CHAPTER 17

Adjuncts to Anesthesia

KEY CONCEPTS

1. Diphenhydramine is one of a diverse group of drugs that competitively blocks H_1 receptors. Many drugs with H_1-receptor antagonist properties have considerable antimuscarinic, or atropine-like, activity (eg, dry mouth), or antiserotonergic activity (antiemetic).
2. H_2 blockers reduce the perioperative risk of aspiration pneumonia by decreasing gastric fluid volume and raising the pH of gastric contents.
3. Metoclopramide increases lower esophageal sphincter tone, speeds gastric emptying, and lowers gastric fluid volume by enhancing the stimulatory effects of acetylcholine on intestinal smooth muscle.
4. Ondansetron, granisetron, and dolasetron selectively block serotonin 5-HT_3 receptors, with little or no effect on dopamine receptors. 5-HT_3 receptors, which are located peripherally and centrally, appear to play an important role in the initiation of the vomiting reflex.
5. Ketorolac is a parenterally administered nonsteroidal antiinflammatory drug that provides analgesia by inhibiting prostaglandin synthesis.
6. Clonidine is a commonly used antihypertensive agent but in anesthesia it is used as an adjunct for epidural and peripheral nerve block anesthesia and analgesia. It is often used in the management of patients with chronic neuropathic pain to increase the efficacy of epidural opioid infusions.
7. Dexmedetomidine is a parenteral selective α_2 agonist with sedative properties. It appears to be more selective for the α_2 receptor than clonidine.
8. Selective activation of carotid chemoreceptors by low doses of doxapram stimulates hypoxic drive, producing an increase in tidal volume and a slight increase in respiratory rate. However, doxapram is not a specific reversal agent and should not replace standard supportive therapy (ie, mechanical ventilation).
9. Naloxone reverses the agonist activity associated with endogenous or exogenous opioid compounds.
10. Flumazenil is useful in the reversal of benzodiazepine sedation and the treatment of benzodiazepine overdose.
11. Aspiration does not necessarily result in aspiration pneumonia. The seriousness of the lung damage depends on the volume and composition of the aspirate. Patients are at risk if their gastric volume is greater than 25 mL (0.4 mL/kg) and their gastric pH is less than 2.5.

Many drugs are routinely administered by anesthetists perioperatively to protect against aspiration pneumonitis, to prevent or reduce the incidence of perianesthetic nausea and vomiting, and to reverse respiratory depression secondary to narcotics or benzodiazepines. This chapter discusses these agents along with other unique classes of drugs that are often administered as adjuvants during anesthesia or analgesia.

Aspiration

Aspiration of gastric contents is a rare, potentially fatal, and often litigious event that can complicate anesthesia. Based on an animal study, it is often stated that aspiration of 25 mL of volume at a pH of less than 2.5 will be sufficient to produce aspiration pneumonia. Many factors place patients at risk for aspiration, including "full" stomach, intestinal obstruction, hiatal hernia, obesity, pregnancy, reflux disease, emergency surgery, and inadequate depth of anesthesia.

Many approaches are employed to reduce the potential for aspiration perioperatively. Many of these interventions, such as the holding of cricoid pressure (Sellick's maneuver) and rapid sequence induction, may only offer limited protection. Cricoid pressure can be applied incorrectly and fail to occlude the esophagus. Whether it has *any* beneficial effect on outcomes even when it is applied correctly remains unproven. Anesthetic agents can decrease lower esophageal sphincter tone and decrease or obliterate the gag reflex, theoretically increasing the risk for passive aspiration. Additionally, inadequately anesthetized patients can vomit with an unprotected airway, likewise leading to aspiration. Different combinations of premedications have been advocated to reduce gastric volume, increase gastric pH, or augment lower esophageal sphincter tone. These agents include antihistamines, antacids, and metoclopramide.

HISTAMINE-RECEPTOR ANTAGONISTS

Histamine Physiology

Histamine is found in the central nervous system, in the gastric mucosa, and in other peripheral tissues. It is synthesized by decarboxylation of the amino acid histidine. Histaminergic neurons are primarily located in the posterior hypothalamus but have wide projections in the brain. Histamine also normally plays a major role in the secretion of hydrochloric acid by parietal cells in the stomach (Figure 17–1). The highest concentrations of histamine are found in the storage granules of circulating basophils and mast cells throughout the body. Mast cells tend to be concentrated in connective tissue just beneath epithelial (mucosal) surfaces. Histamine release (degranulation) from these cells can be triggered by chemical, mechanical, or immunological stimulation

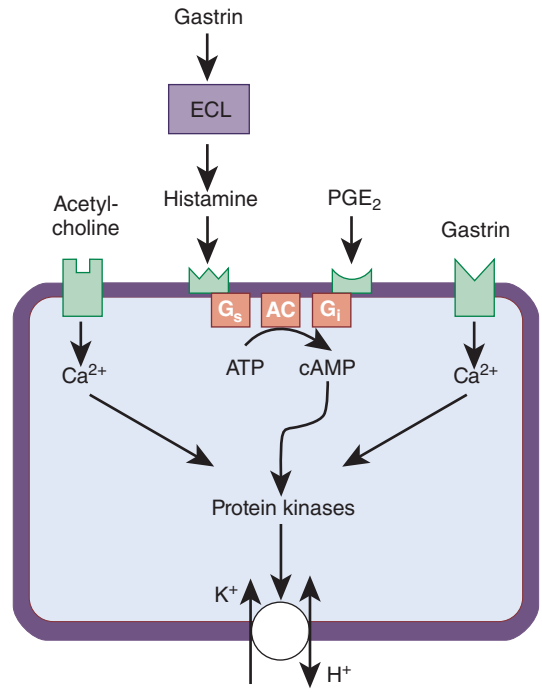

FIGURE 17–1 Secretion of hydrochloric acid is normally mediated by gastrin-induced histamine release from enterochromaffin-like cells (ECL) in the stomach. Note that acid secretion by gastric parietal cells can also be increased indirectly by acetylcholine (AC) via stimulation of M_3 receptors and directly by gastrin through an increase in intracellular Ca^{2+} concentration. Prostaglandin E_2 (PGE_2) can inhibit acid secretion by decreasing cyclic adenosine monophosphate (cAMP) activity. ATP, adenosine triphosphate; G_i, G inhibitory protein; G_s, G stimulatory protein.

Multiple receptors mediate the effects of histamine. The H_1 receptor activates phospholipase C, whereas the H_2 receptor increases intracellular cyclic

adenosine monophosphate (cAMP). An H_3 receptor is primarily located on histamine-secreting cells and mediates negative feedback, inhibiting the synthesis and release of additional histamine. Histamine-*N*-methyltransferase metabolizes histamine to inactive metabolites that are excreted in the urine.

A. Cardiovascular

Histamine reduces arterial blood pressure but increases heart rate and myocardial contractility. H_1-Receptor stimulation increases capillary permeability and enhances ventricular irritability, whereas H_2-receptor stimulation increases heart rate and increases contractility. Both types of receptors mediate peripheral arteriolar dilation and some coronary vasodilation.

