Interventions to Prevent Pneumonia Among Older Adults

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Pneumonia is a common cause of death in older people. Antimicrobial drugs do not prevent pneumonia and, because of increasingly resistant organisms, their value in curing infection will become more limited. Establishing new strategies to prevent pneumonia through consideration of the mechanisms of this devastating illness is essential. The purpose of this review is to discuss how pneumonia develops in older people and to suggest preventive strategies that may reduce the incidence of pneumonia among older adults. Aspiration of oropharyngeal bacterial pathogens to the lower respiratory tract is one of the most important risk factors for pneumonia; impairments in swallowing and cough reflexes among older adults, e.g., related to cerebrovascular disease, increase the risk for the development of pneumonia. Thus, strategies to reduce the volumes and pathogenicity of aspirated material should be pursued. For example, since both swallowing and cough reflexes are mediated by endogenous substance P, pharmacologic therapy using angiotensin-converting enzyme inhibitors, which decrease substance P catabolism, may improve both reflexes and result in the lowering of the risk of pneumonia. Similarly, since the production of substance P is regulated by dopaminergic neurons in the cerebral basal ganglia, treatment with dopamine analogs or potentiating drugs such as amantadine (and, of course, prevention of cerebrovascular disease, which can result in basal ganglia strokes) should affect the incidence of pneumonia. The purpose of this review is to consider promising pharmacologic treatments as methods of preventing pneumonia in older adults and to review other proven strategies, e.g., infection control and cerebrovascular disease prevention that will lessen the incidence of pneumonia. J Am Geriatr Soc 49:85-90, 2001.

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Pneumonia is a common source of morbidity and mortality among older people despite the availability of potent new antimicrobials. Both the increased incidence of pneumonia and high mortality among older people are a consequence of a number of age-related factors including coexisting illnesses, therapeutic interventions, and the aging process itself. Since antimicrobial therapy cannot prevent pneumonia and will have increasingly limited treatment efficacy related to emerging microbial resistance, aggressively employing preventive strategies targeted at the risk factors for pneumonia in older people is essential.

Risk factors for the development of pneumonia in older people can be broadly classified into factors that alter host defenses and factors that increase exposure to bacteria. These factors combine to adversely affect the capacity to defend against pathogens of the upper and lower respiratory tract. Although mortality from infections correlates with decreased IgG levels, cutaneous anergy, and lymphopenia, no proven interventions are known that reverse these age-associated changes in the immune system. However, interventions to improve mechanical airway clearance, implementation of infection control strategies, and prevention of cerebrovascular disease and subsequent dysphagia can all reduce the risk for pneumonia, particularly among high-risk patients. The purpose of this review is to consider pharmacologic, infection-control, and cardiovascular treatments as methods of preventing pneumonia in older adults.

MECHANISMS OF PNEUMONIA IN OLDER PEOPLE

Chemical Pneumonitis

Aspiration is possibly the single most important risk factor for pneumonia in older people. Common medical usage equates aspiration pneumonia with Mendelson’s syndrome, or the acute aspiration of gastric content. Such gross aspiration of large volumes of materials as a cause of aspiration pneumonia is less common, but when it occurs it is probably more like a chemical pneumonitis. The incidence of aspiration increases when the gag reflex is impaired, there is an alteration in the patient’s level of consciousness, certain devices such as nasogastric or endotracheal tubes are used, or esophageal disease is present. The most commonly considered mechanism is pulmonary aspiration of gastric contents producing acid-induced injury. The use
of nebulized beta agonists for treating fever and dyspnea that occur acutely hours after a vomiting episode may help the symptoms, but beta agonists might contribute to gastro-esophageal reflux by decreasing the lower esophageal pressure.9

Silent Aspiration and Pneumonia

Aspiration pneumonia is also used to describe the bacterial infection of the lung that results from aspiration of bacteria contained in oropharyngeal10,11 or gastric secretions.12 Such silent aspiration frequently occurs and is a more important cause of pneumonia than the acute aspiration of gastric content in older people.13 Silent aspiration of oropharyngeal bacterial pathogens to the lower respiratory tract is an important risk factor for community-acquired pneumonia14 and nosocomial pneumonia in older people.15 Normal hosts are less likely to develop pneumonia because they either aspirate smaller volumes or are able to clear bacteria rapidly,16 but an extremely small volume (0.01 ml) of saliva contains pathogenic numbers of bacteria,14 and elderly patients with a predisposition to aspiration frequently aspirate oropharyngeal or gastric secretions with high numbers of bacteria.17

