# Alzheimer's Disease

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| Key Points |
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| ➢ Cause: accumulation of extracellular amyloid beta Aβ plaques and intracellular neurofibrillary tangles<br>➢ Stages: mild behavioural impairment to dementia<br>➢ Diagnosis: Biomarkers, MRI, PET scanning<br>➢ Treatment: |

Alzheimer's disease (AD) is an irreversible neurological disease that impacts everyday living activities and social functioning by impairing mental capacity development, disrupting neurocognitive function, and interfering with daily activities.[1] Alzheimer's disease is a multifaceted disorder caused by the combination of hereditary vulnerability and environmental variables throughout the course of a person's life. Because Alzheimer's disease is thought to begin decades before clinical symptoms appear, interventions addressing many risk factors in non-demented elderly persons, as well as the middle-aged population, may help to prevent or delay the onset of the illness.[2]

**Causes:**

The increasing accumulation of extracellular amyloid beta Aβ plaques and intracellular neurofibrillary tangles (NFTs) are two pathological hallmarks of Alzheimer's disease (AD). Aggregated Aβ plaques are deposited within the brain in Alzheimer's disease as a result of either impaired Aβ clearance or excessive production; plaque deposition occurs 20 years before cognitive impairment. NFTs are created when hyperphosphorylated tau protein accumulates abnormally; they can be discovered 10–15 years before symptoms appear.[3]

**Stages**

AD is a disease that progresses from an asymptomatic stage with biomarker evidence of AD (preclinical AD), through minor cognitive (mild cognitive impairment and/or neurobehavioral (mild behavioural impairment) abnormalities, to dementia. To characterise AD along this continuum, a number of staging schemes have been proposed. While the definitions of each stage differ, they all include the presence or absence of pathologic Aβ and NFTs, as well as cognition, function, and behaviour abnormalities. As a result, there are minor but significant changes in the terminology for each stage of Alzheimer's disease, depending on the clinical and scientific categories used (Figure 1).

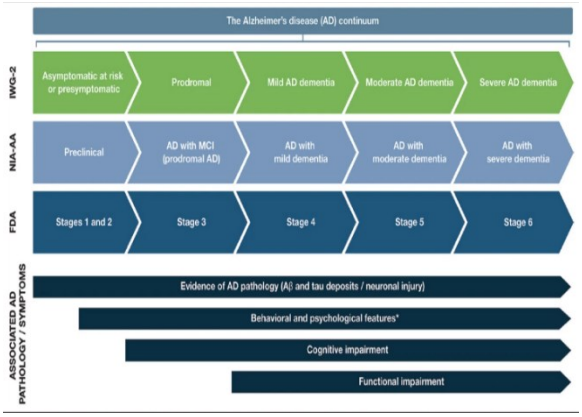


**Figure 1:**

***Source:*** *https://media.springernature.com/*

From preclinical AD to severe AD dementia, the AD continuum can be divided into stages, with variable terminology associated with each stage depending on the clinical and scientific classifications. The symptoms associated with each stage of the continuum are summarized in this diagram. [3]

As the first stage in the Alzheimer's disease continuum, preclinical AD is characterised by a long asymptomatic period during which individuals exhibit indications of AD pathology but no signs of cognitive or functional deterioration, and their everyday lives are undisturbed (Figure 1). Preclinical Alzheimer's disease can last anywhere from 6 to 10 years, depending on the age at which it manifests. A number of variables, including age, sex, and apolipoprotein E (ApoE) status, influence the probability of progression from preclinical AD to MCI due to AD (with/without MBI); however, not everyone with underlying AD pathology will develop MCI or AD dementia. [3]

The symptomatic stage of Alzheimer's disease begins with mild cognitive impairment. Patients in this phase have a slowing or even a plateau in Aβ accumulation from a biomarker standpoint. [4]

When MCI is caused by AD pathology, it is usually followed by AD dementia, which is a later stage of the disease compared to the initial buildup of Aβ AD dementia is a stage in which the Aβ distribution in the brain is most apparent, tau accumulation is at its peak, and neurodegeneration progresses and becomes more macroscopically visible. [5]

**Diagnosis:-**

Patients can engage with their family, caregivers, clinicians, and other members of the larger support team to build advanced care plans after receiving an early diagnosis of AD. It also allows patients to seek early therapy for symptomatic relief, lifestyle adjustments to maintain quality of life, and risk-reduction strategies that can produce clinically relevant reductions in cognitive, functional, and behavioral deterioration. [3]

Alzheimer's disease (AD) is a pathophysiological cascade that begins 20 to 30 years before dementia. Using biomarkers, this pathology can now be detected in vivo.[4] Because the neuropathologic hallmarks of AD ( Aβ plaques and NFTs) can be diagnosed decades before symptoms appear [6, 7,] biomarkers reflecting this underlying pathology constitute an important opportunity for early identification of patients most at risk of developing MCI as a result of AD. [3]

Imaging methods such as magnetic resonance imaging (MRI) and positive emission tomography (PET), which detect early structural and chemical changes in the brain, might provide important biomarker information. CSF indicators can directly represent the presence of Aβ and aggregated tau in the brain. [3]

**Treatment:-**

There is presently no medication that can slow or stop the progression of the disease. Furthermore, the late diagnosis of Alzheimer's disease is a serious hindrance to effective disease management. As a result, better diagnostic techniques and innovative treatments for Alzheimer's disease are critical. The most modern molecular techniques for an AD treatment approach, as well as nanomedicine-based technologies, are being employed to both target medications to the brain and serve as diagnostic indicators for tracking disease development. Modern nanoparticles, such as polymeric, lipid, and metal-based nanoparticles, are being studied extensively for their potential to improve the efficacy of both traditional and innovative medications in the treatment of Alzheimer's disease. [6]

