Indications

- Treatment of motion sickness
- *In patients who are hours to days from death and who can an no longer swallow their own secretions, it is used to decrease production of saliva

- **Agent** Dronabinol (Marinol)

Mechanism of Action
Synthetic delta-9-tetrahydrocannibinol
Cannabinoid 1 (CB1) central receptor agonist

Adverse Effects
- Euphoria
- Dysphoria
- Paranoid delusions
- Cognitive clouding
- Somnolence, sedation
- Hypotension

Clinical Indications
- Breakthrough chemotherapy induced nausea/vomiting
    - AIDs-related anorexia and wasting

SELF STUDY-TOXICOLOGY

Reading assignment: Management of Poisoning and Drug Overdose- Scientific American Medicine (see attached). Review the material in this chapter to address each of the specific learning objectives outlined below.

Key Concepts and Learning Objectives

1. Describe the "ABCDs" of the acute management and stabilization of the poisoned patient

2. List the common causes and mechanisms underlying drug-induced hypotension

3. Identify agents that are known to induce cardiac dysrhythmias and the types of cardiac disturbances they produce

4. List the common causes of drug-induced seizures

5. List the symptoms of the common autonomic syndromes induced by drugs and/or poisons and give examples of agents capable of inducing these effects

6. Describe the empirical intervention used to treat drug/poison-induced autonomic syndromes

7. List methods of acute gastrointestinal decontamination and the situations in which these approaches would be appropriate

8. List the specific treatments available to treat either an overdose or poisoning with each of the following drugs or toxins:
   a) Acetaminophen
   b) Anticholinergic agents
   c) Antihistamine agents
   d) Anticoagulants
   e) Beta blockers
   f) Calcium antagonists
   g) Carbon monoxide
   h) Cocaine, amphetamine & other stimulants
   i) Copper
   j) Cyanide
   k) Digitalis Glycosides
   l) Ethanol, Methanol & Ethylene glycol
   m) Gold
   n) Iron
   o) Lead
   p) Lithium
   q) Methemoglobinemia-inducing agents
   r) Opioids
   s) Organophosphate agents
   t) Salicylates
   u) Sedative Hypnotic agents
   v) Tricylic antidepressants

Antimalarial Drugs Used for Treatment or Prophylaxis

Drug	Method of action	Stage of life cycle inhibited	Use	Unique or major adverse reactions	Use in children	Use in pregnancy	Comments
Chloroquine	Inhibit heme polymerase; incr free heme	RBC Schizont	Treatment and chemo-prophylaxis	Pruritis (Africans)	Safe	Safe	Resistance is major limitation
Quinine, Quinidine	Inhibit heme polymerase; incr free heme (toxic)	RBC Schizont (gametocytes of *P. vivax & ovale)*	Treatment of *P. falciparum*	Cinchonism* Hypoglycemia Blackwater fever	OK	Quinine - **OK, if needed** Quinidine - OK, but contractions in 3rd trimester	Only iv quinidine available in US; DOC for severe malaria; cardiac monitoring recommended; used with a 2nd agent
Mefloquine	Inhibit heme polymerase; incr free heme (toxic)	RBC Schizont	Treatment and chemo-prophylaxis	Neuropsychiatric toxicities (less common with prophylaxis	Safe	OK for prophylaxis (no data for 1st trimester), NO for treatment	DOC for chemoprophylaxis in most regions; Not recommended for treatment of severe malaria
Primaquine	Inhibit heme polymerase; incr free heme (toxic)	Hypnozoite, Gametocyte	Radical cure for *P. vivax & ovale*	Hemolysis in G6PD-deficiency	OK	UNSAFE	Testing for G6PD-deficiency recommended; Terminal prophylaxis is rarely necessary
Proguanil	Inhibit plasmodial DHFR	RBC Schizont, Hepatic Schizont of P. falcip	With chloroquine or atovaquone for chemo-prophylaxis		OK	(never given alone, see atovoquone)	
Atovaquone	Inhibit parasite mitochondial electron transport	RBC Schizont, Hepatic Schizont of P. falcip	With proguanil (Malarone) for chemo-prophylaxis	GI side affects, contraindicated in severe renal impairment	NO, if < 5kg	NO, unless benefit outweighs risk (Category C)	Give with food or milky drink
Doxycycline	Inhibit protein synthesis in parasite organelles	RBC Schizont	Adjuvant treament of *P. falciparum* and chemo-prophylaxis	Photosensitivity, Esophagitis	NO	NO	Used for chemo-prophylaxis in areas with high mefloquine resistance (e.g., areas within Southeast Asia)
Artemisinin	Binds Iron in malaria pigment producing free radicals	RBC Schizont, Gametocyte	Treatment (NOT chemoprophylaxis)	Potential neurotoxicity (ototoxicity) unresolved	Probably OK	Probably OK	Used for treatment in combination with other antimalarial agents