B. Respiratory

Histamine constricts bronchiolar smooth muscle via the H_1 receptor. H_2-Receptor stimulation may produce mild bronchodilation. Histamine has variable effects on the pulmonary vasculature; the H_1 receptor appears to mediate some pulmonary vasodilation, whereas the H_2 receptor may be responsible for histamine-mediated pulmonary vasoconstriction.

C. Gastrointestinal

Activation of H_2 receptors in parietal cells increases gastric acid secretion. Stimulation of H_1 receptors leads to contraction of intestinal smooth muscle.

D. Dermal

The classic wheal-and-flare response of the skin to histamine results from increased capillary permeability and vasodilation, primarily via H_1-receptor activation.

E. Immunological

Histamine is a major mediator of type 1 hypersensitivity reactions. H_1-Receptor stimulation attracts leukocytes and induces synthesis of prostaglandin. In contrast, the H_2 receptor appears to activate suppressor T lymphocytes.

1. H_1-Receptor Antagonists

Mechanism of Action

1 Diphenhydramine (an ethanolamine) is one of a diverse group of drugs that competitively blocks H_1 receptors (Table 17–1). Many drugs with

TABLE 17–1 Properties of commonly used H_1-receptor antagonists.[1]

Drug	Route	Dose (mg)	Duration (h)	Sedation	Antiemesis
Diphenhydramine (Benadryl)	PO, IM, IV	25–50	3–6	+++	++
Dimenhydrinate (Dramamine)	PO, IM, IV	50–100	3–6	+++	++
Chlorpheniramine (Chlor-Trimeton)	PO IM, IV	2–12 5–20	4–8	++	0
Hydroxyzine (Atarax, Vistaril)	PO, IM	25–100	4–12	+++	++
Promethazine (Phenergan)	PO, IM, IV	12.5–50	4–12	+++	+++
Cetirizine (Zyrtec)	PO	5–10	24	+	
Cyproheptadine (Periactin)	PO	4	6–8	++	
Dimenhydrinate (Dramamine)	PO	50	6–12	++	
Fexofenadine (Allegra)	PO	30–60	12	0	
Meclizine (Antivert)	PO	12.5–50	8–24	+	
Loratadine (Claritin)	PO	10	24	0	

[1]0, no effect; ++, moderate activity; +++, marked activity.

H_1-receptor antagonist properties have considerable antimuscarinic, or atropine-like, activity (eg, dry mouth), or antiserotonergic activity (antiemetic). Promethazine is a phenothiazine derivative with H_1-receptor antagonist activity as well as antidopaminergic and α-adrenergic–blocking properties.

Clinical Uses

Like other H_1-receptor antagonists, diphenhydramine has a multitude of therapeutic uses: suppression of allergic reactions and symptoms of upper respiratory tract infections (eg, urticaria, rhinitis, conjunctivitis); vertigo, nausea, and vomiting (eg, motion sickness, Ménière's disease); sedation; suppression of cough; and dyskinesia (eg, parkinsonism, drug-induced extrapyramidal side effects). Some of these actions are predictable from an understanding of histamine physiology, whereas others are the result of the drugs' antimuscarinic and antiserotonergic effects (Table 17–1). Although H_1 blockers prevent the bronchoconstrictive response to histamine, they are ineffective in treating bronchial asthma, which is primarily due to other mediators. Likewise, H_1 blockers will not completely prevent the hypotensive effect of histamine unless an H_2 blocker is administered concomitantly.

The antiemetic and mild hypnotic effects of antihistaminic drugs (particularly diphenhydramine, promethazine, and hydroxyzine) have led to their use for premedication. Although many H_1 blockers cause significant sedation, ventilatory drive is usually unaffected in the absence of other sedative medications. Promethazine and hydroxyzine were often combined with opioids to potentiate analgesia. Newer (second-generation) antihistamines tend to produce little or no sedation because of limited penetration across the blood–brain barrier. This group of drugs is used primarily for allergic rhinitis and urticaria. They include loratadine, fexofenadine, and cetirizine. Many preparations for allergic rhinitis often also contain vasoconstrictors such as pseudoephedrine. Meclizine and dimenhydrinate are used primarily as an antiemetic, particularly for motion sickness, and in the management of vertigo. Cyproheptadine, which also has significant serotonin antagonist activity, has been used in the management of Cushing's Disease, carcinoid syndrome, and vascular (cluster) headaches.

Dosage

The usual adult dose of diphenhydramine is 25–50 mg (0.5–1.5 mg/kg) orally, intramuscularly, or intravenously every 4–6 h. The doses of other H_1-receptor antagonists are listed in Table 17–1.

Drug Interactions

The sedative effects of H_1-receptor antagonists can potentiate other central nervous system depressants such as barbiturates, benzodiazepines, and opioids.

2. H_2-Receptor Antagonists

Mechanism of Action

H_2-Receptor antagonists include cimetidine, famotidine, nizatidine, and ranitidine (**Table 17–2**). These agents competitively inhibit histamine binding to H_2 receptors, thereby reducing gastric acid output and raising gastric pH.

Clinical Uses

All H_2-receptor antagonists are equally effective in the treatment of peptic duodenal and gastric ulcers, hypersecretory states (Zollinger–Ellison syndrome), and gastroesophageal reflux disease (GERD). Intravenous preparations are also used to prevent stress ulceration in critically ill patients. Duodenal and gastric ulcers are usually associated with *Helicobacter pylori* infection, which is treated with combinations of bismuth, tetracycline, and metronidazole. By decreasing gastric fluid volume and hydrogen ion content, H_2 blockers reduce the perioperative risk of aspiration pneumonia. These drugs affect the pH of only those gastric secretions that occur after their administration.

The combination of H_1- and H_2-receptor antagonists provides some protection against drug-induced allergic reactions (eg, intravenous radiocontrast, chymopapain injection for lumbar disk disease, protamine, vital blue dyes used for sentinel node biopsy). Although pretreatment with these agents does not reduce histamine release, it may decrease subsequent hypotension.

TABLE 17–2 Pharmacology of aspiration pneumonia prophylaxis.[1]

Drug	Route	Dose	Onset	Duration	Acidity	Volume	LES Tone
Cimetidine (Tagamet)	PO IV	300–800 mg 300 mg	1–2 h	4–8 h	↓↓↓	↓↓	0
Ranitidine (Zantac)	PO IV	150–300 mg 50 mg	1–2 h	10–12 h	↓↓↓	↓↓	0
Famotidine (Pepcid)	PO IV	20–40 mg 20 mg	1–2 h	10–12 h	↓↓↓	↓↓	0
Nizatidine (Axid)	PO	150–300 mg	0.5–1 h	10–12 h	↓↓↓	↓↓	0
Nonparticulate antacids (Bicitra, Polycitra)	PO	15–30 mL	5–10 min	30–60 min	↓↓↓	↑	0
Metoclopramide (Reglan)	IV PO	10 mg 10–15 mg	1–3 min	1–2 h 30–60 min[2]	0	↓↓	↑↑

[1]0, no effect; ↓↓, moderate decrease; ↓↓↓, marked decrease; ↑, slight increase; ↑↑, moderate increase; LES, lower esophageal sphincter.
[2]Oral metoclopramide has a quite variable onset of action and duration of action.

