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Alzheimer's disease - A neurodegenerative fight

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SUMMARY

Alzheimer's is not about the past - the successes, the accolades, the accomplishments. Alzheimer's is about the present and the struggle, the scrappy bowl, the fight to live with a disease".

Alzheimer's disease may cause a person to become confused, get lost in familiar places, misplace things, or have trouble with language. Groups of nerve cells have special jobs. Some are involved in thinking, learning and memory. Others help us see, hear, smell and tell our muscles when to move. Brain cells operate like tiny factories. They receive supplies, generate energy, construct equipment and get rid of waste. Cells also process and store information and communicate with other cells.

Keeping everything running requires coordination as well as large amounts of fuel and oxygen. Scientists believe Alzheimer's disease prevents parts of a cell's factory from running well. But just like a real factory, backups and breakdowns in one system cause problems in other areas. As damage spreads, cells lose their ability to do their jobs and, eventually, die.

The brains of individuals with Alzheimer's have an abundance of plaques and tangles. Plaques are deposits of a protein fragment called beta-amyloid that build up in the spaces between nerve cells. Tangles are twisted fibers of another protein called tau that builds up inside cells. Though autopsy studies show that most people develop some plaques and tangles as they age, those with Alzheimer's tend to develop far more and in a predictable pattern, beginning in the areas important for memory before spreading to other regions.

Scientists do not know exactly what role plaques and tangles play in Alzheimer's disease. Most experts believe that they disable or block communication among nerve cells and disrupt processes the cells need to survive. The destruction and death of nerve cells causes memory failure, personality changes, problems in carrying out daily activities and other symptoms of Alzheimer's disease.

Keywords: **A**lzheimer's; Plagues; Tangles; Beta-amyloid; Tau; Autopsy

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INTRODUCTION

Alzheimer's disease (AD) is a neurodegenerative disease that usually starts slowly and progressively worsens [1]. It is the cause of 60–70% of cases of dementia [2-4]. The most common early symptom is difficulty in remembering recent events [1]. As the disease advances, symptoms can include problems with language, disorientation (including easily getting lost), mood swings, loss of motivation, self-neglect, and behavioural issues [2]. As a person's condition declines, they often withdraw from family and society [5]. Gradually, bodily functions are lost, ultimately leading to death [6]. Although the speed of progression can vary, the typical life expectancy following diagnosis is three to nine years [3,7].

Alzheimer's disease is characterized by progressive loss of memory and cognitive function in middle aged individuals (**Fig. 1.**). Thus the condition is frequently associated with:

- Memory failure for recent events
- Lack of spontaneous activity and initiative with loss of intellectual functions
- Extra pyramidal and a kinetic hypertonic symptom.
- Loss of spatial orientation.

After 2 or 3 years, dementia (memory loss) becomes well established and focal symptoms occur, such as aphasia (speech disorder), apraxia (inability to perform voluntary movements) and agnosia (inability to recognize objects inspite of intact sensory modality). Similar features in the old age (over 65 years) are called senile dementia [8].

The sequence of events in the affected neurons

Mutation of amyloid precursor protein gene

I

Aggregation of -amyloid peptides

I

Formation of extracellular plaques

(Senile plaques: toxic polypeptide)

I

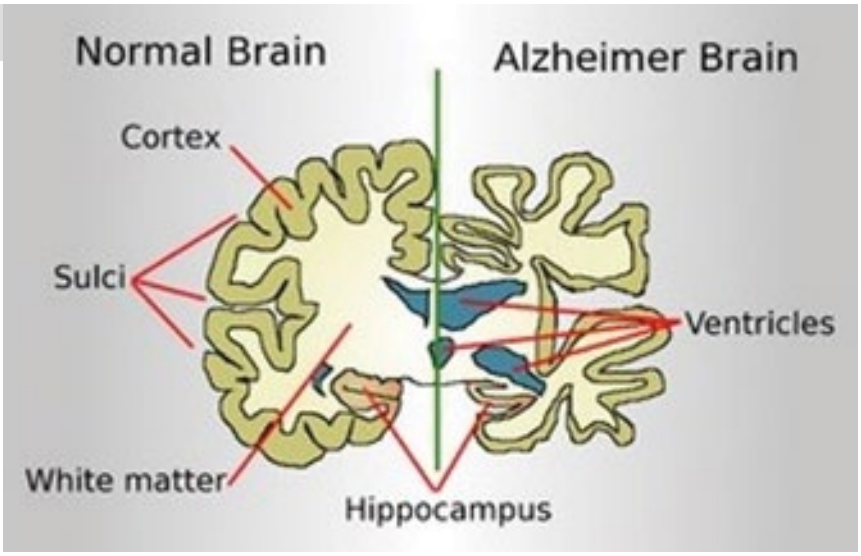
Inflammatory reaction with oxidative damage

Altered nerve

fibers and reactive

glial cells (Gliosis)

Fig. 1. Alzheimer's disease.



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Formation of intracellular neurofibrillary tangles

Degeneration of cholinergic neurons in the cerebral

cortex and hippocampus

I

Alzheimer's disease.

