Primary Care

Aspiration Pneumonitis and Aspiration Pneumonia

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Aspiration is defined as the inhalation of oropharyngeal or gastric contents into the larynx and lower respiratory tract.[1,2] Several pulmonary syndromes may occur after aspiration, depending on the amount and nature of the aspirated material, the frequency of aspiration, and the host's response to the aspirated material.[2] Aspiration pneumonitis (Mendelson's syndrome) is a chemical injury caused by the inhalation of sterile gastric contents, whereas aspiration pneumonia is an infectious process caused by the inhalation of oropharyngeal secretions that are colonized by pathogenic bacteria. Although there is some overlap between these syndromes, they are distinct clinical entities (Table 1). Other aspiration syndromes include airway obstruction, lung abscess, exogenous lipoid pneumonia, chronic interstitial fibrosis, and *Mycobacterium fortuitum* pneumonia.[1,2] This article focuses on the pathophysiology, clinical features, and management of aspiration pneumonia and aspiration pneumonitis.

Pulmonary aspiration is an important cause of serious illness and death among residents of nursing homes as well as hospitalized patients.[1-4] However, the major pulmonary-aspiration syndromes are frequently misdiagnosed and poorly treated. Four common problems are the failure to distinguish aspiration pneumonitis from aspiration pneumonia, the tendency to consider all pulmonary complications of aspiration to be infectious, the failure to recognize the spectrum of pathogens in patients with infectious complications, and the misconception that aspiration must be witnessed for it to be diagnosed.

Epidemiology

The lack of specific and sensitive markers of aspiration complicates the epidemiologic study of aspiration syndromes. Furthermore, most studies do not distinguish between aspiration pneumonitis and aspiration pneumonia. Nevertheless, several studies indicate that 5 to 15 percent of cases of community-acquired pneumonia are aspiration pneumonia.[5-7] Aspiration pneumonia is the most common cause of death in patients with dysphagia due to neurologic disorders, a condition that affects approximately 300,000 to 600,000 people each year in the United States.[8-10] Aspiration pneumonia is also common among residents of nursing homes. In one study of patients with nursing home–acquired pneumonia and controls with community-acquired pneumonia, the incidence of aspiration pneumonia was 18 percent and 5 percent, respectively.[4]

Aspiration pneumonitis occurs in approximately 10 percent of patients who are hospitalized after a drug overdose.[11,12] It is also a recognized complication of general anesthesia, occurring in approximately 1 of 3000 operations in which anesthesia is administered and accounting for 10 to 30 percent of all deaths associated with anesthesia.[13,14]

Aspiration Pneumonitis

Aspiration pneumonitis is defined as acute lung injury after the inhalation of regurgitated gastric contents. This syndrome occurs in patients who have a marked disturbance of consciousness such as that resulting from a drug overdose, seizures, a massive cerebrovascular accident, or the use of anesthesia. Adnet and Baud demonstrated that the risk of aspiration increases with the degree of unconsciousness (as measured by the Glasgow Coma Scale).[15] Historically, the syndrome most commonly described as aspiration pneumonitis is Mendelson's syndrome, reported in 1946 in patients who aspirated while receiving general anesthesia during obstetrical procedures.[16]

Mendelson revealed the importance of acid in the pathogenesis of this syndrome when he showed that acidic gastric contents introduced into the lungs of rabbits caused severe pneumonitis that was indistinguishable from that caused by an equal amount of 0.1 N hydrochloric acid.[16] Later, it was shown that if the pH of gastric contents was neutralized before aspiration, the pulmonary injury was minimal.[17] In experimental studies, the severity of lung injury increased significantly as the volume of the aspirate increased and as its pH decreased.[17-19] Most authors agree that a pH of less than 2.5 and a volume of gastric aspirate greater than 0.3 ml per kilogram of body weight (20 to 25 ml in adults) are required for the development of aspiration pneumonitis.[16-19] However, the stomach contains a variety of other substances in addition to acid. Aspiration of particulate food matter from the stomach may cause severe pulmonary damage, even if the pH of the aspirate is above 2.5.[20,21]

Aspiration of gastric contents results in a chemical burn of the tracheobronchial tree and pulmonary parenchyma, causing an intense parenchymal inflammatory reaction. A study in rats showed that there is a biphasic pattern of lung injury after acid aspiration.[22] The first phase peaks at one to two hours after aspiration and presumably results from the direct, caustic effect of the low pH of the aspirate on the cells lining the alveolar–capillary interface. The second phase, which peaks at four to six hours, is associated with

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TABLE 1. CONTRASTING FEATURES OF ASPIRATION PNEUMONITIS AND ASPIRATION PNEUMONIA.

