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# Don't forget to floss and floss so you don't forget? Emerging evidence linking periodontal disease and dementias

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# Don't forget to floss and floss so you don't forget? Emerging evidence linking periodontal disease and dementias


## Abstract

Patients with periodontal disease are significantly more likely to develop Alzheimer's disease than those who are periodontally healthy. This interaction is thought to be mediated by inflammation, the periodontal microbiome, and the immune reactions to those pathogens that are associated with the oral biofilm. The elderly population in the United States is expected to nearly double by the year 2050. Currently, over 5 million adults in the United States suffer with dementia. The generation that makes up the growing elderly population has rates of total edentulism that are dropping precipitously. Furthermore, medications for dementia often increase symptoms of xerostomia, and higher caries rates are seen in patients with dementia, particularly those with moderate to severe disease and/or those who reside in residential nursing care facilities. It follows, therefore, that many older adults are dentate and suffering with dementia and will require dental care that is delivered or facilitated by primary care providers. There is a need for protocols that allow for effective oral home care for dementia patients, while minimizing care-resistant behaviors, as well as nonsurgical interventions for patients with caries and/or periodontal disease. This course seeks to improve the dental care provider's understanding of the interaction between periodontal disease, dental caries, and dementia. It will also serve as an aid in the clinical decision-making process to optimize dental health for patients with dementia and periodontal disease.


## Educational objectives

Upon completion of this course, the dental professional should be able to:

1. Understand the current scientific literature about the prevalence, etiology, and stages of dementia
2. Recognize and discuss with patients the association of periodontal diseases and oral bacteria with dementia and Alzheimer's disease
3. Develop and implement strategies for communication and delivery of oral hygiene and dental care to patients suffering with dementia
4. Evaluate patients' risk factors and oral hygiene to develop effective intervention and treatment modalities to reduce caries and periodontal disease rates

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Dementia is the most frequent neurological disease and is recognized as a global public health priority by the World Health Organization.[1] Due to the aging of the population, treatment costs for dementia are expected to more than triple by 2050.[1] While treatments to reduce and/or delay dementia symptoms have been studied, there has not been an effective method to prevent or manage dementia for the long term.[2] Dementia causes loss of cognitive function and interferes with a patient's ability to perform activities of daily living and to participate in social activity.[2] Although dementia is not solely a disease of the elderly, the most common form is degenerative brain disease, such as Alzheimer's disease (AD) or vascular dementia.[1,3] As the global elderly population increases, the prevalence of dementias will also likely increase.[1,3] Systemic and environmental factors have been associated with increased incidence of dementia including: low educational attainment, nicotine use, physical inactivity, depression, hypertension in middle age, diabetes mellitus, and overweight/obesity status.[4] Further, systemic inflammation has been associated with dementia development.[5,6] Given these findings, with protocols to treat associated diseases in at-risk patients, it may be possible to prevent and/or delay dementia development and extend the healthy life span.

Oral health status has been strongly associated with dementia.[7-10] This relationship may be bidirectional and multifactorial; impaired cognitive function can impact oral hygiene delivery[7] and inflammation related to periodontal disease, and subsequent tooth loss may impact dementia development.[8-10] Inflammatory mediators closely associated with periodontal disease, e.g., C-reactive protein (CRP), interleukin 6 (IL-6), interleukin 1β (IL-1β), and tumor necrosis factor α (TNF-α), have been identified as playing a potential role in the development and/or progression of dementias.[7-12] An "inflammatory model" linking periodontal disease and dementias posits that systemic inflammatory markers that are elevated in patients with periodontal disease progression can stimulate the production of beta amyloid and tau protein in brain tissue and increase the permeability of the blood-brain barrier, which may increase the risk of development and/or increase the rapidity of symptom onset in individuals with dementia.

This course will discuss the interaction between periodontal disease and dementias, the impact of dementias on overall oral health, and the effect of periodontal therapy on dementia disease activity. In fact, a recent study gained much lay media attention after the authors found that brain tissue from elderly individuals contained higher levels of gingipain enzymes from *Porphyromonas gingivalis (P. gingivalis)* than in healthy controls.[13]

As oral biofilm accumulates, it shifts from a eubiotic biofilm associated with health to a more dysbiotic and periodontopathogenic biofilm.[14,15] Such dysbiotic biofilms are associated with both gingivitis and periodontitis.[14] As the biofilm becomes more pathogenic, the number and proportion of strict anaerobic species present within the biofilm mass increase.[14,15] Anaerobic and motile organisms associated with periodontitis have been associated with systemic bacteremias, particularly in the presence of gingival inflammation.[16] These bacteremias occur during day-to-day procedures such as mastication and toothbrushing.[17] It is feasible, therefore, that in cases of gingival inflammation, either due to gingivitis or periodontitis, the associated systemic translocation of pathogenic bacterial species may result in bacterial entry into brain tissues and potentially negatively impact neural tissues and cognition.

## Epidemiology and etiology of common dementias

Dementia cannot be considered a natural consequence of aging or even extreme forgetfulness. Dementia is defined by its progressive and chronic nature. Patients with dementia experience deterioration in memory, thinking, behavior, and the ability to perform everyday activities.[1]

Currently, more than 55 million people live with dementia worldwide, and there are nearly 10 million new cases every year.[1] Furthermore, global estimates suggest that the total economic costs caused by dementia increased from US $279.6 billion in 2000 to $948 billion in 2016, with an annual growth rate of nearly 16%.[18] It is estimated that attributable dementia spending will reach $1.6 trillion by 2050.[19] Given the considerable economic and societal burdens associated with dementia, understanding the underlying risk factors and implementing public health measures to reduce the overall burden in the future is critically important.

