regulating respiration; and nuclei that control pharyngeal, facial, and tongue movements—coordinate initiation of emesis involving neurokinin NK_1, serotonin 5-HT_3, endocannabinoid, and vasopressin pathways.

Somatic and visceral muscles respond stereotypically during emesis. Inspiratory thoracic and abdominal wall muscles contract, increasing intrathoracic and intraabdominal pressures to evacuate the stomach. Under normal conditions, distally migrating gut contractions are coordinated by an electrical phenomenon, the slow wave, which cycles at 3 cycles/min in the stomach and 11 cycles/min in the duodenum. During emesis, slow waves are abolished and replaced by orally propagating spikes that evoke retrograde contractions to facilitate expulsion of gut contents.

Activators of Emesis Emetic stimuli act at several sites. Emesis evoked by unpleasant thoughts or smells originates in the brain. Motion sickness and inner ear disorders act on labyrinthine pathways. Gastric irritants and cytotoxic agents like cisplatin stimulate gastroduodenal vagal afferent nerves. Nongastric afferents are activated by bowel obstruction and mesenteric ischemia. The area postrema, in the medulla, responds to bloodborne stimuli (emetogenic drugs, bacterial toxins, uremia, hypoxia, ketoacidosis) and is termed the *chemoreceptor trigger zone*.

Neurotransmitters mediating vomiting are selective for different sites. Labyrinthine disorders stimulate vestibular muscarinic M_1 and histaminergic H_1 receptors. Vagal afferent stimuli activate 5-HT_3 receptors. The area postrema is served by nerves acting on 5-HT_3, M_1, H_1, and dopamine D_2 subtypes. NK_1 receptors in the central nervous system (CNS) mediate both nausea and vomiting. Cannabinoid CB_1 pathways may participate in the cerebral cortex and brainstem. Therapies for vomiting act on these receptor-mediated pathways.

■ DIFFERENTIAL DIAGNOSIS

Nausea and vomiting are caused by conditions within and outside the gut, drugs, and circulating toxins **(Table 45-1)**. Unexplained