FEATURE	ASPIRATION PNEUMONITIS	ASPIRATION PNEUMONIA
Mechanism	Aspiration of sterile gastric contents	Aspiration of colonized oropharyngeal material
Pathophysiologic process	Acute lung injury from acidic and particulate gastric material	Acute pulmonary inflammatory response to bacteria and bacterial products
Bacteriologic findings	Initially sterile, with subsequent bacterial infection possible	Gram-positive cocci, gram-negative rods, and (rarely) anaerobic bacteria
Chief predisposing factors	Markedly depressed level of consciousness	Dysphagia and gastric dysmotility
Age group affected	Any age group, but usually young persons	Usually elderly persons
Aspiration event	May be witnessed	Usually not witnessed
Typical presentation	Patient with a history of a depressed level of consciousness in whom a pulmonary infiltrate and respiratory symptoms develop	Institutionalized patient with dysphagia in whom clinical features of pneumonia and an infiltrate in a dependent bronchopulmonary segment develop
Clinical features	No symptoms or symptoms ranging from a nonproductive cough to tachypnea, bronchospasm, bloody or frothy sputum, and respiratory distress 2 to 5 hours after aspiration	Tachypnea, cough, and signs of pneumonia

infiltration of neutrophils into the alveoli and lung interstitium, with histologic findings characteristic of acute inflammation. The mechanisms of the lung injury after gastric aspiration involve a spectrum of inflammatory mediators, inflammatory cells, adhesion molecules, and enzymes, including tumor necrosis factor α, interleukin-8, cyclooxygenase and lipoxygenase products, and reactive oxygen species.[23-27] However, neutrophils and complement appear to have a key role in the development of lung injury. In studies in animals, neutropenia, inhibition of neutrophil function, inactivation of interleukin-8 (a potent neutrophil chemoattractant), and complement inactivation attenuated the acute lung injury induced by acid aspiration.[24,28,29]

Because gastric acid prevents the growth of bacteria, the contents of the stomach are sterile under normal conditions. Bacterial infection therefore does not have an important role in the early stages of acute lung injury after the aspiration of gastric contents. Bacterial infection may occur at a later stage of lung injury, but the incidence of this complication is unknown. Colonization of the gastric contents by potentially pathogenic organisms may occur when the pH in the stomach is increased by the use of antacids, histamine H_2–receptor antagonists, or proton-pump inhibitors.[30,31] In addition, there may be gastric colonization by gram-negative bacteria in patients who receive enteral feedings as well as in patients with gastroparesis or small-bowel obstruction.[32-34] In these circumstances, the inflammatory response in the lungs probably results both from bacterial infection and from the inflammatory response to the particulate gastric matter.

Patients who have aspirated gastric material may present with dramatic signs and symptoms. There may be gastric material in the oropharynx as well as wheezing, coughing, shortness of breath, cyanosis, pulmonary edema, hypotension, and hypoxemia, with rapid progression to severe acute respiratory distress syndrome and death.[35] However, many patients have only a cough or a wheeze, and some patients have what is commonly referred to as silent aspiration, which manifests only as arterial desaturation with radiologic evidence of aspiration. Warner and colleagues studied 67 patients who aspirated while undergoing anesthesia.[14] Forty-two (63 percent) of these patients had no symptoms. Of the 25 who had symptoms, 13 required mechanical ventilatory support for more than six hours, and 4 died.

