

## Alzheimer's Disease in Dentistry: Repercussions and management in oral health



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### ABSTRACT

Alzheimer's disease is one of the most prevalent forms of neurodegenerative dementia that mainly affects elderly individuals, manifesting itself through cognitive disorders that include gradual memory loss, communication difficulties and temporal and spatial disorientation. So far, the etiology of this disease remains uncertain, and its most challenging feature is the lack of a definitive cure, which makes treatment focused on delaying its progression and controlling symptoms. To achieve these goals, it is essential to adopt a multidisciplinary approach involving physicians, nurses, physiotherapists and dentists. The purpose of this work is to present the fundamental principles related to Alzheimer's disease, as well as its implications for oral health, offering guidance to dental professionals on how to conduct care for these patients. The dental surgeon assumes a crucial role in guiding and instructing the patient's caregivers and family members, in order to guarantee the maintenance of the oral health of these individuals. In addition, the professional must plan a treatment that prioritizes adequacy, prevention and promotion of oral health, seeking to provide greater comfort and well-being and, therefore, improving the quality of life of patients with Alzheimer's.

**Keywords:** Alzheimer's disease, Dental management, neurodegenerative diseases, dentistry.

## 1 INTRODUCTION

Alzheimer's disease is currently recognized as the most prevalent cause of dementia in humanity, configuring itself as a global health concern with significant impacts for individuals and society. This scenario becomes more complex in the face of the increasing aging of the world population in recent decades (Lane CA et al., 2017; Weller J et al., 2018). Alzheimer's disease is characterized as a neurocognitive disorder with neurodegeneration, characterized by the progressive loss of neurons (KUMAR et al., 2016). Its signs and symptoms can start with short-term memory loss,



deficits in visual and spatial orientation, language dysfunction, irritability, and cognitive deficits (Alzheimer's Association, 2022).

The discovery of this disease was carried out by Alois Alzheimer, a physician who worked in a psychiatric clinic of the University of Munich during the late nineteenth and early twentieth centuries. On November 3, 1906, he described the first documented case of a degenerative disease, later named "Alzheimer's disease" in his honor (Hippius H et al., 2003; Zhagn et al., 2014). The case of a woman named Auguste D., who at the age of 51 showed signs of progressive memory loss, hallucinations and difficulty concentrating, was crucial for the initial understanding of this disease. Subsequently, language alterations and temporal and spatial disorientation were observed, which progressed rapidly. The patient died four and a half years after the onset of symptoms, presenting an advanced stage of dementia. After the autopsy performed for Alzheimer's, protein deposits were found in the patient's brain, senile plaques in the extracellular space, and neurofilamentary lesions inside neurons distributed throughout the cerebral cortex (Grøntvedt GR et al., 2018; Hippius H et al., 2003).

Initially, Alzheimer's disease was associated with cases of pre-senile neurodegenerative diseases, differentiating itself from the known cases of senile dementia in the early twentieth century. Since then, the term "Alzheimer's disease" has come to encompass cases of neurodegenerative dementia with features of brain lesions, such as senile plaques and neurofibrillary tangles, regardless of the age of symptom onset. Currently, there are no treatments capable of halting the progression of the disease, but there are medications available to treat the symptoms of dementia (Hippius H et al., 2003; Small DH et al., 2006).

The diagnosis of Alzheimer's disease is made through a detailed anamnesis and the clinical history of the patient, starting with the diagnosis of neurocognitive disorder (NCD), which can manifest itself in different degrees, from mild with memory deficits and visual and language disorders, to moderate and severe, characterized by more severe disorders of motor coordination, inability to basic daily activities and aggressiveness (KUMAR et al., 2016).

In addition, Alzheimer's disease can lead to several problems for the oral health of the patient, often leading to deterioration of oral health. It is common to observe active caries disease, periodontal disease and hyposalivation, caused by the medications used for the treatment of Alzheimer's disease (Mancini M et al., 2010). There is a scarcity of preventive measures directed to the oral health of these patients (Boccia A, 1992). Therefore, it is essential that the dentist is properly qualified for the proper and accurate management of patients with this condition, including the instruction and training of caregivers and family members for the correct maintenance of the patient's oral health (Gurgel ALA et al., 2012). In addition, treatment and follow-up should be conducted by a multidisciplinary team aimed at improving the patient's quality of life, focusing on the preservation of comfort and well-being (Frenkel H, 2004).



## 1.1 CONCEPTS AND EPIDEMIOLOGY

### 1.1.2 Concepts

Alzheimer's disease is a fatal and progressive neurodegenerative disorder that is predominantly associated with advanced age, constituting the most common form of neurodegenerative dementia among elderly individuals, accounting for about 70% of all cases recorded globally (APOSTOLOVA et al., 2012). This pathology is typically manifested by the gradual decline of cognitive and neuropsychiatric capacities, leading to progressive difficulty in daily activities. In the early stages of the disease, recent memory loss is noted, while older memories tend to be preserved until a certain stage of the process (Sereniki et al., 2008).

In addition to memory deficits, Alzheimer's disease is accompanied by a number of behavioral disorders, such as depressive symptoms, aggressiveness, hallucinations, hyperactivity, temporal and spatial disorientation, difficulties in communication, reduced discernment and judgment, impaired reasoning, and mood swings (Raskind MA., 1995). This complex interplay of symptoms makes proper diagnosis and treatment a challenge for healthcare professionals and requires a multidisciplinary approach to provide the best care to patients affected by this debilitating disease. Therefore, it is crucial that the scientific community continues to deepen its research on Alzheimer's disease, seeking to better understand its pathophysiology, develop prevention strategies and find more effective therapeutic interventions to improve the quality of life of patients and their families.

### 1.1.3 Epidemiology

Currently, in the Brazilian territory, there is a significant portion of the population, approximately 1.2 million individuals, who live with different manifestations of neurodegenerative dementia, and annually about 100 thousand new cases are officially diagnosed. The magnitude of this problem is not limited only to Brazil, since, according to information released by the World Health Organization (WHO), Alzheimer's disease, one of the most prevalent forms of dementia, affects around 35.6 million people around the globe.

This health condition is revealed, therefore, as a crisis of global scope that demands urgent confrontation. Projections by Alzheimer's Disease International indicate that, by the year 2030, the number of affected individuals could reach the alarming figure of 74.7 million, in view of the aging of the population. Even more impactful is the estimate for the year 2050, when it is projected that approximately 131.5 million people will be facing the disease in question.

