MAYO CLINIC

REVIEW

Aspiration Pneumonia and Related Syndromes

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Abstract

Aspiration is a syndrome with variable respiratory manifestations that span acute, life-threatening illnesses, such as acute respiratory distress syndrome, to chronic, sometimes insidious, respiratory disorders such as aspiration bronchiolitis. Diagnostic testing is limited by the insensitivity of histologic testing, and although gastric biomarkers for aspiration are increasingly available, none have been clinically validated. The leading mechanism for microaspiration is thought to be gastroesophageal reflux disease, largely driven by the increased prevalence of gastroesophageal reflux across a variety of respiratory disorders, including chronic obstructive pulmonary disease, asthma, idiopathic pulmonary fibrosis, and chronic cough. Failure of therapies targeting gastric acidity in clinical trials, in addition to increasing concerns about both the overuse of and adverse events associated with proton pump inhibitors, raise questions about the precise mechanism and causal link between gastroesophageal reflux and respiratory disease. Our review summarizes key aspiration syndromes with a focus on reflux-mediated aspiration and highlights the need for additional mechanistic studies to find more effective therapies for aspiration syndromes.

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Pulmonary aspiration is the pathologic passage of fluid or substances below the level of the vocal cords into the lower airways. Typically, aspiration is considered an acute event that can result in infectious pneumonia, chemical pneumonitis, or even respiratory failure from acute respiratory distress syndrome (ARDS).[1] The pathologic consequence of aspiration has been mostly attributed to the acidity of gastric fluid, but it should be noted that aspiration can occur from multiple sources in addition to the stomach (eg, duodenal, oropharyngeal, exogenous), and the aspirate material may contain other injurious materials (eg, microbes, bile, pepsin, particulates). In this review, we will focus on aspiration syndromes related to gastroesophageal reflux (GER).

In contrast to the more established acute aspiration syndromes, chronic occult pulmonary aspiration, also referred to as *silent aspiration* or *microaspiration*, is considered more often in the outpatient setting and is believed to contribute to the pathophysiology of multiple respiratory disorders, including pulmonary fibrosis, asthma, bronchiectasis, bronchiolitis, chronic bronchitis, pneumonia, chronic cough, and lung transplant rejection (Table 1).[2] Interestingly, these clinical suspicions often go unchallenged with empirical attempts at moderating aspiration, or more typically its prerequisite, GER, by the use of acid suppressants.

The perception that aspiration is an important mechanism and contributor to respiratory disorders is largely due to the apparent increase in the prevalence of gastroesophageal reflux disease (GERD) across both chronic and acute respiratory disorders. However, a well-validated tool to readily diagnose microaspiration is lacking, and many clinicians have adopted the treatment of GERD, typically with a proton pump inhibitor (PPI), into practice in hopes of improving their patient's respiratory condition. Although PPIs do little to directly reduce reflux and are associated with substantial health care costs and potential adverse events, large observational and controlled studies have been increasingly reported in respiratory medicine, more often with negative results. Nonetheless, aspiration remains a dominating concern as the linking mechanism between GERD and chronic respiratory conditions, particularly with fibrotic lung diseases such as idiopathic pulmonary fibrosis (IPF), and to a lesser extent in patients with obstructive lung disorders, including asthma and chronic cough.

ARTICLE HIGHLIGHTS

- Reflux is prevalent across a variety of acute and chronic respiratory disorders and is considered a predisposing mechanism for a variety of pulmonary aspiration syndromes.
- Caution should be used when treating suspected pulmonary aspiration syndromes with gastric acid neutralization alone because standard treatment of reflux has not produced clear clinical benefit and may be of potential harm.
- Additional mechanistic studies are needed to understand the causal role of reflux in aspiration and respiratory disorders to identify effective targets of interventions.

MECHANISMS UNDERLYING GER AND ASPIRATION

Mechanistically, it is inadequate and inappropriate to assume that the presence of GER implies that aspiration is occurring. There are multiple factors that may promote reflux and eventual aspiration of gastric fluid into the lower airways but also multiple defenses that must be bypassed before an aspiration event becomes pathologic (Table 2).

First, it is important to clarify what is meant by GERD. Gastroesophageal reflux is the retrograde movement of gastric fluid into the esophagus and notably not a state of excess gastric acidity, which is the target of most GERD therapies. Furthermore, GERD is heterogeneous and multifactorial, with multiple phenotypes identified in advanced esophageal testing and supported by the current Rome IV classification scheme (eg, erosive esophagitis, functional dyspepsia, nonerosive reflux disease, and asymptomatic GERD).[3] Additionally, standardization and advances in high-resolution esophageal manometry have identified differing patterns in esophageal motility among patients with GERD that may be particularly pertinent in patients with respiratory disorders.[4-6] Finally, novel techniques to image the esophagogastric junction (EGJ) directly with fluoroscopic methods and simultaneously measure pressures in the stomach, esophagus, and EGJ and lower esophageal sphincter (LES) with adaptations of the Dent sleeve catheter (Dentsleeve International Ltd) have further facilitated our understanding of how the transdiaphragmatic (ie, gastric to esophageal) pressure gradient (TDPG) interact with the EGJ/LES complex to facilitate reflux. Specifically, because the striated crural muscles of the diaphragm are important to the competence of the EGJ, this provides at least a potential mechanistic link on how the respiratory system may anatomically and physiologically link with GERD.[7] Fundamentally, these 2 factors, the pressure gradient between the stomach and the esophagus (ie, TDPG) and the competency of the EGJ and LES, are what define whether gastric fluid will abnormally enter into the esophagus, including during physiologic transient LES relaxations.[8]

Second, the composition of gastric fluid is an important consideration. In animal models, it is readily recognized that acid is not the sole issue; gastric particulates also augment airway injury.[9,10] Additionally, both pepsin and bile acids promote epithelial damage, not just to the esophageal mucosa but to airway epithelium as well.[11,12] Thus, the constituency and volume of aspirate material are important in the development of respiratory pathology and perhaps help to account for vastly different phenotypic expressions of gastric aspiration (eg, pneumonitis, ARDS, bronchospasm, bronchiolitis, and lung fibrosis).

Next, if gastric contents do reflux into the esophagus, it must traverse the span of the esophagus up into the pharynx (ie, laryngopharyngeal reflux) by bypassing the important barriers of not only the EGJ and LES but also esophageal peristalsis, which act to clear any residual refluxate from the esophagus, further

TABLE 1. Associated Aspiration Syndromes

Acute
Bronchospasm, asthma
Acute bronchitis, COPD exacerbation
Pneumonia, pneumonitis
Foreign body obstruction
Acute respiratory distress syndrome
Chronic
Bronchiectasis, chronic bronchitis
Exogenous lipoid pneumonia
Interstitial lung disease
Organizing pneumonia
Bronchiolitis obliterans syndrome
Diffuse aspiration bronchiolitis

COPD = chronic obstructive pulmonary disease.