

Vomiting in Children

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Disclosure

- I have no actual or potential conflict of interest in relation to this presentation.

Vomiting in Children

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Education Gaps

1. There are at least 4 known physiologic pathways that can trigger vomiting, 3 of which are extraintestinal.
2. Understanding which pathway is causing a patient's vomiting will help determine best treatment options, including which antiemetic is most likely to be helpful to mitigate symptoms.
3. Bilious emesis in a newborn should indicate bowel obstruction.
4. Cyclic episodes of vomiting may be indicative of a migraine variant.

Objectives

- Understand the main pathways that trigger vomiting via the emetic reflex
- Differentiate between acute, chronic and cyclic causes of vomiting
- Recognize red-flag signs and symptoms of vomiting that should prompt emergent evaluation
- Recognize when to start an antiemetic medication
- Select antiemetic medications according to the presumed underlying pathway of vomiting

Definitions

Vomiting – Forceful expulsion of gastric contents through the mouth and/or nose

Reflux/regurgitation – Effortless retrograde flow of gastric contents into the mouth

Rumination – Regurgitation + rechewing and swallowing of food once again

Why do we vomit?

- Vomiting is the result of the emetic reflex, a neuropathic process by which the body protects itself against toxins, intestinal distention and a number of other triggers
- Protective process!!

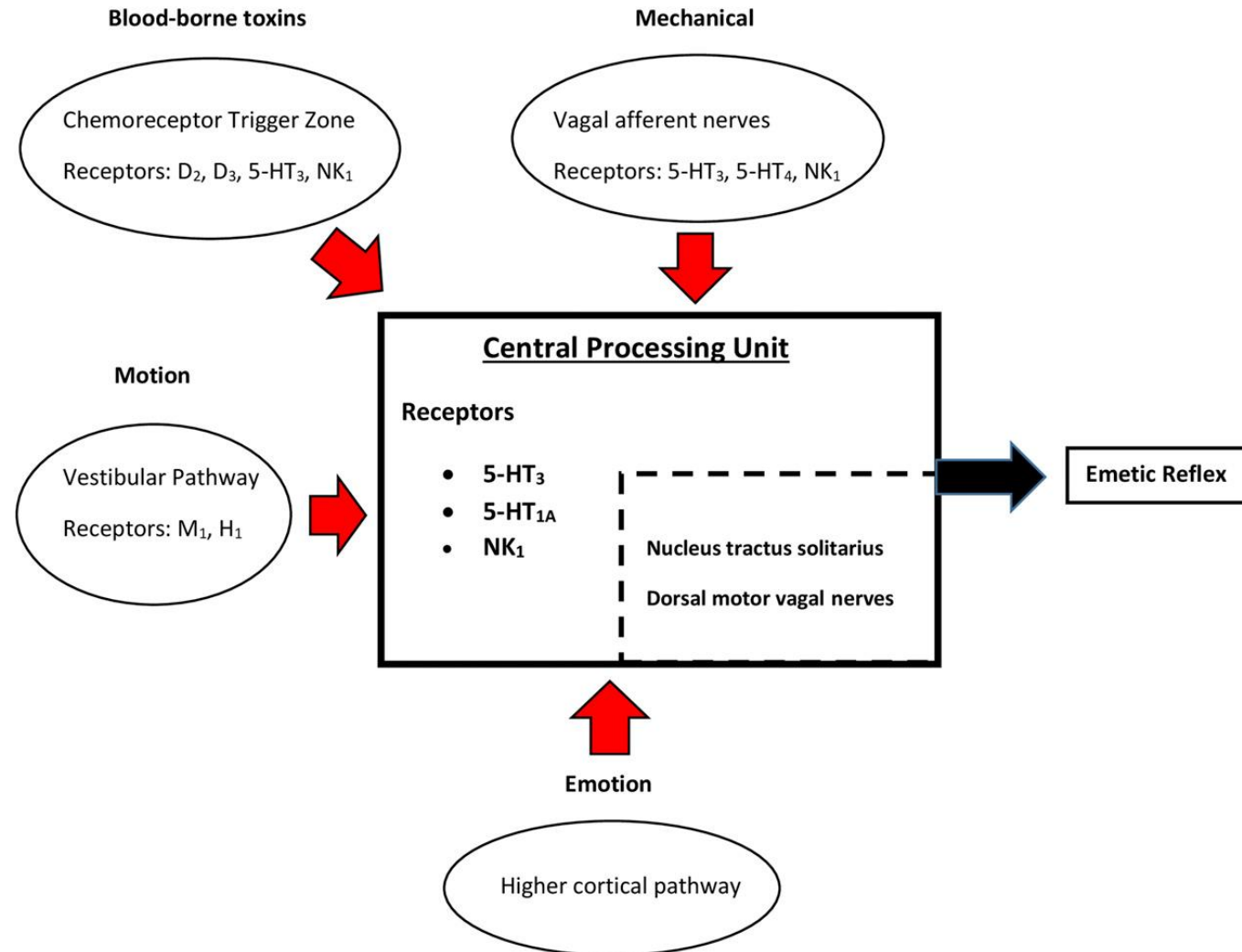
Vomiting is unpredictable!



