Chapter XYZ

Prophylaxis for Aspiration Pneumonitis

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I. Introduction

The American Journal of Obstetrics and Gynecology published a landmark article in the July-December 1946 issue entitled: "The aspiration of stomach contents into the lungs during obstetric anesthesia" by Curtis L. Mendelson, M.D.[1] Dr. Mendelson meticulously observed the causes for the morbidity and mortality experienced by some of his obstetric patients who aspirated gastric contents. He performed careful animal studies, whose outcomes formed the basis for our present day anesthesia theory and practice for the prophylaxis used to prevent Aspiration Pneumonitis (AP).

A. Definitions

Aspirate is derived from the Latin words, *a spirare*, meaning to breathe upon. Aspiration is the inhalation of a bolus of a solid and/or a liquid bolus into the airway.[2,3]

Aspiration pneumonia is an infectious process caused by the aspiration of secretions containing pathogenic oropharyngeal bacteria into the lungs.[4,5]

Aspiration pneumonitis is a direct chemical injury to lung tissues caused by the aspiration of highly acidic gastric contents into the lungs.[4,5] Pulmonary aspiration of gastric contents is believed to occur in 1:3216 anesthetics.[6]

Mendelson's Syndrome describes aspiration pneumonitis (AP): a severe respiratory condition caused by the inhalation of acidic gastric contents into the lungs.[2]

Reflux is from the Latin *refluere*, which means to flow back.[2] Oral and gastric contents normally progress in a one-way direction from the mouth into the stomach,

which then empties into the duodenum. Patients with depressed protective reflexes or who have abnormal anatomic structures can reflux solids or liquids into the esophagus, which can then possibly be aspirated into the lungs.

Stomach is from the Greek word *stomakhos*, meaning gullet. It is the organ that serves as a food reservoir, and is the first major site for the beginning of the digestion of food. (See Figure 1a for the anatomy of the stomach and 1b for the histology of the stomach.). Gastric secretions begin the process of digestion, which is the breakdown of foods and liquids into their basic components for absorption into the bloodstream to support the organs and tissues of the body.

See table 1 for a complete list of the contents and functions of gastric secretions.

Figure 1a The Anatomy of the Stomach[4,7] Anatomy of the Stomach Cancer.gov drawing.

Figure 1b The Histology of the Stomach.[8] Guyton page 796 figure 64-5.

Table 1 The Contents and Functions of Gastric Secretions[2,8,9]

Hydrochloric acid – a potent acid with a pH of 1-2, used for the digestion of food. The parietal cells of the stomach secrete hydrochloric acid when stimulated by cranial nerve X: the vagus nerve.

Gastrin – a hormone whose secretion is triggered by protein-rich foods, which stimulates the release of histamine.

Histamine – an endogenous substance that is synthesized by the degradation of the amino acid histidine, which stimulates gastric hydrochloric acid secretion.

Intrinsic factor – a substance used to absorb Vitamin B_{12} in the ileum.

Mucus – a substance that lubricates the bolus of food, and protects the stomach wall.

Pepsin – a proteolytic enzyme used for the digestion of proteins.

Pepsinogen – a substance which coverts to pepsin upon contact with hydrochloric acid.

B. The physiology of swallowing, coughing, gagging, and laryngospasm as normal protective mechanisms.

1. Swallowing -Swallowing (deglutition) is the complex coordinated effort of the mouth, tongue, pharynx, and esophagus. The pharynx must function in a dual role, first as a passageway for inspiratory and expiratory gases (respiration) of the lungs, and second, as a passageway for the delivery of solids and liquids down the esophagus into the stomach (swallowing). Conduction of respiratory gases is the dominant function of the nose, mouth and pharynx each day. Swallowing requires only a few seconds of oropharyngeal time. Swallowing involves both voluntary and involuntary stages, with built-in protective mechanisms to prevent compromise or interference to respiration.[8] (see Table 2)

Table 2 The Voluntary and Involuntary Stages of Swallowing, Stomach Physiology, and Normal Protective Mechanisms[8]

1. Voluntary initiation of swallowing.

2. Involuntary upward pull of the soft palate to close the posterior nares from the reflux of swallowed oral contents.

3. Involuntary funneling of oral contents into the trachea by the palatopharyngeal folds.

4. Involuntary closure of the trachea by the tight approximation of the vocal cords and the rigidity of the epiglottis cause by muscular contraction.

5. Involuntary peristaltic propulsion of the oral contents from the posterior pharynx past the relaxed upper esophageal sphincter (the upper 3-4 centimeters of the esophagus).

6. Involuntary closure of the upper esophageal sphincter for protection against reflux.

7. Involuntary peristaltic contracture of the esophagus, propelling the oral contents past the relaxed gastroesophageal sphincter into a receptive and relaxed stomach. The gastroesophageal sphincter is normally held tightly closed, and requires 30 torr of pressure to open.

Stomach contents are swept through the stomach from the cardia to the pyloris of by peristaltic waves, at a rate of three to four waves per minute. These powerful peristaltic waves serve to stir and mix the gastric contents. 1% to 3% of the gastric content (chyme) enters the duodenum per minute. The higher the gastric content, the higher the volume of chyme entry into the duodenum.[8,10]

The duodenum possesses a powerful inhibitory reflex to delay gastric emptying, called the enterogastric inhibitory nervous reflex.[8,10] This reflex can be strongly activated within 30 seconds, and can thus increase the probability of stomach contents being regurgitated and then aspirated. (Table 3a lists some factors that can trigger the enterogastric inhibitory reflex.)

Digestion and metabolism of most of the medications administered in anesthesia, and those used for the treatment of AP are performed by the Cytochrome P450 system of enzymes. There are 20 known pharmacogenetic cytochrome enzyme subtypes found in the liver and in the intestines.[11,12] Nearly half of the medications used in anesthesia are

metabolized by one specific pharmacogenetic enzyme variant: CPY 3A4. Interestingly, components of grapefruit juice and grapefruit pulp can interfere with CYP3A4 and other CYP enzyme variants, resulting in can delay or prevent metabolism of drugs metabolized by these enzymes. Thus higher blood levels of these medications occur, causing potential negative effects due to high levels of bioavailability.[13,14]

Table 3a <u>Some Factors that can Trigger the Enterogastric Inhibitory Reflex[8,10]</u>

a. The degree of distension of the duodenum

b. Irritation of the duodenal mucosa – can be due to low pH chyme, hypoosmolar or hyperosmolar chyme, the breakdown products of proteins, and to a lesser extent fats.

2. The protective mechanism of coughing.

Coughing begins with stimulation of the very sensitive trachea and bronchi by foreign matter. The larynx and the carina are also very sensitive to stimulation. Corrosive chemicals can stimulate the cough reflex as far as the terminal bronchi and the alveoli. Stimulation by foreign matter is conducted along the vagus nerve to the medulla of the brain.[8] The process of coughing is outlined in table 3b.

Table 3b <u>The process of coughing</u>[8]

1. Up to 2.5 liters of air is rapidly inspired.

2. The vocal cords tightly close and the epiglottis tightens, trapping the rapidly inspired air.

3. The abdominal muscles and the internal intercostals muscles (which cause voluntary expiration) contract forcefully.

4. Pressures in the lungs can rise ≥ 100 torr.

5. The vocal cords and epiglottis open quickly so that air explodes outward.

6. The resulting negative pressure created in the lungs causes the non-cartilaginous portions of the trachea and bronchi to form slits, propelling the foreign substance out of the lungs.

(The expiration reflex is forceful expiration through the open glottis without the initial inspiration found with the coughing reflex.[15])

3. The pharyngeal protective reflex of gagging.

  The pharyngeal reflex (gagging) begins with a noxious stimulus to the soft palate or the posterior pharynx through the afferent conduction of the Glossopharyngeal nerve (cranial nerve IX). The noxious stimulus is conducted to the nucleus solitarius of the medulla and part of the lower pons. Efferent stimulation then occurs through the nucleus ambiguus of the medulla to the Vagus nerve (cranial nerve X). A noxious thought can also stimulate the pharyngeal reflex. The reflex elicits abdominal walls tightening, closure of the glottis, symmetric lifting of the soft palate, and tongue protrusion which causes the noxious substance to be repelled.[2,8] The pharyngeal reflex can proceed to the process of vomiting.

  Interestingly, stimulation of 5HT-3 serotonin receptors in the brainstem can trigger both the pharyngeal reflex and vomiting.[16]

4. *The protective mechanism of laryngospasm.*[15]

Laryngospasm is a forceful closure of the glottis due to contraction of the laryngeal muscles caused by stimulation from a foreign substance (e.g. saliva, excised tissue, foreign body, excessive positive pressure, certain potent inhaled anesthetics).[11,15] This powerful reflex is used to prevent entry of the foreign substance into the airway, but can quickly prevent airway exchange through the glottis, demanding prompt assessment of the laryngospasm along with appropriate treatment.[12]

C. The mechanisms of aspiration pneumonitis

Many factors can compromise the body's protection against the aspiration of gastric contents into the lungs. Three broad categories of disorder can lead to airway protective mechanism failure and increase the possibility of aspiration pneumonitis:

1. *Depression of protective reflexes.*

2. *Alteration or deviation of normal anatomic structures and functions.*

3. *Iatrogenic disorders.*

Table 4 presents a comprehensive list of factors that can affect our natural protective mechanisms of gastric contents.