These data corroborate the need to address the problem in a comprehensive and systematic way, directing efforts to research, prevention, early diagnosis and adequate treatment of this degenerative disease, in order to mitigate its devastating effects both for patients and for their families and caregivers. In addition, policies of care and support for this vulnerable population should be



implemented and improved, aiming to ensure a better quality of life and well-being for individuals affected by the spectrum of neurodegenerative dementias. Only with effective and committed actions will it be possible to face this growing public health crisis on a global scale.

## 2 CLASSIFICATION AND STAGES OF THE DISEASE

The clinical picture of the disease in question is classified into four stages, and the evolution is generally slow, although there is considerable variation in the duration of these stages. In some cases, the progression of symptoms occurs more slowly, allowing functional levels to be kept reasonable for a longer period. In contrast, in other situations, the deterioration is faster, but occurs constantly. In addition, there are also cases where the disease progresses in bouts of worsening followed by phases of stability, which can last for up to a year or more (Obouidiyat C et al., 2013).

The four stages of the clinical picture are described as follows:

1. Stage 1: Represents the initial form of the disease, characterized by changes in recent memory, changes in personality, visual abilities and notion of time and space.
2. Stage 2: Refers to the moderate form of the disease, manifested by difficulties in speech, communication, performing simple day-to-day tasks and motor coordination. In addition, the presence of agitation and insomnia is common.
3. Stage 3: Configures the severe form of the disease, where individuals face resistance in the execution of daily activities, as well as present aggressiveness, urinary and fecal incontinence, difficulty feeding and progressive motor impairment.
4. Stage 4: Represents the most advanced and terminal form of the disease, with bed limitation, mutism, pain when swallowing, and propensity to intercurrent infections (Alzheimer's Association., 2022).

In addition to these four stages, there are seven other subdivisions with specific characteristics:

- 1) Preclinical stage: Characterized by being silent, without observable cognitive loss.
- 2) Stage of Mild Cognitive Impairment: Presents the first signs of cognitive loss.
- 3) Mild Stage: Symptoms include forgetfulness and loss of recent memory, noticed by family and friends.
- 4) Moderate Stage: Mental confusion, agitation, anxiety, apathy, and aggressiveness are typical of this stage.
- 5) Moderately Severe Stage: Characterized by the inability to deal with personal tasks, loss of the notion of time and space and dependence.
- 6) Severe Form Stage: At this stage, the patient requires full-time care, manifesting urinary and fecal incontinence, delusions and hallucinations, which often requires hospitalization.



7) Very Severe Stage: Speech is lost, the inability to move occurs and consciousness is affected (Albert MS., 2011).

This detailed classification of the stages of the disease allows for a better understanding and identification of the different levels of cognitive and functional impairment that patients may experience throughout the course of the disease.

### 3 PATHOPHYSIOLOGY - WHY DOES ALZHEIMER'S DISEASE OCCUR?

The main changes found in the brain in cases of Alzheimer's disease involve histological and macroscopic modifications. At the histological level, the presence of plaques resulting from the deposition of amyloid protein in the extracellular space is observed, especially in the vicinity of the neuronal connections and in the walls of the blood vessels. These senile plaques are associated with inflammatory processes and abnormal neuronal dysfunction, resulting in synaptic loss and cell death in the brain regions responsible for cognitive functions (Sereniki et al., 2008). In addition, neurofibrillary tangles occur due to hyperphosphorylation of the tau protein, which can affect axons and dendrites. The disease also leads to progressive reduction of brain volume, as well as a decrease in the number of neurons and synapses (KUMAR et al., 2016; CENINI et al., 2012).

Macroscopic changes are evident in the form of cerebral atrophy, characterized by narrower gyri, enlarged grooves, reduced brain weight and increased ventricles (LOTT et al., 2006). The exact mechanism by which amyloid plaques and neurofibrillary tangles cause damage is not yet completely understood, and there are two main hypotheses to explain the pathophysiology of the disease. The first is the amyloid cascade hypothesis, which suggests that the neurodegenerative process begins with proteolytic cleavage of the amyloid precursor protein (APP), leading to the aggregation, deposition, and production of  $\beta$ -amyloid ( $A\beta$ ) and senile plaques. These events eventually result in neuronal death, loss of synapses, and progressive neurotransmitter deficiency (Hardy J et al., 2002).

The second hypothesis is the cholinergic cascade, where cholinergic system disorder results in memory impairment, similar to the symptoms of Alzheimer's disease (Bartus RT et al., 1999). The degeneration of cholinergic neurons and the reduction of cholinergic markers in the cerebral cortex are present in patients with the disease (Auld DS., 2002), which leads to cognitive impairments. In addition, a sustained immune response and inflammation was observed in the brains of patients with Alzheimer's disease, suggesting that inflammation may be a third central pathological feature (Alzheimer's Association., 2022). Experts have proposed that astrocytes and microglia cells are associated with inflammatory responses by releasing pro-inflammatory molecules such as interleukins (IL), prostaglandins (PG), leukotrienes, thromboxanes, clotting factors, complement factors, and proteases (Parihar MS et al., 2002).



Genetic aspects also play a significant role in the etiopathogenesis of the disease. About one-third of Alzheimer's disease cases are familiar with an autosomal dominant monogenic inheritance pattern (Smith MAC., 1999). The allele of the apolipoprotein E type 4 gene (apoE4) has been shown to be associated with increased numbers of senile and vascular plaques, as well as deficiencies in cholinergic function in the brains of patients with the disease (Malamud N., 1972).

Other risk factors for developing Alzheimer's disease include toxicity to infectious agents, aluminum, reactive oxygen substances (ROS), and neurotoxic amino acids. In addition, the presence of hypertension, diabetes, dyslipidemia, smoking, cardiovascular disease, obesity, sedentary lifestyle, inadequate eating habits and traumatic brain injuries also increase the risk of the disease (Alzheimer's Association., 2022). In conclusion, Alzheimer's disease is a complex condition that involves a number of changes in the brain, including amyloid plaques, neurofibrillary tangles, brain atrophy, and inflammatory responses. Genetic and environmental factors also play a significant role in the development of this neurodegenerative pathology. A deeper understanding of these mechanisms is essential for the development of effective therapeutic approaches for Alzheimer's disease.