Side Effects

Rapid intravenous injection of cimetidine or ranitidine has been rarely associated with hypotension, bradycardia, arrhythmias, and cardiac arrest. These adverse cardiovascular effects have been reported following the administration of cimetidine to critically ill patients. In contrast, famotidine can be safely injected intravenously over a 2-min period. H_2-Receptor antagonists change the gastric flora by virtue of their pH effects. Complications of long-term cimetidine therapy include hepatotoxicity (elevated serum transaminases), interstitial nephritis (elevated serum creatinine), granulocytopenia, and thrombocytopenia. Cimetidine also binds to androgen receptors, occasionally causing gynecomastia and impotence. Finally, cimetidine has been associated with changes in mental status ranging from lethargy and hallucinations to seizures, particularly in elderly patients. In contrast, ranitidine, nizatidine, and famotidine do not affect androgen receptors and penetrate the blood–brain barrier poorly.

Dosage

As a premedication to reduce the risk of aspiration pneumonia, H_2-receptor antagonists should be administered at bedtime and again at least 2 h before surgery (Table 17–2). Because all four drugs are eliminated primarily by the kidneys, the dose should be reduced in patients with significant renal dysfunction.

Drug Interactions

Cimetidine may reduce hepatic blood flow and binds to the cytochrome P-450 mixed-function oxidases. These effects slow the metabolism of a multitude of drugs, including lidocaine, propranolol, diazepam, theophylline, phenobarbital, warfarin, and phenytoin. Ranitidine is a weak inhibitor of the cytochrome P-450 system, and no significant drug interactions have been demonstrated. Famotidine and nizatidine do not appear to affect the cytochrome P-450 system.

ANTACIDS

Mechanism of Action

Antacids neutralize the acidity of gastric fluid by providing a base (usually hydroxide, carbonate, bicarbonate, citrate, or trisilicate) that reacts with hydrogen ions to form water.

Clinical Uses

Common uses of antacids include the treatment of gastric and duodenal ulcers, GERD, and Zollinger–Ellison syndrome. In anesthesiology, antacids

provide protection against the harmful effects of aspiration pneumonia by raising the pH of gastric contents. Unlike H_2-receptor antagonists, antacids have an immediate effect. Unfortunately, they increase intragastric volume. Aspiration of particulate antacids (aluminum or magnesium hydroxide) produces abnormalities in lung function comparable to those that occur following acid aspiration. Nonparticulate antacids (sodium citrate or sodium bicarbonate) are much less damaging to lung alveoli if aspirated. Furthermore, nonparticulate antacids mix with gastric contents better than particulate solutions. Timing is critical, as nonparticulate antacids lose their effectiveness 30–60 min after ingestion.

Dosage

The usual adult dose of a 0.3 M solution of sodium citrate—Bicitra (sodium citrate and citric acid) or Polycitra (sodium citrate, potassium citrate, and citric acid)—is 15–30 mL orally, 15–30 min prior to induction.

Drug Interactions

Because antacids alter gastric and urinary pH, they change the absorption and elimination of many drugs. The rate of absorption of digoxin, cimetidine, and ranitidine is slowed, whereas the rate of phenobarbital elimination is quickened.

METOCLOPRAMIDE

Mechanism of Action

Metoclopramide acts peripherally as a cholinomimetic (ie, facilitates acetylcholine transmission at selective muscarinic receptors) and centrally as a dopamine receptor antagonist. Its action as a prokinetic agent in the upper gastrointestinal (GI) tract is not dependent on vagal innervation but is abolished by anticholinergic agents. It does not stimulate secretions.

Clinical Uses

3 By enhancing the stimulatory effects of acetylcholine on intestinal smooth muscle, metoclopramide increases lower esophageal sphincter tone, speeds gastric emptying, and lowers gastric fluid volume. These properties account for its efficacy in the treatment of patients with diabetic gastroparesis and GERD, as well as prophylaxis for those at risk for aspiration pneumonia. Metoclopramide does not affect the secretion of gastric acid or the pH of gastric fluid.

Metoclopramide produces an antiemetic effect by blocking dopamine receptors in the chemoreceptor trigger zone of the central nervous system. However, at doses used clinically during the perioperative period, the drug's ability to reduce postoperative nausea and vomiting is negligible.

Side Effects

Rapid intravenous injection may cause abdominal cramping, and metoclopramide is contraindicated in patients with complete intestinal obstruction. It can induce a hypertensive crisis in patients with pheochromocytoma by releasing catecholamines from the tumor. Sedation, nervousness, and extrapyramidal signs from dopamine antagonism (eg, akathisia) are uncommon and reversible. Nonetheless, metoclopramide is best avoided in patients with Parkinson's disease. Metoclopramide-induced increases in aldosterone and prolactin secretion are probably inconsequential during short-term therapy. Metoclopramide may rarely result in hypotension and arrhythmias.

Dosage

An adult dose of 10–20 mg of metoclopramide (0.25 mg/kg) is effective orally, intramuscularly, or intravenously (injected over 5 min). Larger doses (1–2 mg/kg) have been used to prevent emesis during chemotherapy. The onset of action is much more rapid following parenteral (3–5 min) than oral (30–60 min) administration. Because metoclopramide is excreted in the urine, its dose should be decreased in patients with renal dysfunction.

Drug Interactions

Antimuscarinic drugs (eg, atropine, glycopyrrolate) block the GI effects of metoclopramide. Metoclopramide decreases the absorption of orally administered cimetidine. Concurrent use of phenothiazines or butyrophenones (droperidol) increases the likelihood of extrapyramidal side effects.

PROTON PUMP INHIBITORS

Mechanism of Action

These agents, including omeprazole (Prilosec), lansoprazole (Prevacid), rabeprazole (Aciphex), esomeprazole (Nexium), and pantoprazole (Protonix), bind to the proton pump of parietal cells in the gastric mucosa and inhibit secretion of hydrogen ions.

Clinical Uses

Proton pump inhibitors (PPIs) are indicated for the treatment of duodenal ulcer, GERD, and Zollinger–Ellison syndrome. They may promote healing of peptic ulcers and erosive GERD more quickly than H_2-receptor blockers. There are ongoing questions regarding the safety of PPIs in patients taking clopidogrel (Plavix) because of concerns of inadequate antiplatelet therapy when these drugs are combined.

