Chapter 20
A Minor Hiccup: Singultus, Regurgitation, and Aspiration Under Anesthesia

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Case Presentation

A 46-year-old male (weight 97 kg, height 6′1″, BMI 29) was scheduled for an outpatient right inguinal hernia repair. The patient had no significant past medical history or allergies. His surgical history consisted of a previous right inguinal hernia repair at 6 months of age. Induction of anesthesia proceeded with 150 mcg IV fentanyl, 100 mg IV lidocaine, and 200 mg IV propofol in anticipation of placement of a laryngeal mask airway (LMA). Once the patient was apneic, he began to have hiccups which made laryngeal mask airway placement and ventilation via mask difficult **(Lesson I)**.

The patient then regurgitated clear secretions into his oropharynx **(Lesson II)**. The anesthesiologist turned the head to the right side to suction the oropharynx, deepened anesthesia with 100 mg IV propofol, and paralyzed the patient with 150 mg IV succinylcholine to prepare for endotracheal intubation. The patient regurgitated clear secretions a second time, and the airway was suctioned for a second time. Ventilation via mask was possible at this point. The anesthesiologist performed direct laryngoscopy with cricoid pressure and intubated the patient uneventfully with an 8.0 mm endotracheal tube. A suction catheter was placed through the endotracheal tube, and an orogastric tube was placed in the stomach with no significant return of material through either conduit **(Lesson III)**. The lungs were clear to auscultation bilaterally, and breath sounds were equal throughout the lung fields. During the 70 min case, the patient's oxygen saturation ranged from

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97% to 100% on 50% FiO2. At the end of the case, the anesthesiologist extubated the patient fully awake. During the patient's 3 h postoperative care unit (PACU) stay, his oxygen saturation was 94–97% on 2 L/min nasal cannula which was eventually weaned to room air. The patient had no apparent respiratory distress and was discharged home in stable condition.

On postoperative day 1, the patient came to the emergency department with wheezing, a productive cough with thick brownish-colored sputum, and a fever to 103 °F. Physical exam revealed wheezing and crackles on the right side which correlated with a right middle lobe consolidation on chest radiograph **(Lesson IV)**. The patient was admitted to the hospital for a course of intravenous antibiotics to treat aspiration pneumonia. He was discharged home with oral antibiotics on hospital day 3 after he had been afebrile for 48 h with improvement of his wheezing and cough.

Lesson I: Hiccups Under Anesthesia

Lesson IA: What Is the Definition of a Hiccup?

A hiccup (singultus) is an episodic spasm of the diaphragm and intercostal muscles followed by closure of the vocal cords. During a hiccup, the diaphragm contracts and flattens, and the external intercostal muscles contract, simulating a forceful inspiration [1]. Thirty-five milliseconds after spasm of the respiratory muscles, the vocal cords close suddenly preventing the movement of air into the lungs [2]. The closure of the vocal cords is what creates the characteristic sound of a hiccup [3].

Lesson IB: What Causes Hiccups Under Anesthesia?

Hiccups can occur for many reasons related to anesthesia and surgery. Causes related to anesthesia include gastric distention (i.e., from ventilation via mask) and side effects from induction agents such as propofol [2, 4]. A few case reports have suggested that epidural anesthesia with long-acting local anesthetics such as bupivacaine and ropivacaine can cause hiccups in a dose-dependent manner. This effect could be due to alterations in gastrointestinal, diaphragmatic, or abdominal wall innervation and reflexes [5, 6]. Hiccups appear to occur more frequently in certain types of surgical procedures such as those with direct manipulation of the diaphragm, gastrointestinal surgery, and respiratory procedures such as bronchoscopy and tracheostomy [1]. Another rare but important cause of hiccups is phrenic nerve irritation along its course. Atrial pacing, ablation procedures for atrial fibrillation, and placement of central venous catheters have been reported to cause hiccups due to the anatomical proximity of the right atrium to the right branch of the phrenic nerve [7–9].

Lesson IC: What Is the Reflex Pathway That Causes Hiccups?

