Approach to the adult with nausea and vomiting

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INTRODUCTION — Nausea, the unpleasant sensation of being about to vomit, can occur alone or can accompany vomiting (the forceful expulsion of gastric contents), dyspepsia, or other gastrointestinal symptoms. Retching differs from vomiting in the absence of expulsion of gastric content. In addition, patients may confuse vomiting with regurgitation, which is the return of esophageal contents to the hypopharynx with little effort [1]. (See "Clinical manifestations and diagnosis of gastroesophageal reflux in adults".)

The recommendations made in this topic are generally consistent with the American Gastroenterological Association (AGA) guidelines for nausea and vomiting [2]. The pathophysiology of nausea and vomiting and the overall approach to the patient with these symptoms will be reviewed here. The prevention and treatment of chemotherapy-induced nausea and vomiting and characteristics of antiemetic drugs are discussed separately. (See "Prevention and treatment of chemotherapy-induced nausea and vomiting" and "Characteristics of antiemetic drugs".)

PATHOPHYSIOLOGY — Normal function of the upper gastrointestinal tract involves an interaction between the gut and the central nervous system. The motor function of the gut is controlled at three main levels: the parasympathetic and sympathetic nervous systems; enteric brain neurons; and smooth muscle cells (figure 1). A discussion of the anatomy and physiology of gastric motor function is discussed separately. (See "Pathogenesis of delayed gastric emptying".)

Nausea — Studies that produce motion sickness in humans indicate how some of the physiologic interactions can cause nausea [3,4]. In one report, for example, gastric myoelectrical activity and endogenous neuroendocrine responses were compared in subjects with and without motion sickness elicited by vection (induced by rotating a drum with black and white vertical stripes around seated stationary subjects) [3]. Thirteen subjects developed tachygastria (an increase in gastric slow wave rhythm) and motion sickness during vection, while nine maintained normal gastric rhythms and remained symptom-free. Nausea followed within minutes of and was proportional to the degree of tachygastria. Anticipatory increases in plasma cortisol and beta endorphin occurred in subjects who developed nausea and gastric tachyarrhythmias; endogenous epinephrine and norepinephrine concentrations were also increased in these subjects.

Vomiting — Vomiting is a reflex that allows an animal to rid itself of ingested toxins or poisons. It can be activated by humoral or neuronal stimuli, or both [5]. Multiple afferent and efferent pathways exist which induce vomiting; the following are the major components of these pathways:

- The area postrema in the floor of the fourth ventricle which contains a "chemoreceptor trigger zone" that is sensitive to many humoral factors, including neurotransmitters, peptides, drugs, and toxins.
- An area in the medulla known as the nucleus tractus solitarius (NTS) which may serve as a central pattern generator for vomiting; information from humoral factors via the area postrema and visceral afferents via the vagus nerve may converge at this site [5].
- The central pattern generator presumably projects to the various motor nuclei to elicit the sequential excitation and inhibition that controls the vomiting reflex.

Vagal afferent nerves from the gastrointestinal tract synapse in the NTS. From there, some neurons extend to the area postrema; other neurons from the NTS ascend to the paraventricular nuclei of the hypothalamus and the limbic and cortical regions, where gastric electromechanical events are perceived as normal sensations or symptoms such as nausea or discomfort. Afferent sympathetic neurons mediating nociceptive stimuli synapse in the spinal cord and ascend to brainstem nuclei and the hypothalamus, where vasopressin (antidiuretic hormone) and corticotropin releasing factor can be released (figure 2).

Studies of vomiting in dogs reveal that gastric content is expelled as a result of gastric and lower esophageal sphincter relaxation, retrograde contraction in the proximal small bowel and antrum, abdominal muscle contraction, and initial cricopharyngeus contraction followed by relaxation seconds before vomiting [6]. Retching occurs when the glottis closes and respiratory muscles counteract abdominal muscle contraction to prevent the expulsion of gastric content.

APPROACH TO MANAGEMENT — As a general rule, the following three steps should be considered in patients with persistent nausea and vomiting [1].

