

## REVIEW ARTICLE

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# Postoperative Nausea and Vomiting

*Its Etiology, Treatment, and Prevention*

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### I. Introduction

#### I.A. ROLE OF NAUSEA AND VOMITING

NAUSEA, retching, and vomiting are among the most common postoperative complaints and can occur after general, regional, or local anesthesia. Nausea is defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit. It is usually felt in the back of the throat and epigastrium, and is accompanied by the loss of gastric tone, duodenal contractions, and reflux of the intestinal contents into the stomach.<sup>1,2</sup> Retching is defined as labored, spasmodic, rhythmic contractions of the respiratory muscles including the diaphragm, chest wall, and abdominal wall muscles without the expulsion of gastric contents.<sup>2</sup> Vomiting, or emesis, is the forceful expulsion of gastric contents from the mouth and is brought about by the powerful sustained contraction of the abdominal muscles, descent of the diaphragm, and opening of the gastric cardia.<sup>2,3</sup>

Since the last comprehensive review of postoperative nausea and vomiting by Palazzo and Strunin in 1984,<sup>4</sup> there have been more than 150 new publications in the anesthesia literature describing studies related to this topic. In addition, several newer drugs (*e.g.*, propofol, ketorolac, ondansetron, buprenorphine) and techniques (*e.g.*, patient-controlled analgesia (PCA), spinal opioid administration, total intravenous anesthesia) have become more widely accepted in clinical anesthetic practice. The inci-

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Key words: Analgesics: nonsteroidal antiinflammatory; opioids. Anesthesia: general; regional. Anesthetics, gases: nitrous oxide. Anesthetics: intravenous. Anesthetics: volatile. Complications: vomiting. Drugs: antiemetics.

TABLE 1. Reports from 1936 through 1990 on the Incidence of Postoperative Emesis (modified from Palazzo and Strunin<sup>4</sup>)

Investigators	Year Study Published	Population Size (n)	Incidence of Emesis	Comments
Waters <i>et al.</i> <sup>4,259</sup>	1936	10,000	41%	Follow-up period unknown
Bellville <i>et al.</i> <sup>3,16</sup>	1959	748	19%	Follow-up for only 2.5 h
Adriani J <i>et al.</i> <sup>144</sup>	1961	2,230	23%	Average follow-up 6 h
Rowley <i>et al.</i> <sup>13</sup>	1982	1,183	43%	Limited to children; lower incidence in infants
Stark RD <i>et al.</i> <sup>74</sup>	1985	200	1–3%	High-risk women receiving propofol
Gold <i>et al.</i> <sup>10</sup>	1989	9,616	Severe emesis 0.2%	Outpatients with severe emesis requiring hospitalization
Patel <i>et al.</i> <sup>43</sup>	1989	9,910	9%	Limited to ambulatory surgery in children
Forrest <i>et al.</i> <sup>8</sup>	1990	16,000	Overall incidence 18–25%; severe emesis 0.15%	Multicenter study comparing outcome with halothane, enflurane, isoflurane and fentanyl; highest incidence of emesis with fentanyl (25%)
Karlsson <i>et al.</i> <sup>159</sup>	1990	485	25%	Study limited to children; highest incidence after strabismus surgery
Cohen <i>et al.</i> <sup>9</sup>	1990	29,220	25%	Study limited to children; highest incidence in 6–10-yr age range

dence of postoperative emesis in recent large studies has been reported to be in the 20–30% range (table 1),<sup>3–17</sup> which is consistently lower than the 75–80% incidence reported during the “ether” era.

Nevertheless, persistent nausea and vomiting may result in dehydration, electrolyte imbalance, and delayed discharge, particularly after outpatient (ambulatory) surgery.<sup>11</sup> Persistent retching or vomiting can cause tension on suture lines, venous hypertension, and increased bleeding under skin flaps, and can expose the subject to an increased risk of pulmonary aspiration of vomitus if airway reflexes are depressed from the residual effects of anesthetic and analgesic drugs.<sup>12</sup> Although frequently described as a “minor” postoperative complication, the incidence of severe nausea and vomiting has been reported to be 1 in 1,000 (0.1%).<sup>8,10</sup> Before discussing factors contributing to an increased incidence of nausea and vomiting, as well as its treatment, the physiologic basis for this common postoperative symptom will be reviewed.

#### I.B. PHYSIOLOGY OF EMESIS

Nausea and vomiting are important defense mechanisms against the ingestion of toxins.<sup>18</sup> The act of emesis involves a sequence of events that can be divided into pre-ejection, ejection, and post-ejection phases. The pre-ejection phase comprises prodromal symptoms of nausea, along with autonomic signs such as salivation, swallowing, pallor, tachycardia, and licking (in animals). The ejection phase comprises retching and vomiting. Retching is characterized by rhythmic, synchronous, inspiratory movements of the diaphragm and abdominal and external intercostal muscles, while the mouth and glottis are kept closed. As the antral portion of the stomach contracts, the proximal portion relaxes and the gastric contents oscillate between the stomach and esophagus. During retching the hiatal portion of the diaphragm does not

relax, and intraabdominal pressure increases are associated with decreases in intrathoracic pressure. In contrast, relaxation of the hiatal portion of the diaphragm permits a transfer of intraabdominal pressure to the thorax during the act of vomiting. Contraction of the rectus abdominis and external oblique muscles of the anterior abdominal wall, relaxation of the esophageal sphincter, an increase in intrathoracic and intragastric pressure, reverse peristalsis, and an open glottis and mouth results in the expulsion of gastric contents.<sup>‡</sup> The post-ejection phase consists of autonomic and visceral responses that return the body to a quiescent phase, with or without residual nausea.

The complex act of vomiting involves coordination of the respiratory, gastrointestinal, and abdominal musculature and is controlled by the emetic center (fig. 1). The evidence for such a center is based on electrical stimulation and on brain stem lesion studies.<sup>19</sup> Anatomic studies show that the parvicellular reticular formation has access to the motor pathways responsible for the visceral and somatic output involved in vomiting. This area is situated in the lateral reticular formation close to the tractus solitarius in the brain stem and is thought to be the emetic center.<sup>18,19</sup> Electrical stimulation of the emetic center and the tractus solitarius will cause immediate vomiting. Ablation of the emetic center abolishes the vomiting response to both apomorphine and to direct chemical stimulation (*e.g.*, copper sulfate). However, at present there are no known anesthetic drugs or chemicals that act directly on the emetic center.<sup>18–21</sup>

Stimuli from several areas within the central nervous system can affect the emetic center (fig. 1). These include afferents from the pharynx, gastrointestinal tract, and mediastinum, as well as afferents from the higher cortical

‡ Andrews PLR and Hawthorn J: The neurophysiology of vomiting. *Balliere's Clinical Gastroenterology* 2:141–168, 1988.

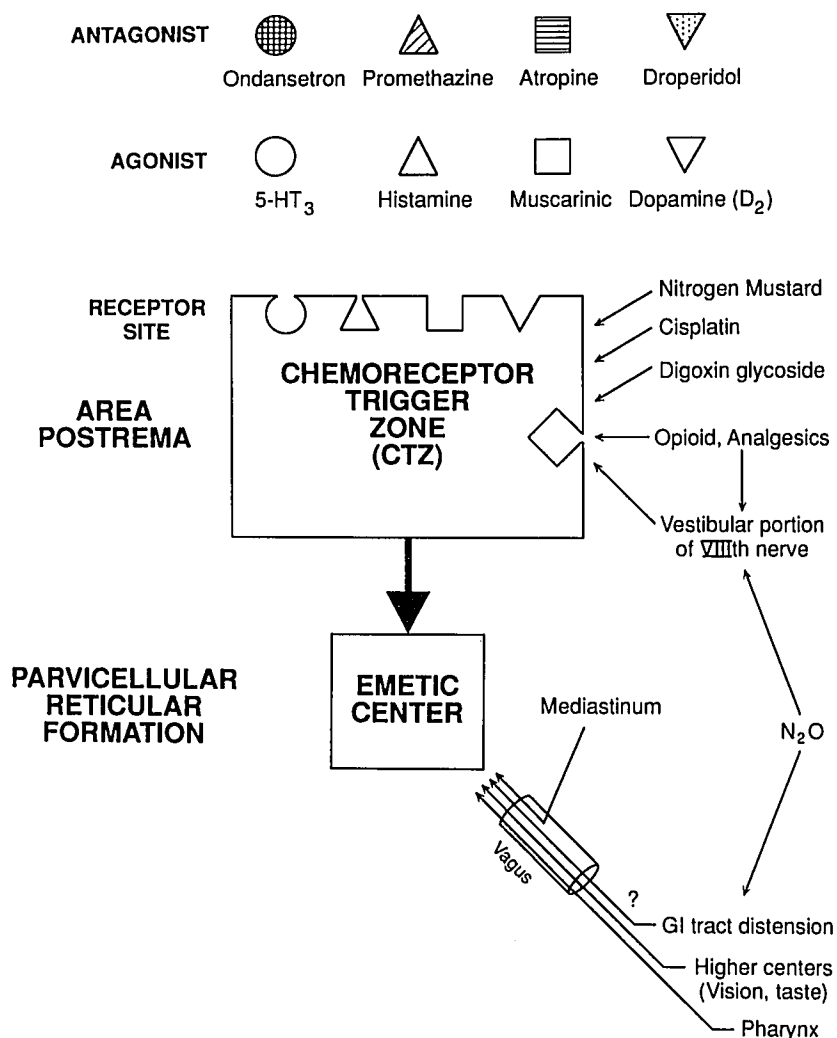


FIG. 1. The chemoreceptor trigger zone and the emetic center with the agonist and antagonist sites of action of various anesthetic-related agents and stimuli.

centers (including the visual center and the vestibular portion of the eighth cranial nerve) and the chemoreceptor trigger zone (CTZ) in the area postrema.<sup>18-25</sup> The area postrema is highly vascularized, and the vessels terminate in fenestrated capillaries surrounded by large perivascular spaces. No effective blood-brain barrier exists in these areas, and thus the CTZ can be activated by chemical stimuli received through the blood as well as the cerebrospinal fluid. However, direct electrical stimulation of the CTZ does not result in emesis.<sup>19</sup>

