

# **Nausea and Vomiting**

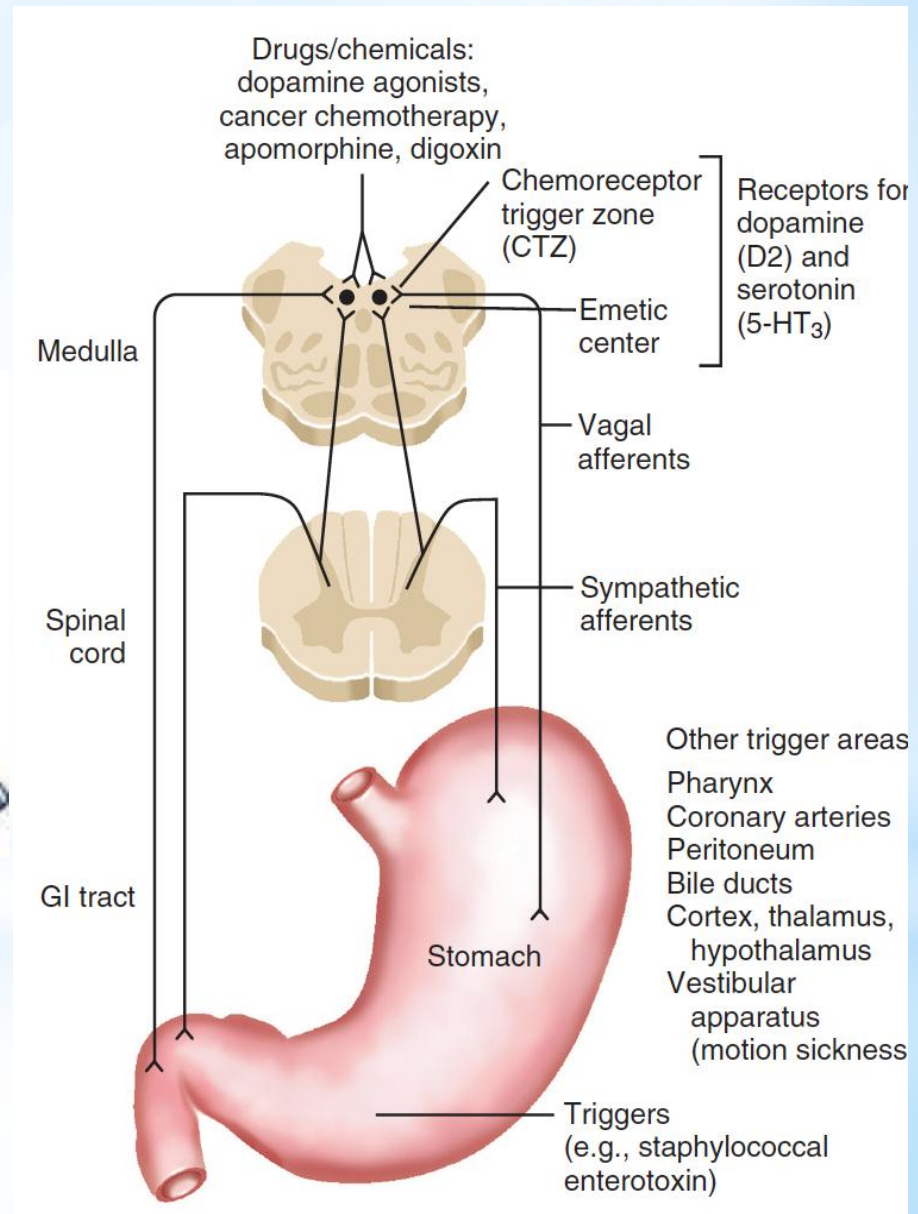
# Definition

Nausea:	Unpleasant subjective sensation Feeling of impending vomiting in epigastrium or throat
Retching:	Spasmodic and abortive respiratory movements with glottis closed Associate with intense nausea and usually culminates in vomiting
Vomiting:	a <b>partially voluntary</b> act of forcefully expelling gastric or intestinal content through the mouth

Differentiated from regurgitation: an **effortless reflux** of gastric contents into the esophagus that sometimes reaches the mouth, not associated with the forceful ejection

