Alzheimer's Disease Overview

Alzheimer's disease (AD) is a neurodegenerative disease of unknown aetiology, characterised by progressive memory loss and cognitive impairment. It is the most common form of dementia, thought to account for 50% to 75% of cases of the disease. AD is an incurable condition with a long preclinical period and progressive course. The exact cause of the disease is unknown.

An estimated 9.8 million people were living with AD and other dementias in the European region in 2019, with women being disproportionately affected. The prevalence is predicted to increase to 18.8 million by 2050 as the population in Europe grows older.

The pathological features of AD are linked to a build-up of harmful proteins in the brain:

- Extracellular beta-amyloid deposits or plaques (amyloid)
- Intracellular neurofibrillary tangles (tau)

These plaques and tangles disrupt connections between brain cells. In addition, the production of brain chemicals, such as acetylcholine is reduced. The combined effect is a loss of brain cell function, as well as brain cell death. Initially, this occurs in the areas of the brain that are responsible for memory. Over time, the disease impacts those areas of the brain responsible for language, reasoning, social behaviour, and performing everyday tasks. In advanced stages, severe loss of brain function can cause dehydration, malnutrition, or infection. These complications can result in death.

Experts are not sure why the buildup of proteins occurs, but research suggests that a combination of lifestyle, environmental, and genetic factors trigger a pathophysiologic cascade that, over time, leads to the characteristic Alzheimer's pathology and dementia.

According to the UK's National Health Service (NHS), risk factors for Alzheimer's disease include age, family history, smoking, obesity, diabetes, high blood pressure, high cholesterol, hearing loss, untreated depression, smoking, hearing loss, social isolation, and a sedentary lifestyle.

Age is the biggest risk factor. The condition mainly affects those 65 years of age and older and the chance of developing the disease after this age doubles every five years. While most cases of AD are sporadic, familial forms do exist and people are more likely to develop AD if a first-degree relative had it. Specific gene mutations are also strong predictors of developing the disease.

While AD cannot entirely be prevented, making modifications to certain lifestyle or environmental factors may decrease the overall risk of developing Alzheimer's disease or another dementia-related condition.

There is no treatment that cures AD. However, medicines may improve or slow the progression of symptoms. Medications currently available for the management of AD include agents for cognitive symptoms, agents for behavioural and psychological symptoms of dementia, as well as agents for sleep disorders. More recently, potential disease-modifying agents are under investigation and have been approved in some jurisdictions.

Cholinesterase inhibitors include the medications donepezil, rivastigmine and galantamine. These medications prevent the neurotransmitter, acetylcholine from breaking down. Acetylcholine supports memory and learning, so by stopping the breakdown of acetylcholine, these medications help to maintain more constant acetylcholine levels and enable more effective communication among nerve cells. Cholinesterase inhibitors may help with symptoms related to memory, judgment, language, and thinking. Donepezil, rivastigmine, and galantamine are approved for use in Europe for mild to moderately severe AD.

Glutamate regulators modify the effects of elevated glutamate levels. Glutamate is a neurotransmitter that helps the brain process information. Elevated levels of glutamate may lead to neuronal dysfunction. Glutamate regulators, such as memantine, may help improve memory, attention, language, reasoning, and the ability to perform basic actions. Memantine is indicated for the treatment of moderate to severe AD in Europe.

Medications like cholinesterase inhibitors and glutamate antagonists offer symptomatic relief without halting progress of the disease or offering a cure. In the last number of years, agents with potential disease-modifying activity have been researched and two such products, lecanemab and donanemab are under evaluation by regulatory bodies in Europe.

Treatment of AD has always been a highly challenging area. There is a huge need for medications that not only slow decline of the condition, but also, improve disease symptoms without causing significant and dangerous side effects. According to the World Health Organization, the number of persons suffering from AD will rise by at least 14% by 2025 as a result of the growing number of adults over age 65.

Therefore, the high demand for improved, cost-effective treatment options from patients, caregivers, and their providers will continue into the foreseeable future for this devastating and deadly disease.

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