

**DENTAL MANAGEMENT OF PATIENTS WITH ALZHEIMER'S DISEASE****DR. M.P.SANTHOSH KUMAR M.D.S.**

*Reader, Department of Oral and Maxillofacial Surgery, saveetha dental college,
Saveetha University, Chennai, Tamil Nadu, India.*

ABSTRACT

Alzheimer's disease (AD), is the most common cause of dementia in adult life and is associated with the selective damage of brain regions and neural circuits critical for memory and cognition. However, the pathogenesis of this disease is complex and involves many molecular, cellular and physiological pathologies. Dental health problems in Alzheimer's patients can lead to pain, unmanageable behaviour and extensive dental treatment. The clinical features, pathophysiology, medical management, dental findings and management of Alzheimer's patients in dental office have been discussed in this review.

KEYWORDS: Alzheimer's disease, Senile plaques, Tangles, Signs

*Corresponding author

DR. M.P.SANTHOSH KUMAR M.D.S

Reader, Department of Oral and Maxillofacial Surgery, saveetha dental college,
Saveetha University, Chennai, Tamil Nadu, India.

INTRODUCTION

Alzheimer's disease (AD), was first described by a German psychiatrist and neuropathologist Alois Alzheimer in 1906.¹ Alzheimer's Foundation of America defined Alzheimer's disease as a "progressive, degenerative disorder that attacks the brain's nerve cells, or neurons, resulting in loss of memory, thinking and language skills, and behavioural changes." It is a progressive and fatal neurodegenerative disorder characterized by cognitive dysfunctions, particularly in learning and memory, and the emergence of behavioural abnormalities.² Deficiencies in the cells responsible for storage and processing of information are the reasons for the cognitive, functional, and behavioural changes seen in patients with the disorder. The disease process appears to be associated with plaques³ and tangles in the brain.⁴ Alzheimer's disease commonly seen in people over 65 years of age. It affects 10% of people over the age of 65 and 50% of people over the age of 85. In 2006, there were 26.6 million people worldwide with Alzheimer's disease.⁵ However, Alzheimer's is not a normal part of aging. Two main types of dental diseases are commonly seen in patients with Alzheimer's disease; periodontal disease and dental caries. This two important finding can cause discomfort or pain which can lead to the development of infection. Both pain and infection can worsen the confusion associated with Alzheimer's disease.⁶

ALZHEIMER'S DISEASE- GENETIC CAUSES

Alzheimer's disease occurs due to a combination of genetic, lifestyle and environmental factors that affect the brain. Less than 5%, the disease is caused by genetic changes.⁷ The disease damages and kills the cells in the brain. Alzheimer's leads to significant brain shrinkage due to the destruction of more and more brain cells. Around 0.1% of the cases are familial forms of autosomal dominant, which usually occurs between the age of 30-60 years.⁸ This form of disease is called as the "Early onset familial Alzheimer's disease." This can occur due to the mutations in one of the three genes- those encoding Amyloid precursor protein (APP) and Presenilins 1 and 2 (PSEN 1 & PSEN 2).⁹

Mutations in these genes increases the production of a small protein called beta-amyloid ($A\beta$ 42), resulting in the formation of "senile plaques"¹⁰ which is the hallmark of this disease. This protein damages and destroys the brain cells by interfering with the cell-to-cell communication. However, the exact cause for brain cell death is unknown, but the primary cause for brain cell destruction is the accumulation of this beta-amyloid protein outside the brain cells.¹¹ But most of the cases reported do not exhibit a autosomal dominant inheritance, but occurs due to environmental and genetic differences that may act as risk factors and this form of disease is called as the "Sporadic Alzheimer's Disease" or "Late onset Alzheimer's" which usually develops at the age of 60 years. The known genetic risk factor is the inheritance of the ϵ 4 allele of the apolipoprotein E (APOE).^{12,13} About 40-80% of the people with AD possess atleast one APOE ϵ 4 allele,¹³ which increases the risk of the disease. Other genes have been identified, which includes; CASS4 (Cas scaffolding protein family member 4), CR1 (Complement receptor 1), TREM2 (Triggering receptor expressed on myeloid cells 2).¹⁴ Mutations in the TREM2 gene is associated with a 3-5 times higher risk of developing Alzheimer's disease. When the TREM2 gene is mutated, the white blood cells in the brain can no longer control the amount of beta-amyloid present.¹⁵

ALZHEIMER'S DISEASE- HYPOTHESIS

Certain hypothesis was putforth to explain the causes of the alzheimer's disease;