In animals, ablation of the CTZ eliminates the emetic actions of apomorphine, glycosides, mechlorothamine, phosphoramidate mustards, and opiates but does not prevent emetic responses to intragastric copper sulfate or to impulses from the gastrointestinal system and the vestibular portion of the eighth cranial nerve.<sup>18-25</sup> In addition to the CTZ, chemosensory inputs to the emetic center can come from the forebrain (e.g., pilocarpine stimulation)

and the nodose ganglion of the vagus nerve (*Veratrum* alkaloids).<sup>24,25</sup>

The area postrema of the brain stem is rich in dopamine, opioid, and serotonin or 5-hydroxytryptamine (5-HT<sub>3</sub>) receptors.<sup>26-28</sup> The nucleus tractus solitarius is rich in enkephalins and in histaminic and muscarinic cholinergic receptors.<sup>29,30</sup> These receptors may play an important role in the transmission of impulses to the emetic center. It has been speculated that blockade of these receptors is an important mechanism of action of the currently used antiemetic drugs (*vide infra*).<sup>31,32</sup>

The complex role of opioids in emesis has been examined by Costello and Borison in the cat.<sup>22</sup> These in-

§ Andrews PLR, Bailey HE, Hawthorn J, Stables R, Tyers MB: GR 38032F, a novel 5-HT<sub>3</sub>-receptor antagonist can abolish emesis induced by cyclophosphamide and radiation in the ferret (abstract). *British Journal of Pharmacology* 91(suppl):417P, 1987.

investigators noted that opioids have both emetic and antiemetic effects in this animal model. The antiemetic effects were blocked by systemic naloxone, but the emetic effects were blocked only by direct intracerebroventricular injection of naloxone.<sup>22</sup> A specific anatomic site for a possible antiemetic center has not been described.<sup>19,22</sup> Although opioid receptors have been identified in the brain stem, their role in emesis is uncertain.<sup>27</sup> Harris has suggested that the opioid receptor in the CTZ is a  $\delta$ -receptor that binds preferentially to enkephalins rather than to naloxone.<sup>32</sup>

The concept of chemosensory activation of the CTZ by a parallel array of independent receptor sites has recently been questioned, and a sequential activation model with linkages between effector nuclei has been suggested.<sup>21</sup> In this model, the control of emesis does not depend on the existence of a discrete group of neurons in an emetic center but is the expression of a local circuit involving sequential stimulation of separate effector nuclei.<sup>21</sup> This model attempts to explain why some of the phenomena usually associated with emesis can occur without the actual expulsion of gastric contents. However, the discovery of the parvicellular reticular formation and its effects on emesis provides support for the parallel array model.<sup>19</sup> Research on the methods by which the body converts blood-borne emetic chemical stimuli to nerve impulses in the CTZ may provide insights on a potential solution to the problem of drug-related emesis.

## II. Nonanesthetic Factors Associated with Postoperative Emesis

Factors affecting postoperative emesis include the patient, the nature of the underlying disease for which surgery is being performed, the type of operation, and the anesthetic technique.<sup>4,6-8,10-13</sup>

### II.A. PATIENT-RELATED FACTORS

#### 1. Age

The incidence of emesis is higher in pediatric patients than in adults. Within the pediatric population, postoperative emesis increases with age to reach a peak incidence in the preadolescent 11-14-yr age group.<sup>9,12,13</sup> While some investigators have suggested that increasing age during adulthood is associated with a decreased incidence of emesis, the relationship between age and emesis is not as clear as the relationship between gender and postoperative nausea and vomiting in the adult population.<sup>4,6-8,10,11,14,15</sup>

#### 2. Gender

Most investigators have reported a significantly lower incidence of nausea and vomiting after surgery in male

adults compared to female adults, including postmenopausal women younger than 60 yr.<sup>4-11</sup> The gender difference is not noted in the preadolescent age group or in patients beyond the 8th decade of life, suggesting that variations in serum gonadotropin (or other hormonal) levels may be a factor in the higher incidence of emesis in women.<sup>4-17</sup> Although Bellville *et al.*<sup>3</sup> did not find a significantly higher emesis rate in women undergoing surgery during the 3rd or 4th week of their menstrual cycle, Beattie *et al.* noted that postoperative nausea and vomiting in women undergoing laparoscopy is increased if the procedure is performed during the menses, with the highest incidence occurring on the 4th and 5th days of the menstrual cycle.<sup>6</sup> This observation may explain differences in rates of postoperative emesis in women undergoing laparoscopic procedures with similar anesthetic techniques.<sup>6</sup>

#### 3. Obesity

There is a positive correlation between body weight and postoperative emesis.<sup>4,33,34</sup> One of the reasons used to explain this relationship is that adipose tissue acts as a reservoir for inhaled anesthetic agents, from which they continue to enter the blood stream even after their administration has been discontinued. In obese patients, the larger reservoir of inhalation agent that will be present at the end of the case may contribute to an increased incidence of postoperative side effects. Other explanations that have been offered include a larger residual gastric volume and increased incidence of esophageal reflux, as well as gallbladder and other gastrointestinal diseases in obese patients. In addition, compared to nonobese subjects, these patients have a higher incidence of airway difficulties, and more gastric inflation occurs during attempts to maintain an adequate airway using a face mask.<sup>3,4,11,17,34</sup>

#### 4. History of Motion Sickness and/or Previous Postoperative Nausea

Patients with a history that suggests that they have a low threshold for vomiting are at increased risk for developing emetic symptoms. These include subjects with a history of vomiting after previous operations or motion sickness.<sup>3,7,11-17,33,34</sup> It has been alleged that these individuals may have a well-developed reflex arc for vomiting.<sup>4</sup>

#### 5. Anxiety

The increased incidence of emesis in patients with a high level of preoperative anxiety is well known to anesthesiologists.<sup>4</sup> The high incidence of emesis when anesthetic agents known to release catecholamines are used

(*e.g.*, ether, cyclopropane, ketamine)<sup>17,35</sup> suggests that catecholamine release may be a contributing factor. In animal studies, injection of epinephrine or norepinephrine into the third and fourth ventricle results in vomiting, whereas the injection of saline does not.<sup>35</sup> Because these effects can be blocked by phentolamine but not propranolol,<sup>35</sup> an  $\alpha$ -adrenergic mechanism has been proposed. An additional explanation for the increased incidence of postoperative emesis in anxious patients may relate to excessive air swallowing, which can increase gastric volume.

#### 6. Gastroparesis

Patients with delayed gastric emptying secondary to an underlying disease may be at increased risk for emesis after surgery.<sup>18,36</sup> These disease processes include gastrointestinal obstruction, chronic cholecystitis, neuromuscular disorders, and intrinsic neuropathies. Gastric hypomotility can complicate conditions such as scleroderma, myotonic dystrophy, and progressive muscular dystrophies (*e.g.*, Duchenne muscular dystrophy), amyloidosis, and familial visceral myopathies.<sup>37-39</sup> Gastroparesis also can be associated with pylorospasm, isolated antral hypomotility, and intrinsic neuropathies in patients with diabetes mellitus.<sup>37</sup>

#### II.B. OPERATIVE PROCEDURE

The incidence of emesis after general anesthesia is influenced by the type of surgical procedure, irrespective of the anesthetic technique used. In a study involving adult outpatients undergoing general anesthesia, the highest incidence of postoperative emesis was reported in women undergoing laparoscopic ovum retrieval procedures (54%); the next highest occurred after laparoscopy (35%).<sup>40</sup> In this study, patients undergoing dental extractions, dilatation and curettage of the uterus, or knee arthroscopy had similar rates of nausea and vomiting (16%, 12%, and 22% respectively).<sup>40</sup> A high incidence of postoperative emesis has also been noted after extracorporeal shock-wave lithotripsy, head and neck surgery, and stomach, duodenum, and gallbladder operations.<sup>4,7,34,40-42</sup>

In children there is a high incidence of emesis after strabismus surgery, orchiopexy, middle ear surgery, and otoplasty.<sup>13,43,44</sup> However, data from these studies are not directly comparable because different anesthetic techniques were used. Nevertheless, the incidence of postoperative emesis appears to be related at least in part to the site of the operation. The effects of antiemetic therapy are often studied in patients undergoing operations with an intrinsically high incidence of postoperative emesis. One commonly used model for these studies involves women undergoing laparoscopy. In the pediatric population, the effects of anesthetic techniques and medications on postoperative emesis have been studied in children

undergoing strabismus surgery and tonsillectomy.