- The etiology should be sought, taking into account whether the patient has acute nausea and vomiting or chronic symptoms (at least one month in duration) [7].
- The consequences or complications of nausea and vomiting (eg, fluid depletion, hypokalemia, and metabolic alkalosis) should be identified and corrected.
- Targeted therapy should be provided, when possible (eg, surgery for bowel obstruction or malignancy). In other cases, the symptoms should be treated.

History and physical examination — An initial careful history and physical examination should be performed. In most cases, the cause of the nausea and vomiting can be determined from the history and physical examination and additional testing is not required [7,8]. If additional testing is needed, it should be guided by the symptom duration, frequency, and severity, as well as the characteristics of vomiting episodes and associated symptoms.

The following clinical features are especially important:

- Abdominal pain with vomiting often indicates an organic etiology (eg, cholelithiasis). (See "Acute cholecystitis: Pathogenesis, clinical features, and diagnosis".)
- Abdominal distension and tenderness suggest bowel obstruction. (See "Epidemiology, clinical features, and diagnosis of mechanical small bowel obstruction in adults" and "Acute colonic pseudo-obstruction (Ogilvie's syndrome)".)
- Vomiting of food eaten several hours earlier and a succussion splash detected on abdominal examination suggest gastric obstruction or gastroparesis. (See "Gastroparesis: Etiology, clinical manifestations, and diagnosis" and "Gastric outlet obstruction in adults".)
- Heartburn with nausea often indicates gastroesophageal reflux disease (GERD), and GERD can present as chronic nausea without typical reflux symptoms [9]. (See "Clinical manifestations and diagnosis of gastroesophageal reflux in adults".)
- Early morning vomiting is characteristic of pregnancy. (See "Clinical manifestations and diagnosis of early pregnancy".)
- Feculent vomiting suggests intestinal obstruction or a gastrocolic fistula. (See "Epidemiology, clinical features, and diagnosis of mechanical small bowel obstruction in adults" and "Acute colonic pseudo-obstruction (Ogilvie's syndrome)".)
- Vertigo and nystagmus are typical of vestibular neuritis and other causes of vertigo. (See "Vestibular neuritis" and "Pathophysiology, etiology, and differential diagnosis of vertigo".)
- Bulimia is associated with dental enamel erosion, parotid gland enlargement, lanugo-like hair, and

calluses on the dorsal surface of the hand [10]. (See "Eating disorders: Overview of epidemiology, diagnosis, and course of illness".)

- Neurogenic vomiting may be positional, projectile, and is usually associated with other neurologic signs or symptoms. (See "Clinical presentation and diagnosis of brain tumors".)

Endoscopy — Chronic dyspepsia often overlaps with nausea and vomiting [11]. Most patients with chronic nausea and vomiting that is unexplained after routine evaluation should undergo esophagogastroduodenoscopy to identify disorders that should have specific therapy.

However, endoscopy and other routine tests are often normal, suggesting an idiopathic (functional) etiology. (See "Functional dyspepsia in adults".)

DIFFERENTIAL DIAGNOSIS — Disorders associated with nausea and vomiting are listed in following table (table 1).

SPECIFIC DISORDERS

Acute disorders

Acute gastroenteritis — Acute gastroenteritis is second only to the common cold as a cause of lost productivity [12]. Bacterial, viral, and parasitic pathogens cause this illness which is characterized by diarrhea and/or vomiting. Vomiting is especially common with infections caused by rotaviruses, enteric adenovirus, and norovirus. (See "Epidemiology and pathogenesis of viral gastroenteritis in adults".)

Laboratory testing usually is unnecessary in adults with domestically acquired illness. In one study, there was no association between abnormal laboratory results and the requirement for intravenous hydration, antibiotic treatment for a positive stool culture, or hospitalization [13]. Stool cultures had higher yields in patients with fever or diarrhea of more than two days' duration.