Four main pathways that cause vomiting

- 1. Mechanical** (5-HT₃, 5-HT₄, NK₁): Stimulation of mechanoreceptors or chemoreceptors in intestinal wall
Examples: Viral gastroenteritis, bowel obstruction
- 2. Blood-borne toxins** (D₂, D₃, 5-HT₃, NK₁): Stimulation of the chemoreceptor trigger zone since it is not protected by the blood-brain barrier
Example: Chemotherapeutic drugs
- 3. Motion** (M₁, H₁): Stimulation of the vestibular system by abnormal movements
Example: Car sickness
- 4. Emotion** (Higher cortical pathway): Stimulation by intense emotions
Example: Child becomes upset about going to school

Pathways that cause vomiting



Emetic Reflex

1. Central processing unit (CPU) receives a stimulus
2. Retrograde contractions of the intestine are initiated by the vagus nerve
3. Retching begins. The UES and glottis close while the diaphragm and abdominal muscles contract, increasing intraabdominal pressure.
4. Esophagus initially contracts and then dilates allowing the stomach to be drawn up into the thoracic cavity (antireflux capabilities of the LES are lost).
5. Cycle of retching repeats itself until the gastric contents are eventually expelled through the mouth.

Vomiting by Symptom Pattern

- Acute Vomiting
 - Symptoms develop over a period of a few hours
 - Dehydration likely
 - Usually requires antiemetics
 - Example: Viral gastroenteritis
- Chronic Vomiting
 - Symptoms develop over several days to weeks
 - Frequent, low volume vomiting
 - Do not usually require antiemetics
 - Example: Peptic ulcer disease
- Cyclic Vomiting
 - Recurrent bouts of vomiting, separated by periods without any symptoms
 - Examples: Cyclical vomiting syndrome, intussusception

Differential diagnosis of vomiting by age and symptom pattern

	0-1 months	1-12 months	1-4 years	5-11 years	12-18 years
Acute	<ul style="list-style-type: none"> - FPIES - Hirschsprung's Disease - Intestinal atresia - Meningitis - Pyloric stenosis - Sepsis 	<ul style="list-style-type: none"> - AOM - Foreign body - FPIES - Gastroenteritis - Intussusception - UTI 	<ul style="list-style-type: none"> - Foreign body - Gastroenteritis - Pharyngitis - Toxic ingestion - UTI - Constipation 	<ul style="list-style-type: none"> - Appendicitis - Diabetic ketoacidosis - Pancreatitis 	<ul style="list-style-type: none"> - Choledocholithiasis - Diabetic ketoacidosis - Drug overdose
Chronic	<ul style="list-style-type: none"> - Adrenal insufficiency - GERD - Hirschsprung's disease - Intestinal atresia 	<ul style="list-style-type: none"> - GERD 	<ul style="list-style-type: none"> - Celiac disease - Eosinophilic esophagitis 	<ul style="list-style-type: none"> - Celiac disease - Eosinophilic esophagitis - Gastritis +/- H. pylori - Gastroparesis - PUD 	<ul style="list-style-type: none"> - Bezoar - CHS/marijuana use - Pregnancy
Cyclical/ Episodic	<ul style="list-style-type: none"> - Adrenal Insufficiency - IEM - Malrotation with volvulus 	<ul style="list-style-type: none"> - Adrenal insufficiency - IEM - Intussusception - Malrotation with volvulus 	<ul style="list-style-type: none"> - Adrenal insufficiency - Constipation 	<ul style="list-style-type: none"> - Abdominal migraine - Cyclical vomiting syndrome - UPJ Obstruction 	<ul style="list-style-type: none"> - Abdominal migraine - CHS/marijuana use - Cyclical vomiting syndrome - Eating disorder - SMA syndrome - UPJ Obstruction