Table 4 Factors that can Affect Normal Protective Mechanisms Against Aspiration of Gastric Contents[5,6,10,11,12,17,18,19,20,21,22,23,24,25,26,27,28]

Depression of protective reflexes

Alcohol

Antipsychotics

Cardiac arrest

Cerebrovascular accident

Depression of consciousness

Depression of gag, coughing, swallowing reflexes

Drug overdose

Extremes of age

Head injury

Neurological diseases

Neuromuscularly impaired reflexes

Opioids

Sedatives

Seizures

Severe hypotension

Stress

Trauma

Alteration or deviation of normal anatomic structures and functions

Achalasia (spasm of the lower portion of the esophagus)

Ascites

Cardiac arrest

Delayed Gastric Emptying

Diabetes mellitus

Difficult airway

Esophageal motility disorders

Foreign body aspiration

Full stomach (gastrodistension)

Dysphagia

Esophageal strictures

Gastroesophageal reflux disease (GERD)

Gastrointestinal obstruction

Gastroparesis (diabetes, medications, infection, uremia)

High gastric pressure

Hiatal hernia

Hyperchlorhydria

Hypotension

Laryngeal incompetency

Reduced lower esophageal sphincter tone

Nausea

Obesity (can be associated with hiatal hernia, and GERD)

Obstetrics[*]

Peptic ulcer disease

Scleroderma

Vomiting

Presence of a Zenker's Diverticulum

Iatrogenic disorders

Anesthetic medications

After-hours surgery

Difficult airway management

Improperly applied cricoid pressure

Inadequate anesthesia

Emergency surgery

Outpatient surgery

Patient positioning (especially lithotomy position)

Poorly compliant patient

Presence of a nasogastric tube

Placement of artificial oral airways

Residual neuromuscular relaxation

Trauma surgery

* Obstetrical patients are always considered to be a full stomach condition, regardless of their nothing-by-mouth status, and should be treated as such prior to any anesthetic therapy. During pregnancy the pylorus is displaced cephalad by the gravid uterus, which decreases gastric emptying, progesterone decreases gastric motility. Also, gastrin is secreted by the placenta.[11,29]

D. The pathophysiology of aspiration pneumonitis.

Aspiration of highly acidic liquid gastric contents with a volume >0.3ml/kg (usually >25ml of gastric volume), and an aspirate pH $\leq$ 2.5, triggers an instant severe inflammatory reaction with acutely damaging histological effects to surfactant-producing cells and the pulmonary capillary endothelium. (Note: a ph > 2.5 elicits a similar response as if distilled water was administered; a ph $\leq$ 1.5 produces maximal pulmonary damage)[5] Hydrochloric acid from the stomach stimulates bronchiolar spasm and tachypnea.

Hydrochloric acid causes a first-phase severe chemical burn of the tracheobronchial tree, and the capillary endothelium. Gastric solids may also be aspirated, causing tracheal or bronchial occlusion.[11,23,25,28,30,31] Liquid and solid aspirate will immediately obstruct the airways, impairing gas exchange and the ability to institute immediate direct treatments to the airway tissues.[25]

Four to six hours after exposure, a second-phase inflammatory response occurs with the infiltration of neutrophils, inflammatory mediators, other inflammatory cells, adhesion molecules, and enzymes. Because of the low pH of the aspirate, bacteria are not present, and bacterial infection does not have a role in early AP.[23]

Severely damaged tissues produce a peribronchiolar exudate, which causes severe congestion. The patient will develop wheezes, a cough, become short of breath, and develop both cyanosis and pulmonary edema. Later, hypotension and hypoxemia will present with rapid progression to adult respiratory distress syndrome (ARDS), tracheal and bronchial infarction, followed by severe hypotension and death. [2,5,11,23,30,31]

Animal studies have shown that gastric volumes that are buffered, and are twice the critical volume of aspirate (>0.3ml/kg; usually >25ml of gastric volume) present less damage to the tracheobronchial tree and capillary endothelium.

E. Treatments for Aspiration Pneumonitis.

Immediate lavage of the tracheobronchial tree can be performed if an endotracheal tube is immediately placed. Inject a small volume (5 - 10ml) of sterile normal saline endotracheally. Large volumes of saline will only serve to push the aspirate

further into the lungs. Box 1 lists other early interventions to be considered for AP in an intubated patient.

Box 1 Early interventions for an intubated patient with Aspiration Pneumonitis[5,10,11,25,26,30,31]

Consider tilting the operating room table 30 degree Trendelenberg (head down) with a turn to right lateral decubitus position to allow for mechanical drainage out of the tracheobronchial tree and the mouth.

Promptly and carefully suction the oropharynx followed by the airway through the endotracheal tube.

Carefully and slowly continue to lavage the airway with 5-10ml of sterile normal saline.

Deliver an increased fraction of inspired oxygen (FIO$_2$).

Begin titrating positive end expiratory pressure (PEEP) as necessary to maintain oxygen saturation.

Auscultate breath sounds periodically for wheezing, ronchi, and rales.

Administer B$_2$ agonists such as albuterol to relieve bronchospasm.

Place an orogastric or nasogastric tube (Salem sump) carefully.

Measure the pH of any remaining gastric fluid.

Obtain an initial chest radiograph (The effects of AP may not be seen for 6-12 hours; early changes could be seen in the lower right lobes of the lung).

Perform a fiberoptic bronchoscopy if aspiration of liquid substance is suspected. Rigid bronchoscopy may be necessary for the removal of solid substances.

Provide comfort and emotional support when needed.

{The use of initial antibiotic therapy has not improved outcomes of AP}

[Intravenous corticosteroid use remains controversial, although some may consider the empirical use of methylprednisolone 30mg/kg I.V. or dexamethasone 1mg/kg I.V.]

Transfer to the intensive care unit with mechanical ventilator support as necessary.

II. Interventions for the Prevention of Aspiration Pneumonitis

The Nurse Anesthetist has many choices to preemptively assuage the morbid effects produced by the aspiration of acidic gastric contents. Table 5 outlines both physical methods used to prevent entry of acidic gastric contents into the respiratory tract, and current pharmaceutical methods used to mobilize gastric contents into the intestinal tract, neutralize gastric contents, or prevent emesis, to reduce chances for accidental entry of noxious substances into the respiratory tract. We will discuss the most current aspiration prophylaxis protocols in the following sections.

Careful attention must be paid to the diabetic patient. Diabetic patients experience microvascular blockage, tissue damage, along with autonomic neuropathy, which leads to decreased circulation and paralytic nerve damage to the stomach (gastroparesis).[2,8]

Table 5 Physical and Pharmaceutical Methods Used for the Prevention of Aspiration Pneumonitis.[5,6,11,24,33,34,35]

1. Physical Methods Used for the Prevention of Aspiration Pneumonitis

   A. Predicting risk factors for the aspiration of gastric contents

   B. Avoidance of General Anesthesia

   C. Proper Fasting

D. Cricoid Pressure (Sellick's Maneuver)

E. Preoperative placement of an orogastric or nasogastric tube

F. Use of a cuffed endotracheal tube

G. Use of an LMA Proseal^{TM} or LMA Supreme^{TM}

H. Preoperative prediction of the potential for nausea and vomiting

I. Extubation of the patient only when they are fully awake and fully able to protect their airway

2. Pharmaceutical Methods Used for the Prevention of Aspiration Pneumonitis

A. *Alkalizers (systemic)* – Citric acid, Sodium citrate, (Bicitra®, Oracit®)

B. *Antiemetics*

> *1. Anticholinergics* – Scopolamine (Transderm Scop®)
>
> *2. Butyrophenones* – Droperidol (Inapsine®)
>
> *3. Nonbarbiturate anesthetic induction drugs* – Propofol, Fospropofol disodium (Lusedra®)
>
> *4. P/neurokinin 1 (NK$_1$) receptor antagonists* – Aprepitant (Emend®)
>
> *5. Serotonin 5-HT$_3$ receptor blockers* – Ondansetron (Zofran®), Alosetron (Lotronex®), Palonosetron (Aloxi®), Dolasetron (Anzemet®), Granisetron (Kytril®)
>
> *6. Synthetic corticosteroids* – Dexamethasone

C. *Gastric motility prokinetic agents* –

> Metoclopramide (Reglan®), Cisapride (Propulsid®), Trimethobenzamide (Tigan®), Prochlorperazine (Compazine®)

D. Histamine (H₂) receptor antagonists –

Cimetidine (Tagamet[®]), Famotidine (Pepcid[®]), Nizatidine (Axid[®]),

Ranitidine (Zantac[®])

E. Proton pump (hydrogen ion) inhibitors –

Omeprazole (Prilosec[®]), Esomeprazole (Nexium[®]), Lansoprazole

(Prevacid[®]), Pantoprazole (Protonix[®]), Rabeprazole (AcipHex[®])

1. Physical Methods Used for the Prevention of Aspiration Pneumonitis

A. Predicting risk factors for aspiration of gastric contents – Table 4 presents a comprehensive list of factors which should alert the anesthetist to the possibility of aspiration pneumonitis in patients presenting with certain signs and symptoms.[6,24]

B. Avoidance of General Anesthesia – The morbid effects of inhaled general anesthetic agents, especially light planes of general anesthesia, combined with the use of potent opioids, can precipitate nausea and vomiting in patients.[10] The anesthetist can consider the using no anesthesia whatsoever; delaying anesthesia as long as safely possible; performing monitored anesthesia care; using local anesthesia, regional anesthesia, or combinations of these techniques when feasible.[6,28]

C. Fasting – General practice guidelines for fasting allow time for normal gastric emptying and normal transit time of chyme through the intestines. Guidelines do not guarantee gastric emptying or a positive outcome, nor serve as an absolute standard of care for the nurse anesthetist. Water administered 2 hours preoperatively promotes gastric emptying in patients with normal gastrointestinal function. It is found that gastric pH did not differ in groups that were administered water preoperatively from those that only fasted using available guidelines.[37]

The use of portable 2-dimensional ultrasound imaging is undergoing study to assess gastric volume. This non-invasive tool (which has found its way into other aspects of anesthetic care such as regional anesthesia) could provide preoperative visual evidence of gastric contents, thus adding another dimension to the prevention of AP.[37]

Consideration of both fasting guidelines and pharmaceuticals for the prevention of aspiration pneumonitis provide optimum patient safety.[6,37]

Table 6 describes of current fasting guidelines to reduce the risk of pulmonary aspiration in healthy children and adults undergoing elective procedures, and excludes the woman in labor.