Side Effects

PPIs are generally well tolerated, causing few side effects. Adverse side effects primarily involve the GI system (nausea, abdominal pain, constipation, diarrhea). On rare occasions, these drugs have been associated with myalgias, anaphylaxis, angioedema, and severe dermatological reactions. Long-term use of PPIs has also been associated with gastric enterochromaffin-like cell hyperplasia and an increased risk of pneumonia secondary to bacterial colonization in the higher-pH environment.

Dosage

Recommended oral doses for adults are omeprazole, 20 mg; lansoprazole, 15 mg; rabeprazole, 20 mg; and pantoprazole, 40 mg. Because these drugs are primarily eliminated by the liver, repeat doses should be decreased in patients with severe liver impairment.

Drug Interactions

PPIs can interfere with hepatic P-450 enzymes, potentially decreasing the clearance of diazepam, warfarin, and phenytoin. Concurrent administration can decrease clopidogrel (Plavix) effectiveness, as the latter medication is dependent on hepatic enzymes for activation.

Postoperative Nausea & Vomiting (PONV)

Without any prophylaxis, PONV occurs in approximately 20–30% of the general surgical population and up to 70–80% in patients with predisposing risk factors (Table 17–3). As anesthetic duration increases, so, too, does PONV risk. When the risk is sufficiently great, prophylactic antiemetic medications are administered and strategies to reduce its incidence are initiated. The Society of Ambulatory Anesthesia (SAMBA) provides simplified risk scoring systems, which assign points for specific risk factors, as well as guidelines that assist in the management of at-risk patients (Table 17–4). Obesity, anxiety, and reversal of neuromuscular blockade are not independent risk factors for PONV.

Drugs used in the prophylaxis and treatment of PONV include 5-HT_3 antagonists, butyrophenones, dexamethasone, neurokinin-1 receptor antagonists (aprepitant, Emend); antihistamines and transdermal scopolamine may also be used. At-risk patients often benefit from one or more prophylactic measures.

TABLE 17–3 Risk factors for postoperative nausea and vomiting (PONV).[1,2]

Patient-specific risk factors:
Female gender
Nonsmoking status
History of PONV/motion sickness
Anesthetic risk factors:
Use of volatile anesthetics
Use of nitrous oxide
Use of intraoperative and postoperative opioids
Surgical risk factors:
Duration of surgery (each 30-min increase in duration increases PONV risk by 60%, so that a baseline risk of 10% is increased by 16% after 30 min)
Type of surgery

[1]Reproduced, with permission, from Gan TJ, Meyer TA, Apfel CC, et al: Society for ambulatory anesthesia guidelines for management of postoperative nausea and vomiting. Anesth Analg 2007;105:1615.

[2]Risk factors are assigned points and an increasing number of points increases the likelihood of PONV. Refer to the Society of Ambulatory Anesthesia (SAMBA) guidelines.

TABLE 17–4 SAMBA guidelines to reduce the risk of postoperative nausea and vomiting (PONV).[1]

1. Identify patients at risk for PONV.
2. Employ management strategies to reduce PONV risk.
3. Employ one to two prophylactic measures in adults at moderate PONV risk.
4. Use multiple interventions in patients at high PONV risk.
5. Administer prophylactic antiemetic therapy to children at high risk using combination therapy.
6. Provide antiemetic therapy to patients with PONV who did not receive prophylactic therapy or in whom prophylaxis failed. Therapy should be with a drug from a different class than that which failed to provide prophylaxis.

[1]Data based on guidelines from the Society of Ambulatory Anesthesia (SAMBA). Refer to Gan TJ, Meyer TA, Apfel CC, et al: Society for ambulatory anesthesia guidelines for management of postoperative nausea and vomiting. Anesth Analg 2007;105:1615.

5-HT$_3$ RECEPTOR ANTAGONISTS

Serotonin Physiology

Serotonin, 5-hydroxytryptamine (5-HT), is present in large quantities in platelets and the GI tract (enterochromaffin cells and the myenteric plexus). It is also an important neurotransmitter in multiple areas of the central nervous system. Serotonin is formed by hydroxylation and decarboxylation of tryptophan. Monoamine oxidase inactivates serotonin into 5-hydroxyindoleacetic acid (5-HIAA). The physiology of serotonin is very complex because there are at least seven receptor types, most with multiple subtypes. The 5-HT$_3$ receptor mediates vomiting and is found in the GI tract and the brain (area postrema). The 5-HT$_{2A}$ receptors are responsible for smooth muscle contraction and platelet aggregation, the 5-HT$_4$ receptors in the GI tract mediate secretion and peristalsis, and the 5-HT$_6$ and 5-HT$_7$ receptors are located primarily in the limbic system where they appear to play a role in depression. All except the 5-HT$_3$ receptor are coupled to G proteins and affect either adenylyl cyclase or phospholipase C; effects of the 5-HT$_3$ receptor are mediated via an ion channel.

A. Cardiovascular

Except in the heart and skeletal muscle, serotonin is a powerful vasoconstrictor of arterioles and veins. Its vasodilator effect in the heart is endothelium dependent. When the myocardial endothelium is damaged following injury, serotonin produces vasoconstriction. The pulmonary and renal vasculatures are very sensitive to the arterial vasoconstrictive effects of serotonin. Modest and transient increases in cardiac contractility and heart rate may occur immediately following serotonin release; reflex bradycardia often follows. Vasodilation in skeletal muscle can subsequently cause hypotension.

B. Respiratory

Contraction of smooth muscle increases airway resistance. Bronchoconstriction from released serotonin is often a prominent feature of carcinoid syndrome

C. Gastrointestinal

Direct smooth muscle contraction (via 5-HT$_2$ receptors) and serotonin-induced release of acetylcholine in the myenteric plexus (via 5-HT$_3$ receptors) greatly augment peristalsis. Secretions are unaffected.

D. Hematological

Activation of 5-HT$_2$ receptors causes platelet aggregation.

Mechanism of Action

4 Ondansetron (Zofran), granisetron (Kytril), and dolasetron (Anzemet) selectively block serotonin 5-HT$_3$ receptors, with little or no effect on dopamine receptors (Figure 17–2). 5-HT$_3$

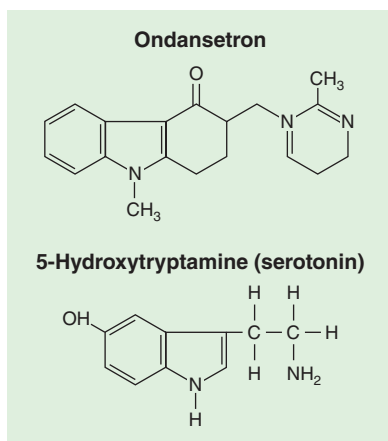

FIGURE 17–2 Ondansetron is structurally related to serotonin.

receptors, which are located peripherally (abdominal vagal afferents) and centrally (chemoreceptor trigger zone of the area postrema and the nucleus tractus solitarius), appear to play an important role in the initiation of the vomiting reflex. The 5-HT_3 receptors of the chemoreceptor trigger zone in the area postrema reside outside the blood–brain barrier. The trigger zone is activated by substances such as anesthetics and opioids and signals the nucleus tractus solitarius, resulting in PONV. Emetogenic stimuli from the GI tract similarly stimulate the development of PONV.