ASPIRATION PNEUMONIA

Aspiration pneumonia develops after the inhalation of colonized oropharyngeal material. Aspiration of colonized secretions from the oropharynx is the primary mechanism by which bacteria gain entrance to the lungs. Indeed, *Haemophilus influenzae* and *Streptococcus pneumoniae* colonize the nasopharynx or oropharynx before they are aspirated and cause community-acquired pneumonia.[36] The term "aspiration pneumonia," however, refers specifically to the development of a radiographically evident infiltrate in patients who are at increased risk for oropharyngeal aspiration.

Approximately half of all healthy adults aspirate small amounts of oropharyngeal secretions during sleep.[37,38] Presumably, the low burden of virulent bacteria in normal pharyngeal secretions, together with forceful coughing, active ciliary transport, and normal humoral and cellular immune mechanisms, results

in clearance of the infectious material without sequelae. However, if these mechanical, humoral, or cellular mechanisms are impaired or if the amount of aspirated material is sufficiently large, pneumonia may follow.

Any condition that increases the volume or bacterial burden of oropharyngeal secretions in a person with impaired defense mechanisms may lead to aspiration pneumonia. Indeed, in patients who have had a stroke and are undergoing an evaluation of swallowing, there is a strong correlation between the volume of the aspirate and the development of pneumonia.[39] Factors that increase the risk of oropharyngeal colonization with potentially pathogenic organisms and that increase the bacterial load may increase the risk of aspiration pneumonia. The risk of aspiration pneumonia is lower in patients without teeth[40] and in elderly patients in institutional settings who receive aggressive oral care[41] than in other patients. These risks largely distinguish aspiration pneumonia from community-acquired pneumonia. However, there is much overlap. For instance, otherwise healthy elderly patients with community-acquired pneumonia have a significantly higher incidence of silent aspiration than age-matched controls.[42]

In patients with aspiration pneumonia, unlike those with aspiration pneumonitis, the episode of aspiration is generally not witnessed. The diagnosis is therefore inferred when a patient at risk for aspiration has radiographic evidence of an infiltrate in a characteristic bronchopulmonary segment. In patients who aspirate while in a recumbent position, the most common sites of involvement are the posterior segments of the upper lobes and the apical segments of the lower lobes (Fig. 1), whereas in patients who aspirate in an upright or semirecumbent position, the basal segments of the lower lobes are usually affected. The usual course is that of an acute pneumonic process, with features similar to those of a typical community-acquired pneumonia. Without treatment, however, these patients have a higher incidence of cavitation and abscess formation in the lungs.[43]

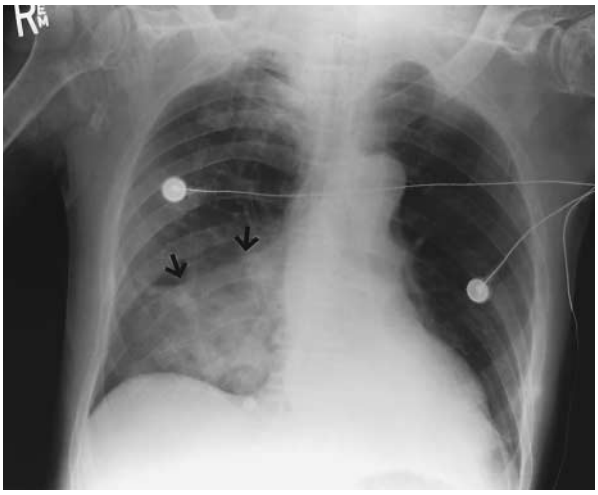

Figure 1. Anteroposterior Radiograph of the Chest, Showing Air-Space Consolidation (Arrows) in the Right Lower Lobe in a Patient Who Had Recently Had a Thrombotic Stroke.