Table 6. A Summary of Current Fasting Recommendations to Reduce the Risk of Pulmonary Aspiration for Healthy Children *and* Adults.[11,37] (Adapted from a report on fasting recommendations from the American Society of Anesthesiologists.)

Ingested Material	Minimum Fasting Period
Clear liquids[*]	2 hours
Breast Milk	4 hours
Infant formula	6 hours
Non-human milk[‡]	6 hours
Light meal[†]	6 hours

*Clear liquids are those that allow the clear passage of light through them. Examples are water, carbonated beverages, clear tea, and black coffee.

‡ Non-human milk is considered the same as solid food in regard to gastric clearance.

† A light meal compares to toast and clear liquids. A full meal should not be considered as this meal can require increased time until gastric emptying.

Children fasting for long periods can experience morbidity prior to non-emergent surgery. Fasting leads to intravascular volume depletion, resulting in a reflex tachycardia, and low blood pressure.

Insertion of intravenous catheters can be more difficult. The use of intraosseous (IO) venous access, serves as an equivalent to intravenous access in urgent/emergent situations. Potent inhaled anesthetic induction can cause a precipitous drop in blood pressure, decreasing perfusion pressures to the brain, and can precipitate vomiting.[20]

D. Cricoid pressure (Sellick's Maneuver) – In August of 1961, The Lancet published a landmark article by Dr. Brian Sellick entitled: Cricoid pressure to control regurgitation of stomach contents during induction of anaesthesia.[39] The simple maneuver he described consisted of temporarily occluding the upper end of the esophagus with backward pressure applied to the cricoid cartilage of the trachea against the bodies of the cervical vertebrae. Cricoid pressure serves two purposes: to control the regurgitation of gastric or esophageal contents, and to prevent inflation of the stomach prior to endotracheal intubation with a cuffed endotracheal tube.[11,39] Cricoid pressure is exerted by a second person applying pressure to the cricoid cartilage with the thumb and index finger. Initially apply the necessary pressure that an awake person can comfortably

tolerate; A greater amount of force is applied after induction of general anesthesia (Specifically a force of 30-40 Newtons after loss of consciousness [1 Newton of acceleration = 1kg meter/second ^{2}]; or about 3 to 4 kilograms (6.7 to 9 pounds) of force).[12,15]

Vigorous application of cricoid pressure to an awake patient, or to a patient not deeply induced prior to intubation, can precipitate pain, retching, and vomiting.[6,15] Cricoid pressure can precipitate tachycardia and hypertension during induction.[15] Manual ventilation can still occur during the application of cricoid pressure. Cricoid pressure is held until purchase of the airway has been accomplished, and the laryngoscopist designates release of the pressure.

E. Preoperative placement of a nasogastric tube (NGT) – The preoperative placement of an NGT allows the evacuation of gastric contents, provides an alternate conduit for the flow of gastric contents or regurgitation away from the airway, and does not interfere with the application of cricoid pressure. Certain conditions such as closed head injury; trauma; esophageal disease such as esophageal erosion or esophageal varices; and life-threatening emergency can preclude the safe placement of an NGT.[6,11,24]

F. Use of a cuffed endotracheal tube – A properly positioned and well-secured high-volume/low-pressure cuffed endotracheal tube is the gold standard for protection of the trachea from both liquid and solid debris. Small amounts of regurgitated material could still potentially leak around the longitudinal folds of the endotracheal cuff, and can be prevented by using water-soluble lubrication around the cuff before insertion.[15]

G. Use of an LMA Proseal^{TM} or LMA Supreme^{TM} – Two models of Laryngeal Mask Airways (LMA) possess a drain tube which will allow passage of a small bore

Salem Sump and allow suctioning of gastric contents with the LMA inserted, which greatly reduces the chances of aspiration.[40]

H. Preoperative prediction of the potential for nausea and vomiting – In 1999 Rhodes, et al presented a paper, which introduced an index to assess the likelihood of patients who could develop nausea, vomiting, and retching. Although this index is intended for use by oncology nurses and physicians, knowledge and awareness of its use by anesthesia providers, along with the other techniques and methods used in clinical anesthesia practice, will be discussed, will help to make anesthetic care more safe and effective for patients.[41]

Figure 2 presents the Rhodes Index of Nausea, Vomiting, and Retching (attempting to vomit without bringing anything up), which can be used as a preoperative assessment tool for patients undergoing anesthetic care.[41,42]

Figure 2 The Rhodes Index of Nausea, Vomiting, and Retching[41]

Patient Initials_____

Date_____

Day of Week_____

Time of Day_____

Directions: Please mark the box in each row that most clearly corresponds to your experience. Please make **one** mark on **each line**.

| 1. In the last 12 hours I threw up _____ times. | 7 or more | 5-6 | 3-4 | 1-2 | I did not throw up |

Question					
2. In the last 12 hours, from retching and dry heaves, I have felt____ distress.	no	mild	moderate	great	severe
3. In the last 12 hours, from vomiting or throwing up, I have felt____distress.	severe	great	moderate	mild	no
4. In the last 12 hours, I have felt nauseated or sick to my stomach.	not at all	1hour or less	2-3 hours	4-6 hours	more than 6 hours
5. In the last 12 hours, from nausea/sickness to my stomach, I have felt____ distress.	no	mild	moderate	great	severe
6. In the last 12 hours, each time I threw up, I produced a _____ amount.	very large (3 cups cups or more)	large (2-3 cups)	moderate (½ – 2 cups)	small (up to ½ cup)	I did not throw up
7. In the last 12 hours, I have felt nauseated or sick to my stomach _____ times.	7 or more	5-6	3-4	1-2	no
8. In the last 12 hours, I have had periods of retching or dry heaves without bringing anything up____ times.	no	1-2	3-4	5-6	7 or more

2. Pharmaceutical Methods Used for the Prevention of Aspiration Pneumonitis

It is essential to review the anatomy and physiology of the vomiting center within

the brain and spinal cord, in order to better understand the variable receptors involved in

sensing and transmitting the signal for the vomiting reflex, which forcefully propels gastric solids and liquids and can be potentially aspirated.

The vomiting center is a complex area of sensory and motor nuclei, located mainly within the medullary and pontile reticular formation, with possible extension into the spinal cord. See Figure 3 for the anatomy of the vomiting center. The vomiting center contains different receptors that can trigger sensory and motor receptors responsible for the sensation and the act of vomiting.[6,8] This area contains receptors for histamine (H_1 receptors); serotonin (5-hydroxytryptamine: 5-HT receptors; specifically 5-HT_3 receptors); dopamine (D_2) receptors, acetylcholine (M_1) receptors; and substance P (NK_1) receptors. See Figure 4 for a schematic representation of the receptors within the chemoreceptor trigger zone.[43]

The Vomiting Center receives stimulus via the circulation from multiple stimuli: the Nucleus Vestibularis, the Nucleus tractus solitarius, the Chemoreceptor Trigger Zone (CTZ) found in the area postrema of the medulla, the labyrinth of the inner ear, and from the Gastrointestinal tract.

Other receptors within these areas are yet to be discovered. Many of the medications we discuss in this section block specific receptors within the vomiting center itself.[8,35,44]

Figure 3 <u>Anatomy of the Vomiting Center</u> (Use figure 45-1, page 778 from Antiemetics chapter in Evers Book)

Figure 4 <u>Schematic Representation of The Receptors within the Chemoreceptor Trigger Zone</u> (Use Antiemetics chapter Evers book Figure 45-2, page 779.)

A. Alkalizers (systemic) – Citric acid and Sodium citrate (*Bicitra, Oracit*) [34,35,45,46]

Mechanism of Action – The combination of sodium citrate and citric acid, along with flavoring agents is a tolerably palatable liquid that mixes quickly with gastric fluid, rapidly buffers gastric fluid, and raises gastric pH.

Clinical Pharmacology

Pharmacokinetics – .34 Molar Sodium citrate with a pH of 8.4 is administered along with pH 0.32 Molar Citric acid; the combination has a pH of approximately 3.15 in the stomach.

Absorption – Sodium citrate/Citric acid passes through the stomach into the small intestine, where it is absorbed into the blood stream, and is metabolized to sodium bicarbonate and rapidly raises the systemic pH.

Distribution – Sodium citrate/citric acid is rapidly soluble in gastric fluid. Sodium bicarbonate circulates systemically.

Metabolism – Sodium citrate is rapidly and efficiently metabolized to sodium bicarbonate.

Elimination – Sodium bicarbonate is excreted in the urine, and sodium citrate/citric acid can be used to alkalinize urine to prevent the formation of renal calculi. Less than 5% of sodium citrate is excreted unchanged in the urine.

Pharmacodynamics – For anesthesia use, sodium citrate dissociates to sodium ions and citrate ions. Citrate anions and chloride ions are free to combine with gastric hydrogen

cations. The presence of sodium citrate with citric acid (Bicitra) also provides a continuous buffering environment in the stomach.

Clinical Uses/Indications – Sodium citrate/Citric acid (30ml) is administered by mouth in a preanesthesia preparation or holding area 10-20 minutes before induction of anesthesia. Sodium citrate makes the solution slightly more palatable. This medication is especially useful for use in obstetrical patients who are about to undergo certain surgical procedures.[11] Sodium citrate/Citric acid is usually combined with other therapies to be discussed later for the prevention of aspiration pneumonitis.

Sodium citrate/citric acid is also used for the alleviation of chronic metabolic acidosis. It is valuable as an alternative systemic alkalizer in patients where potassium salts are undesirable and contraindicated such as in chronic renal failure or renal tubular acidosis.[45]

Comparative pharmacology to other drugs in Class – The combination sodium citrate/citric acid and potassium citrate (Tricitra) is used as a urine alkalizer for treatment of renal calculi.

Side Effects / Contraindications - Sodium citrate/citric acid is considered unpalatable by some patients and may induce a feeling of nausea or vomiting. It is contraindicated for patients on sodium-restricted diets. The medication may cause a saline laxative effect in patients.