# Pathophysiology

## Emetic reflex arc



## Emetic reflex:

### Emetic signals:

1. GI tract (vagal fiber, hormones)
2. Abdominal pain
3. Non-digestive organ: heart, testicles
4. Chemoreceptor trigger zone (CTZ): sensitive detection apparatus for circulating endogenous and exogenous molecules
5. Central nervous system: cortex, brainstem, vestibular system,

## Receptors:

- \* 1. 5-HT<sub>3</sub> (5 Hydroxytryptamine<sub>3</sub>)-> release Dopamine->Dopamine D2 receptor->activate emesis sequence
  - \* Application: Ondansetron (5-HT<sub>3</sub> receptor inhibitor -> treating acute chemotherapy-induced vomiting); metoclopramide (dopamine D2 receptor antagonist)
- \* Histamine H1 and Muscarinic M1 receptor: vestibular center and solitary nucleus
  - \* Application: pharmacologic targets for inhibiting motion sickness, vestibular nausea, pregnancy-related emesis
- \* Cannabinoid CB1 receptors
- \* Neurokinin-1 (NK-1) receptors: part of terminal emetic pathway. Activation of NK-1 receptors by substance P -> chemotherapy induced emesis. NK-1 antagonists reduces emesis induced by peripherally and centrally acting emesis

## Neural efferents

1. Activation of cerebral cortex, stomach relaxes, antral and intestinal peristalsis is inhibited
2. Retching: spasmodic contraction of diaphragm and intercostal muscles, glottis closure
3. Vomiting: simultaneous activation of somatic and visceral components:
  - \* brisk contraction of the diaphragm and abdominal muscles
  - \* relaxation of the lower esophageal sphincter,
  - \* forceful retrograde peristaltic contraction in the jejunum that pushes enteric content into the stomach and from there toward the mouth.
4. Protective reflexes are activated
  - \* The soft palate is raised to prevent gastric content from entering the nasopharynx
  - \* respiration is momentarily inhibited
  - \* the glottis is closed to prevent pulmonary aspiration.

## Other reflex:

1. Hypersalivation
2. Cardiac arrhythmias
3. Pass of gas and stool rectally
4. Alleviate nausea



## Abdominal Causes

- \* Mechanical obstruction
- \* Gastric outlet obstruction
- \* Small bowel obstruction
- \* Motility disorders
- \* Chronic intestinal pseudo-obstruction
- \* Functional dyspepsia
- \* Gastroparesis

## Other intra-abdominal causes

- \* Acute appendicitis
- \* Acute cholecystitis
- \* Acute hepatitis
- \* Acute mesenteric ischemia
- \* Crohn's disease
- \* Gastric and duodenal ulcer disease
- \* Pancreatitis and pancreatic neoplasms
- \* Peritonitis and peritoneal carcinomatosis
- \* Retroperitoneal and mesenteric pathology

## Drugs

*Aspirin and other NSAIDs*

*Antidiabetic agents*

*Antigout drugs*

*Antimicrobial agents:* Acyclovir, Antituberculosis drugs, Erythromycin, Sulfonamides, Tetracycline

*Cancer chemotherapy:* Cisplatin, Cytarabine, Dacarbazine, Etoposide, 5-Fluorouracil, Methotrexate, Nitrogen mustard, Tamoxifen, Vinblastine

*Cardiovascular drugs:* Antiarrhythmics, Antihypertensives, Beta blockers, Calcium channel blockers, Digoxin, Diuretics

*Central nervous system drugs:*

Antiparkinsonian drugs (levodopa and other dopamine agonists), Anticonvulsants

*GI medications:* Azathioprine, Sulfasalazine

*Narcotics*

*Oral contraceptives*

*Theophylline*



## Infectious Causes

- \* Acute gastroenteritis: Viral, Bacterial
- \* Nongastrointestinal (systemic) infections

## Metabolic and Endocrine Causes

- \* Acute intermittent porphyria
- \* Addison's disease
- \* Diabetic ketoacidosis
- \* Diabetes mellitus
- \* Hyperparathyroidism and other causes of hypercalcemia
- \* Hyperthyroidism
- \* Hyponatremia
- \* Hypoparathyroidism
- \* Pregnancy

## Nervous System Causes

- \* Demyelinating disorders
- \* Disorders of the autonomic nervous system

## Hydrocephalus:

Congenital malformations  
Increased intracranial pressure  
Low-pressure hydrocephalus

