The future of geriatric healthcare: Addressing Alzheimer's disease

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Abstract

Alzheimer's disease (AD), the most prevalent kind of dementia, mostly affects the elderly and poses serious problems to worldwide health systems. Several possible therapies exist, but no drug available today can restore or replace destroyed neurons. Researchers are developing novel medicines and treatments for AD. The likelihood of having AD grows with older age. AD has a profound effect on memory, thinking, and behavior. Few new medications showed promise, and most trials concluded that they were either unsafe or did not significantly assist. Although the existing FDA-approved therapies, such as acetylcholinesterase inhibitors and memantine, effectively control symptoms, they do not stop the advancement of the disease. Innovative treatment approaches such as gene therapy, immunotherapy, theragnostic, and metal-based chelators provide renewed optimism. Although significant progress has been made, the ongoing growth of the aging population necessitates the implementation of cutting-edge research and clinical trials to address the rising incidence of Alzheimer's disease (AD) and its impact on society.

Keywords: Geriatric Healthcare, Alzheimer’s Disease, clinical trials

1. Introduction

AD is a degenerative brain illness that causes brain shrinkage and cell death (1). This is the most prevalent kind of dementia, causing problems with everyday tasks, behavioral and cognitive abnormalities, and memory loss. Globally, there are already 55 million cases of dementia; however, as people live longer, this number is predicted to increase to 139 million by 2050

approximately. In 2019, dementia claimed 1.6 million lives and resulted in approximately $1.3 trillion in worldwide costs (2-3). The majority of people afflicted by AD are 75 years of age and older, with women more likely to be impacted in their later years. Approximately 6.5 million Americans who are 65 years of age or older have AD; most of them are over 75. Almost 4 million cases of this illness have been documented in India, and it is responsible for 60% to 70% of dementia cases worldwide (4-5). Forgetting recent discussions or occurrences is one of the early indicators of AD. As the illness worsens, it causes profound memory loss and makes daily chores more difficult to do. Alzheimer's cannot be cured, although drugs can help control symptoms and halt the disease's development (6). Both patients and the people who care for them can get support services. When the illness reaches advanced stages, it can have deadly consequences such as infections or dehydration (7). The causes, current therapies, and diagnostic techniques for AD will be covered in this overview, along with recent developments meant to address problems including inflammation, oxidative damage, and protein accumulation.

2. Phases of Alzheimer's illness

The progression of AD occurs in many phases. Changes in the brain create mild memory loss in the early stage, which can endure for years, although people do not exhibit visible symptoms or have difficulty doing daily chores. The symptoms become more obvious as it progresses towards the intermediate stage.

Individuals may find it difficult to do daily duties, lose track of time or location, and suffer from sadness or mood changes (8). By affecting more brain regions in the intermediate stage, the illness exacerbates memory loss and impairs the ability to identify friends and relatives. It also impacts speaking, writing, reading comprehension, and impulse control. When Alzheimer's reaches a severe stage, it affects the whole brain and significantly impairs cognitive function. Eating, using the bathroom, and recognizing loved ones may be difficult for them. They frequently end up bedridden and may pass away from illness-related complications (9-10). The phases of AD, ranging from moderate cognitive impairment to severe dementia, are depicted in Figure 1.