Regardless of the triggering event, the common pathway for hiccups is a reflex that is incompletely understood. This reflex consists of afferent input from the vagus nerve, phrenic nerve, and sympathetic fibers from T6 to T12. These afferents synapse in the cervical spinal cord at C3-C5 and in the brainstem (likely at the medulla). The efferent output of the reflex is from the phrenic nerve to the diaphragm and respiratory muscles (Fig. 20.1) [1, 2, 10–12]. Neurotransmitters involved in this process include gamma-aminobutyric acid (GABA) and dopamine [3, 13].

Lesson ID: What Are the Treatments for Hiccups Under Anesthesia?

Hiccups are generally self-limited, but treatment may be needed if vocal cord closure or patient movement is preventing a procedure from proceeding. Support for most treatments is largely empirical rather than evidence-based. Therapies are primarily aimed at blocking the reflex discussed above at the level of the gastrointestinal (GI) triggers, respiratory muscles, autonomic nervous system, or neurotransmitters.

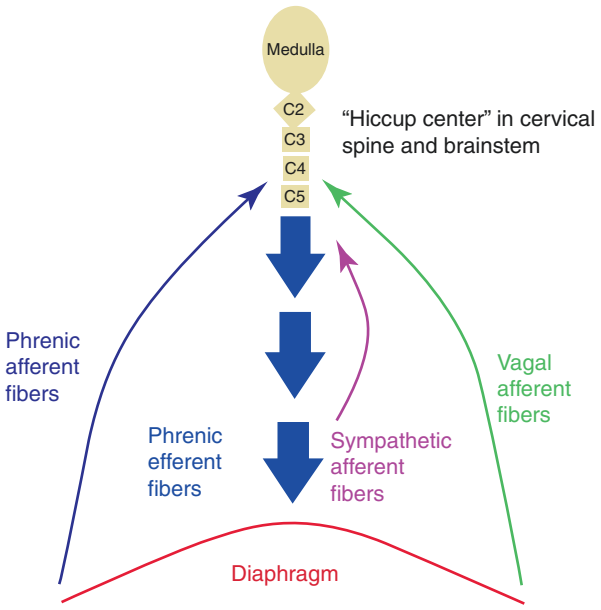

Fig. 20.1 A schematic of the contributions to the reflex arc of a hiccup

Many diverse pharmacological interventions can be used to treat hiccups. To attenuate GI triggers for hiccups such as gastric distention and GI reflux, prokinetic agents such as metoclopramide (Reglan) and proton pump inhibitors (omeprazole) can be used [2, 13]. Neuromuscular blockade is one way to attenuate respiratory muscle and vocal cord movement from hiccups in an anesthetized patient [10]. Baclofen may have an antispasmodic effect on respiratory muscles. Furthermore, baclofen and gabapentin are GABA agonists that may inhibit vagal impulses in the hiccup reflex [14, 15]. Dopaminergic antagonists such as chlorpromazine (Thorazine), the only FDA-approved treatment for hiccups, may also act on brainstem modulation of the hiccup reflex. The suggested dose of Thorazine for this purpose is 25–50 mg IV or IM. Other antidopaminergic agents such as prochlorperazine (Compazine) and droperidol (Inapsine) have been used to treat hiccups in the dosages used for postoperative nausea and vomiting [2]. Medications that inhibit and overcome afferent vagal impulses of the hiccup reflex include sympathomimetic agents such as ketamine and ephedrine and local anesthetics such as lidocaine that may anesthetize vagal afferents [10].

There are also nonpharmacological treatments for hiccups. Airway irritants such as smelling salts or nasopharyngeal stimulation may interrupt vagal afferents in the hiccup reflex [10, 16]. Increased arterial $PaCO_2$ has been shown to decrease the frequency of hiccups which may explain why breath holding may stop hiccups [1, 12]. Breath holding can be simulated under anesthesia with mild hypoventilation, sigh breaths, and continuous positive airway pressure (CPAP). These actions may also stop hiccups by breaking diaphragmatic spasm and restoring phrenic nervous rhythms [1, 2]. The efficacy of blocking vagal afferents may also explain the utility of acupuncture and phrenic nerve blockade for persistent hiccups [1, 10] (Table 20.1).

