



A Comprehensive Review On Alzheimer's Disease: Etiology, Pathogenesis And Current Therapeutic Approaches

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ABSTRACT

Alzheimer's disease (AD) is a long-lasting condition that slowly breaks down the brain's nerve cells, known as neurons, particularly in the cerebral cortex. This leads to problems with memory, thinking, language skills, and changes in behavior. It is the most common type of dementia and typically affects people who are 65 years old or older. Alzheimer's often starts in late middle age and is marked by a gradual decline in memory and mental abilities due to damage in the brain. The condition involves a loss of cognitive function over 10 to 15 years, along with unusual tissue growths and protein clumps in the cerebral cortex. In Alzheimer's, nerve cells in the brain die off, which makes it hard for brain signals to travel correctly. At first, it might be tough to recognize Alzheimer's symptoms. A person with this disease struggles with memory, judgment, and thinking, making daily activities challenging. The loss of nerve cells happens slowly over several years.

Keywords:-cerebral cortex, cognitive.

INTRODUCTION

Alzheimer's disease is the leading cause of dementia, which is a brain disorder that gets worse over time. It affects memory, thinking, and behavior, making it hard for people to do everyday activities. This condition happens because brain cells and connections gradually break down due to issues like the buildup of amyloid plaques and tangles in the brain. Although it isn't just a normal part of getting older, Alzheimer's is a complicated disease influenced by genes, the environment, and lifestyle choices. As symptoms get worse over time, people often become very dependent on others for help.

EPIDEMIOLOGY

Alzheimer's disease is the top cause of dementia, making up 50-70% of all cases. Experts predict that the number of people with Alzheimer's will double every 20 years. This rise is mainly due to more people living longer and the growing number of older adults. The disease mainly impacts elderly individuals, and its occurrence is expected to rise significantly in the coming decades.

TYPES OF ALZHEIMER'S DISEASE: Based on when it starts and what causes it:

1. Early-Onset Alzheimer's: Symptoms show up when a person is between 30 and 65 years old. This uncommon type usually happens because of inherited genetic changes, which is why it's also called Familial Alzheimer's Disease.
2. Late-Onset Alzheimer's: This is the most frequent form of the disease, usually starting after age 65. It often results from a combination of genetic factors and environmental influences.

STAGES OF ALZHEIMER'S DISEASE

Alzheimer's disease is generally divided into three stages:-

- 1.Mild(Early)
- 2.Moderate(Middle)
- 3.Severe(Late)

SYMPTOMS

The early signs of Alzheimer's disease are:

- Poor decision-making
- Asking the same questions over and over
- Struggling to think clearly
- Misplacing things
- Forgetting names, places, or past events.

In the middle stage, symptoms may include:

- Repetitive and obsessive behaviors
- Greater confusion and disorientation
- Sleep disturbances
- Trouble speaking
- Delusions (holding beliefs that aren't based on reality)
- Changes in mood.

In the later stage, which is also known as the final phase of Alzheimer's disease, symptoms can include:

- Difficulty swallowing (dysphagia)
- Trouble moving around without help
- Weight loss
- Unintentional passing of urine (urinary incontinence).

CAUSES & RISK FACTORS:

(A) Age and Genetics: - Older Age: Getting older is the biggest risk factor for Alzheimer's disease, but it's not just a normal part of getting older. - Genetic Factors: Some genes that are passed down can increase the risk. One key gene called APOE (apolipoprotein E) is a major risk factor. While it's rare, certain family genes can guarantee the disease if they are inherited.

(B) Medical and Health Conditions: - Cardiovascular Issues: Having high blood pressure in middle age, high cholesterol, and poorly controlled type 2 diabetes are important risk factors.

Having a history of serious head injuries or brain trauma raises the risk.

Hearing Loss: Not addressing hearing loss has been recognized as a risk factor.

(C) Lifestyle and Environmental Factors

Physical Inactivity: Not getting enough exercise increases the chances of developing Alzheimer's.