Postoperative nausea and vomiting — About one-third of surgical patients have nausea, vomiting or both after receiving general anesthesia. Risk factors include female sex, nonsmoker status, previous history of postoperative nausea and vomiting or motion sickness, and unanticipated use of postoperative opioids. Most research has been directed toward prevention rather than therapy of established symptoms [14]. In a large trial, intravenous doses of 1.25 mg of droperidol and 4 mg of dexamethasone within 20 minutes after the start of anesthesia or 4 mg of ondansetron during the last 20 minutes of surgery each reduced postoperative nausea and vomiting by about 26 percent [14]. Combining drugs had an additive effect, and the combination of droperidol and dexamethasone was more beneficial than ondansetron.

Vestibular neuritis — This acute labyrinthine disorder is characterized by rapid onset of severe vertigo with nausea, vomiting and gait instability. (See "Vestibular neuritis".)

Patients receiving chemotherapy — Nausea and vomiting are common side effects of cancer chemotherapy. Anticipatory antiemetic therapy is indicated when highly emetogenic chemotherapy regimens are given. (See "Prevention and treatment of chemotherapy-induced nausea and vomiting".)

Drugs — Multiple drugs are associated with nausea and thus a careful medication history is mandatory. The history should include non-prescription drugs. Use of marijuana has been associated with recurrent vomiting with features similar to cyclic vomiting syndrome. Compulsive bathing behavior may be a clue to identifying cannabinoid hyperemesis [15,16]. (See "Cyclic vomiting syndrome".)

Chronic disorders

Nausea and vomiting of pregnancy — About 70 to 85 percent of pregnant women suffer nausea and/or vomiting; 50 percent have both nausea and vomiting, and 25 percent have nausea only. Risk factors include increased placental mass (eg, advanced molar gestation, multiple gestation), family history of hyperemesis gravidarum or a personal history of the disorder in a previous pregnancy, female fetus, and a history of motion sickness or migraine headaches.

This disorder nearly always begins within the first nine weeks of pregnancy; onset after the initial nine weeks

should direct especially careful evaluation for another cause within the differential diagnosis of nausea and vomiting in nonpregnant patients. The diagnosis of hyperemesis gravidarum is applied to the most severely affected patients, approximately 0.5 to 2 percent of pregnancies. (See "Clinical features and evaluation of nausea and vomiting of pregnancy".)

Functional nausea and vomiting — Some patients with functional gastroduodenal disorders have nausea and/or vomiting [11,17]. (See "Functional dyspepsia in adults".)

Gastroparesis — Nausea may be a feature of gastroparesis but there is a poor correlation among symptoms, gastric dysrhythmias, and gastric emptying rate. Gastric motor dysfunction can be identified by special tests (such as gastric scintigraphy) in a large proportion of these patients. A noninvasive method of recording gastric myoelectrical activity or slow waves from cutaneous leads placed over the stomach (electrogastrography) reveals abnormalities in some patients. There is no evidence that correction of these abnormalities improves symptoms; thus, the role of this procedure in management is uncertain [18]. (See "Gastroparesis: Etiology, clinical manifestations, and diagnosis" and "Treatment of gastroparesis".)

Gastroesophageal reflux — Nausea can occasionally be the presenting symptom of gastroesophageal reflux disease. (See "Clinical manifestations and diagnosis of gastroesophageal reflux in adults", section on 'Clinical manifestations' and "Medical management of gastroesophageal reflux disease in adults".)

Gastric outlet obstruction — Pyloric stenosis can occur from malignancy or peptic ulcer disease. Inflammatory edema associated with ulcers may respond to acid suppression therapy and nasogastric suction. However, fibrotic strictures may persist after ulcer healing. Treatment of benign fibrotic strictures can be accomplished surgically or endoscopically. The endoscopic approach is the least invasive; however, there is a risk of perforation and recurrence is common after long-term follow-up if the natural history of the underlying ulcer disease is not altered. Conversely, one study revealed that all 23 patients whose obstruction related to peptic ulcer disease was treated with endoscopic dilation, removal of inciting factors, and gastric suppression, had long-term symptom remission [19]. Endoscopic dilation may be most appropriate for patients at high risk for surgery. (See "Overview of the complications of peptic ulcer disease" and "Gastric outlet obstruction in adults".)