Clinical Uses

5-HT_3-receptor antagonists are generally administered at the end of surgery. All these agents are effective antiemetics in the postoperative period. In comparison with other antiemetic agents such as droperidol (1.25 mg) and dexamethasone (4 mg), ondansetron appears equally effective. A new agent, palonosetron (Aloxi), has an extended duration of action and may reduce the incidence of postdischarge nausea and vomiting (PDNV).

Side Effects

5-HT_3 receptor antagonists are essentially devoid of serious side effects, even in amounts several times the recommended dose. They do not appear to cause sedation, extrapyramidal signs, or respiratory depression. The most commonly reported side effect is headache. All three drugs can slightly prolong the QT interval on the electrocardiogram. This effect may be more frequent with dolasetron, although it has not been associated with any adverse arrhythmias. Nonetheless, these drugs, particularly dolasetron, should be used cautiously in patients who are taking antiarrhythmic drugs or who have a prolonged QT interval.

Ondansetron undergoes extensive metabolism in the liver via hydroxylation and conjugation by cytochrome P-450 enzymes. Liver failure impairs clearance several-fold, and the dose should be reduced accordingly. The recommended intravenous dose is 12.5 mg for dolasetron and 1 mg for granisetron. All three drugs are available in oral formulations for PONV prophylaxis.

BUTYROPHENONES

Droperidol (0.625–1.25 mg) was previously used routinely for PONV prophylaxis. Given at the end of the procedure it blocks dopamine receptors that contribute to the development of PONV. Despite its effectiveness, many practitioners no longer routinely administer this medication because of a U.S. Food and Drug Administration (FDA) black box warning related to concerns that doses described in the product labeling ("package insert") may lead to QT prolongation and development of torsades des pointes dysrhythmia. However, the doses relevant to the FDA warning, as acknowledged by the FDA, were those used for neurolept anesthesia (5–15 mg), not the much smaller doses employed for PONV. Cardiac monitoring is warranted when large doses of the drug are used. There is no evidence that use of droperidol at the doses routinely employed for PONV management increases the risk of sudden cardiac death in the perioperative population.

As with other drugs that antagonize dopamine, droperidol use in patients with Parkinson's disease and in patients manifesting extrapyramidal signs should be carefully considered.

The phenothiazine, prochlorperazine (Compazine), which affects multiple receptors (histaminergic, dopaminergic, muscarinic), may be used for PONV management. It may cause extrapyramidal and anticholinergic side effects. Promethazine (Phenergan) works primarily as an anticholinergic agent and antihistamine and likewise can be used to treat PONV. As with other agents of this class, anticholinergic effects (sedation, delirium, confusion, vision changes) can complicate the postoperative period.

DEXAMETHASONE

Dexamethasone (Decadron) in doses as small as 4 mg has been shown to be as effective as ondansetron in reducing the incidence of PONV. Dexamethasone should be given at induction as opposed to the end of surgery, and its mechanism of action is unclear. There appear to be no significant or long-lasting systemic effects from this dose of glucocorticoid.

NEUROKININ-1 RECEPTOR ANTAGONIST

Substance P is a neuropeptide that interacts at neurokinin-1 (NK_1) receptors. NK_1 antagonists inhibit substance P at central and peripheral receptors. Aprepitant (Emend), an NK_1 antagonist, has been found to reduce PONV perioperatively and is additive with ondansetron for this indication.

OTHER PONV STRATEGIES

Several other agents and techniques have been employed to reduce the incidence of PONV. Transdermal scopolamine has been used effectively, although it may produce central anticholinergic effects (confusion, blurred vision, and dry mouth). Acupuncture, acupressure, and transcutaneous electrical stimulation of the P6 acupuncture point can reduce PONV incidence and medication requirements.

As no single agent will both treat and prevent PONV, perioperative management centers on identifying patients at greatest risk so that prophylaxis, often with multiple agents, may be initiated.

Other Drugs Used as Adjuvants to Anesthesia

KETOROLAC

Mechanism of Action

5 Ketorolac is a parenteral nonsteroidal antiinflammatory drug (NSAID) that provides analgesia by inhibiting prostaglandin synthesis.

Clinical Uses

Ketorolac is indicated for the short-term (<5 days) management of pain, and appears to be particularly useful in the immediate postoperative period. A standard dose of ketorolac provides analgesia equivalent to 6–12 mg of morphine administered by the same route. Its time to onset is also similar to morphine, but ketorolac has a longer duration of action (6–8 h).

Ketorolac, a peripherally acting drug, has become a popular alternative to opioids for postoperative analgesia because of its minimal central nervous system side effects. Specifically, ketorolac does not cause respiratory depression, sedation, or nausea and vomiting. In fact, ketorolac does not cross the blood–brain barrier to any significant degree. Numerous studies have shown that oral and parenteral NSAIDs have an opioid-sparing effect. They may be most beneficial in patients at increased risk for postoperative respiratory depression or emesis.

Side Effects

As with other NSAIDs, ketorolac inhibits platelet aggregation and prolongs bleeding time. It and other NSAIDs should therefore be used with caution in patients at risk for postoperative hemorrhage. Long-term administration may lead to renal toxicity (eg, papillary necrosis) or GI tract ulceration with bleeding and perforation. Because ketorolac depends on elimination, it should not be given to patients with kidney failure. Ketorolac is contraindicated in patients allergic to aspirin or NSAIDs. Patients with asthma have an increased incidence of aspirin sensitivity (approximately 10%), particularly if they also have a history of nasal polyps (approximately 20%).

Dosage

Ketorolac has been approved for administration as either a 60 mg intramuscular or 30 mg intravenous loading dose; a maintenance dose of 15–30 mg every 6 h is recommended. Elderly patients clear ketorolac more slowly and should receive reduced doses.

Drug Interactions

Aspirin decreases the protein binding of ketorolac, increasing the amount of active unbound drug. Ketorolac does not affect minimum alveolar concentration of inhalation anesthetic agents, and its administration does not alter the hemodynamics of anesthetized patients. It decreases the postoperative requirement for opioid analgesics.

Other NSAID Adjuvant Drugs

Other NSAID agents are used perioperatively. Ketorolac and other NSAIDs inhibit cyclooxygenase

(COX) isoenzymes. COX-1 maintains gastric mucosa and stimulates platelet aggregation. COX-2 is expressed during inflammation. Whereas ketorolac is a nonselective COX inhibitor, other agents such as parecoxib (Dynastat), celecoxib (Celebrex), and rofecoxib (Vioxx) are specific for COX-2. COX-2 inhibitors spare both the gastric mucosa and platelet function. However, their use is associated with an increased risk of cardiovascular thromboembolic events. Because nonspecific NSAIDs such as ketorolac also inhibit COX-2, their use following cardiac bypass surgery is contraindicated.