Obesity: Being overweight, especially during middle age, is a known risk factor.

Smoking: Smoking cigarettes and being around secondhand smoke raise the risk.

Alcohol Misuse: Drinking too much alcohol is linked to a higher chance of dementia.

Poor Diet: Eating unhealthy foods can add to the risk.

Air Pollution: New research suggests that being exposed to air pollution might increase the risk of dementia.

(D) Mental and Social Well-being

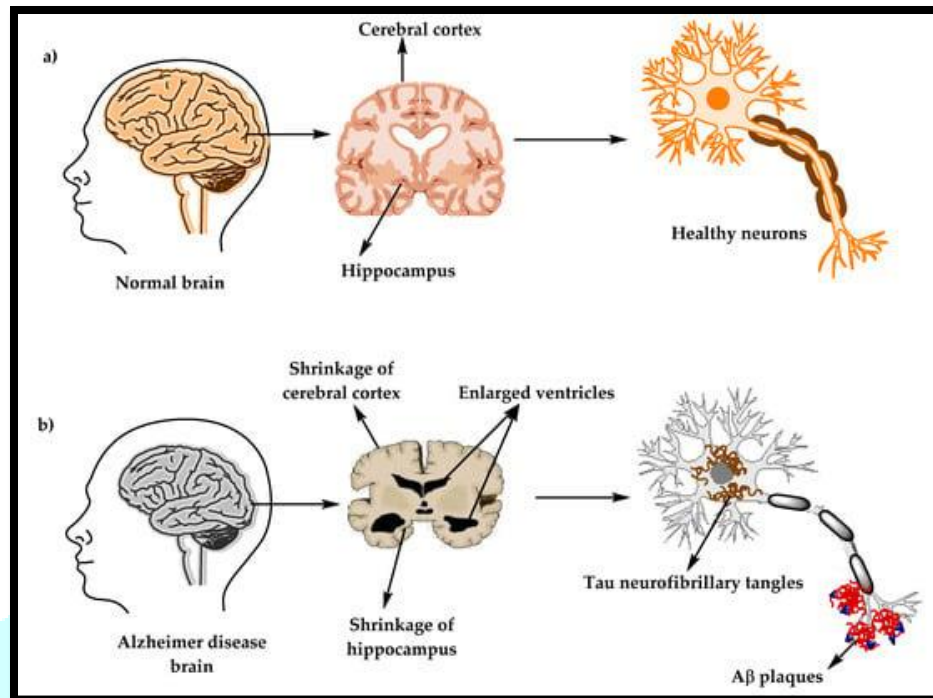
Lack of Mental Stimulation: Living without enough mental challenges can raise your risk.

Sleep Deprivation: Not getting enough good-quality sleep over time allows harmful proteins to build up in the brain, leading to cognitive decline.

Social Isolation: Having little social interaction is connected to a higher rate of Alzheimer's.

Depression and Stress: Ongoing stress and depression are recognized as risk factors.

Low Education: Having less formal education is linked to a greater risk.



PATHOPHYSIOLOGY OF DISEASE:

The pathophysiology of Alzheimer's disease (AD) mainly involves the build-up of amyloid-beta ($A\beta$) plaques, which are deposits outside the cells, and neurofibrillary tangles (NFTs), which are clumps of tau protein found inside neurons. These issues disturb how neurons work, leading to their malfunction and death. This causes a drop in cholinergic neurotransmission, increases oxidative stress, and triggers neuroinflammation, ultimately leading to memory loss and dementia.

Amyloid Plaques: These plaques are made up of amyloid-beta ($A\beta$) peptides that form outside of cells. $A\beta$ comes from the faulty breakdown of the amyloid precursor protein (APP) through a process called the amyloidogenic pathway, which involves special enzymes known as beta- and gamma-secretases. $A\beta$ groups together into oligomers and eventually forms larger senile plaques that can harm nearby neurons and increase oxidative stress.