EPIDEMIOLOGY

Alzheimer's disease is the most common type of dementia diagnosed today, accounting for 60-70% of the estimated 50 million people globally who suffer with dementia [9]. It is a degenerative brain disease which is understood to begin 20 years or more before symptoms become apparent in those affected. Neurons in the brain become damaged or destroyed due to the accumulation of the protein fragment beta-amyloid (Aβ) outside the neurons, called beta-amyloid plaques, as well as accumulations of an abnormal form of the protein tau inside the neurons. As a result of this build-up, the body activates immune system cells called microglia that try to clear the toxic proteins, resulting in chronic inflammation when the microglia can no longer keep up with the amount of toxins produced.

The highest prevalence and incidence rates of AD are reported in North America and Western Europe, followed by Latin America, China, and the Western Pacific. It is officially the sixth leading cause of death in the U.S., where 5.8 million Americans have been diagnosed with the disease. This figure is projected to rise to 14 million by 2050. Approximately 200,000 of those living with AD are younger than 65 years of age, but the vast majority (81%) are over age 75 [10,11].

SYMPTOMS

Alzheimer's disease is a progressive condition, meaning that the symptoms get worse over time. Memory loss is a key feature, and this tends to be one of the first symptoms to develop.

The symptoms appear gradually, over months or years. If they develop over hours or days, a person may require medical attention, as this could indicate a stroke.

Symptoms of Alzheimer's disease include:

- Memory loss: A person may have difficulty taking in new information and remembering information. This can lead to:
- Repeating questions or conversations
- Losing objects
- Forgetting about events or appointments
- Wandering or getting lost
- Cognitive deficits: A person may experience difficulty with reasoning, complex tasks, and judgment. This can lead to:
- A reduced understanding of safety and risks
- Difficulty with money or paying bills
- Difficulty in making decisions
- Difficulty in completing tasks that have several stages, such as getting dressed
- Problems with recognition: A person may become less able to recognize faces or objects or less able to use basic tools. These issues are not Due to problems with eyesight's
- Problems with spatial awareness: A person may have difficulty with their balance, trip over, or spill things more often, or they may have
- **Difficulty orienting clothing to their body when getting dressed**
- Problems with speaking, reading, or writing: A person may develop difficulties with thinking of common words, or they may make more speech, spelling, or writing errors
- Personality or behavior changes: A person may experience changes in personality and behavior that include:

a. becoming upset, angry, or worried more often than before

b. a loss of interest in or motivation for activities they usually enjoy

c. a loss of empathy

d. compulsive, obsessive, or socially inappropriate behavior [12,13]

STAGES OF ALZHEIMER'S DISEASE

You can help support your loved one with Alzheimer's by learning more about how the condition unfolds (**Fig. 2.**).

The stages don't always fall into neat boxes, and the symptoms might vary but they can be a guide and help you plan for your friend or relative's care. Doctors call these different stages the progression of the disease. There is no cure for Alzheimer's disease, so it can help to know what to expect so you can plan to meet your loved one's needs in each stage. There are no hard-and-fast lines between mild and moderate stages, but over time, you can expect changes like the ones below.

There are 3 stages of Alzheimer's:

Stage 1. Early stage Alzheimer's (mild)

Stage 2. Middle stage Alzheimer's (moderate)

Stage 3. Late stage Alzheimer's (severe)

Be aware that it may be difficult to place a person with Alzheimer's in a specific stage as stages may overlap (**Fig. 3. and 4.**).

Stage 1: Early-stage Alzheimer's (mild)

In the early stage of Alzheimer's, a person may function independently. He or she may still drive, work and be part of social activities. Despite this, the person may feel as if he or she is having memory lapses, such as forgetting familiar words or the location of everyday objects.

Symptoms may not be widely apparent at this stage, but family and close friends may take notice and a doctor would be able to identify symptoms using certain diagnostic tools.

Common difficulties include:

- Coming up with the right word or name.
- Remembering names when introduced to new people.
- Having difficulty performing tasks in social or work settings.
- Forgetting material that was just read.
- Losing or misplacing a valuable object.
- Experiencing increased trouble with planning or organizing.

Stage 2: Middle-stage Alzheimer's (moderate)

Middle-stage Alzheimer's is typically the longest stage and can last for many years. As the disease progresses, the person with Alzheimer's will require a greater level of care.

During the middle stage of Alzheimer's, the dementia symptoms are more pronounced. The person may confuse words, get frustrated or angry, and act in unexpected ways, such as refusing to bathe. Damage to nerve cells in the brain can also make it difficult for the person to express thoughts and perform routine tasks without assistance.

Symptoms, which vary from person to person, may include:

Fig. 2. Symptoms of Alzheimer's disease.