## Prevalence and distribution of patients with dementia

Dementia is growing at alarming rates in all regions of the world and is proportional to population aging.[20] It is projected that the number of people with dementia will increase from an estimated 57.4 (50.4 to 65.1) million cases globally in 2019 to an estimated 152.8 (130.8 to 175.6) million cases in 2050.[18] Globally, 1.62 million (0.41–4.21) people were estimated to have died of end-stage dementia in 2019, and mortality due to dementia is expected to rise in coming years.[21,22] The prevalence of dementia increases dramatically with age; 3% of people age 65-74, 17% of people age 75-84, and 32% of people age 85 or older have Alzheimer's dementia.[23]

## Different types of dementias

Alzheimer's disease is the most common form of dementia, causing approximately two-thirds of all cases of dementia. Other major forms of dementia are vascular dementia (affecting up to 20% of patients with dementia), dementia with Lewy bodies (approximately 15% of all dementia cases), frontotemporal dementia (less than 5% of dementia cases).[24] The boundaries between different forms of dementia are indistinct, and mixed forms, as well as dementia as a comorbidity with other diseases, may coexist.[1] Additionally, less common forms of dementia include: Parkinson's disease dementia, Huntington's disease, Creutzfeldt-Jakob disease and other prion diseases, dementia in HIV/AIDS, traumatic brain injury, and Wernicke-Korsakoff syndrome (includes dementia from alcohol abuse).[25]

Risk factors for dementia are multifactorial and vary throughout life.[4] Educational attainment early in life, e.g., number of years spent in education, is

protective against dementia, and a higher level of educational attainment as well as continued education/learning throughout life may delay dementia onset.[26] Additionally, hypertension, diabetes mellitus, hyperlipidemia, alcohol use, diet, and smoking are associated with increased risk of dementia development, whereas increased cognitive activity, social activity, and exercise may negatively influence dementia development.[26,27] Late-onset Alzheimer's, the most common form of dementia, is thought to have multifactorial etiology. This form of dementia is generally thought to be due to a "multihit" hypothesis, where development of the disease is due to a combination of genetic, lifestyle, and environmental factors. Genetically, a polymorphism of the apolipoprotein E (APOE) gene, specifically APOE ε4 on chromosome 19, increases an individual's risk for developing late-onset Alzheimer's disease.[28] This gene and others are thought to increase the risk of Alzheimer's disease development by increasing the production of presenilin and β-amyloid precursor protein (BAPP).[29] The presence of these proteins have been shown to enhance deposition of β-amyloid protein in brain tissue.[29] In addition to these genetic risk factors, epigenetic alterations of the genome (modification of the genome to turn genes off) may play a role for environmental and lifestyle factors to influence gene expression and ameliorate or potentiate underlying genetic risk factors.[30] Studies have also identified blood-brain barrier dysfunction, including: 1) increased permeability, 2) microbleeds, 3) impaired nutrient transport, and 4) impaired learning of neurotoxins, as a mechanism for introduction of neurotoxic substances, e.g., bacteria and bacterial by-products, into the brain.[31]

**TABLE 1: Stages of cognitive impairment/dementia**

| Diagnosis | Stage | Signs and symptoms |
|---|---|---|
| No dementia | Stage 1: No cognitive decline | In this stage, a person functions normally and has no memory loss and is mentally healthy. People without dementia would be in stage 1. |
| No dementia | Stage 2: Very mild cognitive decline | This stage is used to describe normal forgetfulness associated with aging, for example, forgetting names and where familiar objects were left. Symptoms of dementia are not evident to the individual or their physician. |
| No dementia | Stage 3: Mild cognitive decline | This stage includes increased forgetfulness, slight difficulty concentrating, and decreased work performance. People may get lost more frequently or have difficulty finding the right words. At this stage, a person's loved ones will begin to notice a cognitive decline. |
| Early stage | Stage 4: Moderate cognitive decline | This stage includes difficulty concentrating, decreased memory of recent events, and difficulties managing finances or traveling alone to new locations. People have trouble completing complex tasks efficiently or accurately and may be in denial about their symptoms. They may also start withdrawing from family or friends because socialization becomes difficult. At this stage, a physician can detect clear cognitive problems during a patient interview and exam. |
| Midstage | Stage 5: Moderately severe cognitive decline | People in this stage have major memory deficiencies and need some assistance to complete their daily living activities (dressing, bathing, preparing meals, etc.). Memory loss is more prominent and may include major relevant aspects of current lives. For example, people may not remember their address or phone number and may not know the time of day or where they are. |
| Midstage | Stage 6: Severe cognitive decline (middle dementia) | People in stage 6 require extensive assistance to carry out their activities of daily living (ADL). They start to forget names of close family members and have little memory of recent events. Many people can remember only some details of earlier life. Individuals also have difficulty counting down from 10 and finishing tasks. Incontinence (loss of bladder or bowel control) is a problem. Ability to speak declines. Personality/emotional changes, such as delusions (believing something to be true that is not), compulsions (repeating a simple behavior, such as cleaning), or anxiety and agitation may occur. |
| Late stage | Stage 7: Very severe cognitive decline (severe dementia) | People in this stage have essentially no ability to speak or communicate. They require assistance with most activities (e.g., using the toilet, eating). They often lose psychomotor skills, for example, the ability to walk. |