Neurofibrillary Tangles: These tangles are made of hyperphosphorylated tau protein found inside neurons. Normally, tau helps keep microtubules stable, which are important for moving materials within cells. However, in AD, hyperphosphorylated tau comes loose from these microtubules, causing them to malfunction. This leads to problems with transport inside the cell and can result in neuron death.

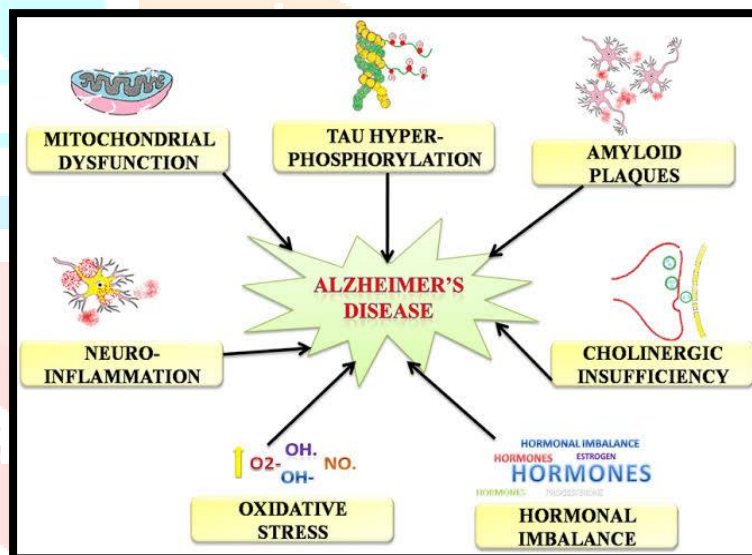
NEUROBIOLOGICAL PROCESS:

Cholinergic Deficit: A key characteristic of Alzheimer's Disease (AD) is a shortage in the cholinergic system, marked by lower levels of choline acetyltransferase (ChAT) and other cholinergic indicators. This shortage is related to the loss of cholinergic neurons, which are essential for memory and learning.

Neuroinflammation: The brain experiences inflammation due to amyloid plaques and tau tangles. This process involves glial cells that increase oxidative stress and make neurons more vulnerable.

Oxidative Stress: In AD, there are higher levels of oxidative stress, which harms neurons and adds to the overall disease progression.

Mitochondrial Dysfunction: Changes in mitochondria are linked to the development of AD, further leading to problems in cell function.



DIAGNOSIS:

A key part of diagnosing Alzheimer's disease is being able to describe your symptoms clearly. It can be helpful to ask a close family member or friend for their views on your symptoms and how they affect your everyday life. Tests that assess memory and thinking skills also play a role in diagnosing Alzheimer's disease. In the past, doctors could only confirm Alzheimer's disease after death by examining the brain for plaques and tangles under a microscope. Nowadays, healthcare professionals and researchers can diagnose Alzheimer's during a person's life with greater confidence.

Tests: To diagnose Alzheimer's disease, the following tests are typically performed:

Physical and Neurological Exam: A healthcare provider will conduct a physical and neurological exam. This may include checking: - Reflexes - Muscle tone and strength - Ability to stand up from a chair and walk across the room - Vision and hearing - Coordination - Balance

Lab Test: Blood tests can help rule out other possible causes of memory issues and confusion, such as thyroid problems or low vitamin levels. Newer blood tests can measure levels of beta-amyloid protein and tau protein, but these may not be widely available or covered by insurance.

Mental Status and Neurological Testing : Your healthcare provider might give you a short mental status test to evaluate your memory and other thinking abilities. Longer versions of this test could provide more detailed information about your mental functions, which can then be compared to others who are similar in age and education level.