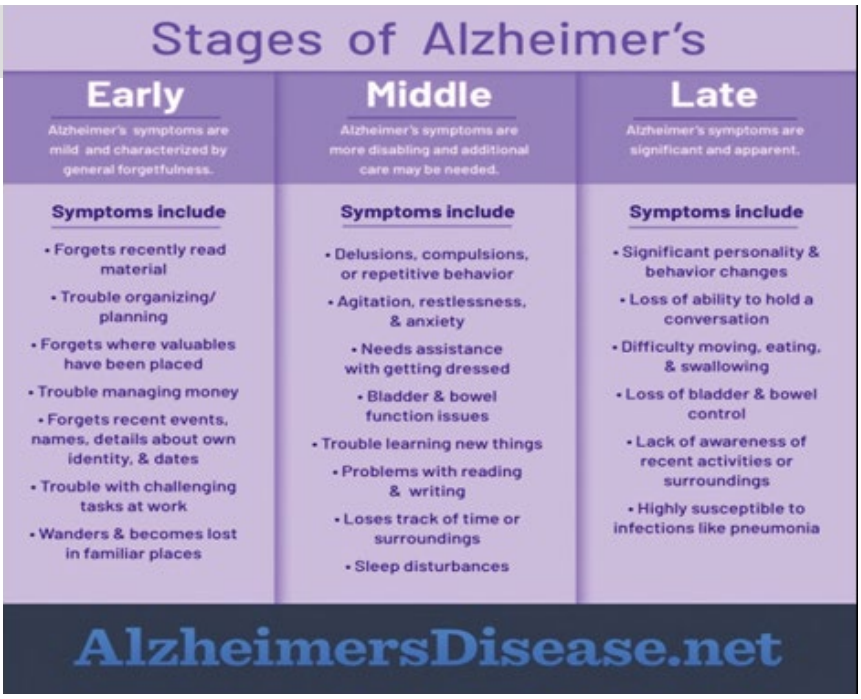

Fig. 3. Stages of Alzheimer's disease.

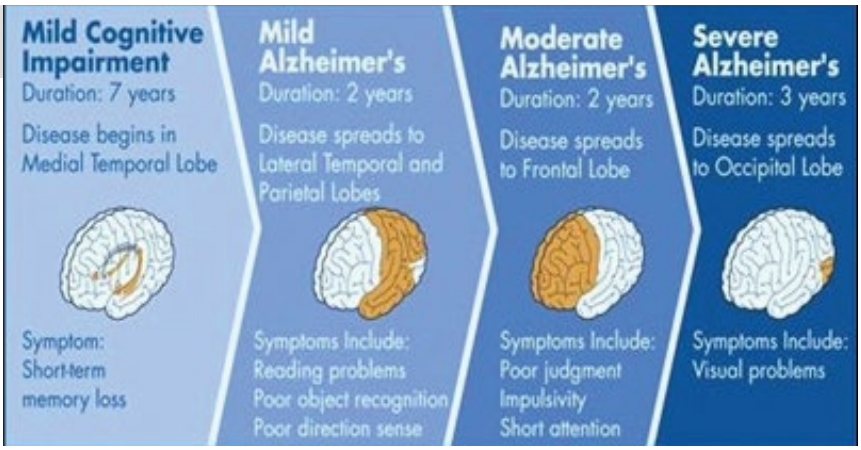

Fig. 4. Symptoms of different stages of Alzheimer's disease.

- Being forgetful of events or personal history.
- Feeling moody or withdrawn, especially in socially or mentally challenging situations.
- Being unable to recall information about themselves like their address or telephone number, and the high school or college they attended.
- Experiencing confusion about where they are or what day it is.
- Requiring help choosing proper clothing for the season or the occasion.
- Having trouble controlling their bladder and bowels.
- Experiencing changes in sleep patterns, such as sleeping during the day and becoming restless at night.
- Showing an increased tendency to wander and become lost.
- Demonstrating personality and behavioral changes, including suspiciousness and delusions or compulsive, repetitive behavior like hand-wringing or tissue shredding.

In the middle stage, the person living with Alzheimer's can still participate in daily activities with assistance. It's important to find out what the person can still do or find ways to simplify tasks. As the need for more intensive care increases, caregivers may want to consider respite care or an adult day center so they can have a temporary break from care giving. While the person living with Alzheimer's continues to receive care in a safe environment.

Stage 3: Late-stage Alzheimer's (severe)

In the final stage of the disease, dementia symptoms are severe. Individuals lose the ability to respond to their environment, to carry on a conversation and, eventually, to control movement. They may still say words or phrases, but communicating pain becomes difficult. As memory and cognitive skills continue to worsen, significant personality changes may take place and individuals need extensive care.

At this stage, individuals may:

- Require around-the-clock assistance with daily personal care.

- Lose awareness of recent experiences as well as of their surroundings.
- Experience changes in physical abilities, including walking, sitting and, eventually, swallowing
- Have difficulty communicating.
- Become vulnerable to infections, especially pneumonia.
- The person living with Alzheimer's may not be able to initiate engagement as much during the late stage, but he or she can still benefit from interaction in ways that are appropriate, like listening to relaxing music or receiving reassurance through gentle touch. During this stage, caregivers may want to use support services, such as hospice care, which focus on providing comfort and dignity at the end of life. Hospice can be of great benefit to people in the final stages of Alzheimer's and other dementias and their families [14].