## Cognitive impairment classifications

It can be difficult to pinpoint the exact onset of dementia as symptoms progress along a spectrum with increasing severity over time and progression speed is dependent on myriad patient-related and environmental factors. Progression generally occurs from no impairment to very severe dementia, with early symptoms being subclinical in many patients.[31] Both the Global Deterioration Scale/Reisberg Scale and the Functional Assessment Staging Test (FAST) assign seven stages to the progression of dementia **(table 1)**.[32]

## Epidemiology and etiology of periodontal disease

Periodontal diseases include inflammatory diseases of the supporting structures around the teeth—the gingiva, periodontal ligament, alveolar bone, and cementum.[33] Research shows all individuals are susceptible to gingivitis, a reversible form of gingival inflammation. Additionally, gingivitis may be the precursor to more serious, irreversible forms of periodontal diseases.[34] Gingivitis is caused by dysbiotic oral biofilm and, in general, gingivitis severity is related to the amount and type of bacteria that have accumulated at and

around the gingival margins throughout the mouth. Oral modifying factors for gingivitis include local factors (oral biofilm retentive factors and oral dryness) and systemic factors (smoking, metabolic factors, nutritional factors, pharmacologic agents, sex steroid hormone elevation, and hematologic conditions).[34-36] Removal of biofilm and local etiologic factors results in the reversal of gingivitis symptoms and reduces local and systemic levels of inflammatory markers in patients with gingivitis.[34,35,37]

Periodontitis is a chronic multifactorial inflammatory disease of the hard and soft tissues supporting the teeth associated with dysbiotic oral biofilm. This dysbiotic biofilm then initiates a host immunoinflammatory response that, over time, may result in progressive destruction of the periodontal ligament and alveolar bone if not adequately resolved.[33,38] Average progression of periodontal disease demonstrates a slow to moderate rate of disease progression with approximately 0.1 mm of attachment loss and 0.2 teeth lost annually.[38] Groups with fastest and slowest disease progression differed considerably, with accelerated attachment loss associated with access to comprehensive dental care as well as local and/or systemic factors.[39]

In an updated classification system from the American Academy of Periodontology (AAP) and European Federation of Periodontology (EFP), individuals are classified with a stage and grade to characterize disease severity and risk of future disease progression.[38,40] Periodontitis stage is assigned as I–IV and is determined by patients' current disease presentation, including attachment, bone, and tooth loss, and the case complexity.[38,40] Periodontitis grade is defined as A–C and is based upon risk and evidence of the rapidity of disease progression over time.[38,40]

The prevalence of periodontitis has been estimated to be over 42% of US adults over 30 years of age.[41] Of those individuals, 7.8% had severe periodontitis, and severe periodontitis was most prevalent among adults 65 years of age or older, Mexican Americans, non-Hispanic blacks, and smokers.[41] These statistics suggest that the prevalence of periodontitis among US adults is nearly fourfold greater than that of diabetes mellitus[42] and over sixfold greater than that of coronary artery disease.[43] Periodontitis is extremely prevalent, and after initiation by bacteria and bacterial virulence factors, disease progression and tissue destruction occurs through host-mediated inflammatory pathways,[35] which may vary based upon genetic and other risk factors.[44-47] The result is a chronic immunoinflammatory disease that may pose a significant systemic burden for individuals.[48]

## Associations between dementias and periodontal disease

Periodontal disease results in systemic inflammation and the potential for bacteremia, both of which may impact other organ systems.[16,17] Periodontitis has been linked to cognitive impairment and dementia after controlling for confounding factors such as age, sex, and educational attainment.[49-51] Disease progression in periodontal disease is associated with dysbiosis and elevated chronic inflammation, and dementia and Alzheimer's disease have been linked to periodontal disease through both inflammatory and bacterial mechanisms.[11,52-54] Periodontal disease has also been linked to increased systemic and neurological markers of Alzheimer's disease.[55-57] Impaired cognitive function has been associated with worsening oral health parameters, including caries rates and periodontal clinical parameters, in cross-sectional studies.[58-60] Epidemiologic studies have also shown that individuals with increased systemic inflammation, including elevated proinflammatory markers and cardiovascular diseases, have a higher risk of developing dementia and more rapid progression of dementia symptoms over time.[11,53] Additionally, patients with dementia and their caregivers must manage delivery of preventive oral hygiene measures, which can be increasingly difficult as dementia severity increases.[61,62] Due to the number of individuals affected by both periodontal disease and dementia and the progressive nature of both diseases, understanding of the interaction between periodontal disease and dementia and treatment strategies for promotion of optimal oral health in patients suffering with dementia is of utmost importance to the dental practitioner.

Chronic inflammation is correlated with the onset and progression of Alzheimer's disease, and it has been postulated that chronic inflammation and neuronal aging induces stress and neuropathological changes.[63] In this model, chronic inflammation primes the microglia and induces a hyperreactive state, which then results in a failure to clear misfolded or damaged neuronal proteins and enhances the aggregation of neuronal proteins associated with dementia, such as Aß1-42.[64,65] Similarly, periodontal tissue breakdown seen in periodontitis is a result of host inflammatory response to bacterial stimuli. Periodontal tissue breakdown is mediated by pro-inflammatory cytokines and mediators such as interleukin-1ß (IL-1ß), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), prostaglandin $E_2$ ($PGE_2$), receptor activator of nuclear factor kappa B ligand (RANKL), and matrix metalloproteinases (MMPs). These pro-inflammatory mediators interact with bacteria and the surrounding tissues. The heterogeneity among individuals in this response can influence disease susceptibility and severity.[65] Additionally, periodontal disease severity is correlated to increased levels of pro-inflammatory mediators systemically.[66-68] Because inflammation may influence the progression of disease in both periodontitis and dementia, one mechanism of interaction between periodontitis and dementia may include increased levels of inflammation and their influence on neuronal function.