## Intracerebral lesions with edema

Abscess  
Hemorrhage  
Infarction  
Neoplasm

## Labyrinthine disorders

Labyrinthitis  
Ménière's disease  
Motion sickness

## Meningitis

## Migraine headaches

## Otitis media

## Seizure disorders

## Visceral neuropathy

## Other Causes

- \* Anxiety and depression
- \* Cannabinoid hyperemesis syndrome
- \* Cardiac disease
  - Heart failure
  - Myocardial infarction, ischemia
  - Radiofrequency ablation for arrhythmias
- \* Collagen vascular disorders
  - Scleroderma
  - Systemic lupus erythematosus
- \* Cyclic vomiting syndrome
- \* Eating disorders
- \* Ethanol abuse
- \* Functional disorders
- \* Hypervitaminosis A
- \* Intense pain
- \* Paraneoplastic syndrome
- \* Postoperative state
- \* Postvagotomy
- \* Radiation therapy
- \* Starvation

# Acute vomiting: <1 week

1. Is emergency action required? Shock, hypokalemia, serious electrolyte disturbances, hollow viscus perforation, organ infarction, cerebral edema, poisoning
2. Is the female patient pregnant?

## Cause of acute vomiting:

1. **Acute intestinal obstruction:** incarcerated hernia, impact stool, distal duodenal or proximal jejunal neoplasms (adenocarcinoma, lymphoma, leiomyosarcoma, carcinoid)
2. **Gastric outlet obstruction:** gastric ulcer disease, gastric volvulus, paraesophageal and post-traumatic diaphragmatic hernias, acute and chronic pancreatitis (inflammation mass, necrosis, pseudocysts, secondary infection), gastric, duodenal and pancreatic malignancies

**3. *Intestinal infarction:*** vascular disorders and thrombotic diatheses in old patients

**4. *Extraintestinal causes***

- \* Myocardial infarction: innitally manifests as acute vomiting (connection between heart and emetic center)
- \* Renal colic
- \* Biliary pain
- \* Torsion of ovarian or testicular
- \* Intraabdominal or retroabdominal inflammation condition...

**5. *Toxins and drugs: common, not difficult to diagnose***

- \* Alcohol abuse
- \* Cancer chemotherapy
- \* Drugs: aspirin, NSAIDs, cardiovascular drugs (digitalis, antiarrhythmics), antibiotics, levodopa, theophylline, opiates, azathioprine

## 6. *Metabolism*

- \* Diabetic ketoacidosis
- \* Hyponatremia, hypernatremia
- \* Addison disease

## 7. *Infection*

Acute gastritis, gastroenteritis (norovirus, bacteria): enterotoxin stimulation of enterochromaffin cells -> 5-HT

## 8. *Neurologic causes*

- \* Meningeal inflammation
- \* Vertigo in vestibular or cerebellar disorder
- \* Motion sickness (5-HT<sub>1B</sub>, 5-HT<sub>1D</sub> receptors in vestibular apparatus)
- \* Migraine headache
- \* Intracerebral lesions: increased intracranial pressure, interference with intracerebral fluid flow, direct compression of the emetic center

## 9. *Postoperative nausea and vomiting*

Risk:

- \* Abdominal, gynecologic, strabismus, and middle ear surgery,
- \* Women > men
- \* General and epidural anesthesia > intravenous anesthesia

Differentiate with other causes in postop. period

# Chronic and relapsing vomiting

Consider the same causes of acute vomiting

Additional considerations: pregnancy, functional vomiting, cyclic vomiting syndrome, pseudovomiting

## **1. *Partial intestinal obstruction***

- \* Relapsing vomiting accompany with abdominal pain, distension
- \* Stenosing Crohn's disease, neoplasms of the intestine, postradiation enteric injury, and ischemic strictures, adhesions from surgery, pelvic inflammatory disease, advanced intra-abdominal cancer
- \* In older: debilitated, and mentally challenged persons, constipation: the colon becomes impacted with stool and ileal outflow is partially impeded

## **2. *Gastric outlet obstruction: PUD***



### **3. *GI motility disorders***

Gastroparesis, chronic intestinal pseudo-obstruction: recurrent vomiting, symptom-free period -> food aversion, poor oral intake, malnutrition; abdominal pain absence, dilated stomach, delayed gastric empty

### **4. *Neurologic disorders***

- \* Migraine
- \* Hydrocephalus
- \* Lesion that compress or irritate the emetic center

