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ORAL INFLAMMATION

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Buffalo, New York

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School of Dentistry
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University of North Carolina
School of Dentistry
Chapel Hill, North Carolina

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Oral Inflammation and Respiratory Diseases

Frank A. Scannapieco, DMD, PhD, Professor and Chair, Department of Oral Biology,
State University of New York at Buffalo School of Dental Medicine

Periodontal disease has been linked to an increased risk of respiratory diseases, such as pneumonia and chronic obstructive pulmonary disease (COPD). This article briefly describes evidence for this association, and the mechanisms by which oral bacteria may promote colonization of the lungs by pathogens.

Pneumonia

Pneumonia is defined as inflammation of the lungs resulting from infection, usually bacterial or viral. Pneumonia cases can be divided into two major types: community-acquired and hospital-acquired (*nosocomial*). About 1.1 million cases of community-acquired pneumonia require hospitalization annually in the United States, with a mortality in hospitalized patients of 12%.¹ Bacteria that often colonize the oropharynx and upper airway, such as *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Mycoplasma pneumoniae*, usually cause community-acquired pneumonia.^{1,2}

Nosocomial pneumonia represents 13-18% of hospital-acquired infections and occurs in 0.4-0.7% of hospitalizations; mortality is about 30%.³ Nosocomial pneumonia is usually caused by bacteria acquired from the environment, such as *Pseudomonas aeruginosa*, *Staphylococcus aureus* and enteric Gram-negative bacteria.^{2,3}

Association Between Oral Bacteria and Pneumonia

Several lines of evidence indicate that people with poor oral health are at higher risk for nosocomial pneumonia. First, a number of oral health factors increase the risk of pneumonia, including having teeth or dentures (versus being edentulous without wearing dentures), being dependent on others for oral care (which leads to higher amounts of plaque), and infrequent tooth brushing.²

Second, microbiological studies reveal a direct association between pneumonia risk and colonization of the teeth and oral cavity by enteric Gram-negative bacteria and respiratory pathogens in intensive care patients.²

Third, in controlled clinical trials, interventions that inhibited dental plaque, such as treatment with oral or

topical antibiotics, chlorhexidine, or povidone-iodine plus tooth brushing, reduced the risk of pneumonia (see Table).² When data from the five trials in the Table were combined in a meta-analysis, oral hygiene intervention reduced the risk of pneumonia by a factor of 3.0 ($p < 0.001$; 95% confidence interval: 2.1-4.4).² The variety of interventions that reduce respiratory disease suggests that other antibacterial treatments could have similar effects. The antibacterial Colgate® Total® Toothpaste, for example, uses a copolymer to improve retention of the bactericide triclosan on oral surfaces, providing 12-hour antibacterial action and direct inhibition of potent inflammatory mediators.⁴ Although its effects on respiratory disease have not been tested, this dentifrice may provide protection because it reduces the growth of oral bacteria and formation of plaque.

Intervention Trials Studying Oral Cleaning and Respiratory Disease

Study	Subjects	Interventions	Major Findings
Pugin, <i>et al.</i> ⁵	ICU patients	Topical solution containing polymyxin B, neomycin and vancomycin vs. PBO	Antibiotics lowered prevalence of pneumonia (16% vs. 78%)
DeRiso, <i>et al.</i> ⁶	ICU patients undergoing heart surgery	Chlorhexidine oral rinse vs. PBO	Chlorhexidine lowered prevalence of respiratory tract infections (0.29% vs. 0.94%) and mortality (1.2% vs. 5.6%)
Fourrier, <i>et al.</i> ⁷	ICU patients requiring mechanical ventilation	Chlorhexidine gel vs. bicarbonate rinse and aspiration	Chlorhexidine lowered prevalence of nosocomial infection (27% vs. 57%) and number of cases of pneumonia per 1000 days of ventilation (10.7 vs. 32.3)
Bergmans, <i>et al.</i> ⁸	ICU patients	Topical gel containing gentamicin, colistin and vancomycin vs. 2 PBO groups	Antibiotics lowered prevalence of pneumonia (10% vs. 23-31%) and colonization by potentially pathogenic microorganisms (10% vs. 59-63%)
Yoneyama, <i>et al.</i> ⁹	Nursing home residents	Supervised tooth-brushing and povidone-iodine vs. no special treatment	Relative risk of pneumonia was 1.67 in untreated patients relative to active care

ICU: intensive care unit; PBO: placebo
Adapted from Scannapieco, *et al.*, 2003²

The association between oral bacteria and pneumonia has implications for the institutionalized,

including those living in nursing homes or hospitals for extended periods of time. People in these situations have a higher exposure to pathogens, are less likely to pay close attention to oral health, and are more likely to have poor general health.¹⁰ In descriptive studies, institutionalized subjects have more dental plaque and are more prone to colonization by respiratory pathogens than controls.² Therefore, institutionalized people represent a high-risk group for pneumonia related to oral bacteria.

Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) was the sixth leading cause of death worldwide in 1990.¹¹ COPD includes chronic bronchitis, in which irritation of the bronchial airway causes increased mucous production and persistent cough, and emphysema, in which dilation of small air passages leads to lung damage.¹⁰

Risk factors for COPD include smoking, chronic exposure to atmospheric pollutants, such as second-hand smoke, and genetic conditions.¹⁰ COPD patients experience periodic exacerbations for unknown reasons, and bacterial infections caused by *H. influenzae*, *S. pneumoniae*, and *Moraxella catarrhalis* may contribute to these episodes.¹⁰

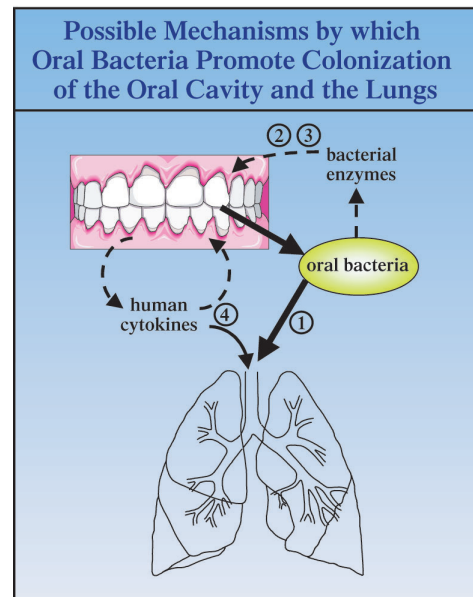
Association Between Periodontal Disease and COPD

Epidemiological studies have revealed an association between periodontal disease and COPD.² For example, among 13,792 participants in a national health survey who received a standardized dental examination, subjects with a history of COPD had a greater mean periodontal attachment loss ($p = 0.0001$).¹² Those with a mean attachment loss of at least 2.0 mm were more likely to have COPD than those with a mean attachment loss of less than 2.0 mm (odds ratio 1.35, 95% confidence interval = 1.07-1.71). However, this association has been reported in epidemiological studies only. To date, no prospective studies have investigated the link between periodontal disease and COPD.²

Potential Mechanisms by which Oral Bacteria Influence Respiratory Disease

At least four mechanisms have been envisioned¹⁰ to explain the role of oral bacteria in the pathogenesis of respiratory disease (see Figure).

First, oral pathogens may be directly inhaled. Organisms living in dental plaque are shed into saliva, and small droplets may be aspirated into the lungs. Normally, the defense mechanisms of the lungs prevent infection. However, bacterial colonization of the lower airway can occur if the



Numbers correspond to the four mechanisms described in the text. Adapted from Scannapieco, 1999¹⁰

immune system is suppressed or defective, if an unusually virulent pathogen is aspirated, or if an overwhelming number of organisms are aspirated simultaneously.

Second, the action of bacterial enzymes on oral epithelial cells may promote colonization by respiratory pathogens. Ordinarily, molecules on the surface of epithelial cells protect against bacterial adhesion, but oral bacteria release enzymes that may degrade these molecules. Poor oral health results in high protease activity in saliva that may damage epithelial cell surfaces and cause increased susceptibility to colonization by pathogenic bacteria.

Third, bacterial enzymes may reduce the protection against colonization provided by mucosal secretions. Proteins in mucosal secretions appear to bind to invading bacteria, inhibiting their adherence to epithelial cells and promoting their elimination from the host. Enzymes from oral bacteria can modify these protective proteins, preventing them from binding to invading pathogens.

Fourth, cytokines may contribute to colonization of the respiratory epithelium. Periodontitis stimulates gum tissue to release cytokines, which may induce changes on the epithelial cell surface. Cytokines also recruit neutrophils to the site of inflammation; neutrophils produce proteases and oxygen radicals that may damage the epithelium. Either of these actions may increase the susceptibility of tissue to bacterial colonization. Contamination of the respiratory epithelium by orally released cytokines, or release of cytokines by the respiratory epithelium itself in response to contact with oral bacteria, may promote

respiratory infection.

Conclusion

Regardless of the mechanism, large numbers of respiratory pathogens in the oral cavity appear to promote respiratory diseases, such as pneumonia and COPD. Although further study is needed to define the relationships between periodontitis and respiratory disease, inhibiting growth of oral bacteria reduces the risk of pneumonia. Therefore, proper attention to oral hygiene, including brushing with an antibacterial dentifrice such as Colgate® Total® and regular flossing, may help prevent respiratory illness, especially in vulnerable populations, such as hospitalized patients and institutionalized elders.

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