Drug Interactions - Sodium citrate/citric acid should not be administered to patients concurrently taking aluminum-based antacids because aluminum-based antacids slow gastric emptying.[34,35]

Guidelines/ precautions – Sodium citrate/citric acid should be used with caution by patients with low urinary output, or in patients with cardiac failure, hypertension, impaired renal function, peripheral edema, pulmonary edema, and toxemia of pregnancy.

Dosage and administration – 15-30 ml of Sodium citrate/citric acid is administered by mouth 10-20 minutes before the induction of general anesthesia. Cricoid pressure must be used at induction, as gastric volume is increased by the ingestion of Sodium citrate/citric acid liquid. Onset is immediately with contact of gastric acids. Duration is based on the gastric emptying time into the duodenum.

B. Antiemetics

      1. Anticholinergics – Scopolamine (*Transderm Scop*®) [2,3,8,33,34,35]

Mechanism of Action –Scopolamine is an anticholinergic agent that blocks the action of acetylcholine on gastrointestinal tract peristalsis. Peristalsis is the movement of digested nutrients along the intestines to expose intestinal nutrients for absorption. Acetylcholine release also facilitates the secretion of gastric acids, and medullary stimulation from the inner ear vestibular apparatus, which can signal motion sickness and nausea.

Clinical Pharmacology

Pharmacokinetics

Absorption – The transdermal scopolamine patch time releases the delivery of scopolamine into the blood stream. The transdermal patch is the commonly used form for anesthesia.

Distribution – Scopolamine circulates systemically. It is highly lipid soluble, and easily crosses the blood/brain barrier.

Metabolism – Scopolamine is efficiently metabolized in the liver, with a half-life of 4.8 hours.

Elimination – Scopolamine metabolites are excreted in the urine, with <1% appearing as the unchanged parent molecule.

Pharmacodynamics – Scopolamine competes with acetylcholine receptor sites, and reversibly combines with each of the five cholinergic muscarinic subtypes. (See Table 7)

The neurotransmitter acetylcholine is responsible for mediating the action between nerves and smooth muscle, skeletal muscle, or cardiac muscle. Acetylcholine also stimulates the vestibular apparatus of the inner ear, which is responsible for balance along with the sense of position, and is involved in the sensation of motion sickness.

See Figure 3 for the relation of the vestibular apparatus as an emetogenic stimulus.

Motion stimulates the cilia in the labyrinth of the vestibular apparatus within the inner ear. This stimulus is then sent to the vestibular apparatus of the cerebellum, which relays its signal to the chemoreceptor trigger zone and finally on to the vomiting center.

The vomiting center is a complex area of sensory and motor nuclei mainly located in the medullary and pontile reticular formation and can extend into the spinal cord.[5] See Figure 4.

Table 7 <u>The Five Cholinergic Muscarinic Receptor Subtypes</u>[35]

M-1: Found at neurons and nerve endings in the Central Nervous System (CNS) and stomach.

M-2: Found on the heart, neurons and nerve endings, and airway smooth muscle.

M-3: Found on exocrine glands (such as the salivary glands), smooth muscle, and neurons and nerve endings.

M-4: Found on the heart and in the CNS. Function is unknown.

M-5: Found in the CNS. Function is unknown.

Clinical Uses/Indications – Transdermal scopolamine is used as an effective and relatively inexpensive means to prevent nausea preoperatively. It can be safely before general anesthetic induction for women having gynecological surgery or obstetric caesarean section. It is also used as an antiemetic adjunct in patients receiving postoperative epidural morphine. High doses of scopolamine are required to block gastric acid secretion, other medications to be discussed later, are efficaciously used due to the numerous side effects of scopolamine at increased dosage.

Comparative pharmacology to other drugs in Class – Scopolamine and atropine are naturally occurring belladonna alkaloids. The molecules of scopolamine and atropine are

highly lipid soluble tertiary amines, possessing a cationic portion that fits into muscarinic cholinergic receptors.

Glycopyrrolate is a quaternary ammonium compound and is poorly lipid soluble and also possesses an affinity for the muscarinic cholinergic receptor. Ipratropium is a synthetic quaternary ammonium analog of atropine, which is inhaled and used primarily for treating bronchospasm.

Side Effects / Contraindications – Side effects of scopolamine are dizziness, drowsiness, confusion, blurred vision, dilated pupils causing photophobia, and difficult urination. Scopolamine in low doses (0.1mg) can produce vagal mimetic effects causing paradoxical bradycardia. High doses of scopolamine can cause tachycardia, and should therefore not be used in patients with coronary insufficiency, myocardial infarction, or coronary artery disease. Scopolamine is contraindicated in patients with narrow angle glaucoma due to the production of mydriasis (dilation of the eye pupil which inhibits the passage of intraocular fluid into the venous circulation) and cycloplegia (relaxation of the ciliary muscle of the eye, occluding the angular space), causing a hazardous raise in intraocular pressure. Scopolamine is contraindicated in patients where conditions of inhibited peristalsis of the ureters would be detrimental, such as in prostatic hypertrophy or urinary retention.

Transdermal scopolamine is slowly released into the bloodstream and can be safely administered without these side effects in most patients.

Drug Interactions – Scopolamine effects increase with patients consuming alcohol, opioids, antihistamines, tricyclic antidepressants, or phenothiazine antipsychotics.

Guidelines/ precautions – Place the transdermal scopolamine patch on a non-hairy area behind the ear. Avoid contact of the medication with the eye, as this can cause anisocoria (an unequal size of the pupils). The transdermal patch may contain metal, and should be removed from patients prior to receiving Magnetic Resonance Imaging (MRI).

Dosage and administration – Transdermal scopolamine is available as 0.5mg or 1mg doses, and is delivered within 72 hours. In anesthesia, a 1mg patch is applied to a hairless area behind the ear, at least 4 hours prior to the induction of general anesthesia, and is used for the duration of the anesthetic and up to 72 hours postoperatively.

Onset – 4 hours prior to surgery.

Duration – Up to seven hours

2. Butyrophenones – Droperidol (Inapsine®) [33,34,35,44]

Mechanism of Action – Droperidol and haloperidol are each a butyrophenone-type molecule, which are dopaminergic antagonists binding to dopamine receptor sites in the central nervous system. Droperidol binds and blocks $dopamine_2$ receptors in the chemoreceptor trigger zone (CTZ) of the medulla.

Clinical Pharmacology

Pharmacokinetics

Absorption – Droperidol is usually administered intravenously, and can be rapidly absorbed if administered intramuscularly.

Distribution – Droperidol is extensively protein-bound, and can cross the blood/brain barrier, and the placenta. Its volume of distribution in children is approximately 0.25-0.9L/kg; and approximately 2L/kg in adults.

Metabolism – Droperidol is metabolized in the liver. It has a half-life of 2.3 hours in adults.

Elimination – Droperidol metabolites are excreted 75% in urine and 22% in feces. <1% of the unchanged parent drug is found in the urine, and 11%-50% of the unchanged parent drug is found in feces.

Pharmacodynamics – Droperidol blocks the action of the neurotransmitter dopamine on the $dopamine_2$ receptors within the CTZ. Droperidol has prolonged CNS effects, which is not believed due its rapid hepatic metabolism, but by retention for prolonged periods on $dopamine_2$ receptors. Droperidol does not affect vomiting originating from vestibular-apparatus-induced motion sickness.

Clinical Uses/Indications – Droperidol is a powerful antiemetic used as a treatment to prevent postoperative nausea and vomiting (PONV) caused by anesthetic medications. Present day use of Droperidol has greatly diminished due to potentially lethal alterations of cardiac electrical conduction.

Comparative pharmacology to other drugs in Class – Haloperidol is not routinely used as an anesthetic antiemetic, but is an antipsychotic agent used for the management of schizophrenia, the vocal utterances caused by Tourette's disorder, and severe behavioral problems in children. Haloperidol has also found use in treating non-schizophrenic psychosis, emergency sedation in patients with severe agitation or delirium, as an adjunct in the treatment of alcohol dependence, and as an antiemetic.

Side Effects / Contraindications -

Drug Interactions

Guidelines/ precautions - Droperidol may prolong the QTc interval of the electrocardiogram, which can precipitate torsades de pointes (polymorphic ventricular tachycardia). Prolonged QTc is defined as >440msec in males, and >450msec in females. Prolongation has occurred with droperidol doses ranging from 0.625mg to 1.25mg and up to 2.5mg. The United States Food and Drug Administration (FDA) issued a black box warning in December of 2001 (the most serious warning for an FDA approved drug) requiring extreme caution before using droperidol. Patients to receive droperidol should undergo a 12-lead electrocardiogram prior to surgery. Patients must be monitored with a continuous EKG for 2-3 hours after receiving droperidol. Prolonged QTc can develop in patients with congestive heart failure, ischemia, myocarditis, bradycardia, cerebrovascular disease, hypokalemia, hyperthyroidism/hypothyroidism, the elderly, and the concomitant use of other QTc prolonging medications (See sidebar 2).[35,47]

Dosage and administration – Give 0.625 – 1.25 mg intravenously at the end of the surgical procedure, upon emergence from anesthesia.

Onset – rapid

Duration – Up to 12 hours.

Sidebar 2 Some Medications Associated with the Prolonging of the QTc interval[47]

Antibiotics – azithromycin, clarithromycin, erythromycin, metronidazole,

Antifungals – fluconazole, ketoconazole

Antivirals – nelfinavir

Antimalarials – chloroquine

Antidysrhythmics – disopyramide, procainamide, quinidine amiodarone, sotalol

Antidepressants – amitriptyline, clomipramine, imipramine, doxepin

Antipsychotics – riperidone, haloperidol, clozapine,

Inhaled Anesthetics - halothane

3. Nonbarbiturate anesthetic induction drugs – Propofol (Diprivan®) and Fospropofol (Lusedra®)[33,34,35,48,49]

Name of Drug - Propofol

Mechanism of Action – Propofol reacts with gamma amino butyric acid receptors subtype A (GABA$_A$) in subcortical centers of the central nervous. Propofol has a postulated function as an antiemetic by either modulation of subcortical neuropathways, or as a direct inhibitor within the vomiting center.

