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Introduction

Aspiration is the introduction of oropharyngeal or gastric contents into the respiratory tract. Three major syndromes may develop as a consequence of aspiration: chemical pneumonitis, bronchial obstruction secondary to aspiration of particulate matter, and bacterial aspiration pneumonia. Less commonly, interstitial lung disease occurs in persons with chronic aspiration. Which of these consequences emerges is determined by the amount and nature of the aspirated material as well as by the integrity of host defense mechanisms.

The term *aspiration pneumonia* refers to the infectious consequences of introduction of relatively large volumes of oral material into the lower airways (macroaspiration). Although healthy persons frequently aspirate small volumes of pharyngeal secretions during sleep, the development of pneumonia after such microaspiration is normally prevented by mechanical (e.g., cough and mucociliary transport) and immunological responses. Pneumonia arises when these host defenses are not able to limit bacterial proliferation either because of microaspiration of highly virulent pathogens to which the host lacks specific immunity (e.g., *Streptococcus pneumoniae* or enteric gram-negative bacteria) or because of macroaspiration of large quantities of organisms that may not necessarily be highly virulent.

Aspiration may be clinically obvious, as when acute pulmonary complications follow inhalation of vomited gastric contents. Such acute chemical pneumonitis, representing damage to lung parenchyma by highly acidic gastric

contents, is often referred to as Mendelson's syndrome. On the other extreme, so-called silent aspiration, as occurs in persons with neurological impairment who lack cough responses, is often followed by the indolent onset of infectious pneumonia consequent to contamination of the lower airways by low virulence mixtures of aerobic and anaerobic microorganisms from the oropharynx. It must be kept in mind, however, that chemical pneumonitis may result in the later development of aspiration pneumonia.

Risk factors

Several factors increase the risk of aspiration pneumonia. First is disturbance of the normal oropharyngeal or gastric flora. The presence of gingivitis, dental plaque, and decayed teeth combined with poor oral hygiene or decreased salivary flow (e.g., due to tube feedings or anticholinergic medications) increases the predisposition to developing pneumonia following an aspiration event by increasing the quantity of relatively low virulence bacteria that colonize the oropharynx. Similarly, decreased gastric acidity (e.g., due to proton pump inhibitor use), enteral feeding, gastroparesis, or small-bowel obstruction increases colonization of gastric contents by pathogenic microorganisms, i.e., enteric gram-negative bacilli such as *Escherichia coli and Klebsiella pneumoniae*. Finally, alcoholism, malnutrition, diabetes, and other severe comorbidities or prior antimicrobial therapy lead to replacement of normal oral flora by more virulent microorganisms such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *K. pneumoniae* and thus also increase the risk of pneumonia following an aspiration event.

For self-evident reasons, conditions that impair cough and other normal mechanical oropharyngeal reflexes that prevent aspiration increase the risk of aspiration pneumonia. These include cerebrovascular and other neurological diseases, alcoholism, drug abuse, general anesthesia, seizures, disorders of the gastrointestinal tract, and uncontrolled postoperative pain (see Table 33.1). In addition, pulmonary clearance defects at the mucociliary level (e.g., secondary to tobacco smoking or influenza), and impairment of normal humoral and cellular host defenses, particularly those conditions that decrease immunoglobulin production (e.g., various hematological malignancies) or result in severe neutropenia, also increase the risk of developing pneumonia after aspiration.

Clinical Epidemiology

In 2010 there were approximately 190,000 inpatient admissions in the United States for which the principal diagnosis was food□vomit (or aspiration) pneumonitis (ICD-9 507.0). These hospitalizations accounted for more than 19,000 inpatient deaths with a total medical care cost of 2.7 billion dollars. Another 370,000 persons received a secondary diagnosis of aspiration pneumonitis. Swallowing disorders due to neurologic diseases affect 300,000 to 600,000 people each year in the United States. Nearly 40% of stroke patients with dysphagia aspirate and develop pneumonia. Overall, aspiration pneumonitis accounts for approximately 0.5% of all hospitalizations, 3% to 4% of inpatient mortality, and 5% to 23% of all cases of community-acquired pneumonia.

More than 70% of cases of aspiration pneumonia are in persons older than 65 years of age. As a corollary, aspiration pneumonia is the second most frequent principal cause of hospitalizations among United States Medicare patients.