Risk Factors for Oropharyngeal Aspiration

Patients with neurologic dysphagia, disruption of the gastroesophageal junction, or anatomical abnormalities of the upper aerodigestive tract are at increased risk for oropharyngeal aspiration. The risk of aspiration is relatively high in elderly persons because of the increased incidence of dysphagia and gastroesophageal reflux in this population. In addition, elderly persons frequently receive poor oral care, resulting in oropharyngeal colonization by potential respiratory tract pathogens, including Enterobacteriaceae, *Pseudomonas aeruginosa,* and *Staphylococcus aureus.*[41,44,45]

In patients with stroke, the prevalence of swallowing dysfunction ranges from 40 to 70 percent.[8,9,46-48] Many of these patients have silent aspiration.[49] Patients with dysphagia who aspirate are at an increased risk for pneumonia. Among patients who have had a stroke, pneumonia is seven times as likely to develop in those in whom aspiration can be confirmed than in those who do not aspirate.[9,50]

Assessing the Risk of Oropharyngeal Aspiration

Assessment of the cough and gag reflexes is an unreliable means of identifying patients at risk for aspiration. A comprehensive swallowing evaluation, supplemented by either a videofluoroscopic swallowing study or a fiberoptic endoscopic evaluation, is required. A speech–language pathologist can perform this evaluation at the bedside.[51-53] In patients found to be at risk for aspiration, further behavioral, dietary, and medical management to reduce this risk can be initiated. In patients with swallowing dysfunction, a soft diet should be introduced, and the patient should be taught compensatory feeding strategies (e.g., reducing the bite size, keeping the chin tucked and the head turned while eating, and swallowing repeatedly). Tube feeding is usually recommended in patients who continue to aspirate pureed food despite these strategies.

Feeding Tubes and Aspiration Pneumonia

In 1995, more than 121,000 percutaneous endoscopic gastrostomy tubes were placed in Medicare recipients in the United States,[54] most commonly because of dysphagia after a stroke.[54,55] However, the use of a percutaneous endoscopic gastrostomy tube has not been shown to be superior to the use of a nasogastric tube for preventing aspiration in these patients.

Two studies compared these two methods of feeding with respect to their efficacy and rates of complications.[56,57] In both studies, gastrostomy-tube feeding was significantly more effective than nasogastric-tube feeding in delivering the prescribed nutrition. However, the incidence of aspiration pneumonia was similar with the two methods. Likewise, among patients who have had a stroke, the incidence of aspiration pneumonia with postpyloric tubes (those placed in the small bowel) has been shown to be similar to that with intragastric tubes.[58-60]

Feeding tubes offer no protection from colonized oral secretions, which are a serious threat to patients with dysphagia. Furthermore, scintigraphic studies have revealed evidence of aspiration of gastric contents in patients fed by gastrostomy tube.[61,62] Over the long term, aspiration pneumonia is the most common cause of death in patients fed by gastrostomy tube. However, because of the problems associated with nasoenteric tubes — including discomfort; excessive gagging; esophagitis; misplacement, displacement, or clogging of the tubes; and poor cosmesis — gastrostomy tubes are usually preferred for long-term nutritional support.[63] Patients who are likely to recover their ability to swallow within a few weeks are not candidates for gastrostomy tubes, and whether patients with a short life expectancy should be considered candidates for gastrostomy tubes is debatable.

Aspiration in Critically Ill Patients

Critically ill patients have an increased risk of aspiration and aspiration pneumonia. A number of factors may increase the risk of aspiration in these patients, including a supine position, gastroparesis, and nasogastric intubation.[64-66] Gastroesophageal reflux occurs in critically ill patients even in the absence of nasogastric tubes and enteral feedings; up to 30 percent of patients who are kept in the supine position are estimated to have gastroesophageal reflux. Clinically important gastrointestinal dysmotility, ranging from a moderate delay in gastric emptying to marked gastroparesis, has been described in critically ill patients with conditions such as burns, sepsis, trauma, surgery, and shock.[67,68] A high gastric residual volume due to gastroparesis, leading to gastric distention and regurgitation, increases the risk of aspiration of gastric contents. Use of a postpyloric tube for feeding may have advantages in these patients.[69]

The risk of aspiration is especially high after removal of an endotracheal tube, because of the residual effects of sedative drugs, the presence of a nasogastric tube, and swallowing dysfunction related to alterations of upper-airway sensitivity, glottic injury, and laryngeal muscular dysfunction.[70-72] Alteration in the swallowing reflex can be detected in patients who have been intubated for as short a time as 24 hours, but this complication usually resolves within 48 hours.[70] I recommend the discontinuation of oral feeding for at least 6 hours after extubation (in case reintubation is required), followed by institution of a diet of pureed food and then soft food for at least 48 hours. A formal evaluation of swallowing may be useful in cases of traumatic intubation and in patients with anatomical or functional abnormalities of the upper airway.