#### II.C. DURATION OF SURGERY

The operative time also has an effect on the incidence of postoperative emesis, with more frequent emesis being reported after longer operations.<sup>4</sup> During longer operations, the patient may receive a larger number of potentially emetic anesthetic drugs.<sup>3,4,16</sup>

### III. Anesthetic-related Factors Associated with Emesis

#### III.A. PREANESTHETIC MEDICATION

Premedication with intramuscular morphine has been associated with an increase in postoperative emesis (table 2).<sup>45,46</sup> Increased emesis also has been noted with intravenous, nasal, oral, and transmucosal routes of opioid administration.<sup>47-49</sup> The addition of atropine or hyoscine to an opioid regimen has been reported to decrease postoperative emesis.<sup>46</sup> It is difficult to determine which opioid premedication is associated with the lowest incidence of postoperative emesis (because these drugs may also have antiemetic actions at low doses).<sup>22</sup> In addition, the avoidance of opioids in the early postoperative period may result in increased emesis secondary to visceral pain.<sup>45,50</sup>

#### III.B. GASTRIC DISTENSION AND SUCTIONING

Gastric distension from vigorous positive pressure ventilation *via* a face mask will predispose a patient to vomit in the postoperative period. This may have contributed to the increased incidence of emesis in patients anesthetized by less experienced trainees.<sup>51</sup> However, gastric suctioning has variable results in reducing emesis. Recent studies found that emptying the stomach had no effect on the incidence of postoperative emesis, even if the nasal or oral gastric tube was removed before airway reflexes returned (to avoid nausea from pharyngeal stimulation).<sup>3,34,41,52,53</sup>

#### III.C. ANESTHETIC TECHNIQUES

##### 1. General Anesthesia

Because anesthesiologists often use more than one drug during an anesthetic, it is difficult to sort out the effects of an individual drug on the incidence of postoperative emesis. The multifactorial etiology of postoperative emesis emphasizes the need for investigators to control perioperative conditions carefully to ensure that differences in the rates of emesis are associated with a specific anesthetic intervention. Data from controlled studies indicate that emesis following the same operative procedure occurs

TABLE 2. Relationship Between the Preoperative Use of Opioids and Postoperative Emesis

Investigators	Opioids	Route and Time of Administration	Study Group	Incidence of Nausea and Vomiting	Comments
Riding <sup>45</sup>	M, M + A, A, placebo	IM, preoperative	870, D & C	Least emesis with M 5 mg + A 1.2 mg	Emesis varies with dose of morphine; reduced by atropine.
Dundee <i>et al.</i> <sup>46</sup>	A, M + A, A, mep + A	IM, 60–90 min preoperative IM	1200, D & C; 20 groups: thiopental, propofol, halothane, cyclopropane, chloroform	More emesis with cyclopropane <i>vs.</i> halothane, propofol <i>vs.</i> thiopental, M + A <i>vs.</i> mep + A <i>vs.</i> A	Complex study with varying techniques of induction and maintenance of anesthesia
Pandit <i>et al.</i> <sup>47</sup>	Placebo, M, mep, F, suf	IV, 30 min before induction	100 women: laparoscopy with N <sub>2</sub> O–isoflurane, droperidol	Placebo 10%, M 25%, mep 20%, F 15%, suf 10%	All patients received preoperative droperidol; no significant differences in emesis
Henderson <i>et al.</i> <sup>48</sup>	Placebo, suf	Nasal, 15 min before induction	80 children, 24-h follow-up	Placebo 42%, Suf (4–5 µg·kg <sup>-1</sup> ) 68%*	Higher-dose sufentanil caused significant emesis
Nelson <i>et al.</i> <sup>49</sup>	F	OTFC <i>vs.</i> no premed, or oral premed (diazepam + mep + A)	75 children	OTFC 41%, no premed 26%, oral premed 5%*	More emesis with OTFC compared to oral combination consisting of diazepam, meperidine, and atropine

\*  $P < 0.05$  versus other groups.  
A = atropine; D & C = dilatation and curettage; F = fentanyl; IM = intramuscular; IV = intravenous; M = morphine; mep = meperidine; OTFC = oral transmucosal fentanyl citrate; suf = sufentanil.

more frequently with some anesthetic agents and techniques than with others.<sup>8,41–47</sup>

a. *Nitrous oxide*: Laparoscopic procedures in women are associated with a high incidence of postoperative emesis, and early studies suggested that the addition of nitrous oxide to potent inhalation agents may increase the incidence and severity of nausea and vomiting (table 3). In two independent studies, Alexander *et al.*<sup>†</sup> and Lonie and Harper<sup>54</sup> noted a significant decrease in postoperative emesis if nitrous oxide was avoided in patients undergoing laparoscopic procedures. Three mechanisms have been suggested as contributing factors to the increase in postoperative emesis associated with nitrous oxide: 1) stimulation of the sympathetic nervous system with catecholamine release<sup>17,35</sup>; 2) middle-ear pressure changes resulting in traction of the membrane of the round window and consequent stimulation of the vestibular system<sup>55</sup>; and 3) increased abdominal distension resulting from the exchange of nitrous oxide and nitrogen in gas introduced into the gastrointestinal tract during mask ventilation.<sup>56</sup>

More recent studies<sup>57–60</sup> have questioned the increased emesis rates that have been reported when nitrous oxide is used as an adjuvant to potent inhalation agents. Unfortunately, none of the published studies regarding the effects of nitrous oxide on emesis after gynecologic laparoscopic procedures was controlled for the day of the menstrual cycle.<sup>54–62</sup> If the association between emesis and the day of the menstrual cycle is stronger than the association between nitrous oxide and emesis, it may explain the differing results that have been reported in this patient population.<sup>54,58–62</sup> The evidence at present suggests that nitrous oxide does not significantly effect the incidence of postoperative emesis in adults when halogenated inhalation agents are used (table 3).

Similarly, the addition of nitrous oxide to a halothane-based anesthetic did not alter the incidence of postoperative emesis in children after strabismus surgery or tonsillectomy.<sup>63,64</sup> In contrast, nitrous oxide appeared to increase emesis in children undergoing strabismus surgery during maintenance anesthesia with propofol.<sup>64</sup> There are few data in adults comparing emesis after nitrous oxide–propofol anesthesia with a propofol-based total intravenous anesthetic technique (*vide infra*).

b. *Inhalation agents*: Although early studies did not control conditions as carefully as the more recent studies, ether and cyclopropane appeared to be associated with a higher incidence of postoperative emesis than the cur-

† Alexander GD, Skupski JN, Brown EM: The role of nitrous oxide in postoperative nausea and vomiting (abstract). *Anesthesia and Analgesia* 63:175, 1984.

\*\* Gibbons P, Davidson P, Adler E: Nitrous oxide does not affect postoperative vomiting in pediatric eye surgery (abstract). *ANESTHESIOLOGY* 67(suppl):A530, 1987.

TABLE 3. Association Between Postoperative Emesis and Use of N<sub>2</sub>O During Surgery

Investigators	Anesthetic Techniques	Number (n)	Incidence of Emesis		Comments
			With N <sub>2</sub> O	Without N <sub>2</sub> O	
Alexander <i>et al.</i> <sup>71</sup>	(1) F + N <sub>2</sub> O (2) I + F + N <sub>2</sub> O (3) I + air	77	N & V 61%	N & V 27.5%*	Women: laparoscopy No isoflurane-N <sub>2</sub> O group
Lonie and Harper <sup>54</sup>	(1) E + N <sub>2</sub> O (2) air + E	87	N 49%, V 49%	N 49%, V 17%	Women: laparoscopy
Sengupta and Plantevin <sup>57</sup>	(1) E + N <sub>2</sub> O (2) E + air	64	N 52%, V 18%	N 38.7%, V 9.7%	Women: laparoscopy
Hovorka <i>et al.</i> <sup>58</sup>	(1) I + N <sub>2</sub> O (2) E + N <sub>2</sub> O (3) I + air	150	N & V Gp 1 58%, Gp 2 48%	N & V Gp 3 52%	Women: laparoscopy; no significant differences
Kortilla <i>et al.</i> <sup>59</sup>	(1) I + N <sub>2</sub> O (2) I + air	110	N & V 67%	N & V 62%	Abdominal hysterectomy
Muir <i>et al.</i> <sup>60</sup>	(1) E + N <sub>2</sub> O (2) E + air (3) I + N <sub>2</sub> O (4) I + air	780	Gp 1 N & V 37.6%, Gp 3 N & V 37%	Gp 2 N & V 37%, Gp 4 N & V 33%	Excluded patients with high risk for emesis, e.g., bowel surgery
Felts <i>et al.</i> <sup>61</sup>	(1) E + N <sub>2</sub> O (2) E + air	185	N & V 29.2%	N & V 9.3%*	Tubal ligation
Melnick <i>et al.</i> <sup>62</sup>	(1) I + N <sub>2</sub> O (2) I + air	60	N & V 25%	N & V 1%*	Gynecologic procedures

E = enflurane; F = fentanyl; Gp = group; I = Isoflurane; N = nausea; N<sub>2</sub>O = nitrous oxide; V = vomiting.

\*  $P < 0.05$  versus with N<sub>2</sub>O group.

rently used potent inhalational agents.<sup>3-8,11-17,34,41,42,45</sup> The high incidence of nausea and vomiting may be related to the increase in endogenous catecholamines associated with the use of the older inhaled agents.<sup>35,45</sup> It has also been suggested that subanesthetic doses of halothane may have an antiemetic effect, analogous to the alleged antiemetic effect following small analgesic doses of opioids.<sup>22,65</sup> However, this observation has not been confirmed in any other study.<sup>65</sup> Although there have been few prospective studies comparing emesis after anesthesia with halothane, enflurane, or isoflurane, data from outcome studies suggest that there are no significant differences between these agents with respect to the incidence of postoperative emesis.<sup>8,9,15,60,66</sup> Early clinical investigations with the less-soluble inhaled agents desflurane and sevoflurane would also suggest that there is little difference in emesis following the use of these agents compared to the currently used inhalation agents.<sup>67,68</sup>

*c. Etomidate:* This intravenous sedative-hypnotic drug is useful during induction and tracheal intubation in patients with limited cardiovascular reserves and/or compromised cerebral perfusion. However, the administration of a continuous etomidate infusion as part of a balanced anesthetic technique markedly increased the incidence of postoperative emesis.<sup>69-71,††</sup> Other side effects (e.g., pain on injection, myoclonus, transient adrenal suppression) have lead to a restricted use of etomidate in anesthesia.