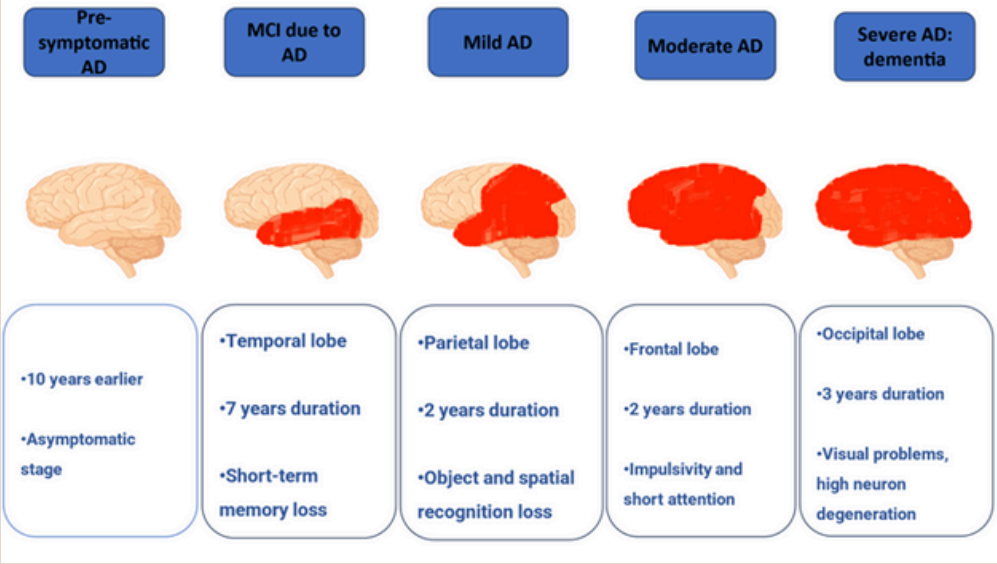

Figure 1. Stages of AD

3. AD diagnostic standards

Multiple tests are employed to identify AD when it is suspected. These include a blood test to measure vitamin B12 levels, a brain MRI, and a neurological examination. Low vitamin B12 can cause brain issues and raise the risk of AD. The brain can also be harmed by high homocysteine

levels, which may be a sign of inadequate vitamin B12. In 1984, guidelines for diagnosing AD were published (11,12). They suggested that symptoms such as progressive memory loss, difficulty with everyday chores, language impairments, or problems with motor skills should be taken into consideration. Between the ages of 40 and 90, the diagnosis should be made, and other illnesses should be checked out. When symptoms point to AD but might also be caused by other conditions, it is referred to as "possible Alzheimer's disease." Examining brain tissue from an autopsy or biopsy confirms a final diagnosis (13). The new criteria include utilizing phrases like "likely AD" and "possible AD dementia" in clinical contexts, as well as searching for indicators of disease processes. Key indicators for diagnosis include brain activity from PET scans and MRI to measure brain atrophy, as well as amyloid levels in CSF fluid or PET scans and tau levels in the same. The most recent approaches to early Alzheimer's disease detection are shown in Figure 2, which highlights improvements in biomarkers and diagnostic tools.

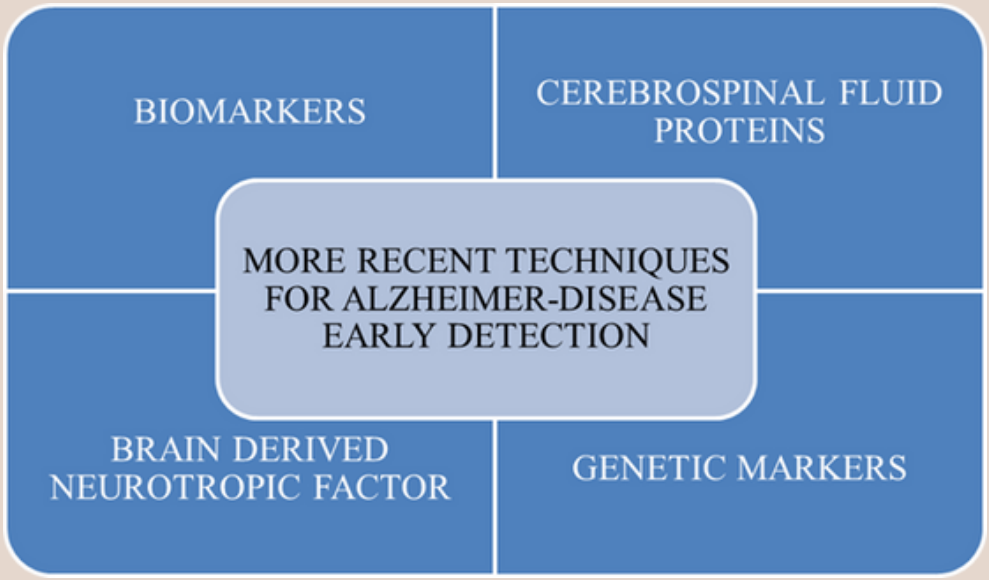

Figure 2. More recent techniques for AD early detection

4. Signs & Symptoms of AD

Memory loss is the main sign of AD. People may have memory loss in the early stages related to recent discussions or occurrences. Memory issues get worse as the illness worsens and new symptoms appear. An individual suffering from AD may first experience memory loss and cognitive impairments. But as symptoms worsen, friends or relatives are likely to notice these problems as well. AD-related brain abnormalities cause problems with a variety of cognitive and functional abilities to get worse:

- AD causes progressive memory loss that begins with trouble recalling recent events. Individuals may become repetitive, lose track of time or conversations, misplace belongings, become lost, and finally forget everyday things and family members' identities. They could have trouble putting their ideas into words (14).

- It becomes difficult to reason and think, especially while juggling many tasks and complicated concepts. It might become difficult to handle chores like cooking or money management.

- Decision-making and judgment deteriorate, resulting in bad decisions and trouble solving common issues, like a burning stove.

- Mood swings, sadness, social disengagement, aggressiveness, and altered sleeping patterns are examples of personality and behavior changes (15).