#### 4 DIAGNOSIS

The diagnosis of Alzheimer's disease (AD) resembles that of other dementias and is carried out through a comprehensive assessment that includes formal mental status examination, clinical history, physical examination, laboratory tests, and neuroimaging (Jack C.R. et al., 2011). However, there is no definitive laboratory test for the diagnosis of AD, and it is necessary to exclude other dementia conditions. The definitive diagnosis of AD can only be confirmed by histological evaluation of brain tissue, through necropsy or biopsy of brain tissue (Caramelli, P et al., 2002).

The initial evaluation begins with the complete anamnesis and the conventional neurological examination, in which the first signs of abnormalities and their evolution, history of previous diseases, medications and habits of the patient are observed. Cognitive, behavioral, and functional changes are also assessed in this context (Alzheimer's Association., 2022). The differential diagnosis of AD is complex, especially to distinguish it from other dementias. The modified Hachinski ischemic score can be used to help distinguish vascular dementia from AD when neuroimaging is not available, but its usefulness is limited (Hachinski VC et al., 1975).

Routine laboratory tests, such as complete blood count, erythrocyte sedimentation rate, glycemia, alkaline phosphatase, transaminases, urea, creatinine, electrolytes, among others, are recommended, as well as neuroimaging tests, such as magnetic resonance imaging and computed tomography, to check for other treatable causes of dementia that may aggravate symptoms (Sayeg, 2012). Biomarkers, such as beta-amyloid levels in cerebrospinal fluid and beta-amyloid deposits in the brain detected by positron emission tomography (PET), are being studied to aid in the accurate





diagnosis of AD, but are not yet widely used in clinical practice (Jack C.R. et al., 2011; McKhann GM et al., 2011).

AD is characterized by the abnormal accumulation of toxic beta-amyloid plaques in the brain, which can arise about 20 years before the onset of symptoms (STAHL, 2014; KUMAR et al., 2016; Panza F et al., 2019). The diagnosis of AD can be established based on the following criteria: onset after the age of 40, most often after the age of 65; presence of dementia confirmed by physical examination and examination of the patient's mental status; absence of systemic or brain disorders that may be responsible for progressive deficits in memory and cognition, although deviations from these criteria do not exclude the diagnosis of AD, as patients may present with mixed dementias; and deficits in more than two areas of cognition (Caramelli, P et al., 2002; Chételat G et al., 2020).

For cognitive assessment, the Mini-Mental State Examination (MMSE), the Alzheimer's Disease Assessment Scale (ADAS) and the Clock Test can be used (Pinto TCC et al., 2019; Sunderland et al., 1989). The Clinical Dementia Rating (CDR) is an instrument used for disease staging and global assessment of dementias (Galvin JE et al., 2009). The Lawton Scale can be useful for assessing functionality in basic and instrumental activities of daily living (Koskas P et al., 2014). The paintings of Carolus Horn, a painter who developed AD, demonstrate changes in color patterns and figures throughout the progression of the disease, with a tendency toward simpler, more childlike depictions (Maurer K et al., 2004).

The prognosis for AD is usually marked by an inevitable cognitive decline, with an average survival of approximately 7 years from diagnosis. In advanced dementia, palliative measures may be more appropriate than aggressive interventions or hospitalizations (Alzheimer's Association., 2022).

## **5 TREATMENT (MEDICATIONS AND INTERACTIONS)**

Alzheimer's disease is a condition still without known cure, requiring an often-multidisciplinary treatment that involves the collaboration of physiotherapists, speech therapists, occupational therapists and psychological support (CARVALHO et al., 2016). Research is ongoing to understand the mechanisms underlying the disease and the development of drugs for its treatment. The main goal is to relieve existing symptoms, slow the progression of the disease and preserve intellectual functions for as long as possible, allowing many patients to maintain their independence in daily activities for longer (STAHL, 2014).

The recommended treatments can be pharmacological or not, and the best results are obtained when treatment is started in the early stages of the disease (CARVALHO et al., 2016). Currently, two groups of drugs are used: cholinesterase inhibitors and glutamate receptor antagonists (STAHL, 2014; Stahl, 2018). Acetylcholine, an important neurotransmitter in memory and learning processes, undergoes reduced activity in Alzheimer's disease due to neuronal degeneration and the action of



enzymes that degrade it (Rees TM et al., 2003). Although several drugs are being tested, acetylcholinesterase inhibitors have been shown to be the most effective treatments, being indicated for mild or moderate forms of the disease (Lane RM et al., 2004). These medications have demonstrated documented efficacy, helping patients maintain their everyday skills and ability to socialize. Among cholinesterase inhibitors, the main ones are donepezil, rivastigmine, and galantamine, which have similar results (Alexander GC et al., 2021). Donepezil is considered first-line due to the single daily dosage and good tolerability. Rivastigmine, in addition to inhibiting acetylcholinesterase, also inhibits butyrylcholinesterase, but may cause adverse cholinergic effects at high doses (Grossberg GT, 2003; Sereniki et al., 2008). Galantamine, in addition to inhibiting acetylcholinesterase, modulates nicotinic receptors, but the clinical impacts of this modulation are not yet fully understood (Maelicke A et al., 2000).

Another class of drugs used are glutamate receptor antagonists, especially Memantine Hydrochloride, which improves the transmission of nerve signals and functional and cognitive capacity in cases of moderate to severe Alzheimer's (Alexander GC et al., 2021; Jarvis et al., 2003; ORESTES V, 2005). This drug can be used in conjunction with cholinesterase inhibitors, but requires special attention in patients with renal failure (Alexander GC et al., 2021).

In addition to the medication approach, non-pharmacological interventions, such as cognitive rehabilitation, occupational therapy, physiotherapy, psychotherapy and music therapy, have been shown to be effective in managing the behavioral and psychological symptoms of the disease (CARVALHO et al., 2016). It is recommended that family members follow the evolution of symptoms in a diary to evaluate the effectiveness of treatment. The continuity of treatment should be reassessed by the physician after one month of initiation, being mandatorily maintained for a minimum period of 3 to 6 months to observe the favorable results. Regular, as-prescribed administration is crucial to achieving the desired outcome (Alzheimer's Association., 2022).