Table 20.1 Summary of treatment options for hiccups

Acute pharmacologic	*Acute nonpharmacologic*
Muscle relaxants	Nasopharyngeal stimulation
Prokinetic agents: metoclopramide (Reglan)	Mild hypoventilation
Proton pump inhibitors (omeprazole)	Sigh breaths
Antidopaminergic agents: chlorpromazine, prochlorperazine, droperidol	Continuous positive airway pressure (CPAP)
	Chronic therapy for refractory hiccups
	Acupuncture
Sympathomimetic agents: ketamine, ephedrine	Phrenic nerve block
IV or nebulized lidocaine	GABA agonists: baclofen, gabapentin
Smelling salts (ammonium chloride)	

Lesson II: Regurgitation

Lesson IIA: What Determines Whether Regurgitation Will Occur?

Regurgitation is the backward, passive expulsion of ingested material or secretions into the oropharynx from the stomach or esophagus [17]. Because regurgitation is a passive process, the movement of material relies primarily on pressure gradients. The three barriers to regurgitation are the following: (1) the lower esophageal sphincter (LES), (2) the upper esophageal sphincter (UES), and (3) the protective laryngeal reflexes [18].

Lesson IIB: Why Are Patients Prone to Regurgitation Under General Anesthesia?

The LES spans the diaphragm and separates the stomach from the esophagus. The tendency to regurgitate from the stomach to the esophagus depends primarily on the barrier pressure, the pressure gradient between the intragastric pressure (normally 5 mm Hg) and the LES pressure (normally 10–25 mm Hg) (Fig. 20.2) [10, 17]. A lower barrier pressure predisposes to regurgitation by creating a gradient favorable for movement of material from the stomach to the esophagus [10]. A typical anesthetic with opioids, muscle relaxants, and inhaled anesthetics decreases lower esophageal sphincter pressure and therefore decreases the barrier pressure [19]. Furthermore, cricoid pressure and laryngeal mask airways (LMAs) seem to reflexively decrease LES and barrier pressure. LMAs, but not cricoid pressure, also appear to increase reflux of materials from the stomach though this is not significant at the level of the upper esophagus unless the patient is placed in lithotomy position [20–22].

The tendency to regurgitate from the esophagus to the hypopharynx is related to the UES. The UES is a band of the cricopharyngeus muscle at the level of the cricoid cartilage that is continuous with the upper esophagus [18]. Most inhaled and intravenous anesthetic techniques, with the notable exception of ketamine, decrease the UES tone from approximately 40 mm Hg to less than 10 mm Hg [23, 24].

Airway reflexesare the final barrier to protect the lungs from aspiration of regurgitated substances. The four protective airway reflexes are (1) apnea with laryngospasm or closure of both the true and false vocal cords, (2) coughing during which a prolonged and forceful expiration follows a brief rapid flow inspiration, (3) sudden isolated expiration with opening of the false vocal cords, and (4) spasmodic panting or shallow breathing with rapid glottic opening and closing [18]. Patients

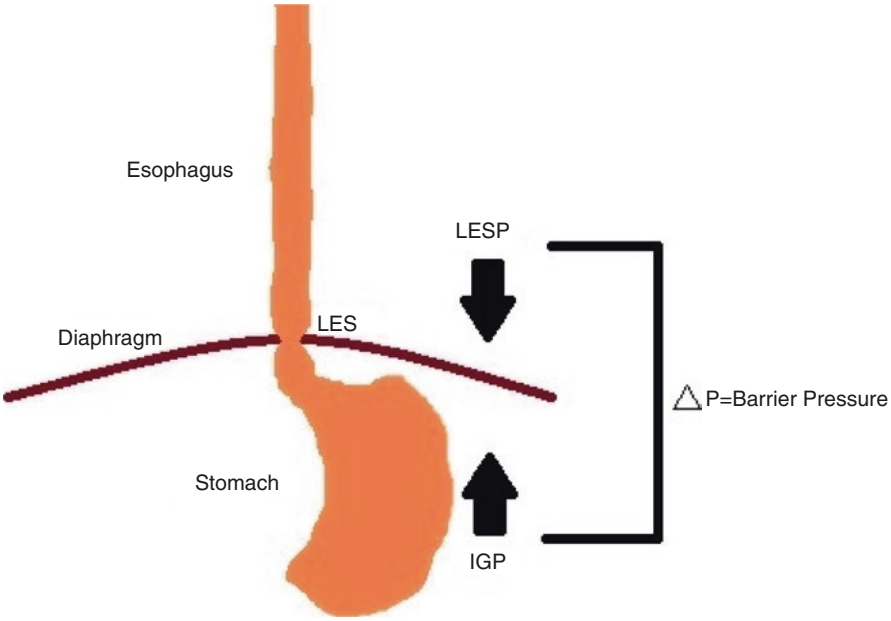

Fig. 20.2 An illustration of barrier pressure, the difference between the lower esophageal sphincter pressure and the intragastric pressure. LES lower esophageal sphincter, LESP lower esophageal sphincter pressure, IGP intragastric pressure