Eosinophilic gastroenteritis — Benign eosinophilic infiltration of the gut is uncommon, but its diagnosis is especially important as steroid therapy is usually effective. (See "Eosinophilic gastroenteritis".) The disease can occur from the esophagus to the colon, and the symptoms depend upon the extent and layer(s) of bowel involved. Gastric mucosal disease is typically associated with nausea and vomiting. (See "Eosinophilic gastroenteritis".)

Cyclic vomiting syndrome — Cyclic vomiting syndrome is characterized by repeated episodes of nausea and vomiting that last for hours to days and are separated by symptom-free periods of variable length [20]. It has been most often described in children in whom symptoms often begin in the early school years and stop spontaneously at puberty. In adults, the disorder consists of episodes of nausea and vomiting lasting for three to six days in a patient-specific stereotypic pattern. (See "Cyclic vomiting syndrome".)

Chronic idiopathic intestinal pseudo-obstruction — Chronic intestinal pseudo-obstruction is usually secondary to an underlying disorder affecting neuromuscular function that suggests mechanical bowel obstruction of the small or large bowel in the absence of an anatomic lesion that obstructs the flow of intestinal contents. (See "Chronic intestinal pseudo-obstruction".)

Rumination syndrome — The rumination syndrome is a behavioral disorder that is most commonly identified among mentally-disadvantaged children, although it is increasingly recognized among adolescents and adults of normal mental capacity. The behavior consists of daily, effortless regurgitation of undigested food within minutes of starting or completing ingestion of a meal. (See "Gastroparesis: Etiology, clinical manifestations, and diagnosis", section on 'Differential diagnosis'.)

TREATMENT — Various therapies, including drugs, gastric electrical stimulation, and surgery, have been used in the treatment of nausea and vomiting. Dietary interventions and the treatment of hypovolemia are discussed elsewhere. (See "Treatment of gastroparesis", section on 'Dietary modification' and "Maintenance and replacement fluid therapy in adults" and "Treatment of severe hypovolemia or hypovolemic shock in adults".)

Drug therapy — Few high quality therapeutic trials have compared the efficacy of different drugs in specified types of nausea and vomiting. As a result, treatment is often based upon clinical experience, costs, and safety.

Antiemetics and prokinetics — Acute or chronic nausea and vomiting can often be helped by antiemetic or prokinetic drugs [21]. The antiemetic drug therapy generally recommended varies according to the etiology (table 2). The efficacy of the available prokinetic drugs is limited [1]. (See "Characteristics of antiemetic drugs".)

- Prochlorperazine is an antiemetic that often partially alleviates acute nausea and vomiting (eg, acute gastroenteritis), but is associated with risks of hypotension and extrapyramidal side effects. Prochlorperazine should usually be considered in such cases before trying serotonin receptor antagonists or prokinetic drugs.

- The dopamine receptor antagonist, metoclopramide, has combined antiemetic and prokinetic properties. However, it can be associated with extrapyramidal side effects. It can be given orally or intravenously. When given intravenously, using a slow infusion over 15 minutes is associated with a lower incidence of akathisia compared with bolus dosing, without a decrease in efficacy [22].

  Another dopamine antagonist, domperidone, penetrates the blood-brain barrier poorly. As a result, anxiety and dystonia are much less common than with metoclopramide. Domperidone is not approved for use in the United States. However, the Food and Drug Administration has encouraged "physicians who would like to prescribe domperidone for their patients with severe gastrointestinal disorders that are refractory to standard therapy to open an Investigational New Drug Application." The FDA domperidone investigational new drug section can be contacted at DomperidoneIND@fda.hhs.gov. (See "Treatment of gastroparesis", section on 'Domperidone'.)

- Agents with mainly prokinetic properties include erythromycin (motilin receptor agonist) and bethanechol (muscarinic receptor agonist).

  Erythromycin has a narrow therapeutic window, above which abdominal pain and nausea are common. Thus, it can improve gastric emptying without improving nausea. A systematic review of published clinical trials of oral erythromycin therapy for various types of gastroparesis revealed that all studies were methodologically weak and that improvement occurred in fewer than 50 percent of patients [23].

  The side effects of bethanechol are similar to those of erythromycin, and trial data are even more limited.