*Cinchonism: tinnitus, headache, nausea, dizzines, flushing and visual disturbances

Antihelmintic drugs used for treatment:

Drug	Disease for which agent is the Drug of Choice	Dose	Special Considerations
Albendazole	Cysticercosis	15 mg/kg/d (Max 800 mg) in 2 divided doses x 21 d	Absorption increased 5-fold with fatty meals, No interaction with corticosteroids
	Hydatid disease	400 mg BID x 3 mos	Check CBC, LFTs Q 2 weeks
Mebendazole	(Pinworm)	100 mg x 1, repeat in 2-4 wks	Absorption increased with fatty meals; chew before swallowing
	(Ascaris, Trichuria, Hookworm)	100 mg BID x 3 d	
Ivermectin	Strongyloidiasis	200 mcg/kg daily x 2	check stool by concentration method x 3 monthly to ensure eradication
	Onchocerciasis	150 mcg/kg x 1, repeat Q 3 mo x 4, then yearly x 10	Mazzotti reaction* occurs due to microfilariae death
Pyrantel pamoate	(Pinworm, Ascaris)	11 mg/kg x 1, repeat 2-4 wks	Treat all family members
Praziquantel	Schistosomiasis**	20 mg/kg Q 4-6 h x 3 doses	Swallow without chewing
	(Cysticercosis)	50 - 60 mg/kg/d in 3 divided doses x 14 d	Bioavailability decreased ~ 50% with phenytoin and corticosteroids
Diethyl carbamazine citrate	Filariasis, Loiasis, Tropical eosinophilia	2 mg/kg TID for 3 weeks, titrate up from Q daily to TID over first 3 d	Reactions to dying microfilariae are common, sometimes serious (BLINDNESS may occur in Onchocerciasis)

*Mazzotti reaction: fever, headache, dizziness, somnolence, weakness, rash, increased pruritis, diarrhea, joint & muscle pains, hypotension, tachycardia,
** Oxamiquine is DOC for S. mansoni

Histamine Antagonists and PPIs

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KEY CONCEPTS AND LEARNING OBJECTIVES .

1. To understand the clinical uses of H_2 receptor antagonists. mechanism of action, elimination and adverse effects.

2. To describe the drug interactions associated with the use of H_2 receptor antagonists.

3. To understand when antacids are used and there mechanism of action.

4. To understand the mechanism of action of PPIs

5. To describe the adverse effects and drugs interactions with PPIs

6. To understand when the histamine antagonists and the PPIs are to be used for treatment

7. To describe the mechanism of action of the mucosal protective agents

8. To describe the drugs used to treat H. pylori infection

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Histamine-2 Antagonists and PPIs

I. Overview of Acid Reflux

A. Acid reflux/GERD occurs when the stomach contents back up into the esophagus or mouth
B. Patients with GERD experience heartburn, regurgitation, vomiting and pain upon swallowing
C. Stomach acid can also affect vocal cords
D. Symptoms of acid reflux/GERD
   1. Heartburn 2-3 times a week
   2. Burning sensation in chest
   3. Acid test in throat
E. Treatment of acid reflux/GERD
   1. Mild symptoms- dietary changes, non-prescription medications
   2. Antacids and H2 antagonists

II. Antacids – used for short term relief

A. Neutralizes gastric acid and reduces delivery of acid to duodenum

B. Contains sodium bicarbonate, aluminium hydroxide, magnesium carbonate or magnesium hydroxide.

B. Adverse effects
   1. Ingestion of large amounts of calcium and alkali can lead to hypercalcemia, alkalosis and renal impairment known as the milk-alkali syndrome
   2. Magnesium containing agents can cause diarrhea

III. H_2 Receptor Antagonists

A. These drugs reduce gastric acid secretion, and are used to treat peptic ulcer disease and gastric acid hypersecretion. These are remarkably safe drugs, and are now available over the counter.