Adequate protective reflexes in the airway are important to prevent aspiration pneumonia, and the suppression or absence of these reflexes is a risk factor for its development.17 For example, Nakajoh et al. reported that the incidence of pneumonia was higher in patients having both a latency of swallowing response longer than 5 seconds following stimulation and a cough threshold for inhalation of citric acid aerosol higher than a concentration of 1.35 (log mg mL⁻¹).18 Thus, the progressive loss of protective swallowing and cough reflexes with age is thought to be one of the major risk factors for aspiration pneumonia in older people,19 and impaired swallowing and cough reflexes have been demonstrated in patients who develop aspiration pneumonia.20,21 These protective reflexes are intact, however, in older individuals who lead active daily lives,22,23 indicating that other involutional and degenerative changes associated with aging (rather than aging itself) lead to loss of these protective reflexes among older adults.24

Disorders of the central nervous system are more likely to develop in older people; pneumonia has been estimated to occur in about one-third of patients with stroke.25,26 The most important recognized factor contributing to the risk of pneumonia in patients with stroke is dysphagia with aspiration.27 Nakagawa et al. showed that the risk of pneumonia was significantly higher in patients with basal ganglia infarcts than in patients with cerebral hemispheric strokes in other locations or without cerebral hemispheric strokes.28 They found that multiple episodes of pneumonia occurred only in patients with bilateral basal ganglia infarcts, that delayed triggering of the swallowing reflex occurred in these patients, and that these patients had a high mortality rate associated with pneumonia. These results strongly suggest that disruption of the basal ganglia is critically important in the development of aspiration pneumonia.

The pharyngeal, laryngeal, and tracheal epithelium, the sites most important for initiation of swallowing and cough reflexes, have an extensive plexus of nerves that contain substance P.29,30 Capsaicin desensitization, which abolishes substance P from the airway and upper digestive tract, or a neurokinin I (NK1) receptor antagonist markedly attenuates the cough response to tussive stimuli31,32 and distilled-water-induced swallowing reflex in guinea pigs.33 These findings from animal studies suggest an important role for substance-P-containing nerves in the initiation of these protective reflexes in humans. Thus, irritation of laryngeal and pharyngeal mucosa by stimuli may activate capsaicin-sensitive sensory nerves, releasing substance P, with the result that protective reflexes are initiated by stimulation of the glossopharyngeal and vagal sensory nerves.34

Dopamine agonist treatments in rats bring about a heightened striosomal expression of substance P, and both dopamine D1 and D2 antagonists decrease substance P.35 Mice lacking the dopamine D1 receptor,36 and those treated with dopamine D1 receptor antagonist,37 show abnormal motor activities and feeding and swallowing problems. An impairment of dopamine metabolism in the basal ganglia is observed in patients with infarcts in the basal ganglia.38-39 Taking these facts together, the mechanisms of silent aspiration may be speculated as shown in Figure 1. Patients with basal ganglion infarcts may suffer from re-

![Figure 1](image.png)

**Figure 1.** Schematic diagram of the mechanism of silent aspiration. The largest pathway of dopamine originates from dopamine-synthesizing neurons of the midbrain substantia nigra complex and innervates the dorsal striatum.39 Patients with basal ganglion infarcts may suffer from reduced dopamine metabolism in the nigrostriatal pathway. Sensory components of swallowing and cough reflexes are illustrated here. See text for explanation.
duced dopamine metabolism, which decreases substance P in the glossopharyngeal and vagal sensory nerves. Depression of substance P concentration in these nerves impairs both swallowing and cough reflexes, which increases the frequency of silent aspiration. Because the act of swallowing and coughing is a fundamental defense mechanism against aspiration of oropharyngeal contents into the respiratory tract, impairment of both reflexes is one of the major reasons for the development of aspiration pneumonia.