## 6 IMPLICATIONS FOR ORAL HEALTH AND DENTAL CARE

Patients diagnosed with Alzheimer's disease (AD) often have deficits in oral health due to difficulty in performing basic self-care activities (BADL) (Rabelo, R. et al., 2020). These problems are usually associated with increased caries index, worsening of periodontal problems (such as gingivitis and periodontitis) due to deficiency in plaque control, accumulation of lingual saburra and hyposalivation caused by the medications administered (Boccia, A., 1992). In addition, it is common the occurrence of lesions in the mucosa due to the use of poorly adapted and worn prostheses, as well as the presence of fungal infections in the mucosa, which can lead the patient to face chewing difficulties and dysphagia. Note the lack of preventive actions aimed at health promotion and adequacy of the oral environment of these patients (Adam, H. et al., 2006).





Aiming at the well-being, quality of life and general health of these individuals, it is crucial that the patient is evaluated in a multidisciplinary approach, so that the dentist can plan and execute a personalized treatment with greater safety (Ettinger, R. L., 2000). As well as other areas of health involved in the care and treatment of people with AD, dentistry should act according to the particularities of each patient, considering the phase of the disease: initial, intermediate and final (Miranda, 2010).

In the initial phase of the disease, which can last on average 4 years, although the patient has recent memory loss, frequent forgetfulness and communication problems, it is still possible to perform the treatment in the office (Frenkel, H., 2004; Little, J. W., 2005). At this stage, it is crucial to carry out planning and preventive treatment, since with the progression of the disease, in-office treatment becomes more difficult (Varjão, F. M., 2006). During the initial phase, it is the ideal time to perform dental procedures, with attendances in the morning, with calm, punctuality and short duration, focusing on the adequacy of the oral environment and the instruction of the patient, family members and caregivers on the correct oral hygiene (Ghezzi, E. M. et al., 2000). During the service, it is important to keep the dental chair in a sitting or semi-inclined position for greater comfort of the patient, to be careful to avoid accidents with sharp instruments and always have the presence of a caregiver or family member during the care. When talking to the patient, one should lower the mask, show a smile and maintain direct and gentle eye contact, conveying tranquility and security. It is essential to provide guidance on oral hygiene, plaque control, periodontal treatment, occlusal adjustments and adequate adaptation of prostheses.

Treatment planning should aim to minimize future problems and anticipate oral health issues, treating as soon as possible and using restorative materials that contribute to the maintenance of oral health (Henry, R. G., 1999). It is also important to apply fluoride and instruct a less cariogenic diet. For patients with hyposalivation, the prescription of artificial saliva may be indicated for greater comfort (Turner, L. N. et al., 2008; Mancini, M. et al., 2010). At this stage, it is easier to train caregivers and family members, and maintenance and investment in dental treatment are extremely important. With the advancement of the disease, the difficulties of hygiene and acceptance of the patient to perform dental procedures increase (Gurgel, A. L. A. et al., 2012).

In the intermediate phase of the disease, which can last on average from 2 to 8 years, memory, language and cognitive loss disorders worsen, leading to a lack of understanding of the patient and more aggressive behaviors. In this phase, it is common the lack and difficulties of expressions and languages to report pain, making the attention of the dentist important (Souza, A. C. A. R. et al., 2006). In-office care becomes more difficult in the intermediate phase, and home care can be initiated for greater comfort of the patient and family. Dental planning and treatment should be directed to the most urgent needs, with the aim of eliminating possible foci of infections and acute inflammatory/infectious



processes, relieving and avoiding episodes of pain and stress of the patient (Henry, R. G., 1999; Fiske, J. et al., 2006). For more invasive procedures, sedation can be used for greater patient comfort, avoiding stress and discomfort. The use of benzodiazepines and anxiolytics should be considered carefully, together with the patient's physician (Friedlander, A. H. et al., 2006). In this phase, caregivers and family members should be trained and obtain the knowledge and skills to perform the correct hygiene of the patient's oral cavity. Special attention should be given to poorly adapted prostheses, the removal of which can provide comfort and a more favorable condition for the patient, avoiding ulcers and traumatic lesions on the mucosa, in addition to preventing possible accidents such as swallowing or aspiration of the prostheses (Turner, L. N., 2006; Chalmers, J. M. et al., 2003).

In the terminal or final phase of the disease, which can last up to 10 years, the patient presents total disorientation, accentuation of cognitive dysfunctions, fecal and urinary incontinence, and total dependence (Little, J. W., 2005; Friedlander, A. H. et al., 2006). In this phase, palliative care is paramount to provide better quality of life to the patient. Complex and invasive treatments should be avoided as much as possible, prioritizing minimum oral health conditions, in order to eliminate and prevent acute foci of infection that can cause aspiration pneumonia and affect the general health status of the patient (Frenkel, H., 2004; Mancini, M. et al., 2010).

The dentist must participate in the home treatment plan or in the intensive care unit (hospital bed care). It is noteworthy the difficulty of caregivers in promoting an adequate maintenance of oral health in this final phase of the disease, making it extremely important the periodic presence of a dentist to perform regular dental care, aiming at the prevention of possible diseases and infectious foci, contributing to improve the quality of life and well-being of the patient (Miranda, A. F. et al., 2010; Frenkel, H., 2004). Recently, studies have indicated that periodontal disease is a risk factor for the progression of Alzheimer's disease. The connection between periodontal disease and AD can be explained by the spread of infectious or inflammatory agents that migrate from the oral cavity to the brain (Ranjan, R. et al., 2018). Research has shown that there is a seven times higher density of oral cavity bacteria found in the brain tissue of patients who have died of AD compared to healthy individuals (Olsen, I. et al., 2015). The oral bacteria most often found in the brain are: Pg, Fn, Pi, H. pylori, B. burgdorferi and spirochetes (treponema). PG, the main pathogen of periodontal disease, is found significantly in the brain tissue of patients who have died of AD (Borsa, L. et al., 2021).

Thus, the presence of a dentist in the general and multidisciplinary treatment plan of the patient with AD becomes extremely important, aiming at the prevention, promotion and maintenance of oral health, avoiding the emergence of foci of infection that may aggravate the systemic condition of the patient (Mansur, F. V., 2006; Miranda, A. F. et al., 2010).



## 7 FINAL CONSIDERATIONS

Based on the above, it is evident that the progressive impairment of cognitive functions in patients diagnosed with Alzheimer's causes significant problems in the maintenance of oral health, resulting in severe complications in the oral cavity, with the manifestation of pain and stress for the affected individual. In this sense, it is extremely important that the dentist acquires in-depth knowledge about the disease and its different stages, as well as being able to deal with this public, thus ensuring due and adequate care. The improvement of the oral health conditions of this group of patients will enable an increase in their general well-being and quality of life.