Clinical Pharmacology (Prototype)

Pharmacokinetics

        Absorption – Propofol is administered intravenously, and is highly protein-bound in the plasma.

        Distribution – Propofol is highly lipophilic and is rapidly distributed throughout the body to fat stores, and crosses the blood brain barrier to react with brain $GABA_A$ receptors. Its volume of distribution is 2-10L/kg.

        Metabolism – Propofol's desirable rapid action is due to uptake by lipophilic tissues, which also accounts for 50% of its rapid decrement effects when used to produce induction of general anesthesia or sedation effect. Propofol is metabolized in the liver to water-soluble sulfate and glucuronide conjugates.

        Elimination – Propofol has a biphasic pattern of elimination. Initial elimination occurs within 40 minutes primarily in the urine (88%) and the feces (<2%). Terminal elimination is 4-7 hours. If propofol is administered for a prolonged period of time, such as in an intensive care unit (ICU), elimination is 1-3 days.

Pharmacodynamics – Propofol interacts with the gamma amino butyric acid receptors ($GABA_A$ receptor) of the CNS. GABA is the principal inhibitory neurotransmitter of the CNS. Propofol is postulated to act by modulation of several subcortical pathways in the CNS inhibiting nausea and vomiting or by direct effects on the vomiting center.

Clinical Uses/Indications – Propofol is a highly favored and useful medication for the induction and maintenance of anesthesia. It is also used off-label as a postoperative antiemetic. Propofol administered in subhypnotic doses is effective in chemotherapy-

induced nausea and vomiting, and as a rapidly effective rescue medication for postoperative nausea and vomiting (PONV). It has been found to be as effective as Ondansetron in the prevention of PONV. Propofol should be used in conjunction with other medications for the prevention of PONV.

When used as an induction and maintenance agent for general anesthesia it is found more effective than ondanestron for the prevention of (PONV).

Comparative pharmacology to other drugs in Class – The American Food and Drug Administration (FDA) recently approved a water-soluble prodrug of propofol, called fospropofol disodium (Lusedra^{TM}), which is undergoing United States Drug Enforcement Agency classification before its release. Fospropofol disodium is hydrolyzed to propofol by alkaline phosphatase found on the surface of endothelial cells, and does not cause discomfort when injected intravenously. It can also be administered as an induction agent or used as bolus doses for anesthetic sedation.[50]

Side Effects / Contraindications – Side effects of Propofol are pain on injection, especially into small peripheral veins, sedation, diminished respiration, tachycardia, decreased blood pressure, and bradycardia. Propofol is contraindicated in patients with hypersensitivity to eggs, egg products, soybeans, and soy products.

Drug Interactions – Propofol is additive to the effects of other classes of CNS depressants; hypnotic anesthetic medications such as the benzodiazepines (e.g.

midazolam, lorazepam); barbiturates such as thiopental; opiates such as fentanyl, sufentanil, alfentanil, remifentanil); and alcohol.

Guidelines/ precautions - Propofol produces sedation and general anesthesia in high doses. It is contraindicated for use by anyone without advanced training in general anesthesia and advanced airway maintenance. It should not be administered by the person conducting the therapeutic or diagnostic procedure for the patient. Use strict aseptic technique

Dosage and administration

The antiemetic effects of propofol can be achieved with a single IV dose of 10mg and effects can be maintained with an infusion of 10 mcg/kg/min.

4. P/neurokinin 1 (NK$_1$) receptor antagonists – Aprepitant (Emend®)[8,33,32,34,35]

Mechanism of Action – Aprepitant is an antagonist to human substance P/neurokinin 1 (NK$_1$) receptors in the brain. This receptor is found in the vomiting center of the brain. Substance P is a neurotransmitter of noxious and adverse pain information into the CNS. Pain sensation is enhanced or aggravated by Substance P. Substance P/NK$_1$ regulates vomiting, and is present in the final common pathway in the metabolism of Substance P.

Clinical Pharmacology (Prototype)

Pharmacokinetics

Absorption – Aprepitant is administered orally with absorption from the gastrointestinal tract. Aprepitant is able to cross the blood/brain barrier.

Distribution – Aprepitant has a volume of distribution of 70L. It is >95% protein bound. Peak plasma levels are achieved in about 3-4 hours.

Metabolism – Aprepitant is metabolized in the liver.

Elimination – Metabolites of Aprepitant are found primarily in the feces. Terminal elimination is within 9-13 hours.

Pharmacodynamics – Aprepitant crosses the blood/brain barrier and blocks the neurotransmitter Substance P/NK$_1$ from binding to receptors in the vomiting center.

Clinical Uses/Indications – Aprepitant is primarily used for chemotherapeutically induced nausea and vomiting. It can be used to prevent PONV if administered 3-4 hours prior to induction. Aprepitant can be used in conjunction with 5-HT$_3$ receptor antagonists (e.g. ondanestron) or corticosteroid receptor (e.g. dexamethasone) antagonists.

Comparative pharmacology to other drugs in Class – Other Substance P antagonists are in development and are being tested in clinical trials.

Side Effects / Contraindications – Aprepitant is contraindicated in patients sensitive to the parent drug or its components of formulation. It is contraindicated in patients receiving pimozide (*Orap*®): an atypical antipsychotic drug used to treat serious motor and verbal tics associated with Tourette's syndrome.

Drug Interactions – Aprepitant is extensively metabolized in the liver, and competes with common medication metabolic pathways such as the benzodiazepines, corticosteroids, dilitiazem, hormone-containing contraceptives (estrogen), rifampin, warfarin, and azole antifungal agents. Patients taking any of these medications could see prolonged effects due to a decrease in the rate of their metabolism.

Guidelines/ precautions – Aprepitant requires no dosage modification for patients with renal impairment or mild to moderate hepatic impairment due to its predominant hepatic metabolism.

Dosage and administration – Administer 40mg orally. Time to peak plasma levels is in approximately 3-4 hours.

5. Serotonin 5-HT$_3$ receptor blockers – Ondansetron (*Zofran*[®]), Alosetron (*Lotronex*[®]), Dolasetron (*Anzemet*[®]), Granisetron (*Kytril*[®]), Palonosetron (*Aloxi*[®])[6,33,32,34,35,44,46,53]

Name of Drug – Ondansetron

Mechanisms of Action – The Serotonin 5-HT$_3$ receptor blockers are highly specific competitive antagonists of the 5-HT$_3$ receptors in the vomiting center, and readily cross the blood-brain barrier. The 5-HT$_3$ receptor blockers also inhibit vagal nerve terminals (Cranial Nerve X) by distributing to peripheral vagal receptors, which play a role in the process of nausea.

Serotonin is released from the enterochromaffin cells located within the mucosa of the duodenum and stimulates efferent vagal nerves with pathways to the vomiting center.

Clinical Pharmacology – Ondansetron

Pharmacokinetics

Absorption – Ondansetron is administered intravenously and has an onset of approximately 30 minutes. It can also be administered orally and intramuscularly.

Distribution – Ondansetron has a volume of distribution of 1.7-3.7 L/Kg in children, and 2.2-2.5 L/Kg in adults. It is 70%-76% protein bound in the plasma.

Metabolism – Ondansetron is extensively metabolized in the liver. It is also metabolized in the plasma by the platelets and the endothelial lining of blood vessels. Its half-life is 2-7 hours in healthy children < 15 years old, and 3-6 hours in healthy adults.

Elimination – Ondansetron is 44%-60% excreted as metabolites. 5%-10% of Ondansetron is excreted unchanged in the urine, and approximately 25% unchanged in the feces.

Pharmacodynamics – There are fourteen 5-HT receptor subtypes that have been discovered thus far. The 5-HT receptor is part of the nicotinic gamma amino butyric acid (GABA) family of receptors. Ondansetron has negligible attraction to any of the other 5-HT receptors, but is highly attracted to the $5-HT_3$ receptors.

Clinical Uses/Indications – Ondansetron is used for patients with moderate to severe cancer chemotherapy induced nausea, in patients receiving total body or abdominal

cancer radiotherapy, and as a preventive or as a rescue for post-operative nausea and vomiting (PONV). Ondansetron has not been found useful for treatment of motion-induced nausea and vomiting.

Ondansetron is found to block the symptoms of opioid withdrawal, and is being investigated as part of the treatments needed for patients with opioid addiction.[52]

Comparative pharmacology to other drugs in Class – The 5-HT$_3$ receptor antagonists differ only in their therapeutic half-life. Dolasetron differs in that is rapidly metabolized by the liver to hydrodolasetron, which is also a highly potent antiemetic.

See Table 8 for a list of the half-life of the Serotonin 5-HT$_3$ receptor antagonists.

Side Effects / Contraindications – The Serotonin 5-HT$_3$ receptor antagonists should not be administered to patients with a hypersensitivity to the medication or any of its components of formulation.

Drug Interactions – Ondansetron is metabolized in the hepatic Cytochrome P450 (CYP3A4) enzyme pathway in the liver. Therefore other medications metabolized by this pathway, will increase the clearance of Ondansetron and shorten its therapeutic half-life, although the manufacturer recommends no dosage adjustments.

Guidelines/ precautions – There are few reported reactions to Ondansetron. Ondansetron can precipitate cardiac dysrhythmias, prolonged QT$_c$ interval, and atrioventricular

conduction disturbances when administered rapidly.[53] It can precipitate headaches, especially in patients prone to migraine headaches. It also can cause malaise, fatigue, or dizziness; and either constipation or diarrhea in some patients.