Oral bacteria and their by-products have been found in brain tissue,[13,69,70] and increased levels of serum antibodies to periodontopathogenic bacteria have been found in patients with Alzheimer's disease and dementia.[54,58,71] These bacteria may enter the brain through several pathways: 1) bacteremia allows for bacteria within the bloodstream, and degradation of the blood-brain barrier is seen in age, chronic infection, and in the presence of inflammation, 2) direct access to the brain may be gained through perivascular spaces, and 3) via olfactory and/or trigeminal nerve pathways.[72] In addition

to the bacteria themselves, influence on the brain by bacterial by-products including virulence factors such as lipopolysaccharide, capsular material, proteolytic enzymes, and gingipains may contribute to the progression of dementia.[13,69,70,73] It should be noted that the presence of gingipains, in particular, has been associated with increases in tau protein and potential worsening of dementia.[13] Finally, epigenetic alterations of the host genome as a result of exposure to bacteria and/or their by-products may alter gene expression and influence the risk conferred by those genes. Bacteria and their by-products have been shown to increase DNA methylation and histone acetylation, which has been indicated in the development of periodontal disease, cancers, and other diseases.[74,75]

Oral hygiene status and oral microbiome composition in elderly dentate patients has also been associated with development of dementia.[76] Alteration of the oral microbiome may be achieved through oral hygiene interventions, which then can alter serum levels of microorganisms and change a potential pathway for bacteria and their by-products to cross the blood-brain barrier.[68,70,77] Oral dysbiosis is indicated as the primary etiology for both periodontitis and gingivitis, and those dysbiotic microbiota have been independently associated with invasion of soft tissues and bacteremias.[14,15] Such systemic translocation of bacteria has been associated with myriad systemic diseases, including dementias.[13,16,17,69-71] Given the impact of oral dysbiosis on systemic health, optimal oral home-care regimens, including care of teeth and dental implants as well as appropriate cleaning of removable prostheses, should be of a part of care delivery for individuals with dementia.[78] Improved oral hygiene delivery is associated with decreases in dental diseases in these populations[79,80] and has been suggested as an intervention to reduce the direct and indirect influences of oral bacteria and their by-products on the brain and the potential influence of these bacteria and their by-products on cognitive decline **(figure 1)**.[81]

## The effect of periodontal therapy on dementia disease activity

Interventional studies assessing the impact of periodontal therapy on dementia are limited. It is well-established that meticulous oral hygiene and the use of some chemotherapeutic agents can address oral dysbiosis.[82-84] While direct evidence of periodontal therapeutic intervention on dementia is limited, a recent study demonstrated that periodontal treatment had a favorable effect on Alzheimer's disease-related brain atrophy.[85] This may indicate that periodontal treatment could prevent or slow disease progression of dementias. Further, there is an ongoing phase II/III trial with the US Food and Drug Administration (FDA) to evaluate the use of a small-molecule inhibitor for gingipains and gingipain-binding sites (atuzaginstat [COR388, Cortexyme Inc.]). Animal studies have demonstrated that application of these inhibitors directly into the brains of mice orally infected with *P. gingivalis* reduced the neural toxicity of gingipains