*d. Ketamine:* Patients receiving ketamine for induction and/or maintenance of anesthesia have experienced delayed discharge, vivid dreams, hallucinations, and a higher incidence of postoperative nausea and vomiting compared

to patients receiving barbiturates with nitrous oxide.<sup>72,73</sup> The emetic effects of ketamine also may be secondary to the release of endogenous catecholamines.<sup>35,45</sup>

*e. Propofol:* Propofol is a novel intravenous anesthetic that is structurally unrelated to barbiturate, benzodiazepine, steroid, or eugenol compounds. Retrospective analysis of data from 200 women undergoing gynecologic procedures with propofol anesthesia revealed a low incidence of postoperative vomiting (1-3%) compared to the usual 10-15% with other intravenous agents.<sup>74</sup> This has been confirmed in numerous prospective studies, including studies in children.<sup>64,75-84</sup> Although some authors have suggested that propofol has a specific antiemetic effect,<sup>74-76</sup> there are no data describing the effects of propofol on the emetic center or the CTZ. Preliminary reports comparing the incidence of postoperative emesis when propofol is used alone (*vs.* a propofol-nitrous oxide regimen) suggest that a total intravenous technique may be associated with less nausea and emesis.<sup>64,76</sup> Propofol is extremely popular in the outpatient setting because of its favorable recovery characteristics, including rapid emergence and a low incidence of postoperative side effects.<sup>77-85</sup>

*f. Balanced anesthesia:* Compared to the use of inhalational or total intravenous techniques, the use of a nitrous oxide-opioid-relaxant technique is associated with an even higher incidence of postoperative emesis (table 4).<sup>3,5,8,17,61,66,86-90</sup> The increased incidence of emesis with the "balanced anesthetic" technique has been attributed to the use of an opioid-nitrous oxide combination and may reflect a direct action of these compounds on the CTZ. Morphine in the usual analgesic doses causes little nausea in the recumbent patient, but it often is associated with emesis when patients move, suggesting a vestibular component to opioid-induced emesis.<sup>91</sup>

†† White PF: Continuous infusions of thiopental, methohexital *vs.* etomidate as adjuvants to nitrous oxide for outpatient anesthesia (abstract). *Anesthesia and Analgesia* 63:282, 1984.

TABLE 4. Comparison of the Incidence of Postoperative Emesis After Inhalation and Opioid-based (Balanced) Anesthetic Techniques

Investigators	Patient Population	Anesthetic Technique	Incidence of Nausea and Vomiting	Comments
Hovorka <i>et al.</i> <sup>66</sup>	180 hysterectomy	(1) I + N <sub>2</sub> O (2) E + N <sub>2</sub> O	Gp 1 27%, Gp 2 48%, Gp 3 48%* in first 24 h	No difference at 24 h
Rising <i>et al.</i> <sup>86</sup>	50 laparoscopic sterilization	(3) F + N <sub>2</sub> O	Gp 1 16%	3 patients in Gp 2 had intraoperative awareness
Zuurmond <i>et al.</i> <sup>87</sup>	42 arthroscopy	(1) I + N <sub>2</sub> O (2) F + N <sub>2</sub> O	Gp 2 = 60%* Gp 1 = 45%* Gp 2 = 14%	More rapid awakening in Gp 1 but longer stay due to more emesis
Howie <i>et al.</i> <sup>89</sup>	40 gynecologic	(1) Alf + N <sub>2</sub> O (2) E + N <sub>2</sub> O	No difference	
Haley <i>et al.</i> <sup>88</sup>	60 gynecologic	(1) Alf + N <sub>2</sub> O (2) F + N <sub>2</sub> O (3) E + N <sub>2</sub> O	Gp 1 = 70%*, Gp 2 = 0% Gp 3 = 10%	All received droperidol
Zuurmond <i>et al.</i> <sup>260</sup>	40 arthroscopy	(1) Suf + N <sub>2</sub> O (2) I + N <sub>2</sub> O	Gp 1 = 45%* Gp 2 = 15%	
Davis <i>et al.</i> <sup>261</sup>	40 children, restorative dentistry	(1) Alf + N <sub>2</sub> O (2) H + N <sub>2</sub> O	Gp 1 = 45%* Gp 2 = 15%	More emesis with alfentanil
Watcha <i>et al.</i> <sup>64</sup>	120 children, strabismus surgery	(1) N <sub>2</sub> O + H + drop (2) Prop (3) prop + N <sub>2</sub> O (4) Prop + N <sub>2</sub> O + drop	Gp 1 = 50%, Gp 2 = 23%* Gp 3 = 60%, Gp 4 = 43%	All patients received morphine

\*  $P < 0.05$  versus other group.

Alf = alfentanil; drop = droperidol; E = enflurane; F = fentanyl;

Gp = group; H = halothane; I = isoflurane; N<sub>2</sub>O = nitrous oxide; prop = propofol; suf = sufentanil.

Studies comparing postoperative recovery following the use of various opioids (morphine and its derivatives, meperidine, fentanyl, alfentanil, and sufentanil) during surgery have failed to demonstrate any consistent, statistically significant differences between these compounds with respect to the incidence of emesis (table 5).<sup>92-98,††</sup> Many of these studies can be criticized for not having a large enough group size to avoid a type II error in the conclusion that the incidence of emesis does not significantly differ among the various opioid compounds. While Phitayakorn *et al.* found sufentanil to be associated with less emesis than fentanyl in women undergoing dilatation and curettage of the uterus,<sup>95</sup> Flacke *et al.* did not find any difference in emesis in patients receiving morphine, meperidine, fentanyl or sufentanil during balanced anesthesia (table 5).<sup>96</sup> However, opioid analgesics vary in their ability to produce nausea and vomiting in individual patients. Hence, in a patient who develops emesis with a specific opioid, it may be advantageous to substitute the opioid with a different analgesic.<sup>98</sup>

In the last few years, several different types of opioid receptors have been described in various parts of the brain and spinal cord.<sup>27</sup> Newer analgesic drugs with a combination of agonistic and antagonistic action at these receptors have been advocated for use in perioperative analgesia.<sup>98-102</sup> Butorphanol, nalbuphine, buprenorphine, and dezocine are alleged to have partial antagonistic action at the  $\mu$  receptor and enhanced agonist activity at the  $\kappa$  re-

ceptor site.<sup>98-102</sup> Because respiratory depression is closely linked to activity at the  $\mu$  receptor, the agonist-antagonist (or partial agonist) drugs have a "ceiling effect" with respect to respiratory depression.<sup>101</sup> Unfortunately, they also have a ceiling effect with respect to their analgesic efficacy.<sup>102</sup> Finally, the agonist-antagonist analgesic drugs have been shown to produce less spasm of the gastrointestinal smooth muscle than morphine and may be useful in treating pain associated with biliary colic.<sup>99,103</sup>

While the side effects of respiratory depression and drug dependence may be lower with the agonist-antagonist agents compared to pure agonists, these compounds appear to be associated with a variable incidence of postoperative emesis.<sup>101,104-109</sup> Although some studies have shown decreased emesis with nalbuphine compared to fentanyl and meperidine, others have found no difference in emetic sequelae or even an increase in emesis (table 6).<sup>104-108</sup> In one of the larger series of patients, Garfield *et al.* found an increased incidence of nausea and vomiting with nalbuphine compared to fentanyl.<sup>108</sup> Similarly, when dezocine was compared to fentanyl in women undergoing laparoscopy, increased emetic sequelae were noted.<sup>109</sup>

Unlike respiratory depression, emesis has not been clearly linked to an interaction between an opioid and a specific type of opioid receptor. Meptazinol, a selective  $\mu_1$  agonist, possesses cholinergic activity and is associated with a very high incidence of emesis.<sup>110</sup> However, nalbuphine, an agonist-antagonist drug, has been used to treat pruritus and nausea after epidural morphine (and hydromorphone) and to reverse respiratory depression produced by fentanyl.<sup>100,101</sup> It is interesting that the ad-

†† Brown JG: Systemic opioid analgesia for postoperative pain management. *Anesthesiology Clinics of North America* 7:51-62, 1989.



TABLE 5. Relationship Between Postoperative Emesis and the Intraoperative Use of Opioids as Part of a Balanced Anesthesia Technique

Investigators	Patient Population	Anesthetic Technique	Results	Comments
Haley <i>et al.</i> <sup>89</sup>	60 gynecologic	(1) E + N <sub>2</sub> O (2) Alf + N <sub>2</sub> O (3) F + N <sub>2</sub> O	Gp 1 10%, Gp 2 70%, Gp 3 0%	All received droperidol
Enright <i>et al.</i> <sup>95</sup>	60 D & C	(1) Alf + N <sub>2</sub> O (2) F + N <sub>2</sub> O	N & V Gp 1 3%, 7% Gp 2 7%, 17%	All received droperidol
White <i>et al.</i> <sup>94</sup>	100 D & C	F by bolus (Gp 1) or infusion (Gp 2) alf by bolus (Gp 3) or infusion (Gp 4)	N Gp 1 60%, Gp 2 68%, Gp 3 52%, Gp 4 68%	No significant differences
Phitayakorn <i>et al.</i> <sup>95</sup>	50 D & C	(1) F + N <sub>2</sub> O (2) suf + N <sub>2</sub> O	N Gp 1 52%, * Gp 2 20%; V Gp 1 32%, Gp 2 16%	More nausea but not emesis with F
Flacke <i>et al.</i> <sup>96</sup>	60 orthopedic or general surgery	(1) Suf + N <sub>2</sub> O (2) M + N <sub>2</sub> O (3) M + N <sub>2</sub> O (4) F + N <sub>2</sub> O	N & V Gp 1 25%, Gp 2 20% Gp 3 25%, Gp 4 12%	
Sfez <i>et al.</i> <sup>97</sup>	39 children, appendectomy	(1) F (2) Alf bolus (3) Alf infusion	Gp 1 33%, Gp 2 30%, Gp 3 33%	
Millar <i>et al.</i> <sup>79</sup>	130 outpatients	(1) Prop (2) TPL + Enf (3) Prop + Alf (4) TPL + E + Alf	Gp 1 0%, Gp 2 35%, * Gp 3 3%, * Gp 4 6%	Less emesis with propofol
Kestin <i>et al.</i> <sup>69</sup>	44 D & C	(1) TPL + F + N <sub>2</sub> O (2) Etomidate + alf + N <sub>2</sub> O	Gp 1 = 9%, Gp 2 = 41%*	Increased emesis may be related to etomidate

\*  $P < 0.05$  versus other group.Alf = alfentanil; E = enflurane; F = fentanyl; Gp = group; H = halothane; I = isoflurane; M = morphine; N = nausea; N<sub>2</sub>O = ni-

trous oxide; Prop = propofol; Suf = sufentanil; TPL = thiopental; V = vomiting.