can have depressed airway reflexes preoperatively due to depressed levels of consciousness, advanced age, and premedication. Inhaled and intravenous general anesthetics also significantly diminish these reflexes both intraoperatively and postoperatively even after other measures of recovery are met [25–27].

Lesson III: Aspiration

Lesson IIIA: What Are Preoperative Risk Factors for Regurgitation and Aspiration?

The main risk factors for regurgitation are increased gastric volume, altered LES tone or anatomy, and loss of protective laryngeal reflexes. Increased gastric volume can arise from delayed gastric emptying which occurs during pregnancy (especially labor), autonomic dysfunction from diabetes mellitus, and conditions that cause peristaltic abnormalities of the gastrointestinal tract (i.e., obstruction, infection, or increased sympathetic tone). Clinical conditions with reduced LES tone include pregnancy and gastroesophageal reflux (GERD). The functionality of the LES may also be altered by anatomical displacement above the diaphragm in pregnancy, obesity, and the presence of a hiatal hernia [10]. Loss of protective laryngeal reflexes occurs from trauma, depressed consciousness, and premedication [18].

Lesson IIIB: How Can One Decrease the Possibility of Regurgitation and Subsequent Aspiration in Patients Who Are at Risk?

An anesthesiologist can decrease the possibility of regurgitation in a patient who is at risk by attempting to reduce the patient's gastric volume and maintain LES tone. The severity of pulmonary damage caused by aspirated gastric contents can also be reduced by increasing the pH of gastric contents (making them less acidic). The ways to accomplish these goals include nil per os (NPO) guidelines, mechanically decompressing the stomach, and specific pharmacologic agents [10, 18, 28].

The two nonpharmacological ways to decrease gastric volume are NPO guidelines and tube decompression of the stomach. NPO guidelines give recommendations regarding the duration of patient fasting for various liquids and solids prior to surgery (Table 20.2) [28]. If NPO guidelines must be by passed and the patient has clear evidence of severely overfilled gastrum (i.e., bowel obstruction, recent oral contrast ingestion), it is advisable to place an 18 French nasogastric (NG) tube and thoroughly suction gastric contents through the tube prior to induction of anesthesia to reduce the risk of aspiration (see Table 20.3). Placement of an NG tube may be complicated by patient discomfort and bleeding from the nasal mucosa. Patient discomfort can be overcome with 4% lidocaine spray to the oropharynx, lidocaine-soaked pledgets into the nare, and serial dilation of the nasal passageway with nasopharyngeal airways of increasing size coated in 5% lidocaine ointment. Bleeding can be avoided by spraying oxymetazoline (Afrin) into the nare. The NG tube should be removed prior to induction of anesthesia to prevent difficulty with preoxygenation and mask ventilation due to the NG tube breaking the seal between the mask and the patient's face. Furthermore, material can travel backward along the sides of the NG tube from the stomach to the oropharynx once the patient is under general anesthesia ("wick effect"). Finally, the NG tube may decrease the efficacy of cricoid pressure. After removal of the NG tube prior to the induction of general anesthesia (for all of the above reasons), a rapid sequence induction (RSI) should still be performed in this setting [29].