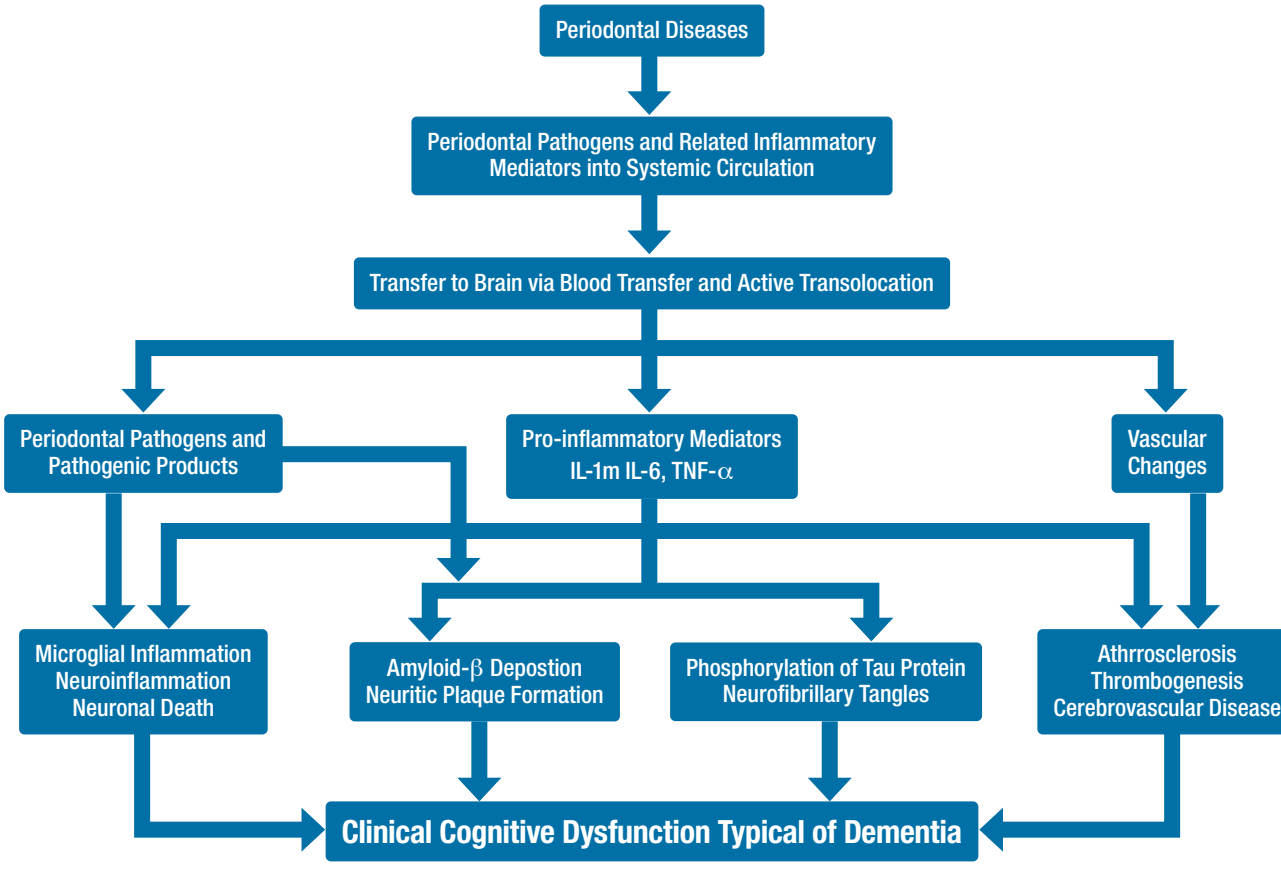


**FIGURE 1:** Mechanisms of interactions between periodontitis and dementia

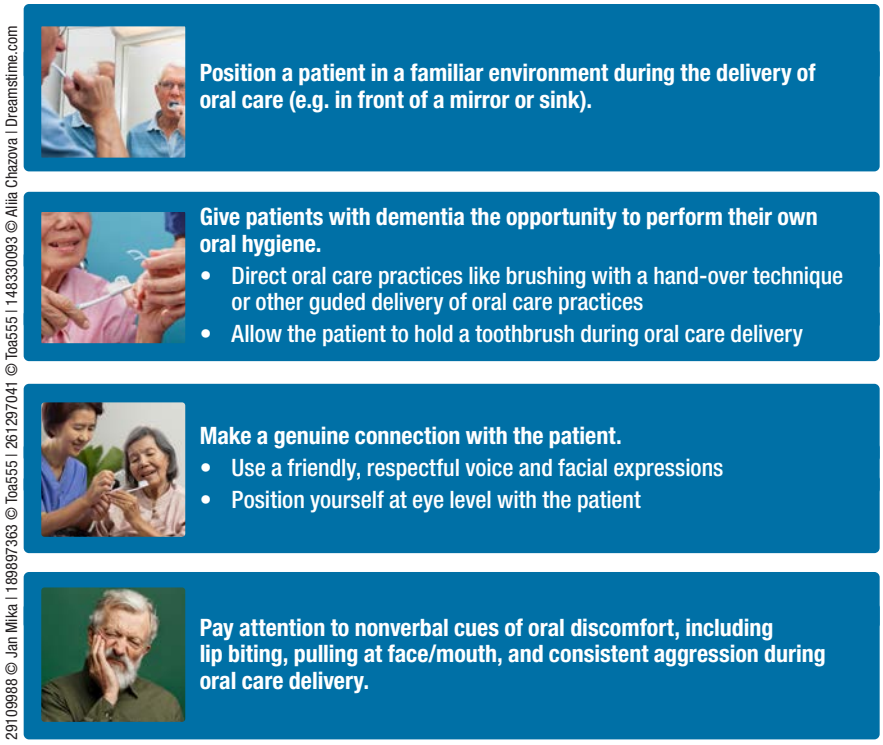




**FIGURE 2:** Strategies to reduce care-resistant behaviors in individuals with dementia during delivery of oral hygiene and professional dental care

and—ultimately—the formation of amyloid plaques and tau tangles.[13,86] The FDA phase Ib small-scale exploratory studies using this inhibitor showed improvements in cognitive function as measured by language and memory ability, inhibition of gingipain cleavage of apolipoprotein E4, and a reduction in cerebrospinal fluid markers for Alzheimer's disease.[87,88] The inhibitor further demonstrated reduction in *Porphyromonas spp.* intraorally and a reduction in periodontal disease destruction.[89]

## Clinical decision-making for dental treatment of patients with dementia

In order to assess and treat patients at risk for dementia or those with a dementia diagnosis, dental health-care professionals need to evaluate patients to determine what alterations to therapy may be needed to best treat them and establish oral health. It is critical to stress the importance of periodontal treatment and maintenance for oral and overall health. Evidence has shown that the risk of developing dementia in a longitudinal analysis was significantly higher in those with untreated periodontal disease when compared to those receiving regular maintenance therapy.[90] Periodontal therapies including mechanical debridement, local antimicrobial use, and extraction of hopeless teeth in patients with Alzheimer's disease have also been shown to result in improvements in cognitive function.[91] While it is unclear on the exact benefits of periodontal therapy in patients with cognitive impairment, the current evidence suggests that in addition to the oral health benefits, careful attention should be paid to this special population given the potential for cognitive benefits as well, due to microbial and inflammatory connections between periodontitis and dementias.[81,92]