- Amyloid cascade hypothesis
- Cholinergic hypothesis
- Tau hypothesis

Amyloid Hypothesis

Amyloid precursor protein (APP) is a protein found widely throughout the body. The amyloid cascade hypothesis postulated that the deposition of the beta-amyloid protein in the brain parenchyma is the crucial step that ultimately leads to Alzheimer's disease.¹⁶ Mutation of APP, PSEN1 and PSEN2 increases the production of $A\beta$ 42 protein which accumulates outside the brain cells resulting in the formation of senile plaques

which is the characteristic feature noticed when examining a section of the affected brain tissue under the microscope.¹⁰

Cholinergic Hypothesis

Acetylcholine (Ach) is an important neurotransmitter in areas of the brain involved in memory formation. Loss of Ach activity increases the severity of Alzheimer's disease.¹⁷

Tau Hypothesis

Brain cells depend on an internal support and transport system to carry nutrients and other essential materials throughout their long extensions. This requires the normal structure and functioning of a protein called tau.¹⁶ In Alzheimer's disease, threads of tau protein twist into abnormal tangles¹⁸ inside the brain cells, resulting in the collapse of the neuron's transport system. This collapse may first result in the malfunctioning of the biochemical communication between the neurons and later results in the death of the brain cells.¹⁹

RISK FACTORS

-Age is the most significant factor. Most commonly affects older people above the age of 65 years. However early onset AD can affect 1 in 20 people around the age of 40 years.²⁰ -The accumulation of amyloid plaques are seen in people with Down's syndrome, which can lead to AD in some people.²¹ - People with severe head injury and neck injury have been found to be at a higher risk of developing Alzheimer's disease.²²

STAGES OF ALZHEIMER'S DISEASE

The disease courses are divided into four stages;

Stage I: Pre-dementia

The most noticeable deficit is memory loss, which shows up as difficulty in remembering recently learned facts and inability to acquire new information. This includes; forgetting things occasionally, misplacing items, minor short-term memory loss, and forgetting that memory lapses happened.²³

Stage II: Early stage Alzheimer's

In people with AD, absent mindedness, forgetting appointments, confusions, language problems are noticed. However, episodic

memory, semantic memory and implicit memory are affected to a lesser degree. In this stage, the person with AD is usually capable of communicating the basic ideas.²⁴

Stage III: Middle stage Alzheimer's

Speech difficulties become evident due to the inability to recall vocabulary, which leads to frequent incorrect word substitutions (Paraphasia).²⁴ Reading and writing skills are lost. Memory problems worsen. Behavioural and neuropsychiatric changes becomes evident. 30% of the people develop illusionary misidentification and delusional symptoms at this stage.²⁵ In this stage, people with AD tend to repeat the same conversation. Urinary incontinence (involuntary urination) can develop.²⁵

Stage IV: Late stage Alzheimer's

During the final stages, the patient completely depends on the caregivers. Patient tend to speak a single phrase or a single word.^{24,25} Sometimes loss of speech also seen. Aggressiveness, apathy and exhaustion are most commonly seen symptoms. Loss of self-awareness. However, death occurs due to other infections and by the disease itself.^{24,25}

TEN WARNING SIGNS OF ALZHEIMER'S

- Memory loss that disrupts daily life
- Challenges in planning and solving problems
- Difficulty in completing the familiar tasks
- Confusion regarding time or place
- Difficulty in understanding visual images
- Difficulty & finding for words while speaking or writing
- Misplacing the things and fail to retrace the misplaced things
- Decreased or poor judgement
- Withdrawal from work or social activities
- Changes in mood and personality.²⁶

DIAGNOSIS

Alzheimer's disease is usually diagnosed based on the person's history, presence of neurological and neuropsychological features. Advanced Medical imaging with Computed Tomography (CT), Magnetic Resonance Imaging (MRI), single-photon emission computed tomography (SPECT) or positron emission tomography (PET) can be used as diagnostic aids.²⁷ Assessment of intellectual

functioning including memory testing can further characterize the state of the disease.