The H_2 antagonists are available OTC:
1. Cimetidine (Tagamet®)
2. Famotidine (Pepcid®)
3. Nizatidine (Axid®)
4. Ranitidine (Zantac®)

All of these have reduce the production of acid by blocking the H2 receptors on the parietal cell. They are used to prevent NSAID-induced ulcers and in the treatment and maintenance of peptic ulcers

B. The H_2 antagonists are rapidly and well absorbed after oral administration (bioavailability 50-90%). Peak plasma concentrations are reached in 1-3 hours, and the drugs have a $t_{1/2}$ of 1-3 hours.

C. Cross the blood-brain and placental barriers

D. Elimination – Hepatic and renal metabolism. Bioavailability is reduced 30-70% by first pass metabolism. Cimetidine exhibits the greatest hepatic metabolism

E. Adverse effects – Rare but can include
Gynecomastia and impotence occur with cimetidine

1. Hematopoietic and immune effects-B 12 deficiency and Idiosyncratic myelosuppression

2. CNS – confusion, agitation

3. Hepatic effects –metabolized by cytochrome P450 and can cause drug interactions

4. Cardiac effects-Brachycardia, hypotension-IV cardiac toxicity-Oral

5. Renal –mild increase in creatinine with cimetidine

Because of the hepatic metabolism and renal excretion, H_2 receptor antagonists should be used with care (lower doses) in patients with hepatic and renal impairment.

IV. Proton Pump Inhibitors

A. Mechanism of action

1. Proton Pump Inhibitors (PPI) irreversibly inhibit the gastric parietal cell proton pump H^+/K^+ ATPase.

2. Activation occurs in 3 phases

a. PPIs are weak bases concentrated in the acid compartment of the parietal cells
b. Prodrugs – activated in acid environment – enter the parietal cells from the blood
c. A sulfhydral group forms a disulfide bond with cysteine residues on the H-K-ATPase pump and inactivates the enzyme

B. Current proton pump inhibitors
1. Omeprazole (Prilosec®)
2. Lansoprazole (Prevacid®)

3. Rabeprazole (Aciphex®)
4. Pantoprazole (Protonix®)
5. Esomeprazole (Nexium®)

- A single dose can inhibit 95% of gastric acid secretion
- H2 antagonist should not be given with PPIs
- PPIs are the drug of choice for treatment of Zollinger-Ellison syndrome and GERD when there is no response with H2 antagonists

C. Drug Interactions of PPIs

1. PPIs are metabolized by Cytochrome P450 and, therefore, can decrease the metabolism and clearance of benzodiazepines (Diazepam), warfarin, phenytoin, etc.

2. PPIs reduce absorption of ketoconazole but increase absorption of digoxin.

3. Prolonged use can result in B12 deficiency

D. Adverse reactions of PPIs

1. Few (<3% of patients) and generally mild

2. Include diarrhea, headache, drowsiness, muscle pain, and constipation.

V. Mucosal Protective Agents

A. Sucralfate (Carafate ®) is aluminum sucrose sulfate.

B. It is thought to polymerize and bind selectively to necrotic tissue, thereby creating a barrier between the gastric contents and the gastric mucosa.

C. Sucralfate is very effective for treating duodenal ulcers, and also suppresses H. Pylori (see below).

D. It is important to note that citric acid, such as that present in grapefruits, promotes absorption of the aluminum in sucralfate. This poses a problem for patients with renal failure who have an impaired ability to eliminate the aluminum.