### **5. *Nausea and Vomiting during pregnancy***

- \* Early in pregnancy, peak around 9 weeks' gestation, rarely continue beyond 22 week
- \* Multiple gestation > single gestation
- \* Origin: unclear, hormone, psychology, increased HCG (stimulate gastric cholecystokinin receptor)
- \* Pharmacotherapy to alleviate discomfort: ondansetron, related 5-HT antagonists, metoclopramide, doxylamine-pyridoxine

*Hyperemesis gravidarum*: severe nausea and vomiting that leads to complications (e.g., dehydration, electrolyte imbalance, Mallory-Weiss tears, malnutrition), may continue beyond the 1<sup>st</sup> trimester

Pathogenesis: hormonal and psychological factors

Treatment:

- \* 1-5% require hospitalization
- \* Fluid and electrolyte replacement, antiemetic drugs, Glucocorticoids, dopamine antagonists, phenothiazines, histamine receptor blockers, erythromycin, and powdered ginger root
- \* Behavior modification and other psychotherapeutic techniques
- \* Small and frequent low-fat, protein-rich meals

## 6. *Functional vomiting*

- \* Consensus criteria (Rome III Consensus Committee on Functional Gastrointestinal Disorders):  $\geq 1$  of vomiting/week for 3 months with the onset of symptoms at least 6 months prior to diagnosis
- \* Excluding the usual organic causes of vomiting
- \* Special motility tests: differentiate functional vomiting from gastroparesis or intestinal pseudo-obstruction

7. Cyclic vomiting syndrome

8. Superior mesenteric artery syndrome

9. Rumination syndrome

# Evaluation

## *Acute Vomiting*

### Basic tests

Carefully obtained history and physical examination: patient's volume status

Urine pregnancy test (HCG) should be performed in women of childbearing potential

Blood test: blood count, kidney function, thyroid function tests, liver biochemical tests, electrolyte, glucose, serum amylase, lipase, arterial blood gases (acid-base status)

### Imaging

Plain abdominal radiographs:

Positive: further tests to ascertain the cause of obstruction

Negative: additional tests: upper GI endoscopy, US, CT, MRI

## Additional tests:

Blood level of drug, toxin

Culture of blood or body fluid if infection is suspected

Cerebrospinal fluid analysis

Serologic tests of hepatitis

## Chronic vomiting

- \* Detain clinical history and physical examination
- \* Upper GI endoscopy, Upper GI barium study for partial gastric outlet obstruction and partial duodenal obstruction
- \* CT: degree of bowel dilation, bowel wall thickness, transitional point of the caliber of intestinal lumen, intra-abdominal mass, retroperitoneal pathology
- \* MRI of abdomen
- \* MRI of the head: CNS lesions
- \* Motility tests to evaluate motor disorder: gastroparesis, chronic intestinal pseudo-obstruction

## **1. Esophageal manometry**

Assess esophageal motor activity: Achalasia, distal esophageal spasm, motor disturbance

## **2. Measurement of gastric emptying**

- \* Radioscintigraphy is the preferred and most accurate method of assessing gastric emptying. Dual marker (1 for solids and 1 for liquids) detected by a dual headed gama camera
- \* Gastric 3-D US: assess emptying of liquid meal and C13 breath test with octanoate acid (labeled with stable isotope and incorporated into meal)
- \* Wireless motility capsule
- \* MRI
- \* Single photon emission CT

### ***3. Cutaneous electrogastrography (EGG)***

Identify dysrhythmia of gastric pacemaker and changes in frequency of pacemaker activity in response to feeding

Non-invasive and simplicity

Unreliability (Certain EGG anomalies may be secondary to nausea rather than the cause of nausea)

### ***4. GI manometry***

Most reliable physiologic test for assessing motor disturbances of the upper GI tract

Pressure sensitive catheter is inserted in antrum and small bowel

Cumbersome, expensive, technical challenge, and available at only a few centers



## ***5. Autonomic function tests***

Assess sympathetic function

- \* Tilt table test (orthostatic challenge to blood pressure and cardiac rate regulation)
- \* Cold hand test (pain reflex test, the hand is immersed in cold water to produce vasoconstriction and, normally, a significant increase in systolic arterial pressure)
- \* Parasympathetic function test measuring variations in the RR interval on the electrocardiogram in response to bradycardia induced by deep respiration

## ***6. Histopathologic study***

- \* mucosal biopsies for quantification of nerve density and morphology to search for evidence of autonomic neuropathy

