late the CTZ, which then transmits signals to the vomiting center. In motion sickness, rapid changes in body motion stimulate receptors in the inner ear (vestibular branch of the auditory nerve, which is concerned with equilibrium), and nerve impulses are transmitted to the CTZ and the vomiting center.

When stimulated, the vomiting center initiates efferent impulses that cause closure of the glottis, contraction of abdominal muscles and the diaphragm, relaxation of the gastroesophageal sphincter, and reverse peristalsis, which moves stomach contents toward the mouth for ejection.

ANTIEMETIC DRUGS

Drugs used to prevent or treat nausea and vomiting belong to several different therapeutic classifications, and most have anticholinergic, antidopaminergic, antihistaminic, or antiserotonergic effects. In general, the drugs are more effective in prophylaxis than treatment. Most antiemetics prevent or relieve nausea and vomiting by acting on the vomiting center, CTZ, cerebral cortex, vestibular apparatus, or a combination of these. Major drugs are described in the following sections and in Drugs at a Glance: Antiemetic Drugs.

Phenothiazines

Phenothiazines, of which chlorpromazine (Thorazine) is the prototype, are central nervous system depressants used in the treatment of psychosis and psychotic symptoms in other disorders (see Chap. 9). These drugs have widespread effects on the body. Their therapeutic effects in nausea and vomiting (as in psychosis) are attributed to their ability to block dopamine from receptor sites in the brain and CTZ (antidopaminergic effects). When used as antiemetics, phenothiazines act on the CTZ and the vomiting center. Not all phenothiazines are effective antiemetics.

Phenothiazines are usually effective in preventing or treating nausea and vomiting induced by drugs, radiation therapy, surgery, and most other stimuli, but are usually ineffective in motion sickness. These drugs cause sedation; prochlorperazine (Compazine) and promethazine (Phenergan) are commonly used.

Antihistamines

Antihistamines are used primarily to prevent histamine from exerting its widespread effects on body tissues (see Chap. 48). Antihistamines used as antiemetic agents are the "classic" antihistamines or H_1 receptor blocking agents (as differentiated from cimetidine and related drugs, which are H_2 receptor blocking agents). The drugs are thought to relieve nausea and vomiting by blocking the action of acetylcholine in the brain (anticholinergic effects). Antihistamines may be effective in preventing and treating motion sickness. Not all antihistamines are effective as antiemetic agents.

Corticosteroids

Although corticosteroids are used mainly as antiallergic, anti-inflammatory, and antistress agents (see Chap. 24), they have antiemetic effects as well. The mechanism by which the drugs exert antiemetic effects is unknown; they may block prostaglandin activity in the cerebral cortex. Dexamethasone and methylprednisolone are commonly used in the management of chemotherapy-induced emesis, usually in combination with one or more other antiemetic agents. Regimens vary from a single dose before chemotherapy to doses every 4 to 6 hours for 24 to 48 hours. With this short-term use, adverse effects are mild (eg, euphoria, insomnia, mild fluid retention).

Benzodiazepine Antianxiety Drugs

These drugs (see Chap. 8) are not antiemetics, but they are often used in multidrug regimens to prevent nausea and vomiting associated with cancer chemotherapy. They produce relaxation and inhibit cerebral cortex input to the vomiting center. They are often prescribed for clients who experience anticipatory nausea and vomiting before administration of anticancer drugs. Lorazepam (Ativan) is commonly used.

5-Hydroxytryptamine$_3$ (5-HT$_3$ or Serotonin) Receptor Antagonists

Ondansetron (Zofran), **granisetron** (Kytril), and **dolasetron** (Anzemet) are used to prevent or treat moderate to severe nausea and vomiting associated with cancer chemotherapy, radiation therapy, and postoperative status. Some anticancer drugs apparently cause nausea and vomiting by combining with a subset of 5-HT$_3$ receptors located in the CTZ and GI tract. These drugs antagonize the receptors and prevent their activation by emetogenic anticancer drugs.

These three drugs may be given intravenously or orally, and are metabolized in the liver. Adverse effects are usually mild to moderate, and common ones include diarrhea, headache, dizziness, constipation, muscle aches, and transient elevation of liver enzymes.

Ondansetron was the first drug of this group. Its half-life is 3 to 5.5 hours in most patients and 9 to 20 hours in patients with moderate or severe liver impairment. With oral drug, action begins in 30 to 60 minutes and peaks in about 2 hours. With intravenous (IV) drug, onset and peak of drug action are immediate.

Granisetron has a half-life of 6 hours with oral drug and 5 to 9 hours with IV drug; its half-life in patients with liver impairment is unknown. Action begins rapidly with IV