PHARMACOLOGIC INTERVENTIONS TO PREVENT PNEUMONIA IN OLDER ADULTS

Because substance P is a neurotransmitter of the swallowing reflex and is depleted in patients with aspiration pneumonia, \textsuperscript{40} capsaicin, the pungent substance in red peppers that stimulates sensory nerves, may improve the swallowing reflex in these patients. Ebihara et al. \textsuperscript{41} measured the swallowing reflex with a bolus injection of 1 ml of solution into the pharynx through a nasal catheter and suggested that the addition of a low dose of capsaicin to liquid or food may stimulate the swallowing reflex and help to prevent aspiration pneumonia in older people.

An adverse effect of angiotensin converting enzyme (ACE) inhibitor therapy is a dry cough. \textsuperscript{42} Substance P is degraded by ACE, \textsuperscript{43} and its action is potentiated by ACE inhibitors. \textsuperscript{44,45} Using ACE inhibitors, substance P might accumulate in the upper respiratory tract because of impaired ACE activity and cause an increase in the sensitivity of the cough reflex. \textsuperscript{12,14} Similar to the cough reflex, ACE inhibitors improve the swallowing reflex in older patients with aspiration pneumonia. \textsuperscript{46} Sekizawa et al. \textsuperscript{47} compared the rate of pneumonia in stroke patients treated with ACE inhibitors with that in stroke patients treated with other antihypertensive drugs. \textsuperscript{47} Figure 2 shows the cumulative proportion of patients without pneumonia in a 2-year follow-up study. According to the Cox regression model, these findings corresponded to a relative risk of 2.56 (95% CI 1.31–3.35, P < .01) for patients who did not receive ACE inhibitors compared with those receiving ACE inhibitors. The authors suggested that the risk of pneumonia is reduced by about one-third if ACE inhibitors are used for hypertension, compared with the use of other antihypertensive drugs in patients with previous strokes. ACE inhibitors, therefore, may have beneficial effects on the prevention of pneumonia in these patients. Araik et al. \textsuperscript{45} also reported that the rate of pneumonia was significantly lower in older hypertensive patients given ACE inhibitors than in those treated with calcium channel blockers. \textsuperscript{48} Teramoto and Ouchi, however, found no advantage in using ACE inhibitors over calcium channel blockers in preventing pneumonia in adults and older people with hypertension. \textsuperscript{49}

Since the severity of the underlying cerebrovascular disease affects susceptibility to pneumonia, ACE inhibitors could be useful in the prevention of aspiration pneumonia in older patients with stroke, but not in those with hypertension.

Irwin et al.\textsuperscript{50} reported a consensus panel report of the American College of Chest Physicians, Managing Cough as a Defense Mechanism and as a Symptom, and did not identify any age-related changes in cough reflex with aging. \textsuperscript{51} However, depression of the cough reflex by anesthetic, sedative hypnotics, or analgesic narcotics should be considered a major risk for aspiration pneumonia in older patients, especially during sleep. Attention to minimizing the use of agents that suppress the cough reflex are crucial in caring for elderly patients.

Delayed triggering of the swallowing reflex occurs in patients with basal ganglia infarctions\textsuperscript{52} and an impairment of dopamine metabolism in the basal ganglia is observed in these patients.\textsuperscript{53,54} Kobayashi et al. investigated whether levodopa improves the swallowing reflex in patients with basal ganglia infarctions who had a history of aspiration pneumonia.\textsuperscript{52} The subjects were given an intravenous drip infusion of levodopa (50 mg in 20 ml saline) for 30 minutes. They found that the administration of levodopa improved the impaired swallowing reflex in these patients.