BACTERIOLOGY

A number of studies in the early 1970s investigated the bacteriology of so-called community-acquired aspiration pneumonia.[43,73-75] Bacteriologic specimens were obtained by percutaneous transtracheal sampling or thoracocentesis. Anaerobic organisms were found to be the predominant pathogens, isolated alone or with aerobes. On the basis of these studies, antibiotics with activity against anaerobic organisms became the standard of care for patients with aspiration pneumonia and aspiration pneumonitis.[2,76] However, in all these studies the microbiologic specimens were obtained late in the course of the illness, frequently after complications such as abscesses, necrotizing pneumonia, or empyema had developed. Furthermore, many of the patients had chronic alcoholism, and most reported having putrid sputum; these patients are unlike the typical patients seen today with acute aspiration pneumonia. In addition, it is possible that the organisms recovered by transtracheal sampling were oropharyngeal flora that contaminated the trachea during the procedure (due to aspiration) or that colonized the trachea, rather than true pulmonary pathogens. This hypothesis is supported by the work of Moser and colleagues, who showed in dogs with experimental pneumonia that there are discrepancies between bacteria recovered by transtracheal sampling and those obtained by transthoracic needle biopsy.[77]

In two studies performed in the 1990s, sampling of the lower respiratory tract with a protected specimen brush, followed by quantitative and anaerobic culturing of the specimens, was performed in patients with acute aspiration syndromes.[78,79] Mier and colleagues studied 52 patients admitted to an intensive care unit with a diagnosis of aspiration pneumonia.[78] Bacterial pathogens were isolated in substantial concentrations ($\geq$1000 colony-forming units per milliliter) from only 19 patients, and the spectrum of organisms identified depended on whether the aspiration syndrome was community acquired or hospital acquired. *Strep. pneumoniae, Staph. aureus, H. influenzae,* and Enterobacteriaceae predominated in patients with a community-acquired aspiration syndrome, whereas gram-negative organisms, including *P. aeruginosa,* predominated in patients with a hospital-acquired aspiration syndrome. No anaerobic organisms were isolated. In a similar study, in which sampling with a protected specimen brush was performed in a blinded fashion in 25 patients with gastric aspiration,[79] bacterial pathogens were isolated from 12 patients, 8 of whom had risk factors for gastric coloni-

zation (small-bowel obstruction or ileus, the presence of a feeding tube, or therapy with histamine H_2 antagonists). The spectrum of pathogens was similar to that reported by Mier and colleagues,[78] and no pathogenic anaerobic organisms were isolated.

MANAGEMENT

The general management of respiratory failure in patients with acute lung injury has been reviewed extensively in the literature and will not be discussed here.[80] This section highlights specific issues relevant to the management of aspiration syndromes.

Aspiration Pneumonitis

The upper airway should be suctioned after a witnessed aspiration of gastric contents. Endotracheal intubation should be considered for patients who are unable to protect their airway (for example, those with a decreased level of consciousness). Although it is common practice, the prophylactic use of antibiotics in patients in whom aspiration is suspected or witnessed is not recommended. Similarly, the use of antibiotics shortly after aspiration in patients in whom a fever, leukocytosis, or a pulmonary infiltrate develops is discouraged, since the antibiotic may select for more resistant organisms in patients with an uncomplicated chemical pneumonitis. However, empirical antibiotic therapy is appropriate for patients who aspirate gastric contents and who have small-bowel obstruction or other conditions associated with colonization of the gastric contents. Antibiotic therapy should be considered for patients with aspiration pneumonitis that fails to resolve within 48 hours after aspiration. Empirical therapy with broad-spectrum agents is recommended (Table 2); antibiotics with anaerobic activity are not routinely required. Sampling of the lower respiratory tract (with a protected specimen brush or by bronchoalveolar lavage) and quantitative culture in intubated patients may allow targeted antibiotic therapy and, in patients with negative cultures, the discontinuation of antibiotics.[81,82]