- The serotonin antagonists form the cornerstone of therapy for the control of acute emesis with chemotherapy agents and can also be used or other causes of nausea and vomiting (table 2). (See "Characteristics of antiemetic drugs", section on 'Serotonin receptor antagonists' and "Prevention and treatment of chemotherapy-induced nausea and vomiting", section on '5-HT3 receptor antagonists'.)

Antidepressants — Some patients have chronic functional nausea and/or vomiting that does not fit the pattern of cyclic vomiting syndrome or other disorders [11,17]. Antinausea drugs are usually ineffective in such patients. Particular attention should be directed to potential psychosocial factors, which should be addressed, if present. There are few data on psychotherapy or low-dose antidepressant therapy in these patients but a trial of such therapy can be considered based upon the efficacy of these approaches in patients with other functional gastrointestinal disorders.

Gastric electrical stimulation — Gastric electrical stimulation via implanted electrodes has been applied to highly selected patients with gastroparesis that is refractory to conventional therapy. A device is available in the United States for humanitarian use, and open-label studies in patients with gastroparesis of various etiologies have found benefit. However, results of controlled trials are less convincing. (See "Electrical stimulation for gastroparesis".)

Surgical therapy — Gastrostomy, jejunostomy, and gastrectomy have been performed in patients with postsurgical, diabetic, and idiopathic gastroparesis, but the reports were uncontrolled, unblinded, and retrospective, and the benefit was unconvincing, except possibly for completion gastrectomy in patients with postsurgical gastroparesis [24].

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient information: Nausea and vomiting in adults (The Basics)" and "Patient information: Upper endoscopy (The Basics)" and "Patient information: Motion sickness (The Basics)")
- Beyond the Basics topics (see "Patient information: Upper endoscopy (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Nausea, the unpleasant sensation of being about to vomit, can occur alone or can accompany vomiting (the forceful expulsion of gastric contents), dyspepsia, or other gastrointestinal symptoms. Retching differs from vomiting in the absence of expulsion of gastric content. In addition, patients may confuse vomiting with regurgitation, which is the return of esophageal contents to the hypopharynx with little effort. (See 'Introduction' above.)
- The consequences or complications of nausea and vomiting (eg, fluid depletion, hypokalemia, and metabolic alkalosis) should be identified and corrected.
- The etiology should be sought. A variety of disorders can produce nausea with or without vomiting (table 1). The diverse differential diagnosis of nausea and vomiting should be approached initially with a careful history and physical examination. In most cases, the cause of the nausea and vomiting can be determined from the history and physical examination and additional testing is not required (eg, in a patient with a history and examination suggestive of gastroenteritis). (See 'History and physical examination' above and 'Differential diagnosis' above.)
- Testing should be guided by the symptom duration, frequency, and severity, as well as the characteristics of vomiting episodes and associated symptoms. (See 'History and physical examination' above.)
- Most patients with chronic nausea and vomiting that is unexplained should undergo esophagogastroduodenoscopy to identify disorders that should have specific therapy. (See 'Endoscopy' above.)
- Targeted therapy should be provided, when possible (eg, surgery for bowel obstruction or malignancy). In other cases symptoms should be treated. Few high-quality therapeutic trials have compared the efficacy of different drugs in specified types of nausea and vomiting. However, acute or chronic nausea and vomiting may be helped by antiemetic or prokinetic drugs depending upon the underlying cause. (See 'Treatment' above.)