Dosage and administration – Administer 4-8 mg of Ondansetron intravenously in adults, and (0.05-0.15 mg/kg) in children, over 2-5 minutes immediately before the induction of general anesthesia[18,19] or 30 minutes before the end of surgery.[34] Administration of Ondansetron with other Serotonin 5-HT$_3$ receptor antagonists has not been found useful. Ondansetron can be administered concomitantly with dexamethasone in patients more prone to PONV. (Droperidol was used concomitantly with Ondansetron prior to its FDA black box warning.)

Onset – Within 30 to 60 minutes after intravenous administration.

Duration – 3-6 hours in healthy patients.

Table 8 The Half-Life of the Serotonin 5-HT$_3$ Receptor Antagonists in Adults (Children)[34,43]

Name	T$_{1/2}$
Ondansetron (*Zofran*®)	3-6 hours (2-7 hours)
Alosetron (*Lotronex*®)	1.5 hours
Dolasetron (*Anzemet*®)	Dolasetron 10 minutes;
	Hydrodolasetron 6-8 hours (4-6 hours)
Granisetron (*Kytril*®)	5-9 hours
Palonosetron (*Aloxi*®)	40 hours

6. Synthetic corticosteroids – Dexamethasone Sodium Phosphate (*Decadron*®)[6,33,32,34,35]

Mechanism of Action – The antiemetic action of Dexamethasone is currently unknown, but is postulated to inhibit prostaglandin synthesis caused from surgery-induced inflammation. As a steroid, Dexamethasone may also stabilize the cell membranes of structures involved with producing PONV, or penetrate to receptors in the central nervous system. Dexamethasone also releases endorphins, which elevate patient mood, and stimulate the appetite.

Clinical Pharmacology

Pharmacokinetics -

Absorption – Dexamethasone is administered intravenously for treatment of PONV, but may also be administered orally or intramuscularly.

Distribution – Dexamethasone sodium phosphate is water soluble, and is rapidly distributed throughout the circulation.

Metabolism – Dexamethasone is metabolized in the liver.

Elimination – Dexamethasone is excreted in the urine and feces.

Pharmacodynamics – Dexamethasone is a fluorinated derivative of the glucocorticoids prednisolone, and is the isomer of betamethasone. Dexamethasone is six times more potent than prednisolone. The elimination half-life is 1.8 – 3.5 hours in a patient with normal renal function. The antiemetic effects of Dexamethasone can persist for 24 hours.

The use of Dexamethasone is discussed in Box 1 as an adjunct for treatment of Aspiration Pneumonitis.

Clinical Uses/Indications – Dexamethasone can be used in conjunction with other single-use antiemetics such as Ondansetron or Palonosetron for the prevention of PONV, and can be used alone for chemotherapeutically induced nausea and vomiting.

Comparative pharmacology to other drugs in Class – Betamethasone is used for the treatment of dermatitis, pruritis, psoriasis, and the inflammatory phase of xerosis, which is abnormal skin dryness. Betamethasone is ineffective for use for the prevention of PONV. None of the other synthetic glucocorticoids possess the antiemetic property of Dexamethasone.

Side Effects / Contraindications – Dexamethasone can exhibit intense peroneal discomfort such as burning or itching when administered to patients. Consider administering Dexamethasone to a sedated patient due to this discomfort. Dexamethasone is contraindicated in patients with an active fungal infection, with an ophthalmic herpes simplex viral infection, or tuberculosis infection. Dexamethasone reduces the humoral inflammatory response, which and can inhibit both the time and quality of wound healing. It is contraindicated in patients who are sensitive to the preservative sodium bisulfite.

Drug Interactions - none

Guidelines/ precautions – Administer the smallest dose possible to prevent PONV due to impairment of the inflammatory response and wound healing. PONV dosages of Decadron are considered relatively small, and are also usually one-time event. Precaution should be considered for repeated Dexamethasone administration to patients requiring multiple surgeries.

Dexamethasone has been implicated as increasing the risk of postoperative bleeding in children undergoing tonsillectomy, probably due to its impairment of wound healing, and should probably be avoided in these patients.[54]

Dosage and administration – Administer (0.5mg/kg, up to 8mg) in pediatric patients. Adult dosage is typically 4mg intravenously. Administer Dexamethasone at the time of induction of anesthesia.

Onset – Immediate

Duration – $\geq$ 24 hours.

C. Gastric motility prokinetic medication - Metoclopramide (Reglan[®]), Cisapride (Propulsid[®] no longer available), Trimethobenzamide (Tigan[®]), Prochlorperazine (Compazine[®])[6,11,33,34,35,44,46]

Name of Drug - Metoclopramide (*Reglan*[®])

Mechanisms of Action – Metoclopramide is a dopamine antagonist, which blocks dopaminergic receptors in the CTZ, and in high doses blocks will block serotonin

receptors in the CTZ. Metoclopramide is a gastrointestinal prokinetic agent: it promotes peristaltic propulsion of gastrointestinal contents through the stomach and intestines by sensitizing gastrointestinal smooth muscle to the effects of acetylcholine.

Clinical Pharmacology

Pharmacokinetics

Absorption – Metoclopramide is administered intravenously or intramuscularly, but can also be administered orally, where it is absorbed directly in the gastrointestinal tract.

Distribution – Metoclopramide is 30% protein bound, and has a volume of distribution of 2-4L/kg, and will readily cross the blood-brain barrier and the placenta.

Metabolism – Approximately 70% of intravenously administered Metoclopramide is conjugated in the liver with sulfate or glucuronic acid for elimination. Orally administered Metoclopramide undergoes rapid first-pass hepatic metabolism, which limits its bioavailability to 75%.

Elimination – Intravenously administered Metoclopramide is excreted 30% unchanged in the urine, and 70% as conjugated forms, which are excreted in the urine and in the bile.

Pharmacodynamics –Metoclopramide, which produces strengthening of the lower esophageal sphincter and the fundus of the stomach, sensitizes gastrointestinal tissue to acetylcholine then motility increases in the stomach and small intestine. The pylorus and the duodenum then become relaxed in order to accept the gastric contents.

Clinical Uses/Indications – Metoclopramide is used preoperatively to stimulate gastric emptying as an aid for the prevention of AP and can even be used preoperatively for the obstetrical patient.[9] It is also used clinically as a treatment for diabetic gastroparesis; as an antiemetic postoperatively or from the effects of chemotherapy; for symptomatic treatment of gastroesophageal reflux; for postpyloric placement of enteral feeding tubes; and for promoting transit of radio opaque dyes in radiological examinations.

Comparative pharmacology to other drugs in Class – Metoclopramide is structurally similar to Procaine (*Novocain*®) an ester local anesthetic that is no longer used, and Procainamide, a benzamide antiarrythmic without any local anesthetic effect. Cisapride (*Propulsid*®) is a gastrointestinal prokinetic agent that is no longer available, since 2000 in the United States, due to reports of severe cardiac dysrhythmias associated with its use.[55] Trimethobenzamide (*Tigan*®) is an antiemetic agent, which acts centrally as a dopaminergic antagonist in the CTZ. Trimethobenzamide can produce seizures, and extrapyramidal symptoms: an old term referring to dysfunctions of motor control.[8]

Prochlorperazine (*Compazine*®) is a piperazine phenothiazine antipsychotic, and is chemically unrelated to Metoclopramide and the other gastrointestinal prokinetic agents already discussed, but Prochlorperazine blocks dopamine receptors in the CTZ. It has the advantage of rectal administration as a suppository for patients who are experiencing active nausea and vomiting, or are unable to take oral medications, or are unable to receive intravenous dosing for nausea and vomiting.

The antibiotic Erythromycin stimulates cholinergic activity, which increases lower esophageal sphincter tone, and promotes gastric emptying. It can be used as an effective gastric prokinetic agent and can be administered to any patient not allergic to the medication.

Side Effects / Contraindications – Metoclopramide is contraindicated in patients experiencing extrapyramidal symptoms, Parkinson's disease, and seizures. It is contraindicated in patients with gastric obstruction and/or bowel obstruction and in patients who have had gastrointestinal surgery.

Drug Interactions – Metoclopramide inhibits the effects of plasma cholinesterase, and can produce prolongation of the anesthetic muscle relaxants succinylcholine and mivacurium (which was discontinued in 2006).

Guidelines/ precautions – Metoclopramide should be administered slowly over 1-2 minutes intravenously to avoid side effects of abdominal cramping, hypotension, tachycardia, bradycardia, and cardiac dysrhythmias.

Dosage and administration – Metoclopramide 10mg is administered intravenously.

Onset – 1-3 minutes.

Duration – 1-2 hours.

D. Histamine (H$_2$) receptor antagonists – Cimetidine (Tagamet[®]), Famotidine (Pepcid[®]), Nizatidine (Axid[®]), Ranitidine (Zantac[®])[6,8,33,34,35,46]

Name of Drug - Ranitidine (*Zantac*®)

Mechanism of Action - Ranitidine (*Zantac*®) competitively inhibits histamine H_2 receptors in the gastric parietal cells, stopping the secretion of gastric acid and hydrogen ions, which reduces gastric volume.

Clinical Pharmacology

Pharmacokinetics

Absorption - Ranitidine (*Zantac*®) is administered intravenously for the preoperative treatment of AP.

Distribution - Ranitidine (*Zantac*®) has a volume of distribution of 1.7L/Kg and minimally penetrates the blood-brain barrier.

Metabolism - Ranitidine (*Zantac*®) undergoes hepatic metabolism to N-oxide, S-oxide, and N-desmethyl metabolites.

Elimination - Ranitidine (*Zantac*®) is excreted 70% unchanged in the urine when administered intravenously, while metabolites are excreted in the feces.

Pharmacodynamics – Histamine (Figure 5) is an endogenous substance that is synthesized by the degradation of the amino acid histidine (Figure 6). Mast cells, found in human connective tissue, store large basophilic granules containing histamine, serotonin, bradykinin, and heparin. These substances are released from the mast cells in response to infection, inflammation, immunological stimulation, mechanical injury, or by certain medications or chemicals.[2,3,35,46] There are 3 histamine receptor subtypes: H_1, H_2, and H_3.