Pharmacologic aspiration prophylaxis is not routinely recommended unless a patient has one or more of the regurgitation and aspiration risk factors described

Table 20.2 Summary of NPO guidelines from the American Society of Anesthesiologists [28]

Ingested material	Interval of fasting prior to elective procedure	Additional comments
Clear liquids	2 h	Excludes alcohol
Human breast milk	4 h	
Nonhuman infant formula	6 h	Low-fat or low-protein foods
Light meal		
Heavy meal	8 h	Fatty or fried foods

Table 20.3 Placement of nasogastric tube in an awake patient prior to the induction of general anesthesia in a patient at high risk for aspiration due to full stomach

Positive consideration	Negative considerations	
Greatly reduce the risk of aspiration of high volume of gastric contents during the induction of general anesthesia	*Specific negative consideration*	*Solution to negative consideration*
	Noxious stimulus	1. Spray nare with lidocaine
		2. Place series of soft nasopharyngeal airways lubricated with lidocaine ointment
		3. Spray posterior oropharynx with lidocaine
	May cause nose bleed	Spray oxymetazoline (Afrin) into nare
	May decrease effective preoxygenation by mask	After thoroughly suctioning gastric contents through NGT, remove the NGT prior to the induction of general anesthesia
	May decrease effective ventilation by mask if needed	
	May decrease effectiveness of cricoid pressure	
	"Wick effect"	
	Still need to perform RSI	Risk of aspiration prior to securing airway has been reduced

above [28]. Pharmacologic options include prokinetic agents (metoclopramide or Reglan), histamine antagonists (H2Bs, ranitidine or Pepcid), proton pump inhibitors (PPIs, omeprazole or Prilosec), and nonparticulate antacids (sodium citrate or Bicitra). Metoclopramide (Reglan) reduces gastric volume via a prokinetic effect mediated by muscarinic agonism, dopaminergic antagonism, and serotonergic antagonism. H2Bs and PPIs decrease gastric volume and increase gastric pH at the level of the parietal cells in the stomach, via histamine receptors and H+/K+ ATPases, respectively. H2Bs work within a few hours of administration, while PPIs should be given in two successive doses starting the night before surgery. Nonparticulate antacids such as sodium citrate (Bicitra) neutralize stomach acid immediately but may slightly increase gastric volume. Antacids and Reglan have also been shown to increase LES tone [18]. There is limited evidence that combining multiple agents increases their efficacy [18, 28]. A summary of aspiration risk reduction can be seen in Fig. 20.3.

The interventions in Fig. 20.3 are listed in the American Society for Anesthesiologists (ASA) "Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration." It is important to note that these guidelines are based largely on expert opinion rather than randomized controlled trials. Furthermore, while the available scientific evidence

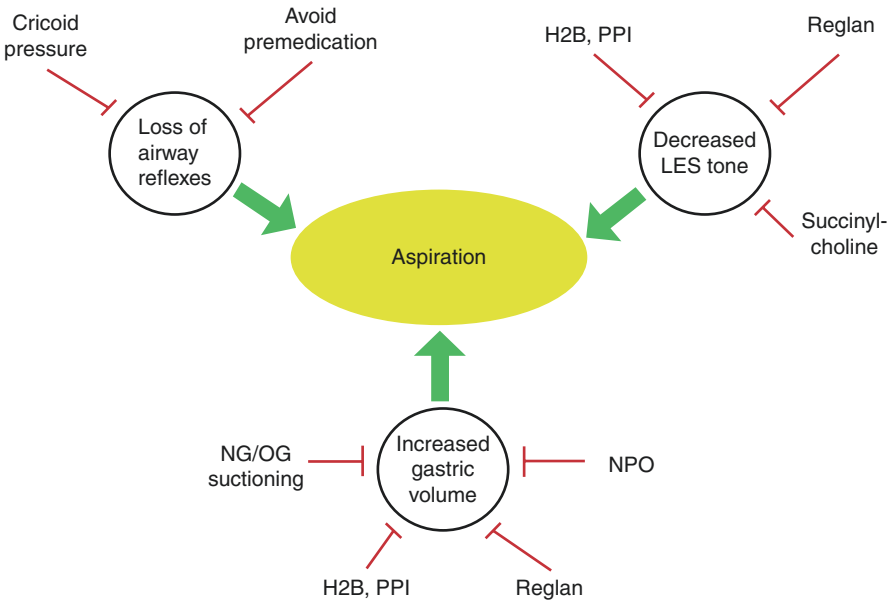

Fig. 20.3 Risk factors for regurgitation and aspiration are indicated by green arrows, and prophylactic measures for each risk factor are indicated with red flathead arrows. H2B H2 blocker, PPI proton pump inhibitor, NPO nil per os, NG/OG nasogastric/orogastric

shows decreased gastric volumes and increased gastric pH when NPO guidelines and appropriate pharmacologic prophylaxis are used, there is inadequate evidence to address the relationship between these measures and the risk of perioperative aspiration into the lungs [28].