Since dopamine supplementation improves the swallowing reflex in patients with cerebral infarctions, Nakagawa et al. investigated whether amantadine, a drug that acts by releasing dopamine from dopaminergic nerve terminals, lowers the incidence of pneumonia in patients with cerebral infarctions.\textsuperscript{55} Patients were randomly assigned amantadine 100 mg per day or no active treatment and were investigated for 3 years. During follow-up, a relative risk of developing pneumonia in patients on no active treatment compared with those on amantadine was 5.92 (95% CI 2.52–13.90, P < .001) (see Figure 3). Their findings suggest that the risk of pneumonia is lowered by about 20% if amantadine is used in patients with previous strokes. Amantadine may, therefore, have beneficial effects on the prevention of pneumonia in these patients. Other recognized effects of amantadine may also have affected the incidence of pneumonia in these studies. For example, amantadine improves the conscious state in patients with brain injury,\textsuperscript{56} and more-agile stroke patients may be less likely to aspirate. In addition, dopaminergic receptors have been identified in the lower esophageal sphincter, and amantadine might reduce gastroesophageal reflux,\textsuperscript{57} and thereby lower the risk of aspiration pneumonia. Finally, antiviral effects and prevention of influenza infection might also lower the incidence of pneumonia over a 3-year period.\textsuperscript{58} Thus, the mechanisms by which
amantadine might positively affect the incidence of pneumonia remain to be proven.57

INFECTION CONTROL MEASURES TO PREVENT PNEUMONIA

Vaccination To Prevent Pneumonia

Influenza vaccination is effective in older adults in preventing not only primary influenza pneumonia but also secondary bacterial pneumonia.58 Although an increased risk of pneumonia mortality is found with limitations in activities of daily living,59,60 even bedridden older patients can be effectively immunized against influenza41 and the duration of febrile days and all respiratory conditions associated with influenza62 can be reduced. The efficacy of pneumococcal vaccine among high-risk patients has been the subject of some controversy. Some investigators estimate an approximately 60% to 95% prevention rate for Pneumovax (pneumococcal vaccine, polyvalent) in immunocompetent older and other high-risk patients.63 It is currently recommended in the United States that all adults 65 years or older and those at risk because of underlying illnesses receive both of these vaccines.44

Oral Hygiene

The microbiologic etiology of aspiration pneumonia is usually traced to organisms that inhabit the oropharynx, and aspiration of pharyngeal contents has been suggested as the mechanism by which these bacteria reach the lower respiratory tract.65 Johanson and Harris speculated that the pulmonary infections caused by bacteria following the introduction of pathogenic organisms by aspiration of oropharyngeal contents is one of the major causes of pneumonia in older people.66 Since aspiration of bacteria in oropharyngeal secretions is an important risk factor for nosocomial pneumonia in older people,67 poor oral health may contribute to the development of pneumonia. Yoneyama et al. assessed the rate of pneumonia in elderly people receiving oral care and in those who did not receive oral care.44 During 2 years of follow-up, pneumonia was diagnosed in 19% of participants who did not receive oral care and 11% of those who received oral care. The relative risk of developing pneumonia on no active oral care compared with oral care was 1.67 (95% CI 1.01–2.75, P < .05). Thus, monitoring the attention given to the oral hygiene of dependent patients can probably lower the incidence of aspiration pneumonia.

Handwashing

Gram-negative bacilli and Staphylococcus aureus commonly colonize on the hands of healthcare providers.69 Although usually transient, hand colonization may persist, particularly in workers with dermatitis. Handwashing before and after patient contact is an effective means of removing transient bacteria,9 but this is often neglected by medical personnel. The use of gloves and gowns can significantly reduce nosocomial infection and pneumonia.70 Hospitals with effective surveillance and infection-control programs have rates of pneumonia 20% lower than hospitals without such programs.71 Adherence to infection-control practices such as handwashing are basic in the prevention of nosocomial pneumonia. Unfortunately, such barrier methods will not be effective in preventing infection with organisms that are part of the critically ill patient's endogenous flora; thus, most gram-negative pneumonias cannot be avoided by isolation methods.72 Improved handwashing practices and appropriate handling of mechanical feeding, suction, and respiratory devices should reduce the spread of infectious agents in institutional settings.