E. Do not give with cimetidine/ranitidine but can be given 2h prior.

F. Colloidal Bismuth (Pepto-Bismol) also acts like sucralfate to bind necrotic tissue and creates a barrier.

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Generic Name	Trade Name	Mechanism	T½ hrs	Elimination
Cimetidine	Tagamet	H2 antagonist	1-3	Hepato-renal
Famotidine	Pepcid	H2 antagonist	1-3	Mainly Renal
Nizatidine	Axid	H2 antagonist	1-3	Mainly Renal
Ranitidine	Zantac	H2 antagonist	1-3	Mainly Renal
Omeprazole	Prilosec	Proton Pump Inhibitor	24	hepatic
Lansoprazole	Prevacid	Proton Pump Inhibitor	24	hepatic
Rabeprazole	Aciphex	Proton Pump Inhibitor	24	hepatic
Carafate	Sulcralfate	Mucosal Protective Agent	6	

OTC = over the counter medication
+Effective = more effective than the H2 antagonists (which are already quite effective!!).

VI. Helicobacter Pylori

A. Bacteria can enter body and live in your digestive system for years. Can eventually cause ulcers in the lining of the stomach and small intestine
B. Transmission is person-to=person or fecal contamination of water and food
C. Pylori is present in only 0.3-0.5 % of the normal healthy population.
D. Presence of H. Pylori increases the risk of recurrent ulcers
E. Combination therapy with a PPI plus 2 antibiotics is used to treat this disease for 2 weeks
F. If PPI is used with 1 antibiotic patient needs longer treatment duration

Histamine Antagonists and PPIs January 11, 2018

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SUMMARY REVIEW TABLE FOR LECTURE

Drug	Classification	Biochemical mechanism of anti-asthmatic action	Routes of administration	Type of therapeutic use	Contraindications	Major side effects	Comments
Cimetidine (Tagamet®)	Histamine **H2 receptor** antagonist	Blocks histamine H2 receptors and decreases gastric acid secretion	1. Oral 2. i.v. 3. injection	1. duodenal ulcers 2. gastric ulcers 3. erosive gastroesophageal reflux disease (GERD) 4. Prevention of upper GI bleeding 5. hypersecretory conditions (Zollinger-Ellison Syndrome)		Gynecomastia with long-term use and in some incidences impotence	1. i.v. bolus reported to cause cardiac arrythmias and hypotension (although rare). 2. H2 antagonists can be added to PPIs to stop nocturnal acid breakthrough -BUT may decrease efficacy of PPIs
Ranitidine (Zantac®)	Histamine **H2 receptor** antagonist	Blocks histamine H2 receptors and decreases gastric acid secretion	1. Oral 2. i.v.	Same as Cimetidine		Rare but include agitation, anemia, confusion and depression	1. May increase risk of developing pneumonia 2. H2 antagonists can be added to PPIs to stop nocturnal acid breakthrough. – BUT may decrease efficacy of PPIs
Omeprazole	**PPI**	1. Inhibits H^+/K^+ pump (proton pump) in the gastric parietal cells	1. Oral	1. Zollinger-Ellison Syndrome 2. GERD 3. short term treatment of duodenal ulcers. 4. Rx of H. Pylori in combination with Antibiotics	1. Can increase concentrations of **diazepam, warfarin, and phenytoin** by decreasing their clearance by the liver. 2. PPIs can reduce absorption of **ketoconazole** and increase absorption of **digoxin.**	Diarrhea, nausea, skin rash, dizziness	Not normally used with H2 antagonists – reduced efficacy of PPIs. **NEW:** long term use may cause Vit B12 deficiency
Rabeprazole	**PPI**	1. Inhibits H^+/K^+ pump (proton pump) in the gastric parietal cells	1. Oral	Same as Omeprazole	Same as for Omeprazole	Headache	Not normally used with H2 antagonists – reduced efficacy of PPIs. **NEW:** long term use may cause Vit B12 deficiency
Sucralfate (Carafate®)	**Mucosal Protective agent**	1. binds selectively to necrotic tissue to form a barrier against gastric acid.	1. Oral	1. Duodenal Ulcers 2. suppresses H. pylori infection	1. Can decrease absorption of cimetidine, ciprofloxacin, digoxin, ofloxacin, ranitidine if given simultaneously with Sucralfate. 2. Grapefruit promotes absorption of Al in sucralfate – problem in patients with renal insufficiency/failure.	Minor: Constipation, flatulence, dry mouth, diarhhea, nausea	Colloidal Bismuth works in same manner as Sucralfate.