Among nursing home patients, aspiration pneumonia accounts for up to 30% of cases of pneumonia, occurs at a rate three times that of age-matched patients in the community and markedly increases the risk of death. Among such patients, difficulty swallowing food, use of tube feedings, requiring assistance with feeding, delirium, and use of sedative medications are the most frequent risk factors for aspiration pneumonia. While the debilitated elderly are at particularly high risk, prior silent aspiration is also common in apparently healthy elderly patients with community-acquired pneumonia.

Aspiration complicates the course of approximately 10% of persons admitted to hospitals for overdosage with sedative or hypnotic agents and 0.05% to 0.8% of persons receiving general anesthesia for surgical procedures. Patient characteristics independently associated with an increased risk of aspiration following general anesthesia include male sex, nonwhite race, age of 60 years, dementia, chronic obstructive pulmonary disease, renal disease, malignancy, moderate to severe liver disease, and emergency surgery.

Clinical course and diagnosis

Aspiration of gastric contents results in acute inflammation of the major airways and lung parenchyma with maximal hypoxemia within 10 minutes of aspiration. Local injury results in complement activation as well as release of TNF-α, IL-8, and other proinflammatory cytokines that in turn are primarily responsible for the acute nonobstructive complications of chemical aspiration. The severity of lung injury is greatest when the pH is less than 2.5, but severe pulmonary injury does occur at higher pH.

Acute symptoms and signs of chemical pneumonitis include respiratory distress, fever, cough, reflex bronchospasm, leukocytosis, and pulmonary infiltrates. Life-threatening hypoxemia may develop as a consequence of atelectasis, pulmonary capillary leak, and direct alveolar damage. These findings are easily attributable to chemical pneumonitis if they follow witnessed vomiting and aspiration of gastric acidic contents. If the event is not witnessed, detection of gastric enzyme pepsin in a tracheal aspirate may serve as a marker for gastric aspiration pneumonitis.

Many patients with chemical pneumonitis improve without any specific antimicrobial therapy. Other patients develop progressive clinical symptoms and worsening radiographic findings for several days after an aspiration event. Such progression indicates the emergence of the acute respiratory distress syndrome and□or bacterial pneumonia. Alternatively, patients may initially improve for several days but then worsen with the onset of recurrent symptoms and signs indicative of secondary bacterial pneumonia.

Differentiation of aspiration pneumonia from progressive chemical pneumonitis is often challenging as there is frequent overlap between these two syndromes. This distinction is important given the desirability of avoiding unnecessary antibiotic use, especially as pneumonia fails to develop in approximately half of all aspiration events. Furthermore, given the differences in microbial etiology of aspiration pneumonia versus community-acquired pneumonia, it is important to consider aspiration in persons with pneumonia who have the risk factors listed in Table 33.1 even if an aspiration event has not been witnessed.

The clinical presentation of aspiration pneumonia is much less dramatic than that of chemical pneumonitis. Many episodes of aspiration pneumonia, especially those involving normal oral flora (i.e., mixed aerobic–anaerobic infections), result from silent aspiration. Clinical characteristics include fever, alteration of general well-being, and respiratory symptoms such as productive cough, dyspnea, and pleuritic pain. In elderly patients with aspiration pneumonia, the early signs and symptoms of pulmonary infection may be muted and overshadowed by nonspecific complaints such as general weakness, decreased appetite, altered mental status, or decompensation of underlying diseases. These patients may have an indolent disease and not develop fever, malaise, weight loss, and cough for 1 to 2 weeks or more after aspiration. This is an especially common presentation for patients who present with mixed aerobic–anaerobic lung abscesses or empyemas after an aspiration event.

Neither routine nor specialized laboratory tests, e.g., c-reactive protein, soluble triggering receptor expressed on myeloid cells (TREM-1), lipid-laden macrophage and serum procalcitonin distinguish between aspiration pneumonitis and aspiration pneumonia. The role of procalcitonin and amylase in bronchoalveolar lavage remains to be established.

Radiographic evaluation is necessary to establish the diagnosis of pneumonia as there is no combination of historical data, physical findings, or laboratory results that reliably confirms the diagnosis. Limitations of chest radiography for the diagnosis of pneumonia include poor specificity in patients with the acute respiratory distress syndrome and decreased sensitivity in persons with previous structural lung disease, very early infection, severe dehydration, or

profound granulocytopenia. Otherwise, the failure to detect an infiltrate essentially rules out the diagnosis of pneumonia. Although spiral computed tomography (CT) of the chest provides a more sensitive means of detecting infiltrates than chest radiography, such infiltrates may not actually represent pneumonia. Esophagography and CT are especially useful in the evaluation of aspiration disease related to tracheoesophageal or tracheopulmonary fistula.