ministration of naloxone, a pure opioid antagonist, can result in nausea and vomiting.<sup>102</sup> As previously described, systemic naloxone blocks the antiemetic effects of morphine in the cat, but direct intracerebroventricular administration is necessary to block the emetic action.<sup>22</sup> It also has been proposed that the opioid receptor in the CTZ is a  $\delta$  receptor that binds preferentially to enkephalins rather than naloxone.<sup>27,32</sup> The choice of an opioid should be based on pharmacodynamic and pharmacokinetic considerations (*e.g.*, onset and duration of action, as well as the potential for side effects.)<sup>99-111</sup>

The incidence of analgesic-induced emesis may be decreased with the development of potent nonsteroidal antiinflammatory drugs. Intraoperative ketorolac has been shown to be as effective as morphine and fentanyl in the prophylaxis of postoperative pain following ambulatory surgery.<sup>112,113</sup> It is associated with a lower incidence of postoperative emesis compared to morphine and dezocine and may prove to be a useful alternative to fentanyl in the outpatient setting.<sup>109,112,113</sup>

Neuromuscular blocking drugs are an integral part of any balanced anesthetic technique. However, at the end

TABLE 6. Relationship Between Agonist-antagonists and Nonsteroidal Antiinflammatory Drug Use and the Incidence of Postoperative Emesis

Investigators	Patient Population	Anesthetic Techniques	Incidence of Nausea and Vomiting	Comments
Hew <i>et al.</i> <sup>104</sup>	150, patients; postoperative pain relief	(1) Nalb (2) mep	Gp 1 2%, Gp 2 22%*	
Crul <i>et al.</i> <sup>105</sup>	63, gynecologic or urologic cases	(1) F + N <sub>2</sub> O (2) nalb + N <sub>2</sub> O	Less emesis with nalb	11 patients in Gp 1 received naloxone
Bone <i>et al.</i> <sup>106</sup>	40 therapeutic abortion	(1) F (2) nalb as premedication	No difference in emesis	
Wandless <sup>107</sup>	50, children orchiopepy	(1) M (2) nalb	No difference in emesis	
Garfield <i>et al.</i> <sup>108</sup>	286 gynecologic laparoscopy	(1) F 1.5 $\mu\text{g} \cdot \text{kg}^{-1}$ (2) nalb 300 $\mu\text{g} \cdot \text{kg}^{-1}$ (3) nalb 500 $\mu\text{g} \cdot \text{kg}^{-1}$	Gp 1 40%, * Gp 2 60%, Gp 3 70%	More patients in Gp 3 needed droperidol
Ding <i>et al.</i> <sup>109</sup>	120 gynecologic	(1) Dezocine (2) ketorolac (3) F	Gp 1 62%, * Gp 2 15%, Gp 3 22%	
Watcha <i>et al.</i> <sup>112</sup>	90 children	(1) Placebo (2) M (3) ketorolac	Gp 1 37%, Gp 2 59%, * Gp 3 25%	All patients received propofol-N <sub>2</sub> O for maintenance
Parker <i>et al.</i> <sup>262</sup>	80 abdominal hysterectomy	(1) ketorolac + m/mep PCA (2) placebo + m/mep PCA	Gp 1 N 66%, V 11%; Gp 2 N 57%, V 11%	

Alf = alfentanil; E = enflurane; F = fentanyl; Gp = group; H = halothane; I = isoflurane; M = morphine; mep = meperidine; nalb = nalbuphine; N = nausea; N<sub>2</sub>O = nitrous oxide; PCA = patient-con-

trolled analgesia; Prop = propofol; Suf = sufentanil; V = vomiting.

\*  $P < 0.05$  versus other group.

of the surgical procedure, most anesthesiologists reverse residual neuromuscular blockade with acetylcholinesterase-inhibiting drugs. The muscarinic effects of these drugs increase gastrointestinal motility, which may contribute to an increased incidence of postoperative vomiting.<sup>114</sup> The increased bowel activity is not affected by the substitution of glycopyrrolate for atropine, suggesting that when muscarinic cholinergic antagonists and anticholinesterases are used in the usual ratios, postoperative emesis may not be affected.<sup>115</sup> With the availability of intermediate (*e.g.*, atracurium, vecuronium) and short-acting nondepolarizing muscle relaxants (*e.g.*, mivacurium, ORG 7616), full recovery from neuromuscular blockade may occur without the need for anticholinesterase agents. The avoidance of neuromuscular reversal agents may decrease postoperative emesis.<sup>114</sup>

## 2. Regional Anesthesia

The incidence of postoperative emesis following regional nerve block procedures is usually lower than with general anesthesia.<sup>116</sup> Most anesthesiologists use concomitant intravenous sedation during regional anesthesia to provide anxiolysis and amnesia for intraoperative events, to prevent spontaneous movements, and to provide analgesia for discomfort associated with positioning.<sup>117</sup> Therefore, it is necessary to separate the emetic effects of the sedative-analgesic medications from those associated with neural blockade.

Emesis with central neuraxial block is greater than that with peripheral nerve blocks because of the associated sympathetic nervous system blockade, which contributes to postural hypotension-induced nausea and vomiting.<sup>41,42,118,119</sup> A rapid decline in arterial blood pressure (to < 80 mmHg) during spinal anesthesia is often associated with the onset of nausea.<sup>118,119</sup> Ratna *et al.* noted that the incidence of nausea and vomiting in these patients was reduced by the administration of 100% oxygen, suggesting that hypoxemia at the vomiting center was the stimulus to emesis.<sup>119</sup> The incidence of nausea and vomiting during spinal anesthesia is decreased by the intravenous administration of atropine, suggesting that vagal stimulation also may play a key role.<sup>4,41,42,118,119</sup>

In women undergoing laparoscopic procedures, postoperative emesis is lower with epidural (*vs.* general) anesthesia.<sup>120</sup> This may be related to improved gastric emptying with epidural anesthesia compared to general anesthesia.<sup>121</sup> However, epidural blockade also may be associated with postoperative emesis. For example, the incidence of emesis was reported to be 17% in a retrospective study in which caudal epidural block was used to supplement general anesthesia for lower abdominal and extremity procedures in children.<sup>122</sup>

During the last decade, anesthesiologists have extended their involvement in patient care to include the manage-

ment of postoperative pain.<sup>123,124</sup> A method that has gained widespread acceptance is the administration of local anesthetics and/or opioids into the subarachnoid or epidural space.<sup>123-139</sup> Opioids have been injected into the epidural space in single or multiple doses, by infusions, and alone or in combination with local anesthetics and  $\alpha_2$ -agonists.<sup>128-138</sup> Epidural techniques are associated with excellent pain relief, but nausea, vomiting, and pruritus are frequent side effects. A 20% incidence of emesis has been reported with epidural morphine 5 mg after elective cesarean section.<sup>128</sup> In two large series, emesis was noted in 40% and 34% of patients after the use of epidural morphine.<sup>130,131</sup> The incidence of nausea after epidural opioid administration may be lower with the more lipid-soluble agents such as fentanyl and sufentanil.<sup>129,132,133,138</sup> The emetic effects of epidural opioids are believed to be related to its rostral spread from the lumbar epidural site of injection to the CTZ and the vomiting center.<sup>132,§§</sup> The more lipid-soluble agents have less rostral spread than do the less soluble opioids such as morphine.

The intrathecal administration of opioids such as morphine has been advocated as a simple, reliable method of providing long-acting postoperative analgesia using low doses and not requiring a catheter.<sup>123,137,139</sup> Until recently, continuous infusions of medications into the intrathecal space were rarely used. However, even with the advent of small-bore catheters for continuous spinal anesthesia, the potential for infections, catheter breakage, and unpredictable, delayed respiratory depression probably will limit the use of continuous opioid infusions into the intrathecal space during the postoperative period. However, single-dose administration of preservative-free morphine with a local anesthetic in the intrathecal space will remain popular, particularly in the management of pain after cesarean section.<sup>137,139-142</sup> The incidence of emesis after intrathecal and epidural morphine appears to be similar when equipotent doses are used (intrathecal 0.3-0.5 mg, epidural 3-5 mg).<sup>137-142</sup>

If carefully titrated, drugs with antagonistic actions at the  $\mu_1$  opioid receptor site (*e.g.*, naloxone 50-100  $\mu$ g) can be used to reverse the side effects of intraspinal opioids, including pruritus and emesis, without significantly decreasing the quality of analgesia provided.<sup>136</sup> Intravenous nalbuphine 2.5-5 mg can reverse the respiratory depressant and emetic effects of epidural morphine without reversing its analgesic actions.<sup>100</sup> The addition of butorphanol 3 mg to epidural morphine 5 mg for postoperative analgesia after cesarean delivery significantly decreased the requirement for antiemetic (and antipruritic) drugs without adversely affecting respiration, sedation, or du-

§§ Chadwick HS, Ross BK: Analgesia for post-cesarean delivery pain. *Anesthesiology Clinics of North America* 7:133-153, 1989.

ration of analgesia.<sup>138</sup> However, administration of naloxone in doses sufficiently large to reverse the respiratory depressant effects of morphine may be associated with emesis.<sup>11,22</sup>

### 3. Monitored Anesthesia Care

Many procedures can be performed using only local anesthetics and intravenous sedation–analgesia techniques (e.g., cosmetic plastic surgery, cataract extractions, breast biopsies, endoscopy, central line or vascular shunt placement).<sup>143</sup> However, the avoidance of general, spinal, and epidural anesthesia does not guarantee the absence of emesis in the postoperative period. The incidence of emesis varies with the type of operation and the sedative–analgesic medications. For example, antiemetic therapy was required in 4–11% of patients undergoing extracorporeal shock-wave lithotripsy with a sedative–analgesic infusion regimen.<sup>144,145</sup> The incidence of nausea in these patients was not significantly altered, regardless of whether one used a midazolam–alfentanil, fentanyl–propofol, or midazolam–ketamine technique.<sup>144,145</sup> It would appear that emesis in these patients is related to the extracorporeal shock-wave lithotripsy procedure and not to the sedative–analgesic technique *per se*.