There are, however, significant challenges in treating patients with cognitive impairment, including communication, memory, at-home plaque control, and compliance with dental care visits. Some of the dilemmas that dental health-care providers can encounter in this patient population include:

- Diagnosis of dental conditions and/or patient complaints if/when the patient cannot relate signs and symptoms of disease to the dental health-care provider
- Assessment of pain/discomfort when sensory changes may influence pain perception
- Determination of diagnostic and therapeutic prognoses to assess likely disease progression without intervention
- Understanding the likely path of dementia disease progression and how that may impact oral care and oral disease progression

Dental health-care providers must also assess the ability of a patient with dementia and/or their caregiver to provide regular oral hygiene outside of the dental office and the behavioral and treatment modifications that may be necessary to deliver care for patients with dental needs. It is critical that dental health-care professionals speak with patients and caregivers about the associations between oral dysbiosis, periodontitis, and dementia and the potential positive impacts of regular preventive and/or interventional dental care in patients with or at-risk for developing dementia.

Patients with dementia can also exhibit care-resistant behaviors, which are defined as behaviors in which persons with dementia resist the help of health-care providers or caregivers. Dental health-care providers can employ techniques, including forming a connection by approaching the patient at or below eye level, using a friendly and calm attitude, and using brief, one-step commands.[93,94] Caregivers should avoid elderspeak (sing-song tone of voice that is often used for babies/children and the elderly). Elderspeak use has been associated with an increase in care-resistant behaviors in adults with dementia.[78,93,94] Additionally, delivery of oral care in a familiar environment and providing a toothbrush or other oral care materials to a patient with dementia can reduce care-resistant behavior.[78,93,94]

It is also imperative to assess nonverbal cues of dental pain/discomfort in patients with severe dementia.[95] Some signs that a patient may be experiencing dental/oral pain include: chewing of lip or tongue, pulling at face or lips, refusing denture wear, and/or aggression in response to oral-related activities of daily living.

Figure 1 demonstrates some strategies that may be utilized to reduce care-resistant behavior both during professional dental care and when oral home care is being delivered by a caregiver **(figure 2)**.

Concerns regarding patients with dementia receiving ongoing dental care can include:

- Ability of the patient and/or caregiver to deliver regular oral hygiene
- Ability of the patient to tolerate dental interventions and the potential need for sedation
- Ability of the patient to give informed consent and/or assent to treatment
- Oral side effects of medications used to treat dementia symptoms and their implications for caries and periodontal disease development and progression

Given these concerns and implications, regular assessment of a patient's cognitive impairment in the dental office and modification of treatment related to the level of cognitive ability are critical to the overall success of dental management for patients with dementia. Niessen et al. developed an index to assess the need for alterations to dental treatment and the likelihood of a patient benefitting from dental treatment **(table 2)**.[96] The most important factor that dental health-care professionals must evaluate is the patient and/or caregiver capacity for delivery of home care. This index assesses the following:

- Patient's ability to perform activities of daily living. This can inform the determination of the level of occlusal functioning and types of prostheses that may be most beneficial to the patient (e.g., if the patient eats solid food and can feed themselves) and whether dental care delivery in an outpatient setting such as an independent dental office is feasible.
- Patient's level of social functioning. This allows assessment of the behavioral expectations for a patient undergoing dental treatment and/or the potential need for conscious sedation and/or general anesthesia to allow for care delivery.
- Condition of the remaining dentition, including plaque index and caries and periodontal conditions. This may determine if teeth with hopeless or poor prognosis are present and should be extracted and the likelihood of worsening oral disease over time as cognitive impairment progresses.

Once the level of cognitive functioning is assessed, the dental health-care provider should determine appropriate treatment and intervention. Dental health-care professionals can educate patients and caregivers about the associations between unmanaged periodontal disease and dementia, as well as the beneficial potential of periodontal therapy in patients at risk for or diagnosed with dementia disease. Further aggressive preventive oral therapy should be employed if possible to potentially reduce future dental needs. The assessment and considerations are summarized in **Table 3**.

**TABLE 2: Index for dental management (Adapted from Niessen et al.)[96]**

| Patient functional activity | 0 | 1 | 2 |
|---|---|---|---|
| Can the patient independently brush teeth and/or clean dentures? | Yes | Needs assistance | No—Cannot perform without complete assistance |
| Can the patient verbalize chief complaint and/or express signs and symptoms? | Yes | Limited ability | No |
| Can the patient follow simple one- and two-step instructions (e.g., sit in chair, stick out your tongue)? | Yes | Occasionally | No |
| Can the patient steadily hold a radiographic intraorally with a bite block, Rinn instrument, etc.? | Yes | Sometimes | No |
| Does the patient exhibit severe care-resistant behaviors, including assaultive behavior? | No | Sometimes | Yes |
| Total dental index score | 0-3: Mild disease (no modification needed)<br>4-7: Moderate disease (modify treatment plan)<br>8-10: Severe disease (emergency treatment only) | | |