## REFERENCES

- Adam H, Preston AJ. The oral health of individuals with dementia in nursing homes. *Gerodontology*. 2006 Jun;23(2):99-105. doi: 10.1111/j.1741-2358.2006.00118.x.
- Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, Gamst A, Holtzman DM, Jagust WJ, Petersen RC, Snyder PJ, Carrillo MC, Thies B, Phelps CH. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011 May;7(3):270-9. doi: 10.1016/j.jalz.2011.03.008.
- Alexander GC, Emerson S, Kesselheim AS. Evaluation of Aducanumab for Alzheimer Disease: Scientific Evidence and Regulatory Review Involving Efficacy, Safety, and Futility. *JAMA*. 2021 May 4;325(17):1717-1718. doi: 10.1001/jama.2021.3854.
- 2022 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2022 Apr;18(4):700-789. doi: 10.1002/alz.12638
- Alzheimer's Society Information Sheet. Dental care and dementia: information sheet. 2001;448-51.
- American Psychiatric Association. Seção II Critérios Diagnósticos e Códigos: Transtornos Neurocognitivos. In: American Psychiatric Association. **Manual Diagnóstico e Estatístico de Transtornos Mentais: DSM-5**. 5. ed. Porto Alegre: Artmed, 2014.
- Apostolova LG, Green AE, Babakchian S, Hwang KS, Chou YY, Toga AW, Thompson PM. Hippocampal atrophy and ventricular enlargement in normal aging, mild cognitive impairment (MCI), and Alzheimer Disease. *Alzheimer Dis Assoc Disord*. 2012 Jan-Mar;26(1):17-27. doi: 10.1097/WAD.0b013e3182163b62.
- Apostolova, Liana G. et al. Dementias. In: DAROFF, Robert B. et al. **Bradley's Neurology in Clinical Practice**. 6. ed. Filadélfia, EUA: Elsevier, 2012.
- Auld DS, Kornecook TJ, Bastianetto S, Quirion R. Alzheimer's disease and the basal forebrain cholinergic system: relations to beta-amyloid peptides, cognition, and treatment strategies. *Prog Neurobiol*. 2002 Oct;68(3):209-45. doi: 10.1016/s0301-0082(02)00079-5. PMID: 12450488.
- Bartus RT, Emerich DF. Cholinergic markers in Alzheimer disease. *JAMA*. 1999 Dec 15;282(23):2208-9. doi: 10.1001/jama.282.23.2208. PMID: 10605966.
- Boccia A. Alzheimer's disease and the dental patient. Recognizing and dealing with dementia. *Ont Dent*. 1992 Apr;69(3):16-8.
- Borghini AC, Sassá AH, de Matos PC, Decesaro Md, Marcon SS. Qualidade de vida de idosos com doença de Alzheimer e de seus cuidadores. *Rev Gaucha Enferm*. 2011 Dec;32(4):751-8. doi: 10.1590/s1983-14472011000400016.
- Borsa L, Dubois M, Sacco G, Lupi L. Analysis the Link between Periodontal Diseases and Alzheimer's Disease: A Systematic Review. *Int J Environ Res Public Health*. 2021 Sep 3;18(17):9312. doi: 10.3390/ijerph18179312.
- Bottino CMC, Laks J, Blay SL. Demência e transtornos cognitivos em idosos. 1ª Ed. Rio de Janeiro: Guanabara-Koogan; 2006.
- Brunetti-Montenegro, FL. Marchini, L. Odontogeriatrics - Uma visão gerontológica. 2013. GEN Guanabara Koogan; 1ª edição.



Camara, FM, Gerez AG, Miranda MLJ, Velardi M. Capacidade Funcional Do Idoso: Formas De avaliação E Tendências”. *Acta Fisiátrica*. 2008 Dez;15(4):249-56. doi:10.11606/issn.2317-0190.v15i4a103005.

Caramelli P, Barbosa MT. Como diagnosticar as quatro causas mais freqüentes de demência. *Braz J Psychiatry*. 2002 Apr; 24:7–10. doi:10.1590/S1516-44462002000500003

Chaves MGAM, de Carvalho MF, Rodrigues PA. Halitose: um estigma social. *hu rev*. 11º 2009 Abr;34(4):273-79. Disponível em: <https://periodicos.ufjf.br/index.php/hurevista/article/view/102>.

Carvalho PDP, Magalhães CMC, Pedroso J da S. Tratamentos não farmacológicos que melhoram a qualidade de vida de idosos com doença de Alzheimer: uma revisão sistemática. *J bras psiquiatr*. 2016Oct;65(4):334–9. doi:10.1590/0047-2085000000142.

Cenini G, Dowling AL, Beckett TL, Barone E, Mancuso C, Murphy MP, Levine H 3rd, Lott IT, Schmitt FA, Butterfield DA, Head E. Association between frontal cortex oxidative damage and beta-amyloid as a function of age in Down syndrome. *Biochim Biophys Acta*. 2012 Feb;1822(2):130-8. doi: 10.1016/j.bbadis.2011.10.001.

Chalmers JM, Carter KD, Spencer AJ. Oral diseases and conditions in community-living older adults with and without dementia. *Spec Care Dentist*. 2003;23(1):7-17. doi: 10.1111/j.1754-4505.2003.tb00283. x.

Chételat G, Arbizu J, Barthel H, Garibotto V, Law I, Morbelli S, van de Giessen E, Agosta F, Barkhof F, Brooks DJ, Carrillo MC, Dubois B, Fjell AM, Frisoni GB, Hansson O, Herholz K, Hutton BF, Jack CR Jr, Lammertsma AA, Landau SM, Minoshima S, Nobili F, Nordberg A, Ossenkoppele R, Oyen WJG, Perani D, Rabinovici GD, Scheltens P, Villemagne VL, Zetterberg H, Drzezga A. Amyloid-PET and 18F-FDG-PET in the diagnostic investigation of Alzheimer's disease and other dementias. *Lancet Neurol*. 2020 Nov;19(11):951-962. doi: 10.1016/S1474-4422(20)30314-8.