## III.D. POSTOPERATIVE FACTORS

Factors that influence the incidence of nausea and vomiting after surgery include pain, dizziness, ambulation, time of first oral intake, and use of opioid analgesics.

### 1. Pain

Visceral or pelvic pain is a common cause of postoperative emesis.<sup>3,11,50,146</sup> Anderson and Krohg found that relief of pain was frequently associated with a relief of nausea.<sup>50</sup> This relationship between pain and vomiting is supported by the increased emesis following naloxone reversal of opioid-mediated pain relief.<sup>4,22</sup>

### 2. Dizziness

Postoperative nausea and vomiting are increased in patients who feel dizzy. Postural hypotension in the postoperative period after a central neuraxis block may be an early sign of mild, unrecognized hypovolemia. When these patients first try to stand up, they may feel dizzy and nauseated, perhaps as a result of decreased medullary blood flow to the CTZ. Elevated vagal tone in the postoperative period may exacerbate the dizziness and nausea in these patients. These emetic symptoms often resolve with adequate hydration and/or sympathomimetic activity.

### 3. Ambulation

Sudden motion, changes in position (e.g. sitting up in a chair), or even transport from the postanesthetic recovery

unit to the postsurgical ward can precipitate nausea and vomiting in patients who have received opioid compounds.<sup>4,11,91,146,147</sup> These data suggest that opioids sensitize the vestibular system to motion-induced nausea and vomiting. Afferent impulses from the vestibular apparatus to the CTZ (via cholinergic and histaminic fibers) may be responsible for emesis following ambulation in the postoperative period.

### 4. Oral Intake

The timing of oral intake after surgery can influence the incidence of emesis in the postoperative period. Vanden berg *et al.* reported that restricting oral intake in the early postoperative period did not decrease the overall incidence of emesis; however, it did delay the first bout of vomiting to the period immediately after the first oral intake.<sup>148</sup> In contrast, Martin *et al.* found that restricting oral intake during the first 8 postoperative hours significantly decreased emesis compared to that in a group who were required to ingest fluids prior to discharge.<sup>149</sup>

### 5. Opioids

Nausea and/or vomiting are common side effects of opioid compounds administered orally during the preoperative period or given parenterally during or immediately after the operation. Irrespective of whether these analgesic drugs are administered by the intranasal, transdermal, oral/transmucosal, intrathecal, subcutaneous, intramuscular, intravenous, or epidural routes, the incidence of nausea and vomiting appears to be similar. In the postoperative period, it is often possible to achieve improved pain control by permitting the patient to titrate his or her own analgesic medications using PCA devices.<sup>150–158</sup>

Most studies have not found differences in the incidence of nausea and vomiting in patients who have received intravenous morphine *via* a PCA delivery system compared to standardized fixed-interval intramuscular injections.<sup>151,153–155,158</sup> Unfortunately, the number of patients in many of these studies is not large enough to determine accurately if there is a difference in the incidence of emesis after intramuscular *versus* intravenous PCA therapy. There are conflicting reports regarding the incidence of emesis in patients receiving epidural opioids compared to intravenous PCA or intramuscular opioid therapy. Eisenach *et al.*<sup>151</sup> found an increase in emesis with epidural compared to intravenous PCA and intramuscular morphine following cesarean section, but in a similar patient population Harrison *et al.*<sup>158</sup> could not confirm this finding. The surgical procedures may also have an effect on the incidence of emesis in patients receiving epidural and intravenous PCA morphine. For example, emetic sequelae have been reported to be more frequent following epidural compared to intravenous PCA morphine in patients

undergoing anterior cruciate ligament surgery and intraabdominal surgery, but not after hip replacement procedures.<sup>152-154</sup>

#### IV. Prevention and Treatment of Postoperative Emesis

##### A. ANTIEMETICS

Routine antiemetic prophylaxis of patients undergoing elective operations is not indicated, since fewer than 30% of patients experience postoperative emetic sequelae. Of those who develop these symptoms, many have transient nausea or only one or two bouts of emesis and do not require antiemetic therapy.<sup>3-17,147</sup> In addition, commonly used antiemetic drugs can produce significant side effects (*e.g.*, sedation, dysphoria, extrapyramidal symptoms). Nevertheless, antiemetic prophylaxis may be justified in subpopulations of patients who are at greater risk for developing postoperative nausea and/or vomiting. These include patients with a history of motion sickness and previous postoperative emesis, women undergoing gynecologic procedures (*e.g.*, laparoscopy),<sup>40</sup> adults undergoing extracorporeal shock wave lithotripsy,<sup>144,145</sup> and children undergoing strabismus surgery, otoplasty, tonsillectomy, and orchiopexy.<sup>9,43,159</sup>

Many different antiemetic drugs are available for the treatment of postoperative nausea and vomiting (table 7). It is difficult to interpret the results of antiemetic studies because the severity of postoperative vomiting and the response to therapeutic agents can be influenced by many variables in addition to the antiemetic drug being studied.

Differences in outcome with the same drugs may be related to the heterogeneity of the patient population studied. Even in what appears to be a homogenous population of patients undergoing the same surgical procedure with an identical anesthetic technique, the severity of emesis varies.<sup>6</sup> Most reliable results are obtained from double-blind, placebo-controlled, comparative studies involving two or more dosages of the study drug. Furthermore, the sample size should be large enough to detect small differences and permit an even distribution of confounding factors that affect emesis among the study groups.

As described above, the vomiting center sends motor output from the dorsal nucleus of the vagus and nucleus ambiguus to initiate the act of vomiting. Although this output is considered the final common pathway of the emetic response, there is no single drug that can block the pathway and thus serve as a universally effective antiemetic agent. The vomiting center receives separate input from different types of receptors (table 7). Antagonism of any one signal may alleviate emesis associated with the stimulation of that receptor. However, no currently available drug will antagonize all receptor sites involved in the emetic response.

Four major neurotransmitter systems appear to play important roles in mediating the emetic response: dopaminergic, histaminic (H<sub>1</sub>), cholinergic muscarinic, and 5-HT<sub>3</sub>. As there are four different types of receptors, there are at least four sites of action of the antiemetic drugs (table 7).<sup>31</sup> Antiemetic agents may have actions at more than one receptor, but they tend to have a more prominent action at one or two receptors. Hence, a combination of drugs will probably have greater antiemetic action than

TABLE 7. Receptor Site Affinity of Antiemetic Drugs (modified from Peroutka *et al.*<sup>31</sup> and Hamik *et al.*<sup>252</sup>)

Pharmacologic Group (drug)	Dopamin (D <sub>2</sub> )	Muscarinic Cholinergic	Histamine	Serotonin
Phenothiazines				
Fluphenazine	++++	+	++	—
Chlorpromazine	++++	++	++++	+
Prochlorperazine	++++			
Butyrophenones				
Droperidol	++++	—	+	+
Haloperidol	++++	—	+	—
Domperidone	++++			
Antihistaminics				
Diphenhydramine	+	++	++++	—
Promethazine	++	++	++++	—
Anticholinergic: scopolamine	+	++++	+	—
Benzamides:				
Metoclopramide	+++	—	+	++
Antiserotonin				
Ondansetron	—	—	—	++++
BRL 43694 (Granisetron)	—	—	—	++++
Zacopride	—	—	—	++++
RG 12915	—	—	—	++++
Tricyclic antidepressants				
Amitriptyline	+++	+++	++++	—
Nortriptyline	+++	++	+++	—

The number of positive (+) signs indicates degree of activity at receptor. The negative (—) sign indicates no activity.

a single drug. Finally, sedation itself may also play a role in preventing vomiting.

### 1. Phenothiazines

These compounds have an aliphatic or heterocyclic ring attached to position 10 of a tricyclic nucleus. Phenothiazines with a piperazine or piperidine ring are more potent and less sedating antiemetics than phenothiazines with an aliphatic chain.<sup>160</sup> The antiemetic actions of phenothiazines have been attributed to their ability to block receptors in the CTZ, specifically the dopaminergic receptors.<sup>161</sup> Chlorpromazine and promethazine have been used for years in the prevention and treatment of postoperative emesis, particularly if opioids have been administered. However, phenothiazines can produce significant sedation and lethargy in patients recovering from a general anesthetic, thereby delaying discharge.<sup>4,7,162,163</sup> Although prochlorperazine and perphenazine are effective therapeutic agents in the management of postoperative emesis when morphine or meperidine have been administered, they have shorter durations of action than the commonly used opioid analgesics, and repeated dosing may be required.<sup>164</sup> In addition, these phenothiazines are associated with a relatively high incidence of extrapyramidal side effects, ranging from restlessness to oculogyric crisis. Promethazine and benztropine are effective in treating these side effects.<sup>165</sup> More recently, dixyrazine, a phenothiazine with less sedative action, has been used successfully as an antiemetic in children undergoing strabismus surgery.<sup>44</sup>

### 2. Butyrophenones

The neuroleptic drugs haloperidol and droperidol are major tranquilizing drugs that possess significant antiemetic activity as a result of their antagonistic properties at the dopamine receptor.<sup>162</sup> Anesthesiologists have greater experience with droperidol than haloperidol in the management of postoperative nausea and vomiting.<sup>162,166-181</sup> Higher doses of droperidol (2.5-5 mg in adults or 50-75  $\mu\text{g} \cdot \text{kg}^{-1}$  in children) are associated with significant drowsiness and can delay discharge. In addition, routine use of droperidol is not recommended for patients undergoing outpatient surgery, as it has extrapyramidal side effects and can cause restlessness and anxiety following discharge.<sup>170-172</sup> Lower doses of droperidol (10-20  $\mu\text{g} \cdot \text{kg}^{-1}$ ) have been used successfully in procedures associated with a moderately high incidence of emesis (*e.g.*, laparoscopy) but have limited efficacy for the more emetic procedures (*e.g.*, strabismus).<sup>171,172,176,179</sup> In children undergoing strabismus surgery, droperidol (50-75  $\mu\text{g} \cdot \text{kg}^{-1}$ ) is a partially effective prophylactic antiemetic, whereas lidocaine probably is not.<sup>44,177-181</sup> Intravenous droperidol 75  $\mu\text{g} \cdot \text{kg}^{-1}$  may be more effective if it is given before eye muscle manipulation.<sup>180</sup> In the pediatric sur-

gical population undergoing lower doses of droperidol (<50  $\mu\text{g} \cdot \text{kg}^{-1}$ ) are not as effective.<sup>179,180</sup> When larger doses of droperidol are used, delayed emergence, drowsiness, and extrapyramidal signs may occur.<sup>44,177,179</sup>