PATHOPHYSIOLOGY OF ALZHEIMER'S DISEASE

The two pathologic hallmarks of Alzheimer disease are:

- Extracellular beta-amyloid deposits (in senile plaques)
- Intracellular neurofibrillary tangles (paired helical filaments)

The beta-amyloid deposition and neurofibrillary tangles lead to loss of synapses and neurons, which results in gross atrophy of the affected areas of the brain, typically starting at the mesial temporal lobe. The mechanism by which beta-amyloid peptide and neurofibrillary tangles cause such damage is incompletely understood. There are several theories. The amyloid hypothesis posits that progressive accumulation of beta-amyloid in the brain triggers a complex cascade of events ending in neuronal cell death, loss of neuronal synapses, and progressive neurotransmitter deficits; all of these effects contribute to the clinical symptoms of dementia. A sustained immune response and inflammation have been observed in the brain of patients with Alzheimer disease. Some experts have proposed that inflammation is the third core pathologic feature of Alzheimer disease (Fig. 5.).

Prion mechanisms have been identified in Alzheimer disease. In prion diseases, a normal cell-surface brain protein called prion protein becomes misfolded into a pathogenic form termed a prion. The prion then causes other prion proteins to misfold similarly, resulting in a marked increase in the abnormal proteins, which leads to brain damage. In Alzheimer disease, it is thought that the beta-amyloid in cerebral amyloid deposits and tau in neurofibrillary tangles have prion-like, self-replicating properties [15].

NEUROANATOMY OF ALZHEIMER'S DISEASE

It is proposed that Alzheimer's disease is initiated by entry of some environmental factor into the brain via the olfactory pathway and that this factor spreads through the brain from neuron to neuron along identified axonal connections. The proposed agent may be a virus or virus-like particle [16]. The objective of this study was to identify the regions of decreased grey matter (GM) volume which were associated with specific neuropsychiatric behaviours in patients with mild Alzheimer's disease. Voxel-based

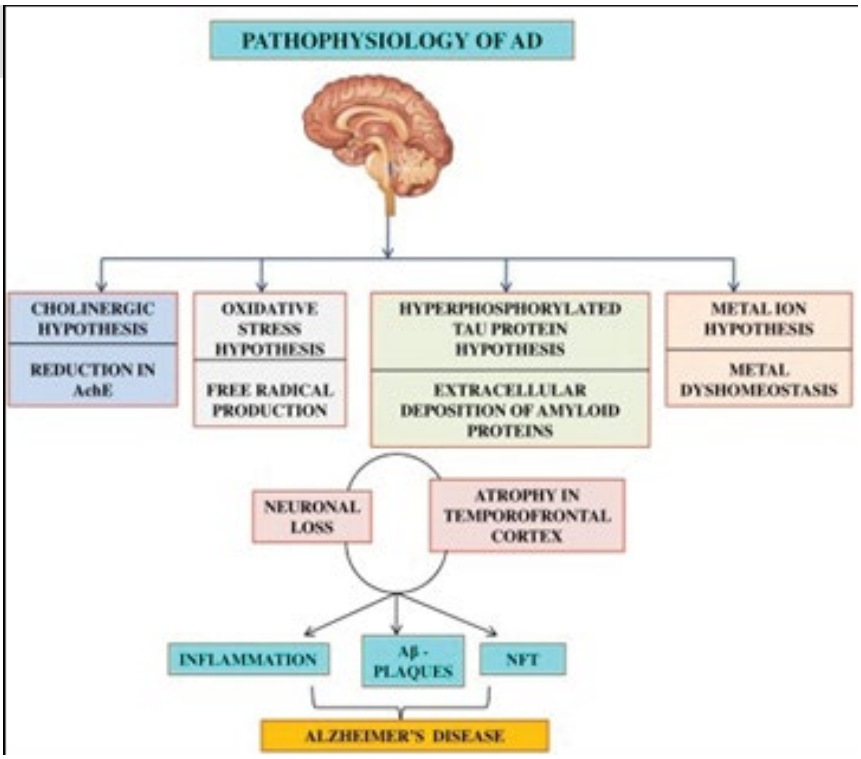

Fig. 5. Pathophysiology of Alzheimer's disease.

morphometry was used to correlate GM derived from T1-weighted MRI images of 31 patients with mild Alzheimer's disease and specific neuropsychiatric symptoms and behaviours measured by the Neuropsychiatric Inventory. Delusions were associated with decreased GM density in the left frontal lobe, in the right front parietal cortex and in the left claustrum. Apathy was associated with GM density loss in the anterior cingulate and frontal cortex bilaterally, the head of the left caudate nucleus and in bilateral putamen. Agitation was associated with decreased GM values in the left insula and in anterior cingulate cortex bilaterally [17].

By controlling for confounds of varying task difficulty and subsequent performance, remarkably similar brain activations were identified during successful paired associate learning in patients with Alzheimer's disease and in healthy comparison subjects. The study methods provide a useful model for further applications of functional imaging involving cognitive activation paradigms in the study of neuropsychiatric disorders [18].

Is Alzheimer's genetics

Family history is not necessary for an individual to develop Alzheimer's. However, research shows that those who have a parent or sibling with Alzheimer's are more likely to develop the disease than those who do not have a first-degree relative with Alzheimer's. Those who have more than one first-degree relative with Alzheimer's are at an even higher risk. When diseases like Alzheimer's and other dementias tend to run in families, either genetics (hereditary factors), environmental factors or both may play a role [14].

Genetics and Alzheimer's

There are two categories of genes that influence whether a person develops a disease: (1) risk genes and (2) deterministic genes. Researchers have identified hereditary Alzheimer's genes in both categories (Fig. 6.).