**TABLE 3: Dental management index score and considerations for dental care (Adapted from Niessen et al.)[96]**

| Treatment planning approach | Dental Index Score | | |
|---|---|---|---|
| | Mild | Moderate | Severe |
| General considerations | Minimal changes in dental practice | Sedation may be necessary; short appointments; more frequent maintenance/ recall visits | Sedation may be necessary; short appointments; more frequent maintenance/ recall visits |
| Specific considerations | Aggressive prevention: Use of topical fluorides, daily oral hygiene, oral education of patient and caregivers; design treatment plan anticipating decline; restore to function as quickly as possible | Aggressive prevention: Use of topical fluorides, daily oral hygiene, oral education of patient and caregivers; design treatment plan to minimize interventions (e.g., reline dentures rather than remake them if possible) | Aggressive prevention: Use of topical fluorides, daily oral hygiene, oral education of patient and caregivers; deliver emergency care; consider function rather than esthetics when making treatment decisions |

## Summary

Research has demonstrated epidemiologic and biologic associations between periodontal disease and a number of dementias. The current theory of the interaction between these conditions focuses on the translocation of the periodontal microflora and periodontitis-associated inflammatory mediators to the central nervous system, where the microflora and their by-products can induce inflammatory and destructive changes in neural tissues. The current and future development of inhibitors to key microflora, such as *P. gingivalis*, through enzyme (e.g., gingipain) inhibition may provide benefits in patients with dementia for oral and other diseases. Improved oral health has been associated with systemic health and well-being improvements including: improved nutritional intake and sleep patterns, decreased agitation associated with discomfort/pain, and improved appearance. Dental health-care providers have a duty to appropriately assess current health conditions and to evaluate the risks and benefits for safely delivering dental care in a manner that enhances patients' oral and overall health.

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## Notes

## ONLINE COMPLETION

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## QUESTIONS

1. A 2019 study examining brain tissue from elderly individuals found that gingipains from *P. gingivalis* were present at ___ levels in brains from individuals with Alzheimer's disease than those who did not have Alzheimer's disease.
   A. Higher
   B. Lower
   C. Similar
   D. Unknown

2. Approximately how many people are diagnosed with dementia every year worldwide?
   A. 2 million
   B. 5 million
   C. 7 million
   D. 10 million

3. The number of people with dementia will increase from an estimated 57.4 million cases globally in 2019 to an estimated ___ million cases in 2050.
   A. 75
   B. 110
   C. 153
   D. 202

4. Which of the following has not been associated with the development of dementia?
   A. Smoking
   B. High level of educational attainment
   C. Diabetes mellitus
   D. Hypertension

5. Which of the following genetic polymorphisms has been linked to an increased risk of late-onset Alzheimer's disease?
   A. APOE e4
   B. IL-1β
   C. Angiotensin converting enzyme (ACE)
   D. Estrogen receptor-2

6. Chronic inflammation influences the progression of dementia. It has been hypothesized that inflammation primes the microglia and increases the production of neuronal proteins associated with dementia.
   A. Both statements are true.
   B. The first statement is true; the second statement is false.
   C. The first statement is false; the second statement is true.
   D. Both statements are false.

7. Studies show that blood-brain barrier dysfunction plays a role in the initiation and disease progression of dementia through the following mechanism:
   A. Increased permeability
   B. Microbleeds
   C. Impaired learning of neurotoxins
   D. All of the above

8. Alzheimer's disease is the most common form of dementia, causing approximately ___ of all cases of dementia.
   A. One-half
   B. Two-thirds
   C. Three-quarters
   D. Seven-eighths

9. Which of the following is not a major form of dementia?
   A. Vascular dementia
   B. Wernicke-Jakob
   C. Dementia with Lewy bodies
   D. Frontotemporal dementia

10. Which of the following is false?
    A. All individuals are susceptible to gingivitis.
    B. Gingivitis is reversible.
    C. Gingivitis severity is generally not related to the amount and type of oral biofilm present at the gingival margins of teeth.
    D. Gingivitis is modified by local factors (dental biofilm retentive factors and oral dryness) and systemic factors (smoking, metabolic factors, nutritional factors, pharmacologic agents, sex steroid hormone elevation, and hematologic conditions).

11. Average progression of periodontal disease demonstrates a slow to moderate rate of disease progression with approximately ___ mm of attachment loss and ___ teeth lost annually.
    A. 0.1; 0.2
    B. 0.2; 0.5
    C. 0.5; 0.5
    D. 0.8; 0.2

12. Periodontitis stage is assigned as A-D and is assessed by patients' current disease presentation, including attachment, bone, and tooth loss, and the case complexity. Periodontitis grade is defined as I-III and is based upon risk and evidence of the rapidity of disease progression over time.
    A. Both statements are true.
    B. The first statement is true; the second statement is false.
    C. The first statement is false; the second statement is true.
    D. Both statements are false.

13. Among US adults over the age of 30, ___% have some form of destructive periodontitis.
    A. 16
    B. 27
    C. 42
    D. 61

14. Pathways by which oral bacteria are thought to enter the brain include:
    A. Bacteremia allows for bacteria within the bloodstream, and chronic infection, age, and inflammation increase the permeability of the blood-brain barrier.
    B. Bacteria may gain direct access to the brain through perivascular spaces.
    C. Bacteria may pass into the brain through olfactory and/or trigeminal nerve pathways.
    D. All of the above

15. Periodontal treatment resulted in ___ in brain atrophy in patients with Alzheimer's disease.
    A. An increase
    B. No change
    C. A decrease
    D. Unknown effects