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Red Flag Signs and Symptoms of Vomiting

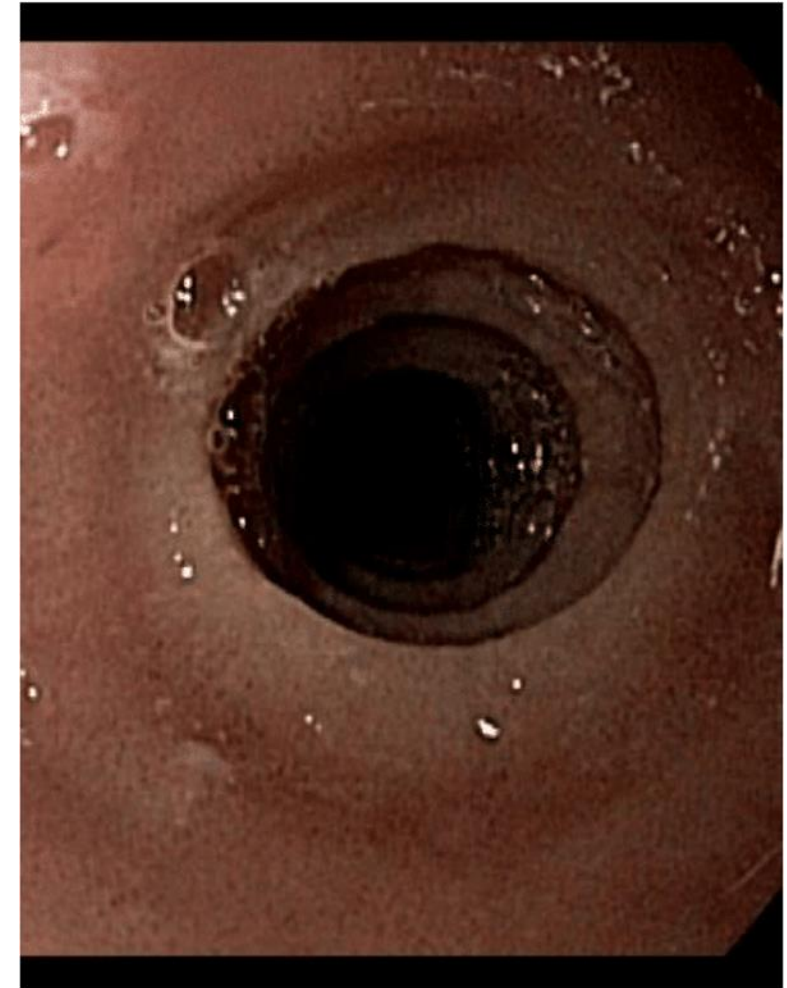
- Hematemesis (especially with first bout of vomiting)
- Bilious emesis
- Focal neurological deficits
- Lack of nausea
- Vomiting that wakes a child from sleep
- Abdominal distention
- Tympanitic bowel sounds
- Vomiting that leads to dehydration