1. Risk genes increase the likelihood of developing a disease but do not guarantee it will happen. Researchers have found several genes that increase the risk of Alzheimer's. APOE-e4 is the first risk gene identified and remains the gene with strongest impact on risk. Researchers estimate that between 40-65% of people diagnosed with Alzheimer's have the APOE-e4 genes.

APOE-e4 is one of three common forms of the APOE gene; the others are APOE-e2 and APOE-e3. We all inherit a copy of some form of APOE from each parent. Those who inherit one copy of APOE-e4 from their mother or father have an increased risk of developing Alzheimer's. Those who inherit two copies from their mother and father have an even higher risk, but not a certainty. In addition to raising risk, APOE-e4 may tend to make symptoms appear at a younger age than usual.

An estimated 20-30% of individuals in the United States have one or two copies of APOE-e4; approximately 2% of the U.S. population has two copies of APOE-e4.

2. Deterministic genes directly cause a disease, guaranteeing that anyone who inherits one will develop a disorder. Scientists have found rare genes that cause Alzheimer's in only a few hundred extended families worldwide. These genes, which are estimated to account for 1% or less of Alzheimer's cases, cause familial early-onset forms in which symptoms usually develop between a person's early 40s and mid-50s. The vast majority of individuals with Alzheimer's have late-onset disease, occurring at age 65 or later [14]. 23 Chromosome Pairs; 4 Alzheimer's Genes Identified: APP PS-1 PS-2 APOE4. Amyloid precursor protein (APP),discovered in 1987, is the first gene with mutations found to cause an inherited form of Alzheimer's [14].

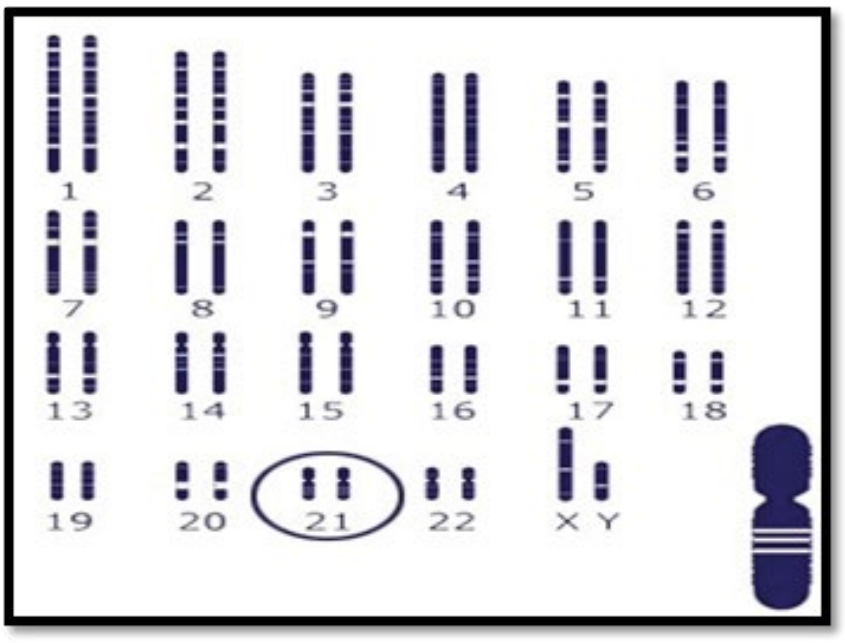

Fig. 6. Genetics of Alzheimer's disease.

3. Genes that increase the risk of developing Alzheimer's disease

The diagram below shows a number of genes associated with Alzheimer's disease according to how common they are. Mutations in the APP, PSEN-1 and PSEN-2 genes are rare, but having a mutation gives a very high risk (or even certainty) of developing Alzheimer's disease, so these genes are shown in the top left of the diagram.

Most people who develop Alzheimer's don't have familial Alzheimer's disease, the particular reason that they develop the disease isn't clear. It's most likely to be due to a combination of factors such as age, environment, lifestyle and genetic risk factors. In these cases, the disease is known as 'sporadic' – there isn't one clear cause.

Some of the 'risk factor' genes are shown in the diagram above. Having one of these genes means you're more likely to develop Alzheimer's disease than someone who doesn't have the gene, but it doesn't mean you'll definitely develop Alzheimer's. These genes increase your risk slightly, but some people with the genes don't get the disease, and vice versa. There are a number of genes that are very common – lots of people have the form of the gene that increases the risk of developing Alzheimer's disease, but they don't have a strong effect. These are shown in the bottom right of the diagram (e.g. CR1, BIN1, and ABCA7). TREM2 on the other hand is fairly rare, but has a greater effect than those more common genes [19,20].

EARLY-ONSET ALZHEIMER'S DISEASE

What is early-onset Alzheimer disease

Alzheimer disease is the most common form of dementia. It affects your memory, thinking, and behavior. It often progresses to the point where it affects daily activities and functions [21-35].

Alzheimer disease most commonly affects older adults, but it can also affect people in their 30s or 40s. When Alzheimer disease occurs in someone under age 65, it is known as early-onset (or younger-onset) Alzheimer disease. A very small number of people with Alzheimer disease have the early-onset form. Many of them are in their 40s and 50s when the disease takes hold.