Avoidance of Antibiotics

Prior use of antibiotics promotes colonization in the oropharynx and gastrointestinal tract by potentially resistant bacteria that can be aspirated and cause pneumonia. The normal anaerobic gastrointestinal flora create resistance to colonization by more-virulent organisms; this colonization resistance is lost when antibiotics are given.73 The gastrointestinal tract has been identified as a potential source of gram-negative organisms that reach the lung, and elevation of gastric pH (by nasogastric feeding, antacids, or histamine-2 receptor antagonists) is a risk factor for bacterial overgrowth in the stomach.74,75,76 Avoiding the unnecessary use of antibiotics can reduce oropharyngeal and gastric colonization and may be beneficial in the prevention of aspiration pneumonia.77

CONTROL OF GASTROESOPHAGEAL REFLUX

Reflux of gastric fluids can damage the respiratory tract. Marked damage to the tracheal mucosa can occur even when the volume of aspirated gastric fluid is too small to cause clinically significant aspiration pneumonia,78 and repeated long periods of aspiration of gastric fluid may even cause interstitial pulmonary fibrosis.79 Damage is always more severe when the pH of the gastric contents is low, but gastric fluid also contains substances besides acid that cause damage and delay healing. Since epithelial damage probably arises through the additive effects of acid, pepsin activity, and low osmolality,40 treatment of gastroesophageal reflux using antacids such as histamine-2 receptor antagonists alone may not improve symptoms caused by aspiration of gastric fluid.40

Gastric reflux is very common in general, and more
common in specific populations. It has been estimated that more than one-third of older people have intermittent symptoms of gastroesophageal reflux. In addition, the supine position, possibly by increasing the likelihood of aspiration of gastric contents into the lung, may lead to pneumonia in patients on mechanical ventilators. Finally, nasogastric tubes promote aspiration of gastric contents by impairing swallowing, causing stagnation of oropharyngeal secretions and reducing the tone of the lower esophageal sphincter. The simplest approach to all of these problems may involve elevating the head of the bed. Meguro et al. showed that elevating the bed after each meal for 2 hours may lower febrile episodes presumptively caused by aspiration of gastric contents. Border et al. emphasized the importance of patient position in the prevention of nosocomial pneumonia.

PREVENTING CEREBRAL VASCULAR DISEASE

Disorders of the central nervous system including dementia and atherosclerotic cerebral vascular disease are more often associated with aspiration than other specific neuro muscular disorders. The mechanisms by which brain injury affects aspiration risk are beginning to be delineated. For example, in healthy people the frequency of swallowing during sleep is slightly less than when awake, but severe delay of the swallowing response at night compared with during day was observed in patients with multiple lacunar infarctions. Cough reflex and spontaneous cough are also suppressed during sleep in patients with evidence of cerebral vascular injury. Thus, patients with cerebral vascular disease are particularly susceptible to the development of aspiration pneumonia during sleep.

Other evidence of the importance of cerebral vascular disease comes from studies of patients with silent cerebral infarction, i.e., patients with radiographic evidence of infarction without frank signs of neurologic impairment. Silent cerebral infarction is quite common among older people. Silent cerebral infarction was observed in 23% of older people in the United States, in 42% of older adults in one Japanese study, and in 51% in another study from Japan. Not only is silent stroke a risk factor for clinical stroke, which obviously increases the risk of aspiration pneumonia, but Nakagawa et al. reported that patients with silent cerebral infarction were more likely to develop pneumonia (20%) than were controls (5%) without silent cerebral infarction over a 2-year period. In this study, deep silent infarcts were more closely associated with the incidence of pneumonia (29%) than superficial infarcts (7%). Thus, silent cerebral infarction should be considered a potential risk for the development of aspiration pneumonia. Taken together, it is reasonable to propose that treatment aimed at reducing the incidence and severity of cerebral vascular disease, e.g., anti-hypertensive therapy, or antiaggregation and anti-platelet therapy in selected populations, should not only prevent future stroke but also reduce the incidence of aspiration pneumonia.

CONCLUSION

Since pneumonia continues to be a serious health problem among older people even with the use of potent antibiotics, prevention strategies should be used whenever possible. Promising pharmacologic approaches that affect the cough reflex and swallowing mechanisms might be tried judiciously, but their efficacy remains to be established in larger well-designed trials. Infection-control interventions, e.g., handwashing, immunization, attention to oral hygiene, and antibiotic avoidance, certainly should always be enforced, and strategies to prevent gastrointestinal reflux should be considered. Finally, large-scale treatment to reduce the incidence of cerebral vascular disease should ultimately reduce the incidence of pneumonia as "the old man's friend."
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