Radiologic findings do not distinguish between chemical pneumonitis and aspiration pneumonia, save for the fact that radiological abnormalities typically have a more rapid onset with chemical pneumonitis. However, when compared with other causes of pneumonia, pneumonia complicating aspiration more often involves the posterior segment of the right upper lobe, the superior segment of the right lower lobe, or both, as well as the corresponding segments in the left lung. Manifestations of severe, mixed aerobic anaerobic infection include necrotizing pneumonia, lung abscess, and empyema (Figures 33.1–33.4). Foreign body aspiration typically occurs in children and manifests as obstructive lobar or segmental overinflation or atelectasis. An extensive, patchy bronchopneumonic pattern may be observed in patients following massive aspiration of gastric contents.

Although the utility of sputum examination is much debated, pleural fluid (if present) and two sets of blood cultures should be obtained and efforts to obtain sputum should be pursued before initiation of antimicrobial therapy in hospitalized patients with aspiration pneumonia. Sputum samples must be carefully collected, transported, and processed to optimize the recovery of common aerobic bacterial pathogens such as *S. pneumoniae*. Because anaerobic

cultures are not performed for sputum specimens, the presence of mixed bacterial flora on the sputum Gram stain is used to suggest the presence of polymicrobial infection with mixed aerobic-anaerobic oropharyngeal flora. Inspection of the sputum Gram stain is also necessary to ensure that the materials being cultured are not unduly contaminated by saliva. Bronchoscopic sampling of the lower respiratory tract (with a protected specimen brush or by bronchoalveolar lavage) and quantitative culture are particularly useful in critically ill patients with hospital-acquired aspiration pneumonia, especially when the response to initial antimicrobial therapy is poor.

Unfortunately, despite extensive evaluation, the microbial cause of pneumonia can be identified in only 40% to 60% of hospitalized patients. However, when successful, identification of the infecting microorganism serves to verify the clinical diagnosis of infection and facilitates the use of specific therapy instead of unnecessarily broad-spectrum antimicrobial agents.

Microbiology

The microbial etiology of aspiration pneumonia is complex and variable. The distribution of responsible pathogens differs in persons with community- versus hospital-acquired illness and varies with the presence or absence of previous antimicrobial exposure, comorbidities, or odontogenic disease.

In many studies performed during the 1970s, bacteriologic specimens were obtained by percutaneous transtracheal sampling, and rigorous laboratory methods were used to optimize the recovery of anaerobic bacteria from patients who were often in the later stages of the disease who had complications such as

abscesses or empyema. Although typical causes of bacterial pneumonia such as *S. pneumoniae* were often recovered, these studies demonstrated that viridans streptococci and anaerobic organisms, including *Peptostreptococcus*, *Bacteroides*, *Prevotella*, and *Fusobacteria*, were the predominant pathogens in aspiration pneumonia.

Although some recent studies show a decreased prevalence of anaerobic bacteria as causes of aspiration pneumonia, the adequacy of attention to anaerobic culture techniques is often uncertain, leaving in doubt whether the true frequency of anaerobic infection has been underestimated. Well-performed studies continue to demonstrate anaerobes in up to 20% of nursing home patients with aspiration pneumonia; increased rates are found in patients with greater levels of debility. Conversely, the frequency of anaerobic infection is somewhat less in edentulous patients. In recent studies, the most frequently recovered aerobic organisms from persons with community-acquired aspiration pneumonia have been *S. pneumoniae, Hemophilus influenzae, Staphylococcus aureus, and Enterobacteriaceae* (eg, *E. coli, Klebsiella* species and *Enterobacter* species).

Aerobic bacteria, particularly *S. aureus*, enteric gram-negative bacilli (ie, *Enterobacteriaceae*), and occasionally *P. aeruginosa*, are more common causes of aspiration pneumonia in persons who develop disease while hospitalized or in a nursing home setting. At least 40% of hospital-associated pneumonias, many of which are due to aspiration, are caused by *S. aureus* and *Enterobacteriaceae*. Patients admitted to a respiratory or intensive care unit have the highest risk of nosocomial gram-negative bacillary pneumonia. *P. aeruginosa* is most common in persons who have received prior intensive antimicrobial therapy or who have

underlying bronchiectasis or severe immunological compromise. Polymicrobial infection is common in patients with aspiration pneumonia.