Dewachter I, Van Leuven F. Secretases as targets for the treatment of Alzheimer's disease: the prospects. *Lancet Neurol*. 2002 Nov;1(7):409-16. doi: 10.1016/s1474-4422(02)00188-6.

Dibello V, Lozupone M, Manfredini D, Dibello A, Zupo R, Sardone R, Daniele A, Lobbezoo F, Panza F. Oral frailty and neurodegeneration in Alzheimer's disease. *Neural Regen Res*. 2021 Nov;16(11):2149-2153. doi: 10.4103/1673-5374.310672.

Engelhardt E, Grinberg LT. Alois Alzheimer and vascular brain disease: Arteriosclerotic atrophy of the brain. *Dement neuropsychol*. 2015Jan;9(1):81–4. doi: 10.1590/S1980-57642015DN91000013.

Ettinger RL. Dental management of patients with Alzheimer's disease and other dementias. *Gerodontology*. 2000 Jul;17(1):8-16. doi: 10.1111/j.1741-2358.2000.00008. x. PMID: 11203516.

Feldman HH, Ferris S, Winblad B, Sfikas N, Mancione L, He Y, Tekin S, Burns A, Cummings J, del Ser T, Inzitari D, Orgogozo JM, Sauer H, Scheltens P, Scarpini E, Herrmann N, Farlow M, Potkin S, Charles HC, Fox NC, Lane R. Effect of rivastigmine on delay to diagnosis of Alzheimer's disease from mild cognitive impairment: the InDDEX study. *Lancet Neurol*. 2007 Jun;6(6):501-12. doi: 10.1016/S1474-4422(07)70109-6.

Fergusson E, Howard R. Donepezil for the treatment of psychosis in dementia with Lewy bodies. *Int J Geriatr Psychiatry*. 2000 Mar;15(3):280-1. doi: 10.1002/(sici)1099-1166(200003)15:3<280: aid-gps108>3.0.co;2-n.



Fiske J, Frenkel H, Griffiths J, Jones V; British Society of Gerodontology; British Society for Disability and Oral Health. Guidelines for the development of local standards of oral health care for people with dementia. *Gerodontology*. 2006 Dec;23 Suppl 1:5-32. doi: 10.1111/j.1741-2358.2006.00140.x. - Fortea J, Vilaplana E, Carmona-Iragui M, Benejam B, Videla L, Barroeta I, Fernández S, Altuna M, Pegueroles J, Montal V, Valldeneu S, Giménez S, González-Ortiz S, Muñoz L, Estellés T, Illán-Gala I, Belbin O, Camacho V, Wilson LR, Annus T, Osorio RS, Videla S, Lehmann S, Holland AJ, Alcolea D, Clarimón J, Zaman SH, Blesa R, Lleó A. Clinical and biomarker changes of Alzheimer's disease in adults with Down syndrome: a cross-sectional study. *Lancet*. 2020 Jun 27;395(10242):1988-1997. doi: 10.1016/S0140-6736(20)30689-9.

Freitas, E. V. Tratado de geriatria e gerontologia. 4. ed. Rio de Janeiro: Guanabara Koogan, 2017.  
Frenkel H. Alzheimer's disease and oral care. *Dent Update*. 2004 Jun;31(5):273-4, 276-8. doi: 10.12968/denu.2004.31.5.273.

Friedlander AH, Norman DC, Mahler ME, Norman KM, Yagiela JA. Alzheimer's disease: psychopathology, medical management and dental implications. *J Am Dent Assoc*. 2006 Sep;137(9):1240-51. doi: 10.14219/jada.archive.2006.0381.

Galvin JE, Meuser TM, Coats MA, Bakal DA, Morris JC. The "portable" CDR: translating the clinical dementia rating interview into a PDA format. *Alzheimer Dis Assoc Disord*. 2009 Jan-Mar;23(1):44-9. doi: 10.1097/WAD.0b013e31817634a0.

Ghezzi EM, Ship JA. Dementia and oral health. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2000 Jan;89(1):2-5. doi: 10.1016/s1079-2104(00)80003-7.

González A, Calfío C, Churruca M, Maccioni RB. Glucose metabolism and AD: evidence for a potential diabetes type 3. *Alzheimers Res Ther*. 2022 Apr 20;14(1):56. doi: 10.1186/s13195-022-00996-8.

Grøntvedt GR, Schröder TN, Sando SB, White L, Bråthen G, Doeller CF. Alzheimer's disease. *Curr Biol*. 2018 Jun 4;28(11):R645-R649. doi: 10.1016/j.cub.2018.04.080.

Grossberg GT. Cholinesterase inhibitors for the treatment of Alzheimer's disease: getting on and staying on. *Curr Ther Res Clin Exp*. 2003 Apr;64(4):216-35. doi: 10.1016/S0011-393X(03)00059-6.

Gurgel ALA, Miranda AF. Atendimento multidisciplinar em paciente idosa com Alzheimer em fase intermediária em domicílio. Relato de caso: o cirurgião dentista como integrante. *Rev Port Divulg*. 2012 Abr; (20):25-34.

Hachinski VC, Iliff LD, Zilhka E, Du Boulay GH, McAllister VL, Marshall J, Russell RW, Symon L. Cerebral blood flow in dementia. *Arch Neurol*. 1975 Sep;32(9):632-7. doi: 10.1001/archneur.1975.00490510088009.

Hardy J, Selkoe DJ. The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics. *Science*. 2002 Jul 19;297(5580):353-6. doi: 10.1126/science.1072994

Henry RG. Alzheimer's disease and cognitively impaired elderly: providing dental care. *J Calif Dent Assoc*. 1999 Sep;27(9):709-17.

Hippius H, Neundörfer G. The discovery of Alzheimer's disease. *Dialogues Clin Neurosci*. 2003 Mar;5(1):101-8. doi: 10.31887/DCNS.2003.5.1/hippius.

Jack CR Jr, Albert MS, Knopman DS, McKhann GM, Sperling RA, Carrillo MC, Thies B, Phelps CH. Introduction to the recommendations from the National Institute on Aging-Alzheimer's Association





workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement.* 2011 May;7(3):257-62. doi: 10.1016/j.jalz.2011.03.004.

Kandel, Eric R. et al. O Encéfalo que Envelhece. *In: KANDEL, Eric R. et al. Princípios de Neurociências.* 5. ed. Porto Alegre: AMGH, 2014.