Domperidone, a benzimidazole that is structurally similar to droperidol, was alleged to be an effective antiemetic with fewer central nervous system side effects than droperidol.<sup>181-186</sup> Domperidone acts by increasing the motility of the upper gastrointestinal tract and has a direct (blocking) effect on the CTZ. It does not readily cross the blood-brain barrier and may be associated with fewer dystonic side effects than metoclopramide. The antiemetic effects of domperidone appear to be highly dependent on the route and timing of its administration.<sup>183</sup> Intravenous domperidone 5 or 10 mg is no more effective than a placebo if given in the preoperative or immediate post-induction period.<sup>169</sup> However, these doses are effective in the treatment of postoperative emesis when administered in the recovery room.<sup>169,181-186</sup>

### 3. Antihistaminics

Dimenhydrinate, hydroxyzine, cyclizine, and diphenhydramine are antihistaminics that act on the vomiting center and the vestibular pathways. These compounds are particularly useful in the prophylaxis and therapy of motion sickness and in the control of emesis following middle ear surgery. In contrast, the phenothiazine class of dopamine ( $D_2$ )-receptor antagonists are usually ineffective in the management of motion sickness. The sedative and antiemetic actions of the piperazine-type antihistaminic compounds, such as hydroxyzine and cyclizine, have made these drugs useful supplements to opioids for premedication. In addition, cyclizine is associated with a lower incidence of side effects than are the phenothiazines and may be more effective in the treatment of postoperative vomiting.<sup>4,7,42,51</sup>

Bhargava *et al.* reported that the emetic effects of intracerebroventricular administration of histamine were effectively blocked by ablation of the area postrema and by pretreatment with specific histaminic ( $H_1$  and  $H_2$ ) antagonists.<sup>184</sup> However, burimamide, a specific  $H_2$  antagonist, was ineffective in controlling emesis caused by apomorphine or copper sulfate. In addition, promethazine, a potent therapeutic and prophylactic agent for the management of motion sickness, is a phenothiazine with both antihistaminic and cholinergic blocking activity.<sup>188,189</sup> Therefore, it is not known if the antiemetic effects of these drugs are secondary to blockade of specific histamine receptors in the central nervous system or are secondary to actions at other receptor sites.

### 4. Anticholinergics

It has been suggested that different cholinergic (muscarinic) receptor sites are present in the cerebral cortex

and the pons and that compounds with specific activity at these receptors could form the basis for effective antiemetic drugs.<sup>190</sup> The addition of anticholinergic drugs such as atropine or scopolamine (hyoscine) to an opioid compound for premedication decreases emesis.<sup>46,189-191</sup> Transdermal scopolamine is effective in controlling motion sickness and significantly decreases the incidence of severe nausea and vomiting after outpatient laparoscopy and after epidural morphine administration.<sup>192-195</sup> However, scopolamine can produce undesirable side effects such as dry mouth, sedation, visual disturbances, memory dysfunction, dysphoria, and occasionally confusion, disorientation, and hallucinations.<sup>192-195</sup> Furthermore, there are conflicting reports about the efficacy of transdermal scopolamine in preventing emesis in children undergoing strabismus surgery. Horimoto and Naide<sup>196</sup> found the transdermal route of administration of scopolamine to be effective in decreasing emesis, whereas Gibbons *et al.*<sup>197</sup> found no difference in emesis rates between children receiving scopolamine and those receiving a placebo patch.

### 5. Benzamides

Metoclopramide is a benzamide with both central and peripheral antiemetic actions. In addition to its ability to block dopaminergic receptors at the CTZ, metoclopramide increases lower esophageal sphincter tone and enhances gastric and small bowel motility, thereby preventing the delayed gastric emptying produced by the opioid analgesics.<sup>181,197-213</sup> Although it is not effective in controlling motion sickness associated with linear or angular acceleration, metoclopramide also has some peripheral cholinergic actions.<sup>198-201</sup>

High doses of metoclopramide (1–2 mg · kg<sup>-1</sup>) are effective in managing chemotherapy-induced emesis.<sup>198-200</sup> More conventional antiemetic dosages (0.1–0.2 mg · kg<sup>-1</sup>) have been used in the prophylaxis and treatment of postoperative emesis in adults and children because these doses are not associated with significant sedative activity.<sup>168,175,176,181,201-209</sup> However, the results of comparative studies involving metoclopramide are not entirely consistent. Factors contributing to the variable results include differing routes of administration; time intervals between the administration of metoclopramide and induction and recovery from anesthesia; types of surgical procedures; and the anesthetic drugs and techniques used during the operation. Whereas Cohen *et al.*<sup>204</sup> found no difference in the incidence of emesis between metoclopramide and placebo-treated patients when given immediately prior to the induction of anesthesia, Cooke *et al.*<sup>186</sup> demonstrated that metoclopramide (and domperidone) were superior

to placebo if given at the time of induction. However, metoclopramide-treated patients in the study by Cooke *et al.* had shorter recovery times compared to placebo and droperidol groups.<sup>186</sup> Metoclopramide appears to be an effective antiemetic in patients receiving opioids analgesics as preanesthetic medication, during surgery or in the immediate postoperative period.<sup>198-200</sup> The higher overall incidence of vomiting in patients receiving opioids increases the likelihood of demonstrating a statistically significant difference between the metoclopramide and placebo treatment groups.

Metoclopramide has a short half-life and should be administered immediately before or just after the end of surgery to have a reliable antiemetic effect in the early postoperative period.<sup>209</sup> This may explain the variable effectiveness of metoclopramide when it is administered prior to the start of the surgical procedure.<sup>191</sup> Conflicting results also have been obtained in a number of single-dose studies in which the antiemetic effects of metoclopramide and droperidol were compared. For example, Korttila *et al.* found no difference in emesis in patients receiving intravenous metoclopramide or placebo, whereas droperidol was an effective antiemetic.<sup>169</sup> However, Diamond *et al.* found oral metoclopramide to be an effective antiemetic compared to placebo.<sup>208</sup> These conflicting results may also be related to the decreased effectiveness of metoclopramide in women compared to men.<sup>206,208</sup>

When metoclopramide is used in the large doses required to prevent emesis during and after chemotherapy, it is associated with a high incidence of dystonic reactions, particularly in children.<sup>210,211</sup> Even in the usual perioperative dose of 0.1–0.2 mg · kg<sup>-1</sup>, children are more prone to develop extrapyramidal side effects from metoclopramide than are adults.<sup>212</sup> However, patients receiving the lower doses of metoclopramide (10–20 mg for adults, 0.1–0.2 mg · kg<sup>-1</sup> for children) are less sedated and have a decreased incidence of extrapyramidal signs than those receiving droperidol.<sup>176,181,202</sup>

Other substituted benzamides which have been evaluated as antiemetics include trimethobenzamide, cisapride, alizapride, domperidone, clebopride, and levosulpiride. Trimethobenzamide has less antiemetic action than metoclopramide but can be administered rectally in children.<sup>213</sup> Cisapride is a benzamide with a strong prokinetic effect on the gastrointestinal system secondary to acetylcholine release at the myenteric plexus. This cholinergic action results in increased lower esophageal sphincter pressure and motility in the entire gastrointestinal tract (including the large bowel).<sup>214,215</sup> Cisapride has a greater ability than metoclopramide to reverse morphine-induced gastric stasis and is not associated with extrapyramidal side effects, since it has no activity at the central dopaminergic receptors. However, cisapride does not block the decrease in lower esophageal tone following the an-

<sup>197</sup> Gibbons PA, Nicolson SC, Betts EK, Rosenberry KR, Jobs DR: Scopolamine does not prevent postoperative emesis after pediatric eye surgery (abstract). *ANESTHESIOLOGY* 61:A435, 1984.

tagonism of neuromuscular blockade by neostigmine, and hence, its role in anesthesia remains unclear.<sup>214,215</sup>

Alizapride is an investigational substituted benzamide with a greater potency than metoclopramide and fewer side effects.<sup>216,217</sup> Compared to a placebo, alizapride is an effective antiemetic for postoperative emesis.<sup>\*\*\*</sup> However, in chemotherapy patients it does not appear to be as effective as high-dose metoclopramide.<sup>218,219</sup> Clebopride is a benzamide with more potent antiemetic activity than metoclopramide.<sup>220,221</sup> It also increases gastrointestinal peristalsis, and at doses that do not result in extrapyramidal symptoms or hyperprolactinemia, it has a mild tranquilizing effect.<sup>220,221</sup> Levosulpride is another investigational benzamide compound with antiemetic action, but it is less potent than metoclopramide.<sup>222</sup>

### 6. Serotonin Antagonists

While studying the antiemetic activity of structural analogues of metoclopramide, investigators discovered that some of these compounds did not have an antagonistic effect at the D<sub>2</sub> receptor site but still possessed significant antiemetic activity.<sup>222-224</sup> Further studies demonstrated that these drugs block the 5-HT<sub>3</sub> receptor. Subtypes of these receptors were identified, and the antiemetic action has subsequently been shown to be secondary to blockade of the 5-HT<sub>3</sub> receptor. Ondansetron (GR 38032F) is the prototype of this new class of drugs, which also includes granisetron, ICS 205-930, MDL 72222, RG-12915, batanopride, and zacopride.<sup>224-236</sup>

Early studies on these compounds were conducted in patients receiving cisplatin and other emetic chemotherapeutic agents. Ondansetron was discovered to be more effective than metoclopramide and droperidol in controlling nausea and vomiting in this patient population.<sup>225-230</sup> The 5-HT<sub>3</sub> receptor antagonists lacked the sedative and dysphoric side effects of droperidol and the extrapyramidal side effects associated with high-dose metoclopramide. Mild sedation, dizziness, headache, and transient elevations of serum alanine aminotransferase have been reported with ondansetron therapy. The other antiserotonin drug that is currently undergoing phase II and phase III clinical trials in the United States is RG 12915 (Rhône-Poulenc-Rorer). Preliminary studies suggest that it may be a more potent antiemetic than ondansetron.<sup>†††</sup> To date, comparative postoperative studies involving the 5-HT<sub>3</sub> antagonists and other commonly used antiemetic drugs have not been performed.