TREATMENT

(A) MEDICATION TREATMENT:

Medicines : Medications for Alzheimer's can help with memory issues and other changes in thinking. There are two main types of medicines used to manage these symptoms:

Cholinesterase inhibitors : These medications help improve communication between brain cells by increasing levels of a chemical messenger that Alzheimer's disease reduces. Doctors usually prescribe these as the first option, and many patients notice slight improvements in their symptoms. Cholinesterase inhibitors may also help with behavior-related symptoms like restlessness or sadness. Patients can take these medicines either by swallowing them or using a patch on their skin. Commonly prescribed cholinesterase inhibitors include donepezil (Aricept, Adlarity), galantamine, and rivastigmine transdermal patch (Exelon). The main side effects of these medications include diarrhea, nausea, decreased appetite, and sleep problems. For individuals with certain heart issues, serious side effects could involve an irregular heartbeat.

Memantine (Namenda) is a medication that affects a different communication system in brain cells. It helps slow down the worsening of symptoms in people with moderate to severe Alzheimer's disease. Sometimes, doctors use it alongside a cholinesterase inhibitor. Although uncommon, some side effects can include dizziness and confusion.

The Food and Drug Administration (FDA) has also approved other medications to help slow down the decline in thinking and functioning caused by Alzheimer's disease. These drugs work by preventing amyloid plaques from sticking together in the brain. They are mainly prescribed for individuals with mild Alzheimer's disease and mild cognitive impairment linked to Alzheimer's.

Some of these medications are:

-Lecanemab-irmb (Leqembi): This drug is administered through an IV infusion every two weeks. Possible side effects include reactions related to the infusion, such as fever, flu-like symptoms, nausea, vomiting, dizziness, changes in heart rate, and difficulty breathing.

- Donanemab-azbt (Kisunla): This medication is given as an IV infusion every four weeks. Side effects may consist of flu-like symptoms, nausea, vomiting, headaches, trouble breathing, and fluctuations in blood pressure.

(B) NON-PHARMACOLOGICAL TREATMENT:

Creating a Safe and Supportive Environment

A key part of any treatment plan is to meet the needs of someone with Alzheimer's disease. Establishing routines and minimizing tasks that require memory can significantly simplify life. Here are some ways to enhance a person's well-being and ability to function:

- Store keys, wallets, mobile phones, and other valuables in the same spot at home to prevent them from getting lost. - Keep medications in a safe place and use a daily checklist to monitor doses. - Set up automatic payments and deposits for finances. - Have the person with Alzheimer's carry a mobile phone equipped with location tracking features. Save important phone numbers in the device. - Install alarm sensors on doors and windows for added security. - Schedule regular appointments for the same day and time whenever possible. - Use a calendar or whiteboard to keep track of daily activities and encourage checking off completed tasks. - Remove unnecessary furniture, clutter, and throw rugs from living spaces. - Put sturdy handrails on stairs and in bathrooms for safety. - Ensure that shoes and slippers fit well and offer good grip. - Limit the number of mirrors, as reflections can be confusing or frightening for people with Alzheimer's. - Make sure the person carries identification or wears a medical alert bracelet. - Display meaningful photos and objects around the house.

Prevention of Alzheimer's Disease



Healthy Brain



Alzheimer's Disease



There is no proven prevention for Alzheimer's, but maintaining a good, healthy lifestyle decreases the risk of Alzheimer's. Below are some of the necessary measures to be taken to prevent the onset of Alzheimer's disease.

- Maintaining a healthy weight
- Controlling blood pressure and blood sugar levels
- Keeping physically and mentally active
- Avoiding alcohol
- Proper sleep
- Avoiding the usage of tobacco
- Preventing head injuries





CONCLUSION

Alzheimer's disease is a complicated brain disorder that affects many people, their caregivers, and healthcare systems. Even though we have made great progress in understanding how Alzheimer's works, finding treatments that can change the course of the disease is still very difficult. More research is necessary to uncover the basic causes of Alzheimer's and to create new ways to prevent, slow down, or stop its progression. In the end, a complete approach that combines improvements in brain science, medication, and lifestyle changes might be the solution for better outcomes for those impacted by this challenging condition.

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