Note: Important to document the absence of these in your note

GI Causes of Vomiting

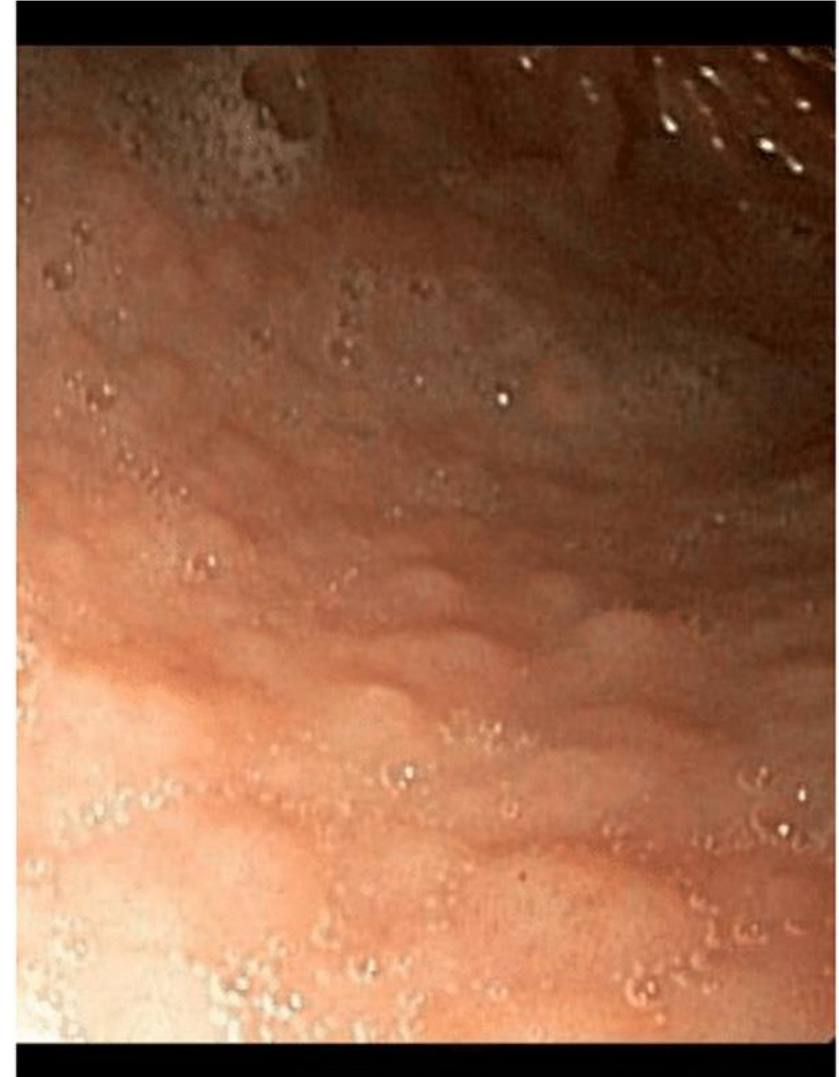
Eosinophilic esophagitis

- Chronic inflammatory condition of the esophagus due to increased eosinophilic activity
- Typically associated with other atopic conditions (asthma, eczema)
- Older patients typically complain of dysphagia but younger children are more likely to refuse food, cry with eating or vomit



H. pylori gastritis

- Diagnosis
 - Stool antigen
 - Urease breath test
 - EGD
- EGD: Presence of nodules in the gastric body
- Treatment
 - Amoxicillin, clarithromycin, PPI (Triple therapy)
 - Bismuth, PPI, metronidazole, doxycycline (Quadruple therapy)



Intestinal malrotation +/- volvulus

- Abnormal positioning of the intestine due to incomplete rotation during gestation
- **Bilious emesis**
- Infants may appear limp/lethargic
- Initial steps: Place NG tube, consult surgery
- Diagnosis
 - Upper GI series, contrast enema
 - US abdomen
 - CT abdomen