Clinical Management

Although corticosteroids have long been used in the treatment of acute chemical pneumonitis due to aspiration, this treatment cannot routinely be recommended. Prospective studies have failed to show a benefit in animal models of acid lung injury or in patients with either aspiration pneumonitis or the acute respiratory distress syndrome.

Antibiotic use is not warranted in most patients who acutely develop fever, leukocytosis, and pulmonary infiltrates following aspiration as these consequences are caused by chemical irritation and inflammation rather than to established infection. Antibiotic use in such patients is essentially prophylactic and may facilitate colonization and infection by more resistant pathogens. However, there may be some benefit in selected populations such as persons with acute life-threatening complications of aspiration or those who have aspirated heavily colonized gastric contents (e.g., in the setting of small bowel obstruction). Antibiotics should generally be administered to patients whose symptoms do not resolve within 48–72 hours or in whom new or progressive signs of pulmonary infection later emerge.

The need to select antibiotics with robust anaerobic activity in the treatment of patients with aspiration pneumonia is controversial. Vigorous antianaerobic therapy may not offer meaningful benefit to patients with uncomplicated pneumonia, especially if therapy is not unduly delayed. However,

specific anti-anaerobic therapy should be given to persons with necrotizing pneumonias, lung abscesses, or empyemas and to persons who present with the indolent onset of aspiration pneumonia. Because of the emergence of β-lactamase-mediated resistance among anaerobes, empirical treatment for mixed aerobic–anaerobic flora requires the use of a β-lactam–β-lactamase inhibitor, clindamycin, or metronidazole combined with a penicillin, ampicillin, or an appropriate cephalosporin (Table 33.2). Because of the inevitable presence of aerobes, metronidazole monotherapy should not be given.

Considering the range of pathogens and antimicrobial resistance, initial therapy of aspiration pneumonia that develops in nursing home or hospitalized patients must be carefully selected. Although monotherapy may be reasonable for immunocompetent patients with mild to moderate diseases who are known or likely to be infected by susceptible strains of *Enterobacteriaceae*, broad-spectrum multidrug therapy is often necessary to ensure coverage of the likely pathogens. The choice of a particular combination must depend on the severity of infection, presence or absence of immunocompromise, and hospital-specific patterns of antimicrobial resistance and infection by specific microorganisms. Therapy should be made more specific when the pathogen(s) has been identified and susceptibilities are known.

With appropriate antimicrobial therapy, 50% of patients treated for aspiration pneumonia defervesce within 2 days of initiation of antibiotic therapy and 80% do so within 5 days. Prolonged fever is more common in patients with lung abscess or with infections by aggressive pathogens such as *P. aeruginosa*.

Prevention

Precautions should be taken to minimize the possibility of aspiration in hospitalized patients. Avoidance of the recumbent position and hypopharyngeal suctioning prevent aspiration among patients who are intubated. Guidelines from the American College of Chest Physicians and the American Gastroenterology Association provide specific recommendations regarding the evaluation of patients who are at risk for aspiration due to dysphagia. These guidelines recommend a multidisciplinary approach to patient evaluation. Patients with documented aspiration during swallowing studies have a 4- to 10-fold increased risk of pneumonia.

Placement of gastrostomy or post pyloric tubes in persons with dysphagia is not superior to the use of a nasogastric tube for the prevention of aspiration or pneumonia. Lack of benefit is likely related to ongoing aspiration of oral secretions and continued aspiration of gastric contents in persons fed by gastrostomy or post pyloric tubes. Nonetheless, decreased local irritation, fewer mechanical problems, and improved nutrition justify the use of gastrostomy tubes in many patients. When used, the residual volume of tube feedings in the stomach should be monitored, and tube feedings should be held if the residual volume exceeds 50 mL.

The use of acid suppressive medications (both proton pump inhibitors and histamine-2 blockers) is associated with a modest increase in the risk of pneumonia, including aspiration pneumonia. Potential mechanisms for this effect include increases in the colonization of the stomach with pathogenic microorganisms and directly impairment of neutrophil function. Minimizing the

use of these medications may reduce the risk of aspiration pneumonia. Conversely, the use of angiotensin converting enzyme inhibitors may reduce aspiration pneumonia by improving swallow and cough reflexes.

Good periodontal care and oral antiseptic decontamination with chlorhexidine decreases the burden of pathogenic bacteria in oral secretions and thereby may prevent aspiration pneumonia. In contrast, prophylactic antibiotic use is not recommended for patients in whom aspiration is suspected or witnessed.