Most types of early-onset Alzheimer disease are the same, but there are a few small distinctions:

- Common Alzheimer disease. Most people with early-onset Alzheimer disease have the common form of the disease. The disease progresses in roughly the same way as it does in older people.
- Genetic (familial) Alzheimer disease. This form is very rare. A few hundred people have genes that directly contribute to Alzheimer disease. These people start showing symptoms of the disease in their 30s, 40s, or 50s.

Who'd gets early onset AD

Although AD isn't an expected part of advancing age, you're at increased risk as you get older. More than 32 percent of people over age 85 have AD. You may also have an increased risk of developing AD if a parent, sibling, or child has the disease. If more than one family member has AD, your risk increases.

A 2016 study Trusted Source showed that African Americans, Native Americans, and Native Alaskans are at higher risk for developing early onset AD compared to white people.

What causes early onset AD

The exact cause of early onset AD hasn't been fully determined. Many researchers believe that this disease develops as the result of multiple factors rather than one specific cause.

Researchers have discovered rare genes that may directly cause or contribute to AD. These "deterministic genes" are:

- Amyloid precursor protein (APP) on chromosome 21
- Presenilin-1 (PS1) on chromosome 14
- Presenilin-2 (PS2) on chromosome 1

These genes may be carried from one generation to the next within a family. Carrying these genes can result in adults younger than age 65 developing symptoms much earlier than expected.

How is early onset AD diagnosed

Talk with a doctor if you or a loved one is finding it increasingly difficult to perform day-to-day tasks, or if you or a loved one is experiencing increased memory loss. They may refer you to a doctor who specializes in AD.

Especially in the case of early onset AD, symptoms may seem to be related to other causes, like stress. There's no one test to diagnose AD. Your doctor may use many different tools to arrive at a diagnosis. These include:

- Medical exam
- Neurological exam
- Cognitive tests
- Talking with family members about changes they've observed
- Reviewing medical and family history
- Blood tests
- Brain imaging, such as magnetic resonance imaging (MRI), positron emission tomography (PET) scans, or computed tomography (CT) scan.
- Recent research has focused on blood tests that can identify proteins associated with AD in the blood. While these show promise, more research is needed.

TREATMENT

The goals of treatment are to achieve improvement

in cognition and to minimize behavioral disturbances (depression, psychosis, agitation, and insomnia).

How to choose a treatment

Your doctor will help you choose the best treatment based on a few things about you, including:

- Your age, overall health, and medical history
- How severe your disease is
- How well a medicine or therapy will work for you and your lifestyle
- Your preferences or those of your family or caregivers [36]

Psychosocial treatment

Environmental manipulation, family support, and prevention of other medical co-morbidities can improve functioning of AD patients. In attempting to maintain patients with AD in their homes for as long as possible, some adjustment of a patient's environment is important. Written daily reminders can be helpful in the performance of daily activities. Prominent clocks, calendars, and windows are important. Patient activities should have minimal changes. Maintaining adequate hydration, nutrition, exercise and cleanliness, is important. Family support is essential, since members are at risk for depression, anxiety syndromes, and insomnia.

Pharmacotherapy

Alzheimer's disease is complex, and it is therefore unlikely that any one drug or other intervention will ever successfully treat it in all people living with the disease. Still, in recent years, scientists have made tremendous progress in better understanding Alzheimer's and in developing and testing new treatments, including several medications that are in late-stage clinical trials.

Several prescription drugs are already approved by the U.S. Food and Drug Administration (FDA) to help manage symptoms in people with Alzheimer's disease. And, on June 7, 2021, FDA provided accelerated approval for the newest medication, aducanumab, which helps to reduce amyloid deposits in the brain and may help slow the progression of Alzheimer's, although it has not yet been shown to affect clinical symptoms or outcomes, such as progression of cognitive decline or dementia.

Most medicines work Alzheimer's. However, it is important to understand that none of the medications available at this time will cure Alzheimer's (Tab. 1.).

Medicines to be used with caution in people with Alzheimer's disease

There are some medicines, such as sleep aids, anti-anxiety drugs, anti-convulsants, and antipsychotics, that a person with Alzheimer's disease should take only:

After the doctor has explained all the risks and side effects of the medicine

After other, safer nonmedication options have not helped treat the problem

People living with Alzheimer's and their caregivers must watch closely for side effects from these medications [37-40].

Sleep aids: are used to help people get to sleep and stay asleep. People with Alzheimer's should not use these drugs regularly because they make the person more confused and

Tab. 1. Drug name, type and use, how they work and common side effects.

