Important GIT reflexes: vomiting

Vomiting Center

Vestibular Triggers
- ACh
- Movement
- Middle ear surgery
- Opioids

Endocrine Triggers
- Estrogen/Progestrone
- Female
- Pregnancy

Cerebral Triggers
- Fear, emotion, stress
- Sights, smells, sounds, tastes
- Memory, anticipation
- Pain

Area Postrema CTZ Triggers
- Inhalation agents
- Opioids
- Dopamine, 5-HT, histamine, ACh, Substance P from drugs, irritation, etc.

Nucleus Tractus Solitarius
Chemoreceptor triggers
- DA, 5-HT, H, ACh

Glossopharyngeal and
Trigeminal Afferent Triggers
- Tonsillectomy
- Otolaryngologic procedures
- Trigeminocardio reflex

Peripheral NS Afferent Triggers
- Pain
- Manipulation of the eyes
- Irritation of the GIT
- Irritation of the kidneys
- Bacteria or viruses
- Cytotoxic drugs
- Radiation
- Eating after surgery

Ondansetron (Zofran) is a popular antiemetic, Photo by Intropin from Wikimedia Commons.

But looking below, should indicate to you that many drug classes impact nausea and vomiting.

Drugs to reduce gastric acid &/or heal ulcers

The H2 receptor blockers are antihistamines that target the H2 receptor in the stomach. They act to inhibit the secretion of gastric acid. These H2 blockers include Cimetidine (Tagamet HB), Famotidine (Pepcid) and Ranitidine (Zantac). They are best taken just before bed as they act mainly on decreasing basal acid secretion.

Antacids should not be taken too often as the neutral pH generated by the antacid triggers the reflex release of gastrin, which triggers gastric acid secretion. This increase in acidity is called acid rebound. Sodium bicarbonate is one of many kinds of antacids.

The proton pump inhibitors (PPI) include Omeprazole (Prilosec). The PPI are used to treat gastric ulcer, GERD, hypersecretory conditions and in combination with an antibiotic, *Helicobacter pylori* infections.

Sucralfate (Carafate) is an antipeptic agent that helps to heal duodenal ulcers by forming a proteinaceous glob over the wound and decreasing the activity of pepsin. It is also used to heal radiation or chemotherapy induced GIT ulcers.

**Misoprostol (Cytotec)**

Misoprostol is a prostaglandin analog. PGE2 acts to decrease secretion of acid and increase mucous secretion. Misoprostol is often given in fixed dose combination with NSAIDs to patients at risk of developing NSAID-induced gastric ulcers. Misoprostol is a potent trigger of uterine contractions.

**GIT Prokinetics**

Drugs used to restart a neurogenic GIT (due to diabetes or surgical anesthetics), are called prokinetics.

**Metoclopramide (Reglan)** is an anti emetic and a prokinetic. It also stimulates lactation and has a risk for EPS because it blocks D2 receptors in the brain.

**Erythromycin** (E-Mycin) is a macrolide antibiotic and a strong prokinetic. It is used less often because it is an antibiotic and can lead to resistance and super infection.
Cathartics & Laxatives

Prolonged use of laxatives leads to a dysfunctional, atonic, dilated colon. Therefore, all laxatives are indicated for short-term use. In general, they are for:

- Treatment of constipation
- Evacuate the bowels prior to procedures (diagnostics, surgery, etc.)
- To prevent straining after:
  - Surgery
  - Delivery
  - Heart attack

**Chemical stimulant laxatives:**

- **Bisacodyl** (Dulcolax) and **Castor oil** (Neoloid)

**Bulk laxatives:**

- **Magnesium hydroxide** (Milk of Magnesia)

**Lubricant laxatives:**

- **Mineral Oil**

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### Digestive Enzymes

**Pancrelipase** ([Ultrase MT 18](#)) is a combination of 3 enzymes, lipase, protease and amylase. Normally produced by the pancreas, they digest fats, proteins and sugars in the diet. Pancrelipase replaces these enzymes.

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### Antidiarrheals

We covered **Diphenoxylate** ([Lomotil](#)), with the opioids. It is a non-narcotic C-V derivative of meperidine that is rapidly metabolized to an active metabolite that does not readily cross the blood brain barrier due to the pumping action of p-Glycoprotein. If taken with a p-GP inhibitor, though, it will have the CNS effects of an opioid. Diphenoxylate acts on the opioid receptors of the GIT to decrease peristalsis.

**Loperamide** ([Imodium](#)) is a synthetic antidiarrheal with no CNS or adrenergic effects. It is an opioid receptor agonist acting on opioid receptors in the myenteric plexus to decrease peristalsis. It is non-narcotic and not controlled.

The opioid-derived antidiarrheals are used for short term treatment of traveler’s diarrhea and irritable bowel syndrome.
Antiemetics

You should know the following acronyms:

1. PONV – Post Op Nausea and Vomiting
2. CINV – Chemical Induced Nausea and Vomiting
3. RINV – Radiation Induced Nausea and Vomiting
4. NVP – Nausea and Vomiting of Pregnancy

There are many classes of drugs with antiemetic effects, in part because the Chemoreceptor Trigger Zone (CTZ) in the brain has so many different types of receptors.

A common anticholinergic antiemetic is **Scopolamine** (*Scopace, Transderm Scop*). It is available OTC for motion sickness, but is also used for PONV because it dries up secretions and has sedative-tranquilizing effects as well.