TREATMENT STRATEGES

There is no cure for Alzheimer's disease. Current treatments can be divided into pharmaceutical, psychosocial and caregiving. Medications are usually palliative in nature. Five medications are currently used out of which four drugs are acetylcholinesterase inhibitors (tacrine, rivastigmine, galantamine and donepezil) and an NMDA (N-Methyl-D-aspartate) receptor antagonist (memantine).²⁸ Antipsychotic drugs are useful in reducing aggression and psychosis in Alzheimer's disease.²⁹ Psychosocial interventions are used as an adjunct to pharmaceutical treatment.³⁰ Caregiving essentially is the treatment and must be carefully managed over the course of the disease.³¹ Feeding tubes can be used for patients developing problems in swallowing, reduced appetite and inability to recognise food.³²

DENTAL FINDINGS SEEN IN ALZHEIMER'S PATIENTS

Patients with a longstanding Alzheimer's disease have poor oral health and do not understand the importance of oral health and function. If oral hygiene measures are inadequate, bacteriologic and fungal disease can result in severe dental caries, periodontal disease and oral candidiasis. However, dental health problems can lead to pain and unmanageable behaviour. The medications given for Alzheimer's disease can cause dry mouth.³³

DENTAL MANAGEMENT

Studies have shown that about 75% of patients with Alzheimer's disease needs dental attention. The stage of the disease and the complexity of the dental treatment will decide if the patient can be treated in the dental clinic, at hospital or at home (bed-ridden). Comprehensive oral rehabilitation is best completed as early as possible since the patients ability to cooperate during dental treatment diminishes with advancing disease.

If long term care is anticipated, full mouth radiographs should be taken for future use. The best alternative is more frequent recall visits including prophylaxis and application of topical fluoride. However, patients with Alzheimer's can also have systemic diseases associated. Hence, a consultation with the patient's physician is required.³⁴ When the patient is unable to take care of the oral health, it is important to educate the partner, caregiver to provide the basic needs for the patients to maintain a good oral hygiene. Electric tooth brushes can be advised, if the patient can tolerate the vibrating sensation.³⁵ For pain and anxiety control, the patient may accept treatment under local anaesthesia in the early stages of the disease. Conscious sedation with short acting benzodiazepine may be required. Nitrous oxide sedation may also be helpful. In patients with loss of ability to cooperate or those with hostile behaviour, general anaesthesia may be required.³⁵ Dental appointments and treatments should be carried out in the mornings when cooperation tends to be the best. Treatments should be carried out in the presence of usual caregivers, in the familiar environment. Time consuming and complex procedures should be avoided. During the advanced stages of the disease, patient has to be positioned upright or slightly reclined, in order to avoid hypotension and aspiration.³⁵

SUMMARY

Alzheimer's disease is not a normal part of aging. It is a disease that affects the brain. Eventhough there are many hypothesis was proposed, the exact cause for the disease is unknown. In the early stages, prevention of the dental disease is the primary factor. However, as the disease progresses, it is difficult to gain cooperation from the patient. Adequate prevention in the early stages of the disease, proper education on oral hygiene maintainence to the patients partner or the caregiver, frequent dental visits, proper diet helps in the proper maintainence of the oral cavity.