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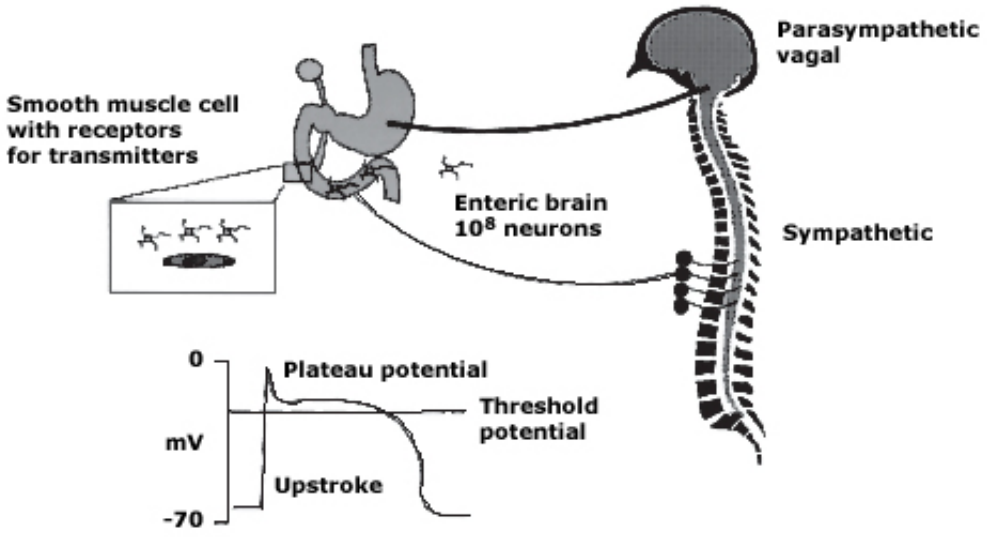
Topic 2537 Version 15.0

GRAPHICS

Control of gastric motility

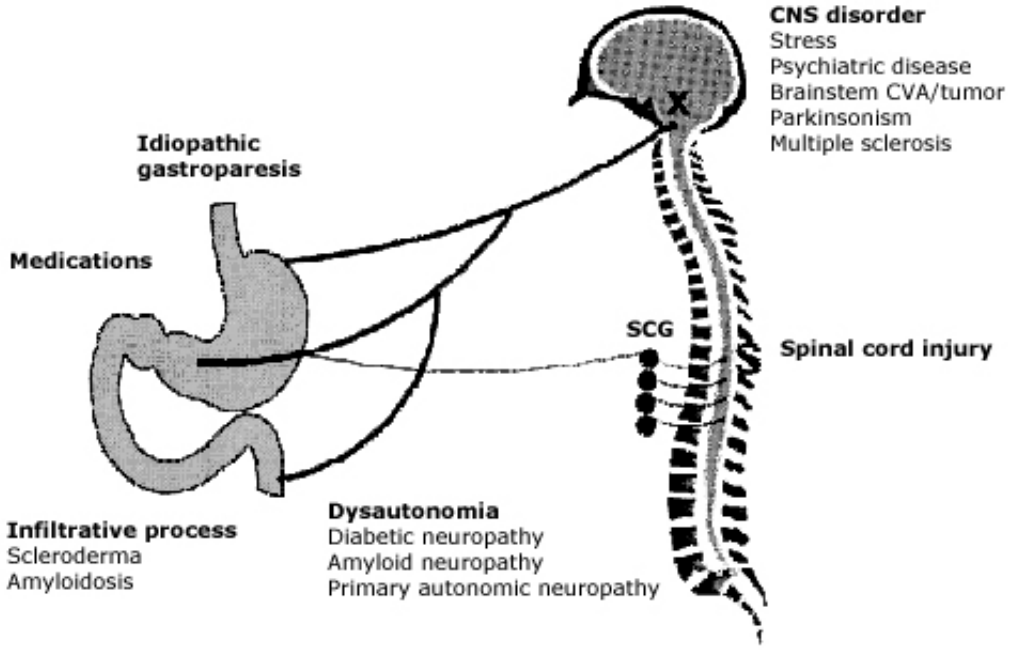


The motor function of the gut is controlled at three main levels: extrinsic neural control (vagal and sympathetic); intrinsic neural control; and excitability of smooth muscle cells controlled by transmitters.

Adapted from: Camilleri M, Prather CM. In: Sleisenger and Fordtran's Gastrointestinal Disease, 6th ed, Feldman M, Scharschmidt BF, Sleisenger MH (Eds), WB Saunders, Philadelphia 1998. p.572.

Graphic 55162 Version 4.0

Neuromuscular disorders impairing gastric motor function



Several common neurologic disorders can affect gastrointestinal motility by altering the parasympathetic or sympathetic supply to the gut.

X: vagal nuceli; CNS: central nervous system; CVA: cerebrovascular accident; SCG: sympathetic chain ganglia.