Drug Name	Drug Type and Use	How it Works	Common Side Effects
Aducanumab (Approved on June 2021)	Disease-'modifying immunotherapy prescribed to treat mild cognitive impairment or mild Alzheimer's	Removes abnormal beta-amyloid to help reduce the number of plaques in the brain	Amyloid-related imaging abnormalities (ARIA), which can lead to fluid buildup or bleeding in the brain; also headache, dizziness, falls, diarrhea, confusion
Donepezil	Cholinesterase inhibitor prescribed to treat symptoms of mild, moderate, and severe Alzheimer's	Prevents the breakdown of acetylcholine in the brain	Nausea, vomiting, diarrhea, muscle cramps, fatigue, weight loss
Rivastigmine	Cholinesterase inhibitor prescribed to treat symptoms of mild, moderate, and severe Alzheimer's	Prevents the breakdown of acetylcholine and butyrylcholine (a brain chemical similar to acetylcholine) in the brain	Nausea, vomiting, diarrhea, weight loss, indigestion, muscle weakness
Memantine	N-methyl D-aspartate (NMDA) antagonist prescribed to treat symptoms of moderate to severe Alzheimer's	Blocks the toxic effects associated with excess glutamate and regulates glutamate activation	Dizziness, headache, diarrhea, constipation, confusion
Galantamine	Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate Alzheimer's	Prevents the breakdown of acetylcholine and stimulates nicotinic receptors to release more acetylcholine in the brain	Nausea, vomiting, diarrhea, decreased appetite, dizziness, headache

more likely to fall. There are lifestyle changes people can make to improve their sleep. Learn more about getting a good night's sleep.

Anti-anxiety drugs: are used to treat agitation. These drugs can cause sleepiness, dizziness, falls, and confusion. For this reason, doctors recommend they should only be used for short periods of time.

Anti-convulsants: are drugs sometimes used to treat severe aggression. Side effects may cause sleepiness, dizziness, mood swings, and confusion.

Antipsychotics: are drugs used to treat paranoia, hallucinations, agitation, and aggression. Side effects of using these drugs can be serious, including increased risk of death in some older people with dementia. They should only be given to people with Alzheimer's when the doctor agrees that the symptoms are severe.

The future of Alzheimer's disease treatments

Alzheimer's disease research has developed to a point where scientists are exploring a variety of avenues to not only treat symptoms but also address underlying disease processes. In ongoing clinical trials, scientists are developing and testing several possible interventions, including immunization therapy, drug therapies, cognitive training, physical activity, and treatments for cardiovascular disease and diabetes [37-40].

Blueberries could be used to fight Alzheimer's, researchers suggest

Our new findings corroborate those of previous animal studies and preliminary human studies, adding further support to the notion that blueberries can have a real benefit in improving memory and cognitive function in some older adults," Krikorian states [41].

The deep blue coloring of blueberries is due to compounds called anthocyanins, which are also found in other fruits and vegetables with similar colors, such as cranberries, red cabbage and eggplants.

Previous research has attributed protection against cardiovascular diseases, neurodegenerative diseases and some forms of cancer to anthocyanins. It is these anthocyanins, as well as high levels of antioxidants in the berries, that the researchers suggest are behind the beneficial effects they believe their studies illustrate.

According to the Alzheimer's Association, in 2015, an estimated 5.3 million Americans had Alzheimer's disease, a neurological disorder in which the death of brain cells causes memory loss and cognitive decline. Of these people, it is estimated that 5.1 million were aged 65 and older.

As the proportion of the US population aged 65 and older increases, the number of people with Alzheimer's disease is expected to increase. The Alzheimer's Association predicts that by 2025, the number of people in this age group with the disease will increase by 40%, to 7.1 million people.

CONCLUSION

AD is the most common of many causes of dementia, and its prevalence is increasing worldwide. Disease pathology starts years before noticeable symptoms. Neuropsychological, imaging, and spinal fluid tests can establish the diagnosis with high accuracy. Although there are currently no treatments that slow the disease process, management of the cognitive and behavioral symptoms of AD dementia can significantly improve the lives of patients and their caregivers. AD pathology consists of -amyloid plaques and phospho-tau neurofibrillary tangles.

AAD pathology can be present in asymptomatic, mildly affected (MCI), or demented individuals. Although advanced age and genetics are the predominant risk factors, several preventable risk factors also contribute to the likelihood of developing AD dementia. There is no perfect diagnostic test for AD, but neuropsychological testing, neuroimaging, and CSF analysis can substantially increase diagnostic accuracy.

There is no cure for AD. Ideal AD management includes a combination of symptomatic treatment for cognitive issues, detection and judicious control of behavioral issues, and caregiver support.