Kihara T, Sawada H, Nakamizo T, Kanki R, Yamashita H, Maelicke A, Shimohama S. Galantamine modulates nicotinic receptor and blocks Abeta-enhanced glutamate toxicity. *Biochem Biophys Res Commun.* 2004 Dec 17;325(3):976-82. doi: 10.1016/j.bbrc.2004.10.132.

Kinney JW, Bemiller SM, Murtishaw AS, Leisgang AM, Salazar AM, Lamb BT. Inflammation as a central mechanism in Alzheimer's disease. *Alzheimers Dement (N Y).* 2018 Sep 6; 4:575-590. doi: 10.1016/j.trci.2018.06.014.

Kivipelto M, Helkala EL, Hänninen T, Laakso MP, Hallikainen M, Alhainen K, Soininen H, Tuomilehto J, Nissinen A. Midlife vascular risk factors and late-life mild cognitive impairment: A population-based study. *Neurology.* 2001 Jun 26;56(12):1683-9. doi: 10.1212/wnl.56.12.1683.

Koskas P, Henry-Feugeas MC, Feugeas JP, Poissonnet A, Pons-Peyneau C, Wolmark Y, Drunat O. The Lawton Instrumental Activities Daily Living/Activities Daily Living Scales: A Sensitive Test to Alzheimer Disease in Community-Dwelling Elderly People? *J Geriatr Psychiatry Neurol.* 2014 Jun;27(2):85-93. doi: 10.1177/0891988714522694.

Kosunen O, Talasniemi S, Lehtovirta M, Heinonen O, Helisalmi S, Mannermaa A, Paljärvi L, Ryyänänen M, Riekkinen PJ Sr, Soininen H. Relation of coronary atherosclerosis and apolipoprotein E genotypes in Alzheimer patients. *Stroke.* 1995 May;26(5):743-8. doi: 10.1161/01.str.26.5.743.

Kumar, Vinay et al. O Sistema Nervoso Central: Doenças Neurodegenerativas. *In: KUMAR, Vinay et al. Robbins & Cotran Patologia: Bases Patológicas das Doenças.* 9. ed. Rio de Janeiro: Guanabara Koogan, 2016.

Lane CA, Hardy J, Schott JM. Alzheimer's disease. *Eur J Neurol.* 2018 Jan;25(1):59-70. doi: 10.1111/ene.13439.

Lane RM, Kivipelto M, Greig NH. Acetylcholinesterase and its inhibition in Alzheimer disease. *Clin Neuropharmacol.* 2004 May-Jun;27(3):141-9. doi: 10.1097/00002826-200405000-00011.

Levin ED, Rezvani AH. Development of nicotinic drug therapy for cognitive disorders. *Eur J Pharmacol.* 2000 Mar 30;393(1-3):141-6. doi: 10.1016/s0014-2999(99)00885-7.

Liccardo D, Marzano F, Carraturo F, Guida M, Femminella GD, Bencivenga L, Agrimi J, Addonizio A, Melino I, Valletta A, Rengo C, Ferrara N, Rengo G, Cannavo A. Potential Bidirectional Relationship Between Periodontitis and Alzheimer's Disease. *Front Physiol.* 2020 Jul 3; 11:683. doi: 10.3389/fphys.2020.00683.

Little JW. Dental management of patients with Alzheimer's disease. *Gen Dent.* 2005 Jul-Aug;53(4):289-96; quiz 297.

Lott IT, Head E, Doran E, Busciglio J. Beta-amyloid, oxidative stress and down syndrome. *Curr Alzheimer Res.* 2006 Dec;3(5):521-8. doi: 10.2174/156720506779025305.



Maelicke A, Albuquerque EX. Allosteric modulation of nicotinic acetylcholine receptors as a treatment strategy for Alzheimer's disease. *Eur J Pharmacol*. 2000 Mar 30;393(1-3):165-70. doi: 10.1016/s0014-2999(00)00093-5.

Malamud, N. *Neuropathology of Organic Brain Syndromes Associated with Aging*. 1972;3. doi: 10.1007/978-1-4684-8503-5\_6.

Mancini M, Grappasonni I, Scuri S, Amenta F. Oral health in Alzheimer's disease: a review. *Curr Alzheimer Res*. 2010 Jun;7(4):368-73. doi: 10.2174/156720510791162359.

Maurer K, Prvulovic D. Paintings of an artist with Alzheimer's disease: visuostructural deficits during dementia. *J Neural Transm (Vienna)*. 2004 Mar;111(3):235-45. doi: 10.1007/s00702-003-0046-2.

McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR Jr, Kawas CH, Klunk WE, Koroshetz WJ, Manly JJ, Mayeux R, Mohs RC, Morris JC, Rossor MN, Scheltens P, Carrillo MC, Thies B, Weintraub S, Phelps CH. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011 May;7(3):263-9. doi: 10.1016/j.jalz.2011.03.005.

Medalia, Alice et al. *Integrando Psicofarmacologia e Remediação Cognitiva para Tratar a Disfunção Cognitiva nos Transtornos Psicóticos*. In: OLIVEIRA, Irismar R. et al, (org.). **Integrando Psicoterapia e Psicofarmacologia: Manual para Clínicos**. Porto Alegre: Artmed, 2015.

Mestel R. Putting prions to the test. *Science*. 1996 Jul 12;273(5272):184-9. doi: 10.1126/science.273.5272.184.

Miranda AF, Lia EM, Leal SC, Miranda MPAF. Doença de Alzheimer: características e orientações em odontologia. *Rev. gaúch. odontol*. 2010;58(1):103-107.

Nunes JD, Saes M de O, Nunes BP, Siqueira FCV, Soares DC, Fassa MEG, et al. Indicadores de incapacidade funcional e fatores associados em idosos: estudo de base populacional em Bagé, Rio Grande do Sul. *Epidemiol Serv Saúde*. 2017Apr;26(2):295-304. doi: 10.5123/S1679-49742017000200007.

Oboudiyat C, Glazer H, Seifan A, Greer C, Isaacson RS. Alzheimer's disease. *Semin Neurol*. 2013 Sep;33(4):313-29. doi: 10.1055/s-0033-1359319.

Olsen I., Singhrao SK A infecção oral pode ser um fator de risco para a doença de Alzheimer? *J. Oral. Microbiol*. 2015; 7 :29143. doi: 10.3402/jom. v7.29143.