**Diphenhydramine** (*Benadryl*) and **Meclizine** (*Bonine*) are common OTC antihistaminic antiemetics. Diphenhydramine has a number of other uses (and/or side effects) than meclizine.

All the benzodiazepines have some antiemetic efficacy, but **Midazolam** (*Versed*) C-IV is used most often for surgical procedures because it is such a strong amnesiac, is sedating and has a very short duration. **Lorazepam** (*Ativan*) C-IV and other BZDs may also be used for PONV, but again, the real reasons behind using a BZD have to due with sedation, anxiolysis, and amnesia. They are not indicated as antiemetics.

We are covering one cannabinoid, **Dronabinol** (*Marinol*) C-III. Dronabinol is an orally active cannabinoid with complex CNS effects that are not clearly understood. It does have sympathomimetic activity that causes tachycardia, but tolerance develops to this with chronic use. It also has psychoactive effects on mood, cognition, memory, perception, and yes, appetite. Tolerance does not develop to the effects on appetite.

NOTE:

All antiemetics may:

1. Mask the symptoms of adverse drug reactions (ADRs) or an overdose (OD), including those of another drug.
2. Interfere with the diagnosis of other conditions, including:
   a. GI obstruction including progressive ileus or GI distension
   b. Brain tumors
   c. Reye’s syndrome
   d. Head trauma
The phenothiazines generally have very good antiemetic activity for CINV and PONV. We covered Promethazine (Phenergan) with the antihistamines in the Autocoids lecture. Promethazine can also be used for motion sickness because it has those antihistaminic effects. Chlorpromazine (Thorazine) is covered with the antipsychotics, it too is a good antiemetic and sedative.

Prochlorperazine (Compazine) is for severe emesis associated with surgery and/or chemotherapy. It is also used for schizophrenia and non-psychotic anxiety. Note that all the phenothiazines can cause tardive dyskinesia and other EPS.

Compazine is available in a formulation called a “Spansule®” sustained-release capsules. What makes the Spansule delivery system unique is that an initial dose is released immediately and the remaining medication is slowly released over several hours. Compazine is also available in tablets, solutions, suppositories and syrups.

Metoclopramide (Reglan) is a non-phenothiazine dopamine antagonist (D2 receptor blocker). It was mentioned earlier for its prokinetic properties, and it is also a very good antiemetic for PONV and CINV.

Haloperidol (Haldol) was covered with the antipsychotics, it too is a D2 receptor blocker and is a very good antiemetic. It is also tranquilizing. Droperidol (Inapsine) is very similar and used to be the most commonly used antiemetic for PONV. The risk of EPS has made the use of the butyrophenones almost unheard of anymore.

Most of the antipsychotic drugs have some antiemetic qualities and because they are also sedating, are used off label as antiemetics, especially for PONV.

Ondansetron (Zofran) is a 5-HT3 receptor blocker. The 5-HT3 receptor is found in the GIT on smooth muscle and mediates increased contractions. It is also found on the CTZ where it triggers vomiting. This is an excellent antiemetic for PONV, CINV and RINV. Ondansetron is a 1st choice drug for PONV.

The antidepressant Mirtazapine (Remeron) and the antipsychotic Olanzapine (Zyprexa) both have activity as 5-HT3 receptor blockers. They are used off label as antiemetics much as Ondansetron would be.

Aprepitant (Emend) is indicated to treat CINV or PONV, it is a Substance P/Neurokinin 1 receptor blocker. Aprepitant is not used alone; it is given with both a 5-HT3 receptor blocker (see above) and a corticosteroid (see below).

Corticosteroids are excellent, inexpensive and well-tolerated antiemetics that often have side effects that are beneficial as well. Dexamethasone (Dexasone) is a 1st choice antiemetic for PONV and CINV. Other links: tablet; monograph.

A rescue antiemetic used in emergency rooms, surgical suites and critical care units is the parenteral general anesthetic Propofol (Diprivan). This is an off label use.

A number of herbs, including (fresh) Ginger, have antiemetic effects and may be useful to treat NVP.

(Antiemetics, continued)
Corticosteroids are used for…. Everything!

Corticosteroids, like Dexamethasone have an astounding number and variety of indications including:

- Adrenocortical or adrenogenital insufficiency
- Hypercalcemia, Multiple Sclerosis, Myasthenia Gravis
- Thyroiditis, Sarcoidosis
- Head trauma, cerebral malaria, bacterial meningitis, cerebral edema
- Rheumatic disorders, collagen diseases
- Dermatologic and Allergic diseases/conditions, Lupus
- Asthma, COPD, Croup, TB, various pneumonias
- Preterm labor and postnatal bronchopulmonary dysplasia
- Hematologic disorders, shock, pericarditis
- GI diseases, Crohn’s disease, CINV, PONV
- Neoplastic diseases, Organ transplants

Homework and Exercises

1. Read the “START HERE” announcement in Laulima for updates and instructions.
2. Read about the GIT in Chapters 61-63 of Adams & Urban, PHARMACOLOGY Connections to Nursing Practice.
3. Review the Powerpoints and listen to the audio from the face-to-face lecture. You may opt to watch the appropriate videos for this lecture. Review any handouts available for this lecture in the Course Index.
4. Complete the SLO practice set for the GIT in Tasks, Tests and Surveys.
5. Use “Chat,” “Discussions and Private Messages” or the lecture “Forum” to ask questions and find answers or to seek assistance.
6. Complete the online quiz in Laulima, Tasks, Tests and Surveys.

If you have any questions, email me at abeale@hawaii.edu