(See Table 9 for a description of the effects of the histamine receptor subtypes)

All 3 histamine receptor subtypes are found on the heart. Ranitidine is a specific histamine H_2 subtype receptor antagonist that competes with histamine for attachment to the basolateral membranes of the hydrogen-ion-secreting gastric parietal cells.

Clinical Uses/Indications – Ranitidine is administered preoperatively for the prevention of AP, and can be used with obstetrical patients.[11]

Comparative pharmacology to other drugs in Class – Cimetidine was the first commercially successful H_2 receptor antagonist introduced in the 1970s. Pharmacologist Sir James W. Black was awarded the 1988 Nobel Prize in medicine for the development of Cimetidine, and for the development of the cardiac beta-receptor antagonist Propanolol.[56] Cimetidine retains the imidazole ring structure similar to histamine, and is assigned a relative H_2 antagonist potency of 1.

Ranitidine utilizes a furan ring structure that increases its potency 4-10 times that of Cimetidine. Nizatidine and Famotidine each utilize a thiazole ring structure giving Nizatidine a potency 4-10 times that of Cimetidine and Famotidine which is 20-50 times more potent than Cimetidine.

Side Effects / Contraindications – Ranitidine is contraindicated in patients sensitive to its chemical structure and components of its formulation. Adverse reactions to Ranitidine are

low, and are characterized as dysrhythmias, dizziness, mental confusion, and somnolence.

Drug Interactions - Ranitidine is metabolized in the hepatic cytochrome P450 system, and can reduce the absorption of Atazanavir (an antiretroviral protease inhibitor for the treatment of Human Immunodeficiency Virus-1), some cephalosporin antibiotics (Cefluroxime, Cefpodoxime), antifungals (itraconazole, ketoconazole), and with warfarin (*Coumadin*®) which has produced either an increase or decrease in Prothrombin time.

Guidelines/ precautions – Ranitidine must be diluted to avoid adverse reactions. Some H_2 receptor antagonists may also block H_3 receptors. H_3 receptors inhibit the synthesis and release of histamine when occupied by an agonist. Therefore histamine release may be enhanced when medications are given that evoke the release of histamine such as atracurium, morphine, or succinylcholine (slight release), and should be used cautiously or avoided if possible.[12,35]

There is evidence of rapid tolerance (within 2-7 days) to the anti-secretory effects of H_2 antagonists in patients who high doses by mouth (Ranitidine 150mg qid) or who take frequent or rapid intravenous doses (Ranitidine 100mg q6h or 50mg bolus and .25mg kg^{-1} h^{-1}). It is therefore suggested that other medications such as proton pump inhibitors be used instead of H_2 receptor antagonists.[56]

New information was published that all patients, and especially those with osteoporosis, who use histamine receptor antagonists or proton pump antagonists (to be discussed in the following section) are subject to an increased risk of hip fractures. The

risk of hip fracture was found to decrease with the use of lower doses. Therefore the lowest effective dose of these medications should be used.[57]

Dosage and administration – Ranitidine 50mg diluted in 20ml of normal saline or D_5W administered intravenously over 5 minutes, or by IV piggyback over 15-20 minutes. The dose of Ranitidine need not be adjusted in patients with hepatic impairment, but must be adjusted in patients with renal insufficiency.

Onset – Within minutes when administered intravenously.

Duration – Elimination Half Lives: Cimetidine 1.5-2.3 hours; Famotidine 2.5-4 hours; Nizatidine 1.1-1.6 hours; Ranitidine 1.6-2.4 hours.

Table 9 Some Effects By Stimulation of the Histamine Receptor Subtypes[35]

H_1 – Coronary artery vasoconstriction, bronchoconstriction, slowed conduction through the atrioventricular node, increases capillary permeability, causes peripheral vascular dilation.

H_2 – Stimulates secretion of hydrogen ions by the gastric parietal cells, CNS stimulation, increases myocardial contractility and heart rate, coronary artery dilation, bronchodilation, increases capillary permeability, causes peripheral vascular dilation.

H_3 – Inhibit the synthesis and release of histamine.
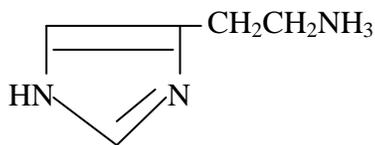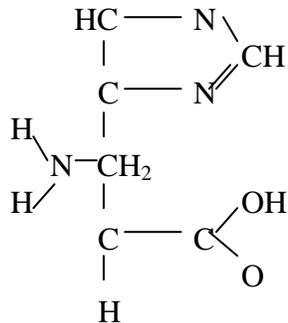
Figure 5 The Molecular Structure of Histamine[35]

Figure 6 The Molecular Structure of the amino acid Histidine[2]

9. Proton pump (hydrogen ion) inhibitors – Omeprazole (Prilosec[®]), Esomeprazole (Nexium[®]), Lansoprazole (Prevacid[®]), Pantoprazole (Protonix[®]), Rabeprazole (AcipHex[®])[2,6,33,34,35,44,46]

Name of Drug - Omeprazole

Mechanism of Action – As discussed previously, hydrochloric acid (with a pH of 0.8 which is 3 million times more acidic than arterial blood) is secreted by the parietal cells of the gastric lining. (See Figures 1a and 1b) Hydrogen ions are produced in the parietal cells by a postulated mechanism involving:

1. Active transport of chloride ions from the parietal cytoplasm into the parietal canaliculi.

2. Sodium ions actively transported out of the canaliculi into the parietal cytoplasm.

3. Dissociation of water into hydrogen ions (H^+) and hydroxyl ions (OH^-).

4. Active <u>pumping</u> of potassium ions (K^+) into the parietal cytoplasm for hydrogen ions (H^+).

This results in hydrogen ion secretion into the canaliculi of the parietal cells. This pump is called H^+/K^+ ATPase (Adenosine Triphosphate) proton pump and whose mechanism is inhibited.[8] (See Figure 7: The Postulated Mechanism for the Secretion of Hydrochloric Acid by the H^+/K^+ ATPase Proton Pump)

Figure 7 The Postulated Mechanism for the Secretion of Hydrochloric Acid by the H^+/K^+ ATPase Proton Pump. (Guyton Figure 64-6, page 796)

Clinical Pharmacology - Omeprazole

Pharmacokinetics

Absorption – Omeprazole can be administered orally. It passes through the stomach into the small bowel (experiencing the first pass effect by the liver), or is also available for intravenous administration.

Distribution – Omeprazole is 95% protein bound, and is distributed via the bloodstream to reach the gastric parietal cells. Omeprazole (a benzimidazole) diffuses into the parietal cell and accumulates in the canaliculi, where it is converted to its active component: a sulphenamide. Its bioavailability is approximately 30-60% with peak serum concentration reached in 0.5-4 hours.

Metabolism – Omeprazole undergoes extensive hepatic metabolism to inactive metabolites.

Elimination – Omeprazole has a half-life of 0.5- 1 hour, and is eliminated in the urine: 77% as inactive metabolites and a negligible amount as the active drug. Metabolites also appear breast milk and the feces.

Pharmacodynamics – The active sulphenamide form of Omeprazole covalently binds to the H^+/K^+ ATPase proton pump, and ceases the function of the pump. As a result, Omeprazole increases gastric pH and decreases gastric fluid volume.

Clinical Uses/Indications – Proton pump inhibitors are used in the treatment of gastroesophageal reflux disease (GERD), treatment of active duodenal ulcers or active benign gastric ulcers (peptic ulcers), erosive esophagitis, hypersecretory disorders such as Zollinger-Ellison syndrome, and as a multidrug regimen for the eradication of Helicobacter pylori. It is also used off-label for the prevention or healing of non-steroidal anti-inflammatory drug (NSAID)-induced ulcers. Although proton pump inhibitors are not currently commonly administered as a first-line therapy for the prevention of AP, patients should continue this medication as ordered by their physician to aid in the prevention of AP, along with additional therapies previously discussed.

Comparative pharmacology to other drugs in Class –

a. Esomeprazole (Nexium®) – is the S-enantiomer of Omeprazole and is therefore structurally and pharmacologically similar to Omeprazole. It has a bioavailability of 85% and a serum half-life of 1.5 hours.

Oral Dosage for GERD

Children <20kg: 10mg once daily

Children ≥20kg: 10-20mg once daily

Adults: 20mg once daily

b. Lansoprazole (Prevacid®) capsule and oral disintegrating tablets available in 15mg or 30mg; intravenous 30mg to be reconstituted in 60mg of liquid mannitol – has the same indications for usage as Omeprazole.

Oral Dosage for GERD

Children ≤ 30kg: 15mg once daily

Children >30kg: 30mg once daily

Adults: 30mg once daily

c. Pantoprazole (Protonix®) - oral tablets available in 20mg or 40mg; intravenous 40mg to be reconstituted in 100ml of Normal Saline or D_5W to be administered over 2-15 minutes. – has the same indications for usage as Omeprazole.

Oral Dosage for GERD

Adults: 40mg once daily

d. Rabeprazole (AcipHex®) - oral tablets available in 15mg or 30mg. – has the same indications for usage as Omeprazole.

Oral Dosage for GERD

Adults >18years and the elderly: 20mg once daily

Side Effects / Contraindications – Omeprazole is contraindicated in patients who are hypersensitive to the medication or components of its formulation, as well as to any other benzamide proton pump inhibitors. Since Omeprazole crosses the blood-brain barrier, rare side effects such as of headache, dizziness, agitation, and confusion can occur. There are also rare instances of nausea, vomiting, diarrhea, constipation, flatulence, and abdominal pain.

As gastric acid levels are decreased by use of the proton pump inhibitors, serum gastrin levels increase, but there has been no experience of significance with long-term proton pump inhibitor use, and eventually gastrin levels become maintained at normal levels.