- Despite these difficulties, certain abilities such as reading, writing, and listening to music may be retained for a longer period as they involve brain regions that are impacted later in the illness.

5. Risk factors

- **Age:** Age is the most important risk factor for AD, with most instances occurring in those 65 years of age and older. AD can occur with an early start and can be misdiagnosed, even though it is less frequent in people under 65 (16,17).

- **Risk to other family members:** If a parent or sibling has AD, your chances of getting the illness are increased. Although the precise reasons are yet unknown, a person's genetics, lifestyle, and environment may all increase their risk (16,17).

- **Minimal cognitive decline:** Although moderate cognitive impairment (MCI) impairs cognitive ability, it has little effect on day-to-day activities. Individuals with MCI, particularly those who have memory problems, are more likely to get Alzheimer's. MCI, however, does not necessarily advance in some circumstances, it can even become better (16,17).

- **Heart-related conditions:** Heart and blood vessel health are related to brain health. Those who smoke, are obese, have diabetes, have high blood pressure, or have high cholesterol may be more susceptible to AD and other dementias (16,17).

- **Brain trauma:** AD risk is increased by traumatic brain injuries, such as those resulting from a severe blow to the head or prolonged unconsciousness. Dementia risk may also increase with repeated brain trauma, such as those sustained in sports or battle (16,17).

6. Current treatments available

6.1 **FDA-approved drugs:** Memantine and other acetylcholinesterase inhibitors are examples of current Alzheimer's medications that only treat symptoms rather than the illness itself. Drugs that target the tau and amyloid proteins are being investigated in ongoing studies; early intervention and immunotherapy are other priorities (18).

6.2 **Gene therapy:** Gene therapy for Alzheimer’s is exploring methods like inserting new genes using viruses to address faulty genes and proteins. Recent studies show promise with techniques like NGF gene therapy and PGC1-alpha delivery, but this approach faces challenges in effective delivery across the blood-brain barrier, ensuring target specificity, managing safety concerns, and addressing high costs and ethical issues. Long-term efficacy and regulatory hurdles also pose significant limitations but further research is needed to confirm the effectiveness and safety (20).

6.3 **Theragnostic:** Theragnostic combines diagnosis and treatment for Alzheimer’s using technologies like gold nanorods and fluorescent probes to detect and target amyloid plaques. Challenges include achieving precise targeting across the blood-brain barrier, ensuring safe and effective use of nanomaterials, and balancing the complexity and cost of integrating diagnostic and therapeutic functions. Long-term safety and regulatory approval remain significant hurdles (21).

6.4 **Immunotherapy:** Aβ immunotherapy aims to target amyloid plaques using mechanisms like neutralizing antibodies, enhancing phagocytosis, and preventing plaque spread. Active and passive immunization strategies, including monoclonal antibodies, are being tested, with newer engineered antibodies showing promise for fewer side effects (22).

6.5 Metal-based chelators: Metal chelators help treat Alzheimer's by removing excess metals like copper, iron, and zinc from the brain, which reduces toxicity and oxidative stress. Compounds like clioquinol and hybrid modulators show promise by restoring metal balance and preventing Aβ aggregation (23).

6.6 Drugs under clinical testing: The important medications undergoing clinical testing are listed in Table 1, highlighting the latest advancements in AD treatments (19).

Table 1. Important medications undergoing clinical testing

S. No.	Name of Drug	Mechanism of Action	Clinical Trial	Indications to be Alleviated
1.	Nabilone	Semisynthetic derivative of a cannabinoid.	Small-scale phase III	Agitation
2.	Suvorexant	Antagonists on both sides of the orexin receptor.	Phase III	Insomnia
3.	Brexpiprazole	D2 partial agonist.	Phase III	Agitation
4.	Lemborexant	Antagonists on both sides of the orexin receptor.	Phase II	Insomnia
5.	Pimavanserin	Selective 5-HT2A serotonin inverse agonist.	Phase II/III	Psychotic

7. Conclusion

There are now no effective therapies to stop or reverse AD progresses and it remains a serious medical concern. Contemporary medications mostly target symptom relief; however, advancements in monoclonal antibody therapy, such as aducanumab and lecanemab, have demonstrated potential in mitigating Aβ plaques and delaying cognitive deterioration. Additionally, novel experimental treatments including genistein, losartan, and atomoxetine are being investigated. To ensure that these therapies are safe and successful, additional study is needed, as many of them are still in the trial stage. The effects of AD are most severe in the elderly because they disproportionately affect people 65 years of age and beyond, making them more vulnerable and lowering their quality of life. The need to identify efficient therapies grows as the population ages. To close the gap between existing scientific understanding and effective medicines, clinical trials and collaborative research are crucial in providing individuals and families struggling with the symptoms of AD with hope.

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