While representing a major advance in the manage-

ment of chemotherapy-induced emesis, the role of the 5-HT<sub>3</sub> antagonists in anesthesia is yet to be defined.<sup>225-230</sup> Preliminary studies with the 5-HT<sub>3</sub> antagonists suggest that these compounds may be effective in the treatment and prevention of surgically related emetic sequelae.<sup>236-240</sup> Bodner *et al.*,<sup>237</sup> Rosenblum *et al.*,<sup>238</sup> and Larijani *et al.*<sup>239</sup> found intravenous ondansetron 8 mg was a more effective antiemetic than was placebo in women undergoing gynecologic procedures. Lessin *et al.* demonstrated that ondansetron lacked the dysphoric and extrapyramidal side effects commonly seen with other antiemetic drugs.<sup>240</sup> Wetchler *et al.* reported that ondansetron was effective when given as a prophylactic antiemetic in the outpatient setting.<sup>241</sup>

### 7. Other Drugs

Ephedrine, an indirectly acting sympathomimetic drug, can prevent motion sickness.<sup>167</sup> It is also effective in treating emesis that occurs secondary to the hypotension associated with spinal anesthesia. Anecdotal reports regarding its effectiveness in managing patients who developed emesis with postural changes led Rothenberg *et al.* to compare the antiemetic effects of ephedrine and droperidol after general anesthesia.<sup>242</sup> In a double-blind placebo-controlled study, ephedrine was found to be similar to droperidol with respect to antiemetic activity, without its centrally mediated side effects.<sup>242</sup> In a placebo-controlled study, Poler and White reported that emetic sequelae in the postanesthesia recovery unit were slightly decreased when intramuscular ephedrine 25 mg was administered intraoperatively to women undergoing laparoscopic procedures.<sup>243</sup> However, the ephedrine-treated patients received less fluid in the early recovery period and actually had a higher incidence of vomiting after discharge.

Interest in the antiemetic potential of cannabinoids has decreased because the use of these agents has been associated with a high incidence of side effects (*e.g.* vertigo, dizziness, ataxia, postural hypotension, vision disturbances, and confusion).<sup>244-247</sup> However, cannabinoids have been used with some success in the management of chemotherapy-induced emesis refractory to conventional treatment modalities.<sup>†††</sup> Tetrahydrocannabinol does not appear to have a role in anesthetic-induced emesis.<sup>244-247</sup> However, sublingually administered tetrahydrocannabinol (dronabinol) can be effective in treating intractable postoperative nausea.<sup>§§§</sup>

\*\*\* Booij LH, Rachmat S, Bulder ER: Alizapride in prevention of postoperative nausea and vomiting. *Netherlands Journal of Surgery* 40:6-9, 1988.

††† White PF: Unpublished observations, 1991.

††† Venner P, Bruerra E, Drebit D, Shankowsky H: Intensive treatment scheduling of nabilone plus dexamethasone (DM) vs. metoclopramide plus DM in cisplatin-induced emesis (abstract). *Proceedings of the Annual Meeting of American Society of Clinical Oncology* 5: 253 (abstract 988), 1986.

§§§ Taylor E: Personal communication, 1991.

### 8. Combination Antiemetic Therapy

Because antiemetic drugs have differing sites of action, better results can be obtained by using a multi-drug approach. However, if a combination of drugs with a similar site of action is used, the incidence of side effects may be increased. The role of combination therapy has been examined in chemotherapy-induced emesis.<sup>245,248-251</sup> For example, the side effects of cannabinoids are reduced by the addition of a phenothiazine.<sup>247</sup> In another study, the combination of dexamethasone and metoclopramide was superior to nabilone plus dexamethasone and to high-dose metoclopramide alone.<sup>251</sup> The addition of a phenothiazine and/or a benzodiazepine to the metoclopramide-corticosteroid combination appeared to enhance its effectiveness.<sup>248</sup> A combination of metoclopramide, thiethylperazine, diphenhydramine, dexamethasone, and diazepam prevented nausea and vomiting in 45% of patients undergoing highly emetic chemotherapy.<sup>¶¶¶</sup> There are no data available on the effects of combining ondansetron (or other 5-HT<sub>3</sub> blocking agents) with metoclopramide, steroids, phenothiazines, or benzodiazepines.

There are few, if any, data regarding combination antiemetic prophylaxis or therapy for postoperative emesis. Drug combinations have been avoided in postsurgical patients because of concerns about additive central nervous system toxicity (*e.g.*, delayed emergence, drowsiness, and extrapyramidal reactions). However, the combination of low-dose droperidol (0.5–1.0 mg intravenously) with metoclopramide (10–20 mg intravenously) appeared to be more effective than droperidol alone for outpatient gynecologic procedures.<sup>\*\*\*\*</sup> Combinations of metoclopramide and a phenothiazine or 5-HT<sub>3</sub> antagonist may prove useful for patients at increased risk of postoperative emesis (*e.g.*, women undergoing laparoscopic procedures during their menses). Further studies evaluating the efficacy of drug combinations during the postoperative period are clearly needed.

### IV.B. Nonpharmacologic Approaches: Acupuncture and Acupressure

Nonpharmacologic techniques (*e.g.*, acupuncture and acupressure) have also been evaluated for the prevention of postoperative emesis with varying degrees of success.<sup>252-256</sup> Dundee *et al.* studied women undergoing mi-

nor gynecologic procedures after receiving an opioid analgesic for preanesthetic medication.<sup>252</sup> These investigators found that manual stimulation of the P-6 acupuncture point (Neiguan) by a needle resulted in a significant reduction in postoperative emesis. Similar results were obtained when low-frequency electrical stimulation of the P-6 point was performed. It is interesting that higher-frequency electrical stimulation had no antiemetic activity.<sup>253</sup> The efficacy of P-6 acupuncture as an antiemetic in patients receiving chemotherapy is limited to approximately 6 h.<sup>254</sup> Application of pressure every 2 h to this acupuncture point was reported to produce an antiemetic action for up to 24 h.<sup>254</sup> A commercially available elastic wrist band with a plastic stud (Sea Band<sup>®</sup>) was alleged to be an effective method of applying pressure to the P-6 point and may possess some antiemetic activity.<sup>254,255</sup> However, Lewis *et al.* was unable to demonstrate a significant antiemetic effect using acupressure in children undergoing strabismus surgery.<sup>256</sup> The future role of acupuncture and acupressure in the prevention of postoperative vomiting is unclear.

### V. Summary

In a recent editorial, Kapur described perioperative nausea and vomiting as “the big ‘little problem’ following ambulatory surgery.”<sup>257</sup> Although the actual morbidity associated with nausea is relatively low in health outpatients, it should not be considered an unavoidable part of the perioperative experience. The availability of an emesis basin for every patient in the postanesthesia recovery unit is a reflection of the limited success with the available therapeutic techniques.<sup>257</sup> There had been little change in the incidence of postoperative emesis since the introduction of halothane into clinical practice in 1956. However, newer anesthetic drugs (*e.g.* propofol) appear to have contributed to a recent decline in the incidence of emesis.

Factors associated with an increased risk of postoperative emesis include age, gender (menses), obesity, previous history of motion sickness or postoperative vomiting, anxiety, gastroparesis, and type and duration of the surgical procedure (*e.g.*, laparoscopy, strabismus, middle ear procedures). Anesthesiologists have little, if any, control over these surgical factors. However, they do have control over many other factors that influence postoperative emesis (*e.g.*, preanesthetic medication, anesthetic drugs and techniques, and postoperative pain management).

Although routine antiemetic prophylaxis is clearly unjustified, patients at high risk for postoperative emesis should receive special considerations with respect to the prophylactic use of antiemetic drugs. Minimally effective doses of antiemetic drugs can be administered to reduce the incidence of sedation and other deleterious side effects. Potent nonopioid analgesics (*e.g.*, ketorolac) can be

¶¶¶ Plezia PM, Alberts DS, Kessler JF, Berens PL, Chase JL, Roe DJ: Randomized crossover comparison of high dose intravenous metoclopramide versus a five-drug antiemetic regimen. *Journal of Pain Symptom Management* 5:101–108, 1990.

\*\*\*\* Doze VA, Shafer A, White PF: Nausea and vomiting after outpatient anesthesia: Effectiveness of droperidol alone and in combination with metoclopramide (abstract). *Anesthesia and Analgesia* 66: S41, 1987.



used to control pain while avoiding some of the opioid-related side effects. Gentle handling in the immediate postoperative period is also essential. If emesis does occur, aggressive intravenous hydration and pain management are important components of the therapeutic regimen, along with antiemetic drugs. If one antiemetic does not appear to be effective, another drug with a different site of action should be considered. With the availability of new antiserotonin drugs, the incidence of recurrent (intractable) emesis could be further decreased.<sup>258</sup>

Research into the mechanisms of this common postoperative complication may help in improving the management of emetic sequelae in the future. As suggested in a recent editorial,<sup>257</sup> improvement in antiemetic therapy could have a major impact for surgical patients, particularly after ambulatory surgery. Patients as well as those involved in their postoperative care look forward to a time when the routine offering of an emesis basin after surgery becomes a historical practice.

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