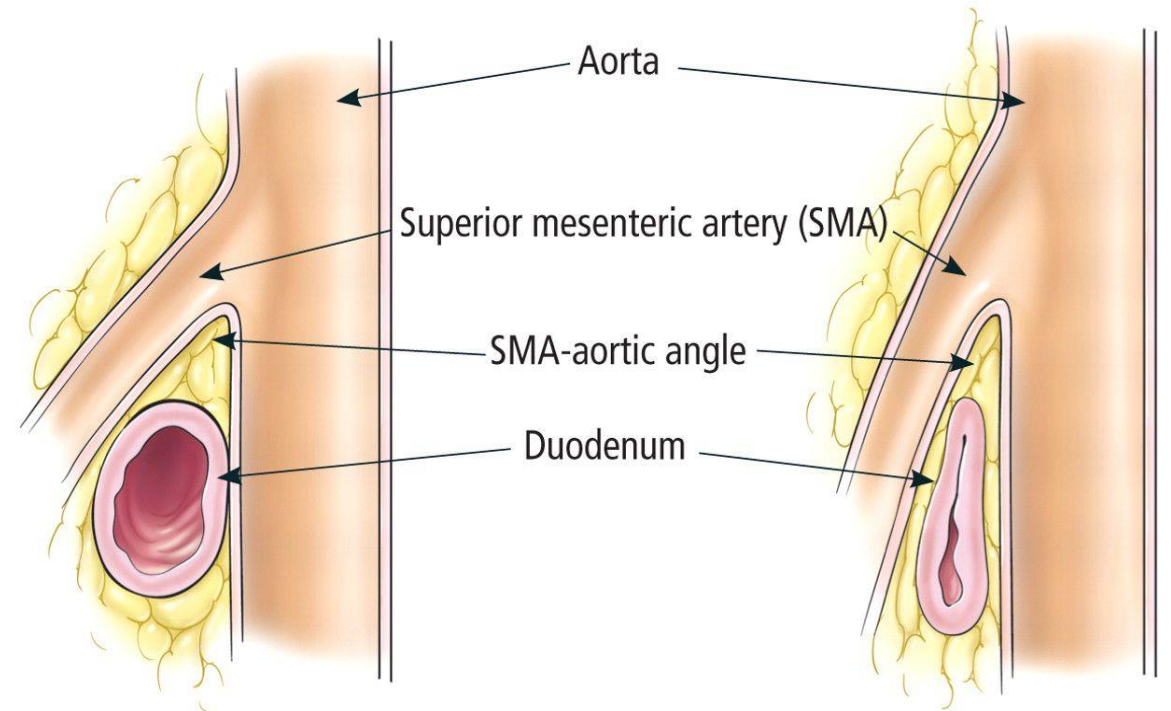


Gastroparesis

- Functional delay in stomach emptying
- Symptoms: Nausea, early satiety, vomiting undigested food several hours after eating, weight loss
- Causes
 - Viral infections
 - Type 1 DM
 - Cerebral palsy
 - Post-surgical with injury to vagus nerve
 - Opioids, anticholinergics
 - Acidosis
- Diagnosis: Gastric emptying scan, antroduodenal manometry
- Treatment: Frequent, low-fat meals; prokinetic medications
- Can take several weeks to months to resolve

Superior Mesenteric Artery (SMA) Syndrome

- Adipose tissue that normally suspends the SMA over the third portion of the duodenum is reduced
- “Nutcracker effect” whereby the SMA compresses the duodenum, resulting in a partial or complete bowel obstruction
- Symptoms: Vomiting but just typically with eating



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Superior Mesenteric Artery (SMA) Syndrome

- At risk patients: PICU patients, athletes with weight restrictions (wrestling, figure skating, gymnastics, crew)
- Diagnosis: Upper GI series will demonstrate a stasis or pooling of contrast in the proximal duodenum
- Treatment: Liquid diet until weight improves, or feeding distal to the obstruction (NJ tube) in more severe cases