REFERENCES

1. **Knopman DS, Amieva H, Petersen RC, et al.** Alzheimer disease. *Nat Rev Dis Primers*. 2021;7(1):33.
2. Dementia Fact sheet. World Health Organization. 2020.
3. **Querfurth HW, LaFerla FM.** Alzheimer's disease. *N Engl J Med*. 2010;362(4):329-344. \
4. **Simon RP, Greenberg DA, Aminoff MJ.** Clinical neurology (10th Ed.). [New York]: McGraw Hill. 2018;pp:111.
5. **Burns A, Iliffe S.** Alzheimer's disease. *BMJ*. 2009;338:b158.
6. **Todd S, Barr S, Roberts M, et al.** Survival in dementia and predictors of mortality: a review. *Int J Geriatr Psychiatry*. 2013;28(11):1109-1124.
7. Textbook of physiology volume 2 by AK JAIN (Avichal publishing company) (4th Edn).
8. World Health Organization. Dementia – key facts. 2019.
9. Alzheimer's Association. Alzheimer's disease facts and figures. *Alzheimers Dement*. 2019;15(3):321-387.
10. **Reitz C, Mayeux R.** Alzheimer disease: epidemiology, diagnostic criteria, risk factors and biomarkers. *Biochem Pharmacol*. 2014;88(4):640-651.
11. **Kinney W, Bemiller SM, Murtishaw AS, et al.** Inflammation as a central mechanism in Alzheimer's disease. *Alzheimers Dement*. 2018;4:575-590.
12. De Gruyter the neuroanatomy of Alzheimer's disease RCA persons, TPD Powell Reviews in the neuros. 1989;2(2):101-122.
13. **Bruen PD, McGeown WJ, Shanks MF, et al.** Neuroanatomical correlates of neuropsychiatric symptoms in Alzheimer's disease. *Brain*. 2008;131(9):2455-2463.
14. **Gould RL, Brown RG, Owen AM, et al.** Functional neuroanatomy of successful paired associate learning in Alzheimer's disease. *Am J Psychiatry*. 2005;162(11):2049-2060.
15. **Guerreiro R , Wojtas A, Bras J, et al.** TREM2 variants in Alzheimer's disease. N Engl J Med. 2013;368(2):117-127.
16. Image supplied by Alzheimer's Research UK in the article "Global research team discovers new Alzheimer's risk gene. 10 early signs and symptoms of Alzheimer's. (n.d.).
17. Alzheimer's disease facts and figures. 2019.
18. Alzheimer's disease and related dementia. 2020.
19. **Chen HY, Panegyres PK.** The role of ethnicity in Alzheimer's disease: Findings from the C-Path Online Data Repository. *J Alzheimers Dis*. 2016; 51(2):515-523.
20. **Heymann D, Stern Y, Cosentino S, et al.** The association between alcohol use and the progression of Alzheimer's disease. *Curr Alzheimer Res*. 2016;13(12):1356-1362.
21. If you have younger-onset Alzheimer's disease. (n.d.).
22. **Kumar A, Sidhu J, Goyal A, et al.** Alzheimer disease. *StatPearls*. 2021.
23. **Mendez MF.** Early-onset Alzheimer's disease. *Neurol Clin*. 2017;35(2):263-281.
24. **Reynolds S.** Blood tests show promise for early Alzheimer's diagnosis. *Nat Institute Aging*. 2020.
25. **Weller J.** Current understanding of Alzheimer's disease diagnosis and treatment. *F1000Res*. 2018;7:1161.
26. **Alzheimer A, Stelzmann RA, Schnitzlein HN, et al.** An English translation of Alzheimer's 1907 paper, "Über eine eigenartige Erkankung der Hirnrinde." *Clin Anat*. 1995;8(6):429-431.
27. **Alzheimer's Association, Thies W, Bleiler L.** 2011 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2011;7:208-244.
28. **Barnes DE, Yaffe K.** The projected effect of risk factor reduction on Alzheimer's disease prevalence. *Lancet Neurol*. 2011;10(9):819-828.
29. **Ballard C, Gauthier S, Corbett A, et al.** Alzheimer's disease. *Lancet*. 2011;377(9770):1019-1031.
30. **Castillo-Carranza DL, Guerrero-Muñoz MJ, Kayed R.** Immunotherapy for the treatment of Alzheimer's disease: Amyloid-□ or tau, which is the right target? *Immunotargets Ther*. 2014;3:19-28.
31. **Meeks TW, Ropacki SA, Jeste DV.** The neurobiology of neuropsychiatric syndromes in dementia. *Curr Opin Psychiatry*. 2006;19(6):581-586.
32. **Dubois B, Feldman HH, Jacova C, et al.** Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS-ADRDA criteria. *Lancet Neurol*. 2007;6(8):734-746.
33. **Savva GM, Zaccai J, Matthews FE, et al.** Prevalence, correlates and course of behavioural and psychological symptoms of dementia in the population. *Br J Psychiatry*. 2009;194(3):212-219.
34. **Ballard CG, Gauthier S, Cummings JL, et al.** Management of agitation and aggression associated with Alzheimer disease. *Nat Rev Neurol*. 2009;5(5):245-255.
35. **McKhann G, Drachman D, Folstein M, et al.** Clinical diagnosis Of Alzheimer's disease: Report of the Nincds-Adrda work group under the auspices of the Department of Health And Human Services task force on Alzheimer's disease. *Neurology*. 984;34(7):939-944.
36. **Harvey RJ, Skelton-Robinson M, MN.** The prevalence and causes of dementia in people under the age of 65 years. *J Neurol Neurosurg Psychiatr*. 2003;74(9):1206-1209.
37. American Geriatrics Society 2012 Beers Criteria Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2012;60(4):616-631.
38. **Knopman DS, DeKosky ST, Cummings JL, et al.** Practice parameter: diagnosis of dementia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001;56(9):1143-1153.
39. **Doody RS, Stevens JC, Beck C, et al**. Practice parameter: Management of dementia (an evidence based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001;56(9):1154-1166.
40. **Ballard C, Waite J.** The effectiveness of atypical antipsychotics for the treatment of aggression and psychosis in Alzheimer's disease. *Cochrane Database Syst Rev*. 2006;1:CD003476.
41. **Rochon PA, Normand SL, Gomes T, et al.** Antipsychotic therapy and short-term serious events in older adults with dementia. *Arch Intern Med*. 2008;168(10):1090-1096.