There are currently just four FDA-approved treatments for Alzheimer's disease, all of which are tied to the two biochemical pathways involving Aβ peptide buildup and p-tau protein neurofibrillary tangles (NFT).[6] However, it was eventually recognized that these drugs were inefficient in addressing the root of AD pathogenesis, instead focusing on the symptoms in order to enhance a patient's cognitive function. As a result, a hunt for improved disease-modifying alternatives continues.[8] It is believed that the discovery of novel biomarkers would lead to early AD diagnosis and the identification of additional molecular targets, which could lead to new treatments. [6]

Cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) and an N-methyl-D-aspartic acid

receptor antagonist (memantine), which are now approved drugs for the treatment of Alzheimer's disease, are symptomatic but have little effect on disease progression. [7]

LNPs (lipid-based nanoparticles) are one of the most widely utilised controlled drug delivery technologies for delivering medications to the brain. These systems are appealing for therapeutic nanocarriers because of their safety, biocompatibility, and biodegradability. Because of their ubiquitous use in nanomedicine, metal-based NPs (MNPs) are the most relevant inorganic nanocarriers. Gold, silver, iron, zinc, and copper are often used to make MNPs, each of which gives the final nanocarrier various features. [8]

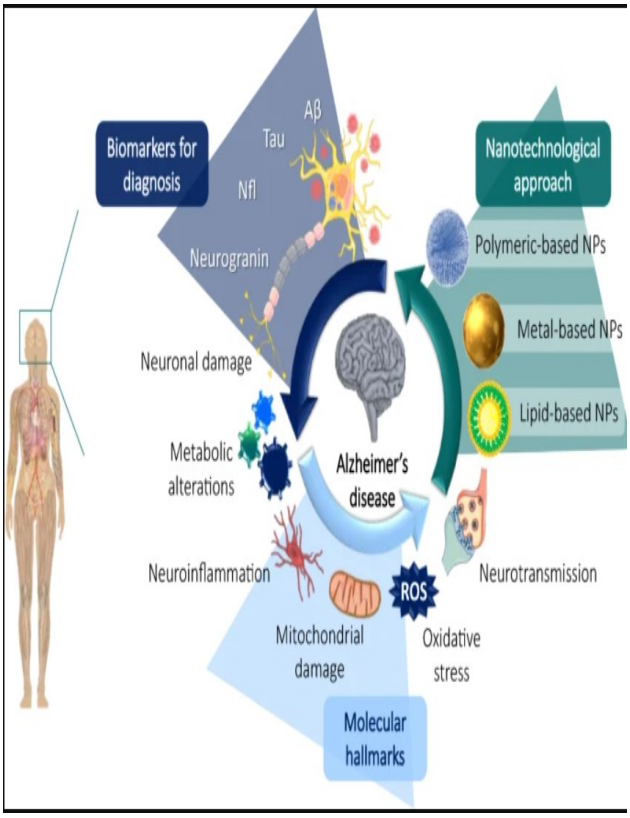


**Figure 2:**

***Source:*** *Https://Media.Springernature.*

## References


1. Srivastava S, Ahmad R, Khare SK. Alzheimer's disease and its treatment by different approaches: A review. European Journal of Medicinal Chemistry. 2021 Apr 15;216:113320.
2. Zhang XX, Tian Y, Wang ZT, Ma YH, Tan L, Yu JT. The epidemiology of Alzheimer's disease modifiable risk factors and prevention. The journal of prevention of Alzheimer's disease. 2021 Jul;8(3):313-21.
3. Porsteinsson AP, Isaacson RS, Knox S, Sabbagh MN, Rubino I. Diagnosis of early Alzheimer's disease: clinical practice in 2021. The journal of prevention of Alzheimer's disease. 2021 Jul;8(3):371-86.
4. Van der Schaar J, Visser LN, Bouwman FH, Ket JC, Scheltens P, Bredenoord AL, van der Flier WM. Considerations regarding a diagnosis of Alzheimer's disease before dementia: a systematic review. Alzheimer's research & therapy. 2022 Dec;14(1):1-2.
5. Liss JL, Seleri Assunção S, Cummings J, Atri A, Geldmacher DS, Candela SF, Devanand DP, Fillit HM, Susman J, Mintzer J, Bittner T. Practical recommendations for timely, accurate diagnosis of symptomatic Alzheimer's disease (MCI and dementia) in primary care: a review and synthesis. Journal of Internal Medicine. 2021 Aug;290(2):310-34.
6. Cano A, Turowski P, Ettcheto M, Duskey JT, Tosi G, Sánchez-López E, García ML, Camins A, Souto EB, Ruiz A, Marquié M. Nanomedicine-based technologies and novel biomarkers for the diagnosis and treatment of Alzheimer's disease: from current to future challenges. Journal of Nanobiotechnology. 2021 Dec;19(1):1-30.
7. Zhang F, Zhong RJ, Cheng C, Li S, Le WD. New therapeutics beyond amyloid-β and tau for the treatment of Alzheimer's disease. Acta Pharmacologica Sinica. 2021 Sep;42(9):1382-9.
8. Thoe ES, Fauzi A, Tang YQ, Chamyuang S, Chia AY. A review on advances of treatment modalities for Alzheimer's disease. Life sciences. 2021 Jul 1;276:119129.