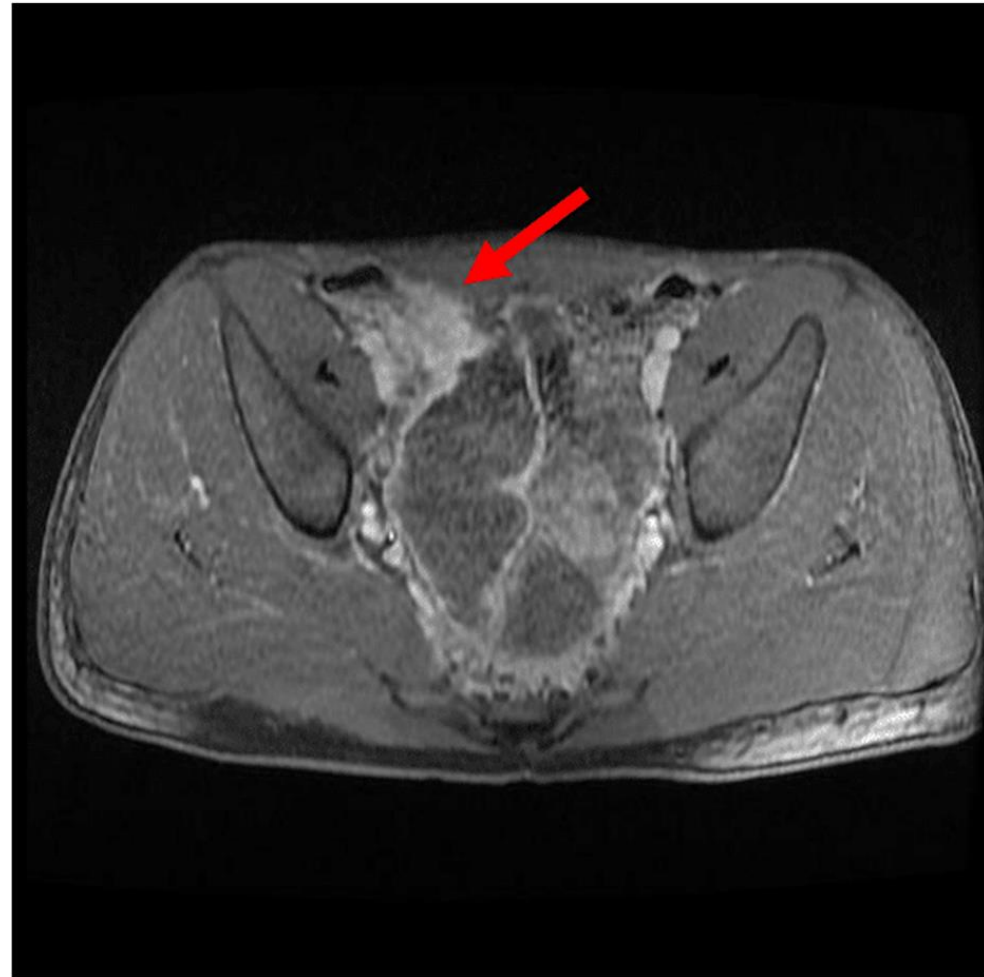
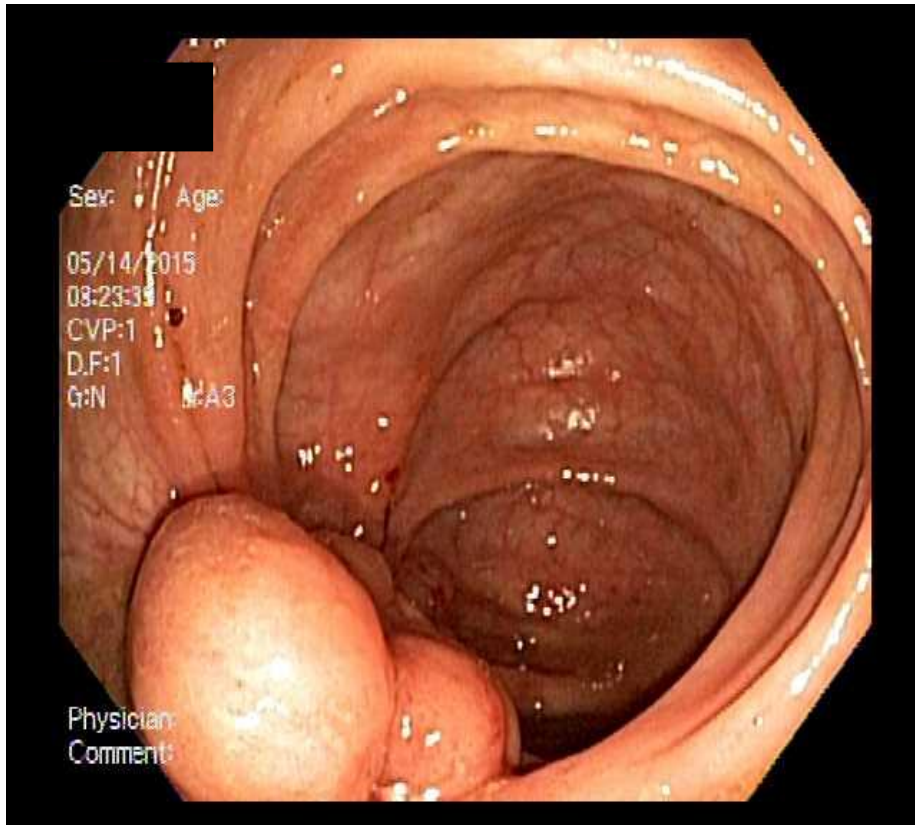
Crohn's Disease (Strictureing variant)