Intravenous acetaminophen (Ofirmev) has recently become available for perioperative use in the United States. Acetaminophen is a centrally acting analgesic with likely central COX inhibition and with weak peripheral COX effects resulting in a lack of gastric irritation and clotting abnormalities. A maximal adult (>50 kg weight) dose of 1 g is infused to a maximum total dose of 4 g/d. Patients weighing 50 kg or less should receive a maximal dose of 15 mg/kg and a maximal total dose of 75 mg/kg/d. Hepatoxicity is a known risk of overdosage, and the drug should be used with caution in patients with hepatic disease or undergoing hepatic surgery.

CLONIDINE

Mechanism of Action

Clonidine (Catapres, Duraclon) is an imidazoline derivative with predominantly α_2-adrenergic agonist activity. It is highly lipid soluble and readily penetrates the blood–brain barrier and the placenta. Studies indicate that binding of clonidine to receptors is highest in the rostral ventrolateral medulla in the brainstem (the final common pathway for sympathetic outflow) where it activates inhibitory neurons. The overall effect is to decrease sympathetic activity, enhance parasympathetic tone, and reduce circulating catecholamines. There is also evidence that much of clonidine's antihypertensive action occurs via binding to a nonadrenergic (imidazoline) receptor. In contrast, its analgesic effects, particularly in the spinal cord, are mediated entirely via pre- and possibly postsynaptic α_2-adrenergic receptors that block nociceptive transmission. Clonidine also has local anesthetic effects when applied to peripheral nerves and is frequently added to local anesthetic solutions.

Clinical Uses

6 Clonidine is a commonly used antihypertensive agent that reduces sympathetic tone, decreasing systemic vascular resistance, heart rate, and blood pressure. In anesthesia, clonidine is used as an adjunct for epidural, caudal, and peripheral nerve block anesthesia and analgesia. It is often used in the management of patients with chronic neuropathic pain to increase the efficacy of epidural opioid infusions. When given epidurally, the analgesic effect of clonidine is segmental, being localized to the level at which it is injected or infused. When added to local anesthetics of intermediate duration (eg, mepivacaine or lidocaine) administered for epidural or peripheral nerve block, clonidine will markedly prolong both the anesthetic and analgesic effects.

Unlabeled/investigational uses of clonidine include serving as an adjunct in premedication, control of withdrawal syndromes (nicotine, opioids, alcohol, and vasomotor symptoms of menopause), and treatment of glaucoma as well as various psychiatric disorders.

Side Effects

Sedation, dizziness, bradycardia, and dry mouth are common side effects. Less commonly, bradycardia, orthostatic hypotension, nausea, and diarrhea may be observed. Abrupt discontinuation of clonidine following long-term administration (>1 mo) can produce a withdrawal phenomenon characterized by rebound hypertension, agitation, and sympathetic overactivity.

Dosage

Epidural clonidine is usually started at 30 mcg/h in a mixture with an opioid or a local anesthetic. Oral clonidine is readily absorbed, has a 30–60 min onset, and lasts 6–12 h. In the treatment of acute hypertension, 0.1 mg can be given orally every hour until the blood pressure is controlled, or up to a maximum of 0.6 mg; the maintenance dose is 0.1–0.3 mg twice daily. Transdermal preparations of clonidine can also be used for maintenance therapy. They are available as 0.1, 0.2, and 0.3 mg/d patches that are replaced

every 7 days. Clonidine is metabolized by the liver and excreted renally. Dosages should be reduced for patients with renal insufficiency.

Drug Interactions

Clonidine enhances and prolongs sensory and motor blockade from local anesthetics. Additive effects with hypnotic agents, general anesthetics, and sedatives can potentiate sedation, hypotension, and bradycardia. The drug should be used cautiously, if at all, in patients who take β-adrenergic blockers and in those with significant cardiac conduction system abnormalities. Lastly, clonidine can mask the symptoms of hypoglycemia in diabetic patients.

DEXMEDETOMIDINE

Mechanism of Action

7 Dexmedetomidine (Precedex) is a parenteral selective α_2 agonist with sedative properties. It appears to be more selective for the α_2 receptor than clonidine. At higher doses it loses its selectivity and also stimulates α_1-adrenergic receptors.

Clinical Uses

Dexmedetomidine causes dose-dependent sedation anxiolysis and some analgesia and blunts the sympathetic response to surgery and other stress. Most importantly, it has an opioid-sparing effect and does not significantly depress respiratory drive; excessive sedation, however, may cause airway obstruction. The drug is used for short-term (<24 h), intravenous sedation of mechanically ventilated patients. Discontinuation after more prolonged use can potentially cause a withdrawal phenomenon similar to that of clonidine. It has also been used for intraoperative sedation and as an adjunct to general anesthetics.

Side Effects

The principal side effects are bradycardia, heart block, and hypotension. It may also cause nausea.

Dosage

The recommended initial loading dose is 1 mcg/kg intravenously over 10 min with a maintenance infusion rate of 0.2–0.7 mcg/kg/h. Dexmedetomidine has a rapid onset and terminal half-life of 2 h. The drug is metabolized in the liver and its metabolites are eliminated in the urine. Dosage should be reduced in patients with renal insufficiency or hepatic impairment.

Drug Interactions

Caution should be used when dexmedetomidine is administered with vasodilators, cardiac depressants, and drugs that decrease heart rate. Reduced requirements of hypnotics/anesthetic agents should prevent excessive hypotension.

DOXAPRAM

Mechanism of Action

Doxapram (Dopram) is a peripheral and central 8 nervous system stimulant. Selective activation of carotid chemoreceptors by low doses of doxapram stimulates hypoxic drive, producing an increase in tidal volume and a slight increase in respiratory rate. At larger doses, the central respiratory centers in the medulla are stimulated.

Clinical Uses

Because doxapram mimics a low Pao_2, it may be useful in patients with chronic obstructive pulmonary disease who are dependent on hypoxic drive yet require supplemental oxygen. Drug-induced respiratory and central nervous system depression, including that seen immediately postoperatively, can be *temporarily* overcome. Doxapram is not a specific reversal agent, however, and should not replace standard supportive therapy (mechanical ventilation). For example, doxapram will not reverse paralysis caused by muscle relaxants, although it may transiently mask respiratory failure. The most common cause of postoperative hypoventilation—airway obstruction—will not be alleviated by doxapram. For these reasons, many anesthesiologists believe that the usefulness of doxapram is very limited.

Side Effects

Stimulation of the central nervous system leads to a variety of possible side effects: changes in mental

status (confusion, dizziness, seizures), cardiac abnormalities (tachycardia, dysrhythmias, hypertension), and pulmonary dysfunction (wheezing, tachypnea). Vomiting and laryngospasm are of particular concern to the anesthesiologist in the postoperative period. Doxapram should not be used in patients with a history of epilepsy, cerebrovascular disease, acute head injury, coronary artery disease, hypertension, or bronchial asthma.