REFERENCES

1. Alzheimer Alois. About a Peculiar Disease of the Cerebral Cortex. *Alzheimer disease and associated disorders*.1(1):3-8.(1987).
2. Alzheimer's Association. Alzheimer's disease facts and figures. *Alzheimer's Dement*. 8(2):131-68.(2012)
3. Selkoe DJ. Translating cell biology into therapeutic advances in Alzheimer' disease. *Nature*. 399(6738 Suppl):A23-31(1999).
5. Geodert M, Spillantini MG, Crowther RA. Tau proteins and Neurofibrillary Degeneration. *Brain pathology (Zurich, Switzerland)*.1(4):279-86.(1991).
6. Burns A, Iliffe S. Alzheimer's disease. *BMJ (Clinical research ed)* 338:b158.(2009).
7. Arthur H. Freidlander, DMD, Dean C.Norman, Michael E.Mahler et al- Alzheimer's disease- Psychopathology, medical management, and dental implications. *The Journal of American Dental Association* 137, 1240-1251.(2006).
8. "What We Know Today About Alzheimer's Disease". Alzheimer's Association.(2011).
9. Blennow K, de Leon MJ, Zetterberg H. Alzheimer's Disease. *Lancet*. 368(9533):387-403. (2006).
10. Warning SC, Rosenberg RN. Genome-wide association studies in Alzheimer's disease. *Archives of neurology*.;65(3):329-34(2008).
11. Gatz M, Reynolds CA, Fratiglioni L et al- Role of genes and environments for explaining Alzheimer's disease. *Arch Gen Psychiatry*. ;63(2):168-74.(2006).
12. Jonsson T, Atwal JK, Sulem P, Lu Y et al- Mutation in APP protects against Alzheimer's disease and age-related cognitive decline. 488(7409):96-99.(2012).
13. Strittmatter WJ, Saunders AM, Enghild J et al- Apolipoprotein E: high-avidity binding to beta-amyloid and increased frequency of type 4 allele in late-onset familial Alzheimer disease. *Proceedings of the National Academy of Sciences of the United states of America*. ;90(5):1977-81.(1993).
14. Mahley RW, Weisgraber KH, Huang Y. Apolipoprotein E4; a causative factor and therapeutic target in neuropathology including Alzheimer's disease. *Proceedings of the National Academy of Sciences of the United States of America*. ;103(15):5644-51.(2006).
15. Lambert JC. Meta analysis of 74,046 individuals identifies 11 new susceptibility loci for Alzheimer's disease. *Nature Genetics* 45(12):1452-8.(2013).
16. Guerreiro R, Wojtas A, Bras J et al- TREM2 variants in Alzheimer's disease. *The New England Journal of Medicine*. 368(2):117-27.(2012).
17. Mudher A, Lovestone S. Alzheimer's disease- do tauists and bapists finally shake hands?. *Trends in Neurosciences*.;25(1):22-26(2002).
18. Francis PT, Palmer AM, Snape M, Wilcock GK. The Cholinergic Hypothesis of Alzheimer's Disease: a Review of Progress. *Journal of Neurology, Neurosurgery and Psychiatry*.;66(2):137-47.(1996).
19. Chun W, Johnson GV. The Role of Tau Phosphorylation and Cleavage in Neuronal Cell Death. *Frontiers in Bioscience: A Journal and Virtual Library*. 12:733-56.(2007).
20. Iqbal K, Alonso Adel C, Chen S et al- Tau Pathology in Alzheimer Disease and other Tauopathies. *Biochimica Et Biophysica Acta*. ;1739 (2-3):198-210 (2005).
21. Alzheimer's Association. Alzheimer's disease facts and figures, (2013).
22. Tanzi RE. The genetics of Alzheimer disease. *Cold Spring Harbor Perspectives in Medicine*. volume 2, issue 10.(2012).
23. Alzheimer's Association. Traumatic Brain Injury. (2013.)
24. Arnaiz E, Almkvist O. Neuropsychological Features of Mild Cognitive Impairment and Preclinical Alzheimer's Disease. *Acta Neurologica Scandinavica*. 179:34-41(2003).
25. Frank EM. Effect of Alzheimer's Disease on Communication Function. *Journal of*

- the South Carolina Medical Association. ;90(9):417-23(1994).
26. Forstl H, Kurz A. Clinical Features of Alzheimer's Disease. *European Archives of Psychiatry and Clinical Neuroscience*. 249(6):288-290.(1999).
 27. Alzheimer's Association. Know the 10 signs- Early detection matters (2009).
 28. Dementia: In: Quick Reference Guide. London (UK) National Institute for Health and Clinical Excellence.(2006.)
 29. Pohanka M. Cholinesterases, a target of pharmacology and toxicology. *Biomedical Papers of the Medical Faculty of the University Palacky, Olomouc, Czech Republic*. 155(3):219-229.(2011).
 30. Ballard C, Waite J. The Effectiveness of Atypical Antipsychotics for the Treatment of Aggression and Psychosis in Alzheimer's Disease. *The Cochrane Database of Systemic Reviews*. (1):CD003476.(2006)
 31. Rabins PV, Blacker D, Rovner BW et al- American Psychiatric Association Practice Guideline for the treatment of patients with Alzheimer's disease and other dementias. *The American Journal of Psychiatry*. December ;164(12 Suppl):5-56.(2007)
 32. Dunne TE, Nearing SA, Cipolloni PB. Visual Contrast Enhances Food and Liquid Intake in Advanced Alzheimer's Disease. *Clinical Nutrition(Edinburgh, Scotland)*. 23(4):533-538.(2004).
 33. Chernoff R. Tube feeding patients with Dementia. In: *Nutrition in Clinical Practice*. 21(2):142-6.(2006).
 34. Edward W Odell, *Textbook of Clinical Solving Problems in Dentistry*, 3rd Edn, Elsevier India. 2011.
 35. Peter B. Lockhart. John, *Textbook of Oral Medicine and Medically Complex Patients*, 6th Edn, Wiley & Sons, 2012.
 36. Crispian Scully, Pedro Diz Dios, Navdeep Kumar, *Textbook of Special Care in Dentistry- Handbook of Oral Healthcare*. Elsevier Health Sciences. 38-40.(2006).