



Surveillance Spotlight: Current Concepts in Oral-Systemic Health

Relationship Between Periodontal Disease and Dementia: Real or Imagined?

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Recently, there has been much interest in the possible connection between poor oral health and the onset of dementia in later life. The inflammatory hypothesis of various neurodegenerative diseases such as Alzheimer disease and Parkinson disease (the most common neurodegenerative disorders leading to dementia in the elderly) has evolved from being on the fringe of medical speculation to part of mainstream thinking.^{1,2}

Brain mononuclear phagocytes, especially microglia (brain resident macrophages), function to protect the nervous system by scavenging for debris, killing microbial pathogens and regulating immune responses. Microglia are activated by a variety of environmental stimuli, including pro-inflammatory cytokines and bacterial lipopolysaccharides, which initiate a cascade of events that can best be characterized as a neuroinflammatory process.¹ Recent evidence suggests that systemic inflammation is associated with signals that pass from the blood to the brain via perivascular macrophages and microglia.³ The resultant neuroinflammatory responses include secretion of neurotoxic factors causing cell injury and death throughout the central nervous system. Over a period of years, this smouldering inflammation in the brain may destroy sufficient amounts of neurons to cause the clinical signs of Alzheimer or Parkinson dementia. Indeed, a recent population-based prospective cohort study⁴ has demonstrated that serum C-reactive protein and pro-inflammatory cytokine levels are increased before the clinical onset of dementia.

These interactions suggest that systemic infections, or indeed any systemic challenge that promotes a systemic inflammatory response, may contribute to the outcome or progression of chronic neurodegenerative disease. This scenario provides a potential link between periodontitis-induced bacteremia or endotoxemia and subsequent neuronal injury.⁵ Some recent studies⁶⁻⁸ have examined oral disease as a potential risk factor in the development of dementia. One of the most interesting of these is the Nun study, a longitudinal study of aging and Alzheimer disease in 144 participants aged 75–98 years old. The study used 40 years of dental data and 12 years of findings from annual cognitive assessments and brain autopsies, which provided an unparalleled opportunity to study dental health, dementia and neuropathology. The findings demonstrated for the first time an association between a history of oral disease and the development of dementia in a longitudinal population-based design. Participants with the most tooth loss due to periodontal disease had the highest risk of prevalence and incidence of dementia (overall risk for dementia increased by 120%).

Most recently, findings¹⁰ were published regarding relationships between systemic exposure to periodontal pathogens (as measured by immunoglobulin G [IgG] against *Porphyromonas gingivalis*) and cognitive test outcomes in 2,355 participants from the Third National Health and Nutrition Examination Survey, a nationally representative cross-sectional observation study among older adults in the United States. This study was significant due to its large sample size and findings of poor immediate verbal memory, impaired delayed recall and difficulty with serial subtractions in individuals with *P. gingivalis* IgG (the relationship was dose-dependent as individuals with higher IgG levels exhibited more severe deficits in cognitive function). This is the first demonstration that a serological marker of periodontitis is associated with impaired cognition.

This cross-sectional analysis does not prove directionality of the association between cognition and oral health. An argument can be made for cognitive impairment leading to poor oral health (for example, people with impaired cognition could

be inattentive to oral hygiene or oral health maintenance as cognitive impairment progresses). However, a growing body of evidence supports a possible association between poor oral health and dementia. Thus, additional studies of relationships between oral health and cognition are required. ✦

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