- Three phenotypes of Crohn's disease: Inflammatory, penetrating and stricturing disease
- Strictureing Crohn's disease can result in obstruction as a result of chronic inflammation and fibrosis
- Typically occurs in the terminal ileum
- Consider a stricture in any patient with a history of bowel resection with anastomosis or inflammatory process (Examples: Necrotizing enterocolitis, gastroschisis)

Crohn's disease (Stricturing variant)

- 17-year-old male with 3 recurrent ED visits for NBNB vomiting, afebrile
- Symptoms ultimately would resolve after a few hours of bowel rest and was diagnosed with a viral gastroenteritis on each occasion
- Complained intermittently of RLQ abdominal pain and weight loss
- Stool for occult blood was positive

Crohn's Disease (Stricturing disease)



Other GI Causes of Vomiting to remember

- Constipation
- GER/GERD
- Viral gastroenteritis
- Foreign body
- Bezoar
- Toxic ingestion
- Pancreatitis
- Gastric outlet obstruction
 - Pyloric stenosis
 - Antral web
- Intestinal atresia
- Hirschsprung disease
- Pseudoobstruction

Non-GI Causes of Vomiting

Food Protein-Induced Enterocolitis Syndrome (FPIES)

- Non-IgE mediated reaction to the protein component of food
- Different than the more common diagnosis of cow's milk protein intolerance (food protein induced enteropathy)
- Usually presents during infancy and resolves by 3 years of age
- Presents 2-6 hours after ingestion of food
- Presents with vomiting and often diarrhea in the absence of respiratory symptoms, hives or swelling
- Common causes: Oats, cow's milk, soy, sweet potatoes



Cyclical Vomiting Syndrome (CVS)

- Characterized by episodic spells of sudden vomiting, usually early in the morning (3 AM-6 AM)
- Often there is a family history of migraines
- Rome IV Criteria for the diagnosis of CVS
 - Occurrence of 2 or more periods of intense, unremitting vomiting lasting hours to days within a 6 month period
 - Episodes are stereotypical in each patient
 - Episodes are separated by weeks to months and return to baseline in between
 - *After appropriate evaluation*, the symptoms cannot be attributed to another condition

Cyclical Vomiting Syndrome

- Differential diagnosis: Intestinal malrotation, gastroparesis, IEM, increased ICP
 - Consider an upper GI series, GE scan
 - Inquire about developmental delay, vomiting brought on by high protein meal, fasting, etc.
 - Consider imaging of the brain/head as clinically indicated
- Exclude marijuana use in adolescents
- Treatment: Cyproheptadine \leq 5 years; amitriptyline $>$ 5 years

Cannabinoid Hyperemesis Syndrome (CHS)

- Emerging condition associated with chronic marijuana exposure which results in severe vomiting
- Pathophysiology of CHS is unclear as cannabinoids can also be used as an anti-emetic in some patients
- Hypothesis for pathophysiology of CHS:
 - Receptors for THC are located in the brain and the intestine (TRPV1, CB1)
 - TRPV1 in the intestine affects the rate of gastric emptying
 - With initial use of marijuana, receptors in the brain are stimulated resulting in an anti-emetic effect
 - With chronic use, receptors in intestine become increasingly sensitive to THC downregulating TRPV1 resulting in gastroparesis

Financial burden of CHS

- Retrospective observational study
- 17 patients presenting to the ED with CHS were enrolled between 2010 and 2015
- 3 medical centers (2 academic centers, 1 community hospital)
- Average number of ED visits for the 17 patients: 17.9 (5-38)
- Calculated total cost of ED services and imaging

Financial burden of CHS

Average Number of ED Admissions Per Patient	17.9
Average Total ED Charge	\$ 36,188.52
Average Number of X-Rays	0.9
Average Total Cost of X-Rays	\$756.78
Average Number of AAS (acute abdominal series)	5
Average Total Cost of AAS	\$4,189.50
Average Number of CTs	4.9
Average Total Cost of CTs	\$31,092.23
Average Number of US	2.4
Average Total Cost of US	\$4,063.89
Average Total Cost of All Imaging	\$40,102.40
Average Total Cost Incurred Per Patient	\$76,290.92