As mentioned in the section on histamine receptor blockers, any patients who use either histamine receptor antagonists or proton pump antagonists are subject to an increased risk of hip fractures. The risk of hip fracture was found to decrease with the use of lower doses, and the lowest effective dose of these medications should be used.[57]

Drug Interactions – Omeprazole may decrease the absorption of the protease inhibitors (atazanvir, indinavir) and should not be used concurrently. Omeprazole may increase the levels and the effects of the R-isomer of warfarin, so warfarin levels should be continuously monitored.

Absorption of drugs dependent on low gastric pH, such as the imidazole antifungals (itraconazole, ketoconazole), ampicillin esters, and iron may be affected by the profound acid suppression effects of Omeprazole.

Phenytoin elimination may be prolonged in patients taking Omeprazole, and the levels and effects of Omeprazole maybe decreased in these same patients.

Since Omeprazole is metabolized by the Cytochrome P450 (CYP) enzyme system, levels of benzodiazepines that are metabolized by oxidation within the Cytochrome P450 system (diazepam, midazolam, triazolam) become increased.

Guidelines/ precautions – Omeprazole should be used with caution in lactating women.

Dosage and administration – Omeprazole is available as either a 10mg or 20mg oral capsule, and in 40 mg vials. Vials must be reconstituted in 100ml of normal saline or D_5W and infused over 30 minutes.

For GERD:

Children < 2 years – 10mg once daily

Children ≥ 2 years – 20mg once daily

Adults – 20 mg/day for up to 4 weeks (Anesthesia providers may consider a one-time dosage as part of their preoperative treatment regimen for patients with GERD)

For patients with an indwelling patent nasogastric tube who are unable to swallow the medication, capsules may be opened and flushed with water into the stomach.

Onset – Omeprazole 20mg by mouth has a gastric acid antisecretory onset within 2-6 hours. Preoperative administration of Omeprazole should be >3 hours before the time of induction of anesthesia. Omeprazole administered intravenously has a gastric acid antisecretory effects within 3 minutes to > 2hours, and can be used to maintain plasma levels of the drug necessary for the treatment of bleeding gastric or duodenal ulcers.[58]

Duration – Despite the short half-life of Omeprazole, its affects may be >24 hours due to its concentration within the acidic environment of the gastric parietal cells, and its acid-inhibitory effects increase with repeated dosing.

III. Summary of Key Points and Anesthesia Implications

Respiration is the dominant function of the nose, the mouth and pharynx. The swallowing pathway shares a parallel conduit with the respiratory pathway with both voluntary and involuntary protective mechanisms to protect the respiratory pathway. Coughing and the pharyngeal reflex (gagging) are two quick and strong protective mechanisms. Coughing forcefully and explosively expels foreign matter from the respiratory pathway, while the pharyngeal reflex blocks the respiratory pathway and allows pharyngeal and/or gastric contents to be forcefully expelled. The body's protective mechanisms can become ineffective or fail by the depression of protective reflexes, the alteration or deviation of normal anatomic structures, and by iatrogenic disorders.

Aspiration pneumonitis is the inflow of a critical volume of highly acidic gastric contents, which triggers a severe inflammatory reaction along and produces injurious histological effects to the trachea, bronchioles, lung tissue, and the pulmonary capillary endothelium.

The anesthetist has tools available to assess the patient's probable risks of developing aspiration pneumonitis, and can utilize both physical and pharmaceutical methods to prevent this catastrophic event from occurring.

IV. Conclusions

1. Legal considerations –

Code 1.2 oft the American Association of Nurse Anesthetists Code of Ethics for the Certified Registered Nurse Anesthetist in, **"Responsibility to Patients"** states: The CRNA protects the patient from harm and is an advocate for the patient's welfare.[44] This statement states a duty for CRNAs to diligently guard for the safety and well-being of the patient at all times, especially to those patients with a potential to develop aspiration pneumonitis.

A duty of care is a requirement that a person act toward others and the public with the watchfulness, attention, caution, and prudence that a reasonable person in the circumstances would use. If a person's actions do not meet this standard of care, then the acts are considered negligent, and any damages resulting may be claimed in a lawsuit for negligence.[59]

Negligence is a failure to exercise care toward others (our patients), which a reasonable or prudent person would do in similar circumstances, or by taking action, which such a reasonable person would not. Negligence is one of the greatest sources of litigation.

In order for negligence to be a claim for damages, the injured party (plaintiff) must prove three things:

a) The party alleged to be negligent had a duty to the injured party, specifically to the one injured or to the general public.

b) The defendant's action (or failure to act) was negligent: not what a reasonably prudent person would have done.

c) The damages were caused ("proximately caused") by the negligence.

An added factor in the formula for determining negligence is whether the damages were "reasonably foreseeable" at the time of the alleged carelessness. If the injury is caused by neglect of common standards of care, negligence can be found based on the doctrine of res ipsa loquitor (Latin for "the thing speaks for itself").[60]

While we have discussed physical and pharmaceutical methods used for the prevention of Aspiration Pneumonitis (see Table 5), no guarantee can be afforded the CRNA that Aspiration Pneumonitis will be averted by the use of the materials and methods discussed. But if the CRNA acts *with the watchfulness, attention, caution, and prudence that a reasonable person in the circumstances would use*, the plaintiff could have a difficult time claiming damages.[61]

2. Closed Claim Studies for Aspiration Pneumonitis

With the advent of physical methods, pharmaceutical methods, and well-taught protocols commonly used for the prevention of aspiration pneumonitis, it is helpful to put aspiration pneumonitis into perspective by studying malpractice claims pertaining to the occurrence of aspiration and for respiratory events from the most recent malpractice closed-claim data.

The American Society of Anesthesiologists (ASA) studies closed anesthesia malpractice claims data from 35 insurance companies, representing 14,500

anesthesiologists. Most malpractice claims arise from death (22%), nerve injury (21%), and brain damage (7%).[62]

Aspiration-related malpractice claims have remained a constant 3-3.5% of all respiratory malpractice claims from the 1970's to the 1990's and the highest incidence of aspiration malpractice claims was during the induction of a general anesthetic. Damaging respiratory-related events have decreased from 30% to 15% from the 1970's to the 1990's. This led the author to conclude, and for us to realize, that the current practice of treating aspiration pneumonitis is effective, and that the hazard of gastric aspiration is not a major liability hazard.[62,63]

Other conclusions reached from the ASA closed anesthesia malpractice claims were:

1. Obstetric anesthesia malpractice claims were lead by maternal death (19% of claims); headache/pain during anesthesia/back pain/emotional distress (together 49% of all claims).

It is important to note that while 30% of respiratory complications in obstetrics (5% is attributed to aspiration pneumonitis) which lead to maternal injury (difficult intubation, pulmonary aspiration, esophageal intubation, inadequate ventilation/oxygenation, bronchospasm, etc.) was low in leading to malpractice claims.[64]

2. Pediatric anesthesia malpractice claims were lead by cardiovascular events (27%); respiratory events (25%); equipment events (17%: intravenous line placement, airway equipment, warming device burns, electrocautery); and medication-related events (14%: adverse drug reactions, malignant hyperthermia, wrong dose). Pediatric anesthesia

malpractice claim trends are decreasing due to the vast improvements in techniques, medications, monitors, and other adjunctive equipment.[65]

3. Trauma anesthesia malpractice claims show aspiration to be a rare event (2.6% of claims) and that anesthetic care during trauma appears to be adequate.[66]

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VI. Critical Thinking Study Questions

Questions

1. Aspiration pneumonitis is a chronically developed infection of lung tissues.

True or False

2. Aspiration pneumonitis can develop because of all but one of the following:

a. A diminished cough reflex.

b. Reduced lower esophageal sphincter tone.

c. Inadequate reversal of neuromuscular blockade.

d. Gastric pH $\geq$ 2.5

3. The certified nurse anesthetist may anticipate the likelihood of aspiration pneumonitis

by the preoperative assessment of all but one of the following physical findings:

a. Fasting for > 6 hours.

b. An obtunded motorcycle injury patient.

c. Awake patient with reflexes intact.

d. An obstetric patient.

4. Which of the following pharmaceutical types is not currently recommended as a first

line medication for the prevention of aspiration pneumonitis?

a. Proton pump (hydrogen ion) inhibitors

b. Histamine (H_2) receptor antagonists

c. Antiemetics

d. Alkalizers (systemic)

5. Aspiration pneumonitis and respiratory claims are the major cause for anesthesia-related malpractice claims.

a. True

b. False

Answers and Discussion

1. False

Aspiration pneumonitis is an acute direct chemical injury to lung tissues caused by the aspiration of highly acidic gastric contents, while aspiration pneumonia is an infectious process caused by the continual aspiration of secretions containing pathogenic oropharyngeal bacteria.

2. d. The pH of gastric contents is typically 1-2. Aspiration pneumonitis is most damaging with aspirated gastric contents of a $pH \leq 2.5$ with a critical gastric fluid volume of 0.3ml/kg or greater.

3.c. An awake patient with reflexes intact on assessment will have the least chance of developing aspiration pneumonitis. Consideration should be made for alternatives to general anesthesia, as many different factors could increase chances for aspiration. Also, fasting for > 6 hours does not guarantee empty stomach contents.

4. a. Proton pump inhibitors are not currently routinely used as a first line pharmaceutical for the preoperative treatment of aspiration pneumonitis. The proton pump inhibitors are used in the treatment of gastroesophageal reflux disease, duodenal and peptic ulcers, and for other ulcerative diseases. These medications should be used concurrently with other pharmaceuticals used for the preoperative prevention of aspiration pneumonitis.

5. Current practices for the treatment and prevention of aspiration pneumonitis are effective, and that the hazard of gastric aspiration is not a major liability hazard. Aspiration-related malpractice claims have remained constant at 3-3.5% of all respiratory malpractice claims from the 1970's to the 1990's as practitioners are acutely aware of both the dire consequences to the patient who aspirates, and aspiration pneumonitis prevention protocols.