Dosage

Bolus intravenous administration (0.5–1 mg/kg) results in transient increases in minute ventilation (the onset of action is 1 min; the duration of action is 5–12 min). Continuous intravenous infusions (1–3 mg/min) provide longer-lasting effects (the maximum dose is 4 mg/kg).

Drug Interactions

The sympathetic stimulation produced by doxapram may exaggerate the cardiovascular effects of monoamine oxidase inhibitors or adrenergic agents. Doxapram should probably not be used in patients awakening from halothane anesthesia, as halothane sensitizes the myocardium to catecholamines.

NALOXONE

Mechanism of Action

Naloxone (Narcan) is a competitive opioid receptor antagonist. Its affinity for opioid μ receptors appears to be much greater than for opioid κ or δ receptors Naloxone has no significant agonist activity.

Clinical Uses

9 Naloxone reverses the agonist activity associated with endogenous (enkephalins, endorphins) or exogenous opioid compounds. A dramatic example is the reversal of unconsciousness that occurs in a patient with opioid overdose who has received naloxone. Perioperative respiratory depression caused by excessive opioid administration is rapidly antagonized (1–2 min). Some degree of opioid analgesia can often be spared if the dose of naloxone is limited to the minimum required to maintain adequate ventilation. Low doses of intravenous naloxone reverse the side effects of epidural opioids without necessarily reversing the analgesia.

Side Effects

Abrupt reversal of opioid analgesia can result in sympathetic stimulation (tachycardia, ventricular irritability, hypertension, pulmonary edema) caused by severe, acute pain, and an acute withdrawal syndrome in patients who are opioid-dependent. The extent of these side effects is proportional to the amount of opioid being reversed and the speed of the reversal.

Dosage

In postoperative patients experiencing respiratory depression from excessive opioid administration, intravenous naloxone (0.4 mg/mL vial diluted in 9 mL saline to 0.04 mg/mL) can be titrated in increments of 0.5–1 mcg/kg every 3–5 min until adequate ventilation and alertness are achieved. Doses in excess of 0.2 mg are rarely indicated. The brief duration of action of intravenous naloxone (30–45 min) is due to rapid redistribution from the central nervous system. A more prolonged effect is almost always necessary to prevent the recurrence of respiratory depression from longer-acting opioids. Therefore, intramuscular naloxone (twice the required intravenous dose) or a continuous infusion (4–5 mcg/kg/h) is recommended. Neonatal respiratory depression resulting from maternal opioid administration is treated with 10 mcg/kg, repeated in 2 min if necessary. Neonates of opioid-dependent mothers will exhibit withdrawal symptoms if given naloxone. The primary treatment of respiratory depression is always establishment of an adequate airway to permit spontaneous, assisted, or controlled ventilation.

Drug Interactions

The effect of naloxone on nonopioid anesthetic agents such as nitrous oxide is insignificant. Naloxone may antagonize the antihypertensive effect of clonidine.

NALTREXONE

Naltrexone is also a pure opioid antagonist with a high affinity for the μ receptor, but with a significantly longer half-life than naloxone. Naltrexone is used orally for maintenance treatment of opioid addicts and for ethanol abuse. In the latter instance, it appears to block some of the pleasant effects of alcohol in some individuals.

FLUMAZENIL

Mechanism of Action

Flumazenil (Romazicon), an imidazobenzodiazepine, is a specific and competitive antagonist of benzodiazepines at benzodiazepine receptors.

Clinical Uses

10 Flumazenil is useful in the reversal of benzodiazepine sedation and the treatment of benzodiazepine overdose. Although it promptly (onset <1 min) reverses the hypnotic effects of benzodiazepines, amnesia has proved to be less reliably prevented. Some evidence of respiratory depression may linger despite an alert and awake appearance. Specifically, tidal volume and minute ventilation return to normal, but the slope of the carbon dioxide response curve remains depressed. Effects in elderly patients appear to be particularly difficult to reverse fully, and these patients are more prone to resedation.

Side Effects & Drug Interactions

Rapid administration of flumazenil may cause anxiety reactions in previously sedated patients and symptoms of withdrawal in those on long-term benzodiazepine therapy. Flumazenil reversal has been associated with increases in intracranial pressure in patients with head injuries and abnormal intracranial compliance. Flumazenil may induce seizure activity if benzodiazepines have been given as anticonvulsants or in conjunction with an overdose of tricyclic antidepressants. Flumazenil reversal following a midazolam–ketamine anesthetic technique may increase the incidence of emergence dysphoria and hallucinations. Nausea and vomiting are not uncommon following administration of flumazenil. The reversal effect of flumazenil is based on its strong antagonist affinity for benzodiazepine receptors. Flumazenil does not affect the minimum alveolar concentration of inhalation anesthetics.

Dosage

Gradual titration of flumazenil is usually accomplished by intravenous administration of 0.2 mg/min until reaching the desired degree of reversal. The usual total dose is 0.6–1.0 mg. Because of flumazenil's rapid hepatic clearance, repeat doses may be required after 1–2 h to avoid resedation and premature recovery room or outpatient discharge. A continuous infusion (0.5 mg/h) may be helpful in the case of an overdose of a longer-acting benzodiazepine. Liver failure prolongs the clearance of flumazenil and benzodiazepines.

CASE DISCUSSION

Management of Patients at Risk for Aspiration Pneumonia

A 58-year-old man is scheduled for elective inguinal hernia repair. His past history reveals a persistent problem with heartburn and passive regurgitation of gastric contents into the pharynx. He has been told by his internist that these symptoms are due to a hiatal hernia.

Why would a history of hiatal hernia concern the anesthesiologist?

Perioperative aspiration of gastric contents (Mendelson's syndrome) is a potentially fatal complication of anesthesia. Hiatal hernia is commonly associated with symptomatic GERD, which is considered a predisposing factor for aspiration. Mild or occasional heartburn may not significantly increase the risk of aspiration. In contrast, symptoms related to passive reflux of gastric fluid, such as acid taste or sensation of refluxing liquid into the mouth, should alert the clinician to a high risk of pulmonary aspiration. Paroxysms of coughing or wheezing, particularly at night or when the patient is flat, may be indicative of chronic aspiration. Aspiration can occur on induction, during maintenance, or upon emergence from anesthesia.

Which patients are predisposed to aspiration?

Patients with altered airway reflexes (eg, drug intoxication, general anesthesia, encephalopathy, neuromuscular disease) or abnormal pharyngeal or esophageal anatomy (eg, large hiatal hernia, Zenker's diverticulum, scleroderma, pregnancy, obesity) are prone to pulmonary aspiration.

11 Does aspiration consistently result in aspiration pneumonia?

Not necessarily. The seriousness of the lung damage depends on the volume and composition of the aspirate. Traditionally, patients are considered to be at risk if their gastric volume is greater than 25 mL (0.4 mL/kg) and their gastric pH is less than 2.5. Some investigators believe that controlling acidity is more important than volume and that the criteria should be revised to a pH less than 3.5 with a volume greater than 50 mL.

