

UNDERSTANDING ALZHEIMER'S DISEASE PROGRESSION

Alzheimer's disease (AD), the most common cause of dementia, is a **progressive neurodegenerative disease** that typically affects **memory, thinking, decision-making and mood**, which impacts a person's ability to perform daily activities.^{1,2} Dementia, including AD, has **physical, psychological, social and economic** impacts, not only for people living with dementia, but also for their caregivers, families and society.³

Prevalence



60-70%

of all dementia cases may be attributable to **AD**³



14.1 million

people are living with dementia in **Europe**⁴



10 million

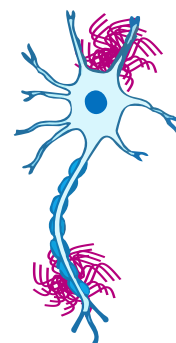
new cases of dementia **globally** every year⁴

Brain changes in AD

Several brain changes are associated with AD, including inflammation and loss of brain volume, however the hallmark pathologies of AD are the accumulation of two different proteins in the brain:

- › **amyloid beta** ($A\beta$) which forms plaques outside neurons
- › **tau** which forms twisted strands inside neurons

These changes interfere with neuronal function and are thought to contribute to damage and death of neurons.⁵



There is **scientific evidence that the $A\beta$ pathway contributes to neurodegeneration in AD**, as $A\beta$ accumulation occurs long before the onset of clinical symptoms and before other brain changes in AD.⁶ $A\beta$ can exist in several forms including plaques which are deposited within the brain interfering with neuronal communication at synapses.^{5,6} A smaller formation of $A\beta$ called protofibrils are thought to be particularly harmful.⁶

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AD Progression

AD is **progressive**, meaning that symptoms gradually develop and worsen over time as damage to the brain accumulates. There are three broad stages, **preclinical AD**, **mild cognitive impairment (MCI) due to AD**, and **Alzheimer's dementia** (further split into mild, moderate, and severe). The length of time an individual spends in each stage varies.⁵

- 1 Preclinical AD**
Individuals have measurable brain changes that indicate the earliest signs of AD such as abnormal levels of A β but have not yet developed symptoms
- 2 MCI due to AD**
Individuals start experiencing symptoms as subtle problems with memory and thinking
- 3 Mild dementia due to AD**
Individuals have noticeable symptoms that start to interfere with some daily activities and they may need help for these
- 4 Moderate dementia due to AD**
Individuals have symptoms that interfere with many daily activities, and they may develop problems with communication and personality changes. This is often the longest stage
- 5 Severe dementia due to AD**
Individuals have symptoms that interfere with most daily activities and likely require full-time care

References

1. Alzheimer's Disease International. Alzheimer's Disease. <https://www.alzint.org/about/dementia-facts-figures/types-of-dementia/alzheimers-disease/> (Accessed November 2022). 2. Alzheimer's Disease International. About Alzheimer's & Dementia. <https://www.alzint.org/about/> (Accessed November 2022). 3. WHO. Dementia. <https://www.who.int/news-room/fact-sheets/detail/dementia> (Accessed November 2022). 4. WHO. Global status report on the public health response to dementia. 2021. Available at: <https://www.who.int/publications/i/item/9789240033245> 5. Alzheimer's Association Report. 2021 Alzheimer's disease facts and figures. Alzheimer's & dementia. 2021 Mar;17(3):327-406. 6. Hampel H, et al. The amyloid- β pathway in Alzheimer's disease. Molecular Psychiatry. 2021. 26(10):5481-5503.