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Graphic 52708 Version 5.0

Differential diagnosis of nausea and vomiting

Medications and toxic etiologies
Cancer chemotherapy
Severe-cisplatinum, dacarbazine, nitrogen mustard
Moderate-etoposide, methotrexate, cytarabine
Mild-fluorouracil, vinblastine, tamoxifen
Analgesics
Aspirin
Nonsteroidal anti-inflammatory drugs
Auranofin
Antigout drugs
Cardiovascular medications
Digoxin
Antiarrhythmics
Antihypertensives
β-blockers
Calcium channel antagonists
Diuretics
Hormonal preparations/therapies
Oral antidiabetics
Oral contraceptives
Antibiotics/antivirals
Erythromycin
Tetracycline
Sulfonamides
Antituberculous drugs
Acyclovir
Gastrointestinal medications
Sulfasalazine
Azathioprine
Nicotine
CNS active drugs
Narcotics

Infectious causes
Gastroenteritis
Viral
Bacterial
Nongastrointestinal infections
Otitis media
Disorders of the gut and peritoneum
Mechanical obstruction
Gastric outlet obstruction
Small bowel obstruction
Functional gastrointestinal disorders
Gastroparesis
Chronic intestinal pseudo-obstruction
Nonulcer dyspepsia
Irritable bowel syndrome
Organic gastrointestinal disorders
Pancreatic adenocarcinoma
Inflammatory intraperitoneal disease
Peptic ulcer disease
Cholecystitis
Pancreatitis
Hepatitis
Crohn disease
Mesenteric ischemia
Retroperitoneal fibrosis
Mucosal metastases

CNS causes
Migraine
Increased intracranial pressure
Malignancy
Hemorrhage
Infarction
Abscess
Meningitis
Congenital malformation
Hydrocephalus
Pseudotumor cerebri
Seizure disorders
Demyelinating disorders
Cranial radiation
Emotional responses
Psychiatric disease
Psychogenic vomiting
Anxiety disorders
Depression
Pain
Anorexia nervosa
Bulimia nervosa
Labyrinthine disorders
Motion sickness
Labyrinthitis
Tumors
Ménière disease
Iatrogenic
Fluorescein angiography
Endocrinologic and metabolic causes
Pregnancy
Other endocrine and metabolic
Uremia
Diabetic ketoacidosis
Hyperparathyroidism
Hypoparathyroidism

Antiparkinsonian drugs
Anticonvulsants
Antiasthmatics
Theophylline
Radiation therapy
Ethanol abuse
Jamaican vomiting sickness
Hypervitaminosis

Hyperthyroidism
Addison's disease
Acute intermittent porphyria
Miscellaneous causes
Postoperative nausea and vomiting
Cyclic vomiting syndrome
Cardiac disease
Myocardial infarction
Heart failure
Radiofrequency ablation of the liver
Starvation
Radiation therapy to the upper abdomen and lower chest

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Graphic 78422 Version 7.0

Selection of antiemetics by clinical situation

Situation	Associated neurotransmitters	Recommended antiemetic
Migraine headache	Dopamine (probably a primary mediator)	For headache and nausea: metoclopramide (reglan) or prochlorperazine (compazine)
		For nausea: oral antiemetics, metoclopramide, prochlorperazine, serotonin antagonists
Vestibular nausea	Histamine, acetylcholine	Antihistamines and anticholinergics (equally effective)
Pregnancy-induced nausea	Unknown	For nausea: ginger, vitamin B6
		For hyperemesis gravidarum: promethazine (phenergan, first-line agent); serotonin antagonists and corticosteroids (second-line agents)
Gastroenteritis	Dopamine, serotonin	First-line agents: dopamine antagonists
		Second-line agents: serotonin antagonists
		Use in children is controversial
Postoperative nausea and vomiting	Dopamine, serotonin	Prevention: serotonin antagonists, droperidol (inapsine), dexamethasone
		Treatment: dopamine antagonists, serotonin antagonists, dexamethasone

Adapted from: Flake ZA, Scalley RD, Bailey AG. Practical selection of antiemetics. Am Fam Physician 2004; 69:1169.

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