16. A small-molecule inhibitor for gingipains and gingipain-binding sites (atuzaginstat [COR388, Cortexyme Inc.]) has been tested in animals. Application of these inhibitors directly into the brains of mice orally infected with *P. gingivalis* resulted in:
    i. Reduced formation of amyloid plaques and tau tangles
    ii. Decreased gingipain toxicity
    iii. Reduction in *Porphyromonas spp.* intraorally
    iv. Reduction in periodontal disease destruction
    A. iii and iv
    B. iii only
    C. ii, iii, and iv
    D. All of the above

## ONLINE COMPLETION

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## QUESTIONS

17. Periodontal therapies, including mechanical debridement, local antimicrobial use, and extraction of hopeless teeth, in patients with Alzheimer's disease have also been shown to result in ___ in cognitive function.
    A. An improvement
    B. No change
    C. Worsening
    D. Unknown effects

18. Which of the following is not a challenge in the treatment of patients with dementia?
    A. Diagnosis of dental conditions and/or patient complaints if/when the patient cannot relate signs and symptoms of disease to the dental health-care provider
    B. Delivering sedation and/or general anesthesia in patients for behavioral management
    C. Assessment of pain/discomfort when sensory changes may influence pain perception
    D. Determination of diagnostic and therapeutic prognoses to assess likely disease progression without intervention

19. Care-resistant behavior is defined as:
    A. Persons with dementia withstand or oppose the helping efforts of caregivers
    B. Caregivers that induce agitation in persons with dementia
    C. Patients with dementia related to preference for one caregiver over another
    D. Caregivers who decrease the effectiveness of health-care delivery

20. Which of the following is a technique caregivers can implement to reduce care-resistant behavior?
    A. Approaching the patient above eye level
    B. Using elderspeak
    C. Using polite, one-step commands
    D. All of the above

21. Which of the following are signs of oral discomfort that may be recognized in a nonverbal patient with dementia?
    i. Chewing of lip or tongue
    ii. Pulling at face or lips
    iii. Refusing denture wear
    iv. Aggression in response to oral-related activities of daily living
    A. i, iii
    B. i, ii, iii
    C. i, ii, iii, iv
    D. iv only

22. Which is the most important factor that dental health-care professionals must evaluate when determining a dental treatment plan?
    A. Number of remaining teeth
    B. Insurance coverage for dental care
    C. Patient and/or caregiver capacity for delivery of home care
    D. Likelihood of improved cognition with periodontal care

23. Dental health-care providers should assess cognitive functioning, which can then allow for determination of appropriate interventions based upon a risk-benefit analysis. In patients with more severe cognitive impairment, more aggressive interventions are indicated.
    A. Both statements are true
    B. The first statement is true; the second statement is false
    C. The first statement is false; the second statement is true
    D. Both statements are false

24. Which of the following is not seen with improved oral health in patients with dementia?
    A. Improved nutritional intake
    B. Worsening sleep patterns
    C. Decreased agitation associated with discomfort/pain
    D. Improved appearance

25. There are seven stages of dementia. The most severe stage is categorized by:
    A. Essentially no ability to speak or communicate and assistance required with most activities (e.g., using the toilet, eating)
    B. Increased forgetfulness, difficulty concentrating, and decreased work performance; individuals get lost more frequently or have difficulty finding the right words
    C. Memory loss may include major relevant aspects of current lives
    D. Personality/emotional changes, such as delusions (believing something to be true that is not), compulsions (repeating a simple behavior, such as cleaning), or anxiety and agitation

26. Niessen et al. developed an index for dental management of patients with dementia. This index evaluates all of the following except:
    A. Ability of the patient/caregiver to brush teeth or clean dentures
    B. Ability of the patient to verbalize their chief complaint
    C. Care-resistant behavior, including assaultive behavior
    D. Ability of the patient to remember a series of unrelated words

27. The Niessen et al. dental index stratifies patients into the following categories:
    i. No dementia disease
    ii. Mild dementia disease
    iii. Moderate dementia disease
    iv. Severe dementia disease
    A. i, ii, iii
    B. i, ii, iii, iv
    C. ii, iii, iv
    D. ii and iii

28. In patients with mild dementia disease, which of the following specific treatment considerations is recommended?
    A. Aggressive prevention: use of topical fluorides, daily oral hygiene, oral education of patient and caregivers
    B. Design treatment plan anticipating decline
    C. Restore to function as quickly as possible
    D. All of the above

29. In patients with moderate dementia disease, which of the following general treatment considerations is not recommended?
    A. Sedation may be necessary.
    B. Consider patient and caregiver esthetic needs.
    C. Shorten appointments.
    D. Provide more frequent maintenance/recall visits.

30. In patients with mild dementia disease, which of the following specific treatment considerations is recommended?
    A. Deliver emergency care.
    B. Reduce recommendations for oral hygiene based upon what the patient can perform.
    C. Consider esthetics when making treatment decisions.
    D. Restore patient with fixed rather than removable prostheses.

| | |
|---|---|
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ANSWER SHEET

# Don't forget to floss and floss so you don't forget? Emerging evidence linking periodontal disease and dementias

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## Educational Objectives

1. Understand the current scientific literature about the prevalence, etiology, and stages of dementia
2. Recognize and discuss with patients the association of periodontal diseases and oral bacteria with dementia and Alzheimer's disease
3. Develop and implement strategies for communication and delivery of oral hygiene and dental care to patients suffering with dementia
4. Evaluate patients' risk factors and oral hygiene to develop effective intervention and treatment modalities to reduce caries and periodontal disease rates

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   Objective #1: Yes No Objective #3: Yes No

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