Lesson IIIC: What Is an Appropriate Action Plan to Manage a Witnessed Aspiration Event?

The immediate treatment of witnessed or suspected aspiration in an anesthetized patient includes turning the patient's head to the right side, suctioning the oropharynx, and tracheal intubation with a cuffed endotracheal tube. As soon as tube placement is confirmed with end- tidal carbon dioxide (EtCO2), the trachea should be suctioned through the endotracheal tube with a 14 French soft suction catheter. It is highly desirable to examine the tracheobronchial tree with a fiber-optic bronchoscope following a known or suspected aspiration and perform localized, small volume saline lavage and suctioning of the inhaled gastric contents under the control of an appropriately sized fiber-optic bronchoscope. Blind

saline lavage of the airway is never recommended. Alkali lavage of the tracheobronchial tree is also not recommended because the toxic effect of gastric aspirate on the airways is immediate [30].

Disposition of a patient who aspirates gastric contents before or during anesthesia depends on the patient's level of clinical stability. A patient with compromised oxygenation or cardiovascular instability after aspiration should remain intubated and be admitted to the intensive care unit (ICU) for observation, pulmonary toilet, and repeated fiber-optic examinations. Occasionally, aspiration can lead to pneumonia, acute respiration distress syndrome (ARDS), multi-organ failure, sepsis, and death [31]. A stable patient can be extubated after anesthesia provided the patient is observed for 4–6 h after extubation for the development of cough, wheezing, and hypoxemia. Outpatient follow-up may be appropriate if none of these symptoms develop and the patient is given explicit instructions to return to a medical facility if symptoms of pneumonia arise. Inpatient monitoring may be needed after extubation if the likelihood of severe aspiration is high or the patient has significant comorbidities such as preexisting lung disease. Treatment of aspiration with corticosteroids is not helpful and may increase the risk of bacterial infection. Prophylactic treatment with antibiotics is not indicated because not all aspiration results in pneumonia and unnecessary antibiotics may facilitate the colonization of resistant organisms [30].

Lesson IV: Aspiration Pneumonia

Lesson IVA: How Do You Diagnose and Treat Aspiration Pneumonia?

Bacterial pneumonia can develop after aspiration due to the transference of nasopharyngeal, oropharyngeal, and gastrointestinal bacteria into the airways. Aspiration pneumonia usually has a rather indolent course because the causative agents are oral anaerobes and streptococci which are less virulent than the bacteria that cause other types of pneumonia. The onset of symptoms of pneumonia such as fever and productive cough after aspiration is typically days to weeks. The presence of purulent or malodorous sputum is regarded as diagnostic of anaerobic infection [32]. The treatment for aspiration pneumonia is a 7–10 day course of antibiotics. Regimens include clindamycin, amoxicillin-clavulanate, or a penicillin plus metronidazole (Flagyl) for 7–10 days [33–35]. While this clinical course is common in mild to moderate aspiration in a healthy patient, occasionally, aspiration pneumonia can be severe and lead to ARDS, sepsis, and death as mentioned above.

The differential diagnosis for postoperative aspiration pneumonia includes chemical pneumonitis and atelectasis. Chemical pneumonitis occurs when bile and stomach acid cause an acute (within 2 h) inflammatory process in lungs that leads to hypoxemia and respiratory distress. Clinical recovery from pneumonitis occurs in 24–36 h of aspiration [31, 36]. Atelectasis, or collapse of the lung parenchyma,

occurs during almost all inhaled and intravenous anesthetics due to compression of lung tissue by altered chest wall and diaphragm mechanics, slower rate of gas entry into the alveolus than absorption of gas into the blood, and altered surfactant function. While atelectasis from surgery improves within 24 h, it can be a significant cause of hypoxemia and even mild fever [37]. The treatment for both pneumonitis and atelectasis is supportive care of pulmonary function (deep breathing, coughing, noninvasive positive pressure ventilation) unless there is progression of symptoms or development of superimposed pneumonia.