Patients who have eaten immediately prior to emergency surgery are obviously at risk. Traditionally, "NPO after midnight" implied a preoperative fast of at least 6 h. Current opinion allows clear liquids until 2–4 h before induction of anesthesia, although solids are still taboo for 6 h in adult patients. Some patients who have fasted for 8 h or more before elective surgery also meet the at-risk criteria, however. Certain patient populations are particularly likely to have large volumes of acidic gastric fluid: patients with an acute abdomen or peptic ulcer disease, children, the elderly, diabetic patients, pregnant women, and obese patients. Furthermore, pain, anxiety, or opioid-agonists may delay gastric emptying. Note that pregnancy and obesity place patients in double jeopardy by increasing the chance of aspiration (increased intraabdominal pressure and distortion of the lower esophageal sphincter) and the risk of aspiration pneumonia (increased acidity and volume of gastric contents). Aspiration is more common in patients undergoing esophageal, upper abdominal, or emergency laparoscopic surgery.

Which drugs lower the risk of aspiration pneumonia?

H_2-Receptor antagonists decrease gastric acid secretion. Although they will not affect gastric contents already in the stomach, they will inhibit further acid production. Both gastric pH and volume are affected. In addition, the long duration of action of ranitidine and famotidine may provide protection in the recovery room.

Metoclopramide shortens gastric emptying time and increases lower esophageal sphincter tone. It does not affect gastric pH, and it cannot clear large volumes of food in a few hours. Nonetheless, metoclopramide with ranitidine is a good combination for most at-risk patients. Antacids usually raise gastric fluid pH, but, at the same time, they increase gastric volume. Although antacid administration technically removes a patient from the at-risk category, aspiration of a substantial volume of particulate matter will lead to serious physiological damage. For this reason, clear antacids (eg, sodium citrate) are strongly preferred. In contrast to H_2 antagonists, antacids are immediately effective and alter the acidity of existing gastric contents. Thus, they are useful in emergency situations and in patients who have recently eaten.

Anticholinergic drugs, particularly glycopyrrolate, decrease gastric secretions if large doses are administered; however, lower esophageal sphincter tone is reduced. Overall, anticholinergic drugs do not reliably reduce the risk of aspiration pneumonia and can reverse the protective effects of metoclopramide. Proton pump inhibitors are generally as effective as H_2 antagonists.

What anesthetic techniques are used in full-stomach patients?

If the full stomach is due to recent food intake and the surgical procedure is elective, the operation should be postponed. If the risk factor is not reversible (eg, large hiatal hernia) or the case is emergent, proper anesthetic technique can minimize the risk of aspiration pneumonia. Regional anesthesia with minimal sedation should be considered in patients at increased risk for aspiration pneumonia. If local anesthetic techniques are impractical, the patient's airway must be protected. Delivering anesthesia by mask or laryngeal mask airway is contraindicated. As in every

anesthetic case, the availability of suction must be confirmed before induction. If there are signs suggesting a difficult airway, intubation should precede induction. Otherwise, a rapid-sequence induction is indicated.

How does a rapid-sequence induction differ from a routine induction?

- The patient is always preoxygenated prior to induction. Patients with lung disease require 3–5 min of preoxygenation.
- Prior curarization with a nondepolarizing muscle relaxant may prevent the increase in intraabdominal pressure that accompanies the fasciculations caused by succinylcholine. This step is often omitted, however, as it can decrease lower esophageal sphincter tone. If rocuronium has been selected for relaxation, a small priming dose (0.1 mg/kg) given 2–3 min prior to induction may speed its onset of action.
- A wide assortment of blades, video laryngoscopes, and endotracheal tubes are prepared in advance.
- An assistant may apply firm pressure over the cricoid cartilage prior to induction (Sellick's maneuver). Because the cricoid cartilage forms an uninterrupted and incompressible ring, pressure over it is transmitted to underlying tissue. The esophagus is collapsed, and passively regurgitated gastric fluid cannot reach the hypopharynx. Excessive cricoid pressure (beyond what can be tolerated by a conscious person) applied during active regurgitation has been associated with rupture of the posterior wall of the esophagus. The effectiveness of Sellick's maneuver has been questioned.
- A propofol induction dose is given as a bolus. Obviously, this dose must be modified if there is any indication that the patient's cardiovascular system is unstable. Other rapid-acting induction agents can be substituted (eg, etomidate, ketamine).
- Succinylcholine (1.5 mg/kg) or rocuronium (0.9–1.2 mg/kg) is administered immediately following the induction dose, even if the patient has not yet lost consciousness.
- The patient is not artificially ventilated, to avoid filling the stomach with gas and thereby increasing the risk of emesis. Once spontaneous efforts have ceased or muscle response to nerve stimulation has disappeared, the patient is rapidly intubated. Cricoid pressure is maintained until the endotracheal tube cuff is inflated and tube position is confirmed. A modification of the classic rapid-sequence induction allows gentle ventilation as long as cricoid pressure is maintained.
- If the intubation proves difficult, cricoid pressure is maintained and the patient is gently ventilated with oxygen until another intubation attempt can be performed. If intubation is still unsuccessful, spontaneous ventilation should be allowed to return and an awake intubation performed.
- After surgery, the patient should remain intubated until airway reflexes have returned and consciousness has been regained.

What are the relative contraindications to rapid-sequence inductions?

Rapid-sequence inductions are usually associated with increases in intracranial pressure, arterial blood pressure, and heart rate. Contraindications to succinylcholine also apply (eg, thermal burns).

Describe the pathophysiology and clinical findings associated with aspiration pneumonia.

The pathophysiological changes depend on the composition of the aspirate. Acid solutions cause atelectasis, alveolar edema, and loss of surfactant. Particulate aspirate will also result in small-airway obstruction and alveolar necrosis. Granulomas may form around food or antacid particles. The earliest physiological change following aspiration is intrapulmonary shunting, resulting in hypoxia. Other changes may include pulmonary edema, pulmonary hypertension, and hypercapnia.

Wheezing, rhonchi, tachycardia, and tachypnea are common physical findings. Decreased lung compliance can make ventilation difficult. Hypotension signals significant fluid shifts into the alveoli and is associated with massive lung injury.

Chest roentgenography may not demonstrate diffuse bilateral infiltrates for several hours after the event. Arterial blood gases reveal hypoxemia, hypercapnia, and respiratory acidosis.

What is the treatment for aspiration pneumonia?

As soon as regurgitation is suspected, the patient should be placed in a head-down position so that gastric contents drain out of the mouth instead of into the trachea. The pharynx and, if possible, the trachea should be thoroughly suctioned. The mainstay of therapy in patients who subsequently become hypoxic is positive-pressure ventilation. Intubation and the institution of positive end-expiratory pressure or continuous positive airway pressure are often required. Bronchoscopy and pulmonary lavage are usually indicated when particulate aspiration has occurred. Use of corticosteroids is generally not recommended and antibiotics are administered depending upon culture results.

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