Panza F, Lozupone M, Logroscino G, Imbimbo BP. A critical appraisal of amyloid- $\beta$ -targeting therapies for Alzheimer disease. *Nat Rev Neurol*. 2019 Feb;15(2):73-88. doi: 10.1038/s41582-018-0116-6.

Parihar MS, Hemnani T. Alzheimer's disease pathogenesis and therapeutic interventions. *J Clin Neurosci*. 2004 Jun;11(5):456-67. doi: 10.1016/j.jocn.2003.12.007.

Pinto TCC, Machado L, Bulgacov TM, Rodrigues-Júnior AL, Costa MLG, Ximenes RCC, Sougey EB. Is the Montreal Cognitive Assessment (MoCA) screening superior to the Mini-Mental State Examination (MMSE) in the detection of mild cognitive impairment (MCI) and Alzheimer's Disease (AD) in the elderly? *Int Psychogeriatr*. 2019 Apr;31(4):491-504. doi: 10.1017/S1041610218001370.



Poirier J, Delisle MC, Quirion R, Aubert I, Farlow M, Lahiri D, Hui S, Bertrand P, Nalbantoglu J, Gilfix BM, Gauthier S. Apolipoprotein E4 allele as a predictor of cholinergic deficits and treatment outcome in Alzheimer disease. *Proc Natl Acad Sci U S A*. 1995 Dec 19;92(26):12260-4. doi: 10.1073/pnas.92.26.12260.

Rabelo RG, Ferraz-Mello SM, Neto AT, Araujo, NS. A doença de alzheimer e o cuidado em saúde bucal alzheimer's disease and oral health care. *Revista Da Faculdade De Odontologia da UFBA*. 2017;50(1):71–77. doi:10.9771/revfo.v50i1.37120

Ranjan R, Abhinay A, Mishra M. As infecções microbianas orais podem ser um fator de risco para neurodegeneração? Uma revisão da literatura. *Neurol. Índia*. 2018;66 :344–351. doi: 10.4103/0028-3886.227315.

Raskind MA. Alzheimer's disease: treatment of noncognitive behavioural abnormalities. In: Bloom FE, Kupper DJ. *Psychopharmacology: the fourth generation of progress*. New York: Raven Press; 1995. p. 1427-35.

Rees TM, Brimijoin S. The role of acetylcholinesterase in the pathogenesis of Alzheimer's disease. *Drugs Today (Barc)*. 2003 Jan;39(1):75-83. doi: 10.1358/dot.2003.39.1.740206.

Sayeg, Norton. Como diagnosticar e tratar a doença de Alzheimer. 2008. Campinas, v. 68, n. 12, p. 79-163.

Selkoe DJ. Alzheimer's disease: genes, proteins, and therapy. *Physiol Rev*. 2001 Apr;81(2):741-66. doi: 10.1152/physrev.2001.81.2.741.

Sereniki A, Vital MABF. A doença de Alzheimer: aspectos fisiopatológicos e farmacológicos. *Revista de Psiquiatria Do Rio Grande Do Sul*. 2008;30(1 suppl). doi:10.1590/s0101-81082008000200002

Silva AH, Costa LA, Sena SR, Silva RF. Ressonância magnética no diagnóstico da Alzheimer precoce. *Rev Bras Interdiscip Saúde*. 2023;5(1):16-23.

Small DH, Cappai R. Alois Alzheimer and Alzheimer's disease: a centennial perspective. *J Neurochem*. 2006 Nov;99(3):708-10. doi: 10.1111/j.1471-4159.2006.04212. x.

Smith M de AC. Doença de Alzheimer. *Braz J Psychiatry*. 1999Oct; 21:03–7. doi:10.1590/S1516-44461999000600003.

Souza ACAR, Rosa CFBD, Elias R. Doença de Alzheimer: protocolo de atendimento odontológico. CISPRES 2006

Stahl, Stephen M. Demência e seu Tratamento. In: STAHL, Stephen M. **Psicofarmacologia: bases neurocientíficas e aplicações práticas**. 4. ed. Rio de Janeiro: Guanabara Koogan, 2014.

Stahl, Stephen M. **Stahl's Essential Psychopharmacology: Prescriber's Guide**. 6. ed. Reino Unido: Cambridge University Press, 2017.

Sunderland T, Hill JL, Mellow AM, Lawlor BA, Gundersheimer J, Newhouse PA, Grafman JH. Clock drawing in Alzheimer's disease. A novel measure of dementia severity. *J Am Geriatr Soc*. 1989 Aug;37(8):725-9. doi: 10.1111/j.1532-5415.1989.tb02233. x. PMID: 2754157.

Tarulli, Andrew. **Neurology: A Clinician's Approach**. 2. ed. Suíça: Springer, 2016.



Turner LN, Balasubramaniam R, Hersh EV, Stoopler ET. Drug therapy in Alzheimer disease: an update for the oral health care provider. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2008 Oct;106(4):467-76. doi: 10.1016/j.tripleo.2008.06.009.

Varjão FM. Assistência odontológica para o paciente portador da doença de Alzheimer. *Rev Odonto Ciência.* 2006;21(53):284-8.

Veras, Renato Peixoto *et al.* Avaliação dos gastos com o cuidado do idoso com demência. **Revista de Psiquiatria Clínica**, São Paulo, 2007. doi:[10.1590/S0101-60832007000100001](https://doi.org/10.1590/S0101-60832007000100001)

Waldemar G, Dubois B, Emre M, Georges J, McKeith IG, Rossor M, Scheltens P, Tariska P, Winblad B; EFNS. Recommendations for the diagnosis and management of Alzheimer's disease and other disorders associated with dementia: EFNS guideline. *Eur J Neurol.* 2007 Jan;14(1): e1-26. doi: 10.1111/j.1468-1331.2006.01605. x.

Weller J, Budson A. Current understanding of Alzheimer's disease diagnosis and treatment. *F1000Res.* 2018 Jul 31;7: F1000 Faculty Rev-1161. doi: 10.12688/f1000research.14506.1.

Zhagn L, Li Z. [Alzheimer and the discovery of Alzheimer's disease]. *Zhonghua Yi Shi Za Zhi.* 2014 Sep;44(5):288-90. Chinese.

Zuluaga DJM. Manejo odontológico de pacientes com demências. *Rev Fed Odontol Colomb.* 2002;(203):28-39.