Note: This study does not include cost of hospitalization, EGD/colonoscopy or surgery

CHS and Hot Showers

- Taking a hot shower is known to alleviate symptoms of CHS
- Pathophysiology unclear
 - Vasodilation results in decreased blood flow to the intestine?
 - Upregulation of TRPV1 receptor which has anti-nausea effects?
- Hot showers can exacerbate dehydration
- Capsaicin cream has the same effect as a hot shower possibly through upregulation of TRPV1 receptor (Dezieck, et al. 2017)



Functional Vomiting

- Criteria for diagnosis
 - On average, 1 or more episode of vomiting per week
 - Absence of self-induced vomiting or criteria for an eating disorder or rumination
 - After *appropriate evaluation*, the vomiting cannot be fully explained by another medical condition
- Many patients also have comorbidities including anxiety and depression
- Treatment options
 - Mental health evaluations
 - Cognitive behavioral therapy
 - Hypnotherapy
 - Cyproheptadine (weak evidence)

Other non-GI causes of vomiting to remember

- Increased ICP
- Pregnancy
- Ureteropelvic junction obstruction
- Eating disorder
- Diabetic ketoacidosis
- Meningitis
- Adrenal Insufficiency
- Inborn errors of metabolism (Organic acidemia, Urea cycle defect)

Evaluation of vomiting

Acute	Chronic	Cyclic
Electrolytes (Na+, K+, Cl-) BUN Creatinine Abdominal radiograph	Electrolytes (Na+, K+, Cl-) BUN Creatinine Celiac screen Amylase Lipase Urine β -HCG Hepatic function panel Stool <i>H. pylori</i> antigen Upper Endoscopy MRI Brain/CT Head	Electrolytes (Na+, K+, Cl-) BUN Creatinine Glucose Upper GI Series US abdomen Serum amino acids Urine organic acids Urine ketones Carnitine profile Ammonia Lactate Pyruvate

Note: There is little role for upper endoscopy in evaluating causes of vomiting

Medication	Dose	Receptor	Notes
Ondansetron	0.3-0.4 mg/kg/dose q 4-6 hours	5-HT ₃	Diarrhea is a side effect
Granisetron	40 mcg/kg/dose q 12 hours	5-HT ₃	
Ginger	250 mg TID	5-HT ₃ (?)	The mechanism of action of ginger is not completely understood.
Cyproheptadine	0.25-0.5 mg/kg/day	5-HT _{2A} , 5-HT _{2B} , H ₁	Stimulates appetite
Amitriptyline	0.25 mg/kg/day (Max 1 mg/kg/day)	Serotonin	Increased risk of cardiac arrhythmia
Erythromycin	5 mg/kg/dose q 6 hours	Motilin	Can increase risk of pyloric stenosis in infants
Diphenhydramine	5 mg/kg/day divided TID or QID	H ₁ , D ₂	
Promethazine	0.25-1 mg/kg/dose q 4-6 hours	H ₁	Contraindicated in children < 2 years old due to respiratory depression
Meclizine	25-50 mg 1 hour before travel	H ₁	For patients 12 years and older
Prochlorperazine	5-10 mg q 6-8 hours (≥40 kg)	D ₁ , D ₂	
Metoclopramide	0.1-0.2 mg/kg/dose q 6-8 hours	D ₂	Black box warning: Increased risk of tardive dyskinesia
Scopolamine	1 mg transdermal disc applied behind ear q 3 days	M ₁	
Aprepitant	Children 6-30kg: 3 mg/kg on Day 1, then 2 mg/kg on Day 2 and Day 3 Children >30 kg: 125 mg on Day 1, then 80 mg on Day 2 and Day 3	NK ₁	Indicated for chemotherapy-induced nausea Causes fatigue, dizziness Not for long-term use

Take-Home Points

- There are 4 main physiologic pathways that can trigger the emetic reflex: mechanical, blood-borne toxin, motion and emotion
- Establishing a cause of vomiting should take into account the patient's age and the temporal nature of the vomiting
- Document presence or absence of the red-flag symptoms
- Bilious emesis, especially in an infant, should always prompt urgent evaluation
- Cannabinoid hyperemesis syndrome is a growing problem and is expected to get worse with the legalization of marijuana in Massachusetts

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