Suggested reading

Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2005;171;388–416.

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Table 33.1 Risk Factors for Aspiration

Altered Level of Consciousness
General anesthesia
Narcotic and sedative drugs
Drug overdose and ethanol toxicity
Metabolic encephalopathies (electrolyte imbalances, liver failure, uremia, sepsis)
Hypoxia and hypercapnia
Central nervous system (CNS) infections
Dementia
Abnormal Glottic Closure
Anesthetic induction or postanesthetic recovery
Postextubation
Structural lesions of the CNS (tumors, cerebrovascular accident, head trauma)
Seizures
Infection (eg, diphtheria, pharyngeal abscess)
Gastroesophageal Dysfunction
Alkaline gastric pH
Gastrointestinal tract dysmotility
Esophagitis (infectious, postradiation)
Hiatal hernia
Scleroderma
Esophageal motility disorders (achalasia, megaesophagus)
Tracheoesophageal fistula
Ascites (increased intra-abdominal pressure)
Intestinal obstruction or ileus
Diabetes (functional gastric outlet obstruction)
Neuromuscular Diseases
Guillain-Barré syndrome
Botulism
Muscular dystrophy
Parkinson’s disease

Polymyositis
Amyotrophic lateral sclerosis
Multiple sclerosis
Myasthenia gravis
Poliomyelitis
Tardive dyskinesia
Mechanical Factors
Nasogastric or enteral feeding tubes
Upper endoscopy
Emergency and routine airway manipulation
Surgery or trauma to the neck and pharynx
Tumors of the upper airway
Tracheostomy
Endotracheal tube
Zenker’s diverticulum
Other Factors
Obesity
Pregnancy

Table 33.2 Suggested Empiric Therapy for Inpatients with Aspiration Pneumonia

Suspected Pathogens	Preferred Agents	Alternative Agents
Mixed aerobic–anaerobic flora	β-lactam plus metronidazole, β-lactam–β-lactamase inhibitor[a]	Clindamycin, moxifloxacin, ertapenem
Enterobacteriaceae	β-lactam–β-lactamase inhibitor[a], cefepime, carbapenem[b]	Third-generation cephalosporinc or fluoroquinolone[d], both +/− aminoglycoside[f]
P. aeruginosa	Antipseudomonal β-lactam[e] +/− aminoglycoside[f], carbapenem +/- aminoglycoside[f]	Ciprofloxacin + aminoglycoside, ciprofloxacin + antipseudomonal β-lactam[f]
S. aureus	Vancomycin	Linezolid, quinupristin–dalfopristin, telavancin

Note: Therapy should be modified when the identity and susceptibility of the responsible pathogen(s) is determined.

[a] Ticarcillin–clavulanate and piperacillin–tazobactam are the preferred β-lactam–β-lactamase inhibitors for the treatment of nosocomial pneumonia due to *Enterobacteriaceae*. Ampicillin–sulbactam lacks adequate activity against many nosocomial enteric gram-negative bacilli.

[b] Ertapenem, imipenem, and meropenem have equivalent activity against Enterobacter spp. mixed aerobic–anaerobic flora. Only imipenem and meropenem have activity against *P. aeruginosa*.

[c] Third-generation cephalosporins: cefotaxime, ceftriaxone, and ceftazidime.

[d] Levofloxacin and ciprofloxacin generally have equivalent activity against *Enterobacter spp*. and *P. aeruginosa*. High resistance rates, particularly for nosocomial isolates of limit the empiric usefulness of these agents in many settings.

[e] Antipseudomonal β-lactams: ceftazidime, cefepime, imipenem, meropenem, mezlocillin, piperacillin or piperacillin-tazobactam.

[f] Addition of an aminoglycoside should be strongly considered in serious ill patients to ensure adequate breadth of antimicrobial therapy.

Figure Captions

Figure 33.1 *K. pneumoniae* infection causing left lower lobe pneumonia in a 47-year-old woman who aspirated during a period of depressed consciousness due to alcohol intoxication.

Figure 33.2 Bilateral lower lobe pneumonia due to *P. aeruginosa* in a dialysis-dependent nursing home patient following episode of vomiting.

Figure 33.3 Mixed aerobic–anaerobic lung abscess following aspiration.

Figure 33.4 Mixed aerobic–anaerobic empyema following aspiration.