While all of the above diagnoses cause hypoxemia and respiratory distress, aspiration pneumonia can be differentiated from pneumonitis and atelectasis by its clinical progression with high fevers, elevated white blood cell count, and purulent sputum. However, these symptoms may take days to develop after aspiration. A chest radiograph may be diagnostically useful to differentiate early pneumonia from atelectasis due to differences in their pathophysiology (Fig. 20.4). Generally, chest radiograph from aspiration shows bilateral air space opacification without volume loss. Opacification from atelectasis is often accompanied by signs of volume loss including diaphragm elevation and displacement of ribs, fissures, or mediastinal structures toward the area of collapse [38].

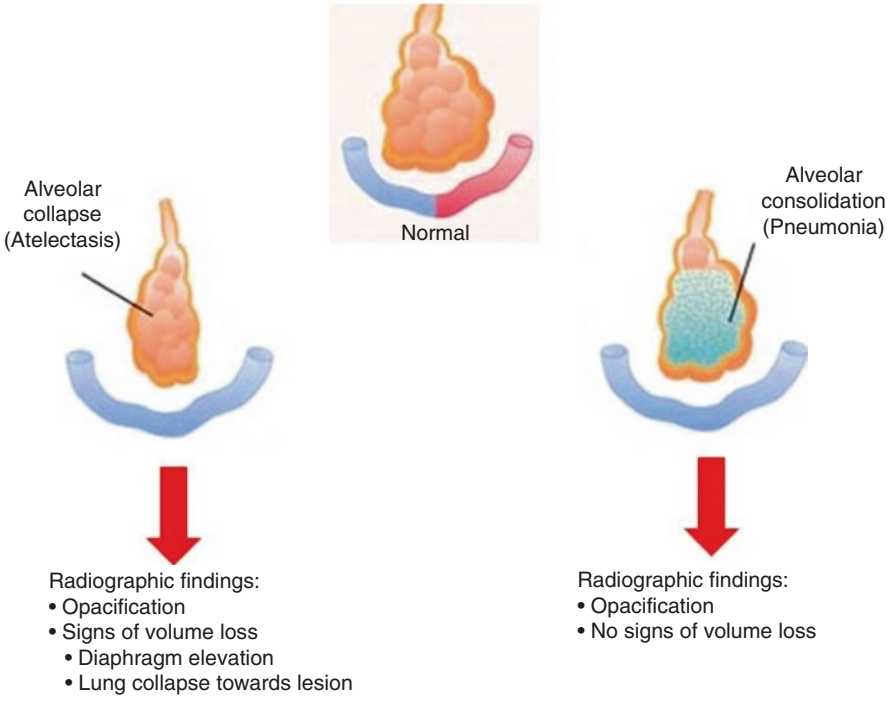

Fig. 20.4 Illustration of how atelectasis and pneumonia differ at the level of the alveoli which creates the differences apparent on chest radiography

Summary of Key Teaching Points

- A hiccup is an episodic spasm of the diaphragm followed by vocal cord closure that is caused by activation of a reflex involving phrenic and vagal afferents, integration in the spinal cord and brainstem, and phrenic efferents.
- Hiccups can be caused by a number of anesthetic and surgical factors, and the treatment of hiccups under anesthesia includes dopamine antagonists, muscle paralysis, prokinetic agents, breath holding, and maneuvers to inhibit vagal impulses.
- Regurgitation under anesthesia occurs when the development of a favorable pressure gradient allows gastric contents to move backward by overcoming the lower esophageal sphincter, the upper esophageal sphincter, and the protective airway reflexes.
- Risk factors for regurgitation and aspiration include increased gastric volume, decreased LES tone, and loss of protective airway reflexes. NPO guidelines, awake NG tube gastric emptying, and appropriate pharmacologic prophylaxis are measures for risk reduction.
- Witnessed or suspected aspiration under anesthesia should be treated with right lateral head positioning, oral suctioning, and endotracheal intubation. Tracheal lavage, corticosteroids, and prophylactic antibiotics are not indicated.
- The differential diagnosis for hypoxemia and respiratory distress after aspiration is chemical pneumonitis, atelectasis, and aspiration pneumonia. These can be distinguished by clinical course and radiological findings.
- On chest radiography, aspiration pneumonia will show infiltrates but no volume loss, while atelectasis will show infiltrates with evidence of volume loss.

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