Corticosteroids have been used for decades in the management of aspiration pneumonitis.[83] However, there are limited data on the role of these agents. In a prospective, placebo-controlled study, Sukumaran and colleagues found that radiographically evident lung injury improved more quickly in the patients given corticosteroids than in those given placebo; however, the patients given corticosteroids had a longer stay in the intensive care unit, and there were no significant differences between the two groups in the incidence of complications or the outcome.[84,85] In a case–control study, Wolfe and colleagues found that pneumonia due to gram-negative bacteria was more frequent after aspiration among patients treated with corticosteroids than among those who were not.[86] Similarly, studies in animals have failed to demonstrate a beneficial effect of corticosteroids on pulmonary function, lung injury, alveolar–capillary permeability, or outcome after acid aspiration.[87,88] Furthermore, given the failure of two multicenter, randomized, controlled trials to demonstrate a benefit of high-dose corticosteroids in patients with the acute respiratory distress syndrome, the administration of corticosteroids cannot be recommended.[89,90]

TABLE 2. EMPIRICAL ANTIBIOTICS RECOMMENDED FOR THE MOST COMMON ASPIRATION SYNDROMES.

SYNDROME AND CLINICAL SITUATION	ANTIBIOTIC (USUAL DOSE)*
Aspiration pneumonitis	
Signs or symptoms lasting >48 hr	Levofloxacin (500 mg/day)† or ceftriaxone (1–2 g/day)
Small-bowel obstruction or use of antacids or antisecretory agents	Levofloxacin (500 mg/day)† or ceftriaxone (1–2 g/day) or ciprofloxacin (400 mg every 12 hr) or piperacillin–tazobactam (3.375 g every 6 hr) or ceftazidime (2 g every 8 hr)
Aspiration pneumonia	
Community-acquired pneumonia	Levofloxacin (500 mg/day)† or ceftriaxone (1–2 g/day)
Residence in a long-term care facility	Levofloxacin (500 mg/day)† or piperacillin–tazobactam (3.375 g every 6 hr) or ceftazidime (2 g every 8 hr)
Severe periodontal disease, putrid sputum, or alcoholism	Piperacillin–tazobactam (3.375 g every 6 hr) or imipenem (500 mg every 8 hr to 1 g every 6 hr) or a combination of two drugs: levofloxacin (500 mg/day)† or ciprofloxacin (400 mg every 12 hr) or ceftriaxone (1–2 g/day) plus clindamycin (600 mg every 8 hr) or metronidazole (500 mg every 8 hr)

*The doses listed are those for patients with normal renal function.

†Levofloxacin is given by slow infusion over a 60-minute period. Levofloxacin (500 mg/day) may be replaced by gatifloxacin (400 mg/day).

Aspiration Pneumonia

Antibiotic therapy is unequivocally indicated in patients with aspiration pneumonia. The choice of antibiotics should depend on the setting in which the aspiration occurs as well as the patient's general health (Table 2). However, antibiotic agents with activity against gram-negative organisms, such as third-generation cephalosporins, fluoroquinolones, and piperacillin, are usually required. Penicillin and clindamycin, which are often called the standard antibiotic agents for aspiration pneumonia, are inadequate for most patients with aspiration pneumonia.[78] Antibiotic agents with specific anaerobic activity are not routinely warranted and may be indicated only in patients with severe periodontal disease, putrid sputum, or evidence of necrotizing pneumonia or lung abscess on radiographs of the chest.[78,79]

CONCLUSIONS

In the management of aspiration syndromes, it is vitally important to distinguish aspiration pneumonitis from aspiration pneumonia. Although some over-

lap exists, they are distinct clinical syndromes. Antibiotics are not indicated (at least initially) in the majority of patients with aspiration pneumonitis, and corticosteroids have no proven benefit. Aspiration pneumonia should be considered in the differential diagnosis for any patient with dysphagia and an infiltrate in a dependent bronchopulmonary segment. Broad-spectrum antibiotics are indicated in most patients with aspiration pneumonia.

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