Alzheimer Disease: A Review

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***Abstract*- Alzheimer's disease (AD) is a progressive neurodegenerative disease. It is characterized by progressive cognitive deterioration together with declining activities of daily living and behavioral changes. It is the most common type of pre-senile and senile dementia. According to the World Health Organization (WHO), 5% of men and 6% of woman of above the age of 60 years are affected with Alzheimer's type dementia worldwide. The clinical manifestation of Alzheimer disease (AD) is dementia that typically begins with subtle and poorly recognized failure of memory and slowly becomes more severe and, eventually, incapacitating.**

***Index terms*- Alzheimer, Management, Diagnosis, treatment, Causes, Facts, Drug therapy**

INTRODUCTION

Alzheimer's disease (AD) is the most common cause of dementia and is clinically characterized by a progression from episodic memory problems to a slow general decline of cognitive function. In 2013, ~44 million of the world-wide population was estimated to be affected by dementia and a steep rise to ~136 million has been predicted by 2050 2. To date, there are no treatments with proven disease-modifying effects and AD remains the largest unmet medical need in neurology. AD pathology presents a complex interplay between several biochemical alterations, including changes in amyloid precursor protein metabolism, phosphorylation of the tau protein, oxidative stress, impaired energetics, mitochondrial dysfunction, inflammation, membrane lipid dysregulation and neurotransmitter pathway disruption. Most of these pathological features can be directly linked to metabolic abnormalities and it is now clear that metabolic dysfunction is an important factor in AD. For example, impaired cerebral glucose uptake occurs decades prior to the onset of cognitive dysfunction and is an invariant feature of AD. The well-documented neurotoxicity associated with Aβ42 is thought to participate in impaired neuronal energetics through initiating a cascade of pathological events; interaction between Aβ42 and mitochondrial enzymes leads to increased release of reactive oxygen species (ROS), affecting glycolysis, the TCA cycle and mitochondrial respiratory-chain activity through the accumulation of deleterious intermediate metabolites in the mitochondria.

ALZHEIMER'S DISEASE

Alzheimer's is a disease that robs people of their memory. At first, people have a hard time remembering recent events, though they might easily recall things that happened years ago.

As time goes on, other symptoms can appear, including:

- Trouble focusing
- A hard time doing ordinary activities
- Feeling confused or frustrated, especially at night
- Dramatic mood swings -- outbursts of anger, anxiety, and depression
- Feeling disoriented and getting lost easily

- Physical problems, such as an odd walk or poor coordination
- Trouble communicating

People with Alzheimer's might forget their loved ones. They might forget how to dress themselves, feed themselves, and use the toilet.

The disease makes brain tissue break down over time. It usually happens to people over age 65.

A person can live with Alzheimer's disease for just a few years or for a few decades. More often, however, people live with it for about 9 years. About 1 in 8 people age 65 and over has the disease. Women are more likely to have it than men.

SYMPTOMS OF ALZHEIMER'S DISEASE

To receive a diagnosis of Alzheimer's, the person must have experienced a decline in cognitive or behavioral function and performance compared with how they were previously. This decline must interfere with their ability to function at work or in usual activities.

The cognitive decline must be seen in at least two of the five symptom areas listed below:

1. Reduced ability to take in and remember new information, which can lead, for example, to:

- repetitive questions or conversations
- misplacing personal belongings
- forgetting events or appointments
- getting lost on a familiar route

2. Impairments to reasoning, complex tasking, and exercising judgment, for example:

- poor understanding of safety risks
- inability to manage finances
- poor decision-making ability
- inability to plan complex or sequential activities

3. Impaired visuospatial abilities that are not, for example, due to eye sight problems. These could be:

- inability to recognize faces or common objects or to find objects in direct view
- inability to use simple tools, for example, to orient clothing to the body

4. Impaired speaking, reading and writing, for example:

- difficulty thinking of common words while speaking, hesitations
- speech, spelling, and writing errors

5. Changes in personality and behavior, for example:

- out-of-character mood changes, including agitation, apathy, social withdrawal or a lack of interest, motivation, or initiative
- loss of empathy
- compulsive, obsessive, or socially unacceptable behavior

If the number and severity of symptoms confirm dementia, the following factors can then confirm Alzheimer's.

- a gradual onset, over months to years, rather than hours or days
- a marked worsening of the individual's normal level of cognition in particular areas

If symptoms begin or worsen over the course of hours or days, you should seek immediate medical attention, as this could indicate an acute illness.

Alzheimer's is most likely when memory loss is a prominent symptom, especially in the area of learning and recalling new information.

Language problems can also be a key early symptom, for example, struggling to find the right words.

If visuospatial deficits are most prominent, these would include:

- inability to recognize objects and faces
- difficulty comprehending separate parts of a scene at once
- difficulty with reading text, known as alexia

The most prominent deficits in executive dysfunction would be to do with reasoning, judgment, and problem-solving.

CAUSES OF ALZHEIMER'S DISEASE

People who get Alzheimer's disease are usually older, but the disease isn't a normal part of aging. Scientists aren't sure why some people get it and others don't. But they do know that the symptoms it causes seem to come from two main types of nerve damage:

- Nerve cells get tangles, called neurofibrillary tangles.
- Protein deposits called beta-amyloid plaques build up in the brain.
- Researchers aren't sure what causes this damage or how it happens, but it could be a protein in blood called ApoE (for apolipoprotein E), which the body uses to move cholesterol in the blood.
- There are a few types of ApoE that may be linked to a higher risk of Alzheimer's. It could be

that certain forms of it cause brain damage. Some scientists think it plays a role in building the plaques in the brains of people with Alzheimer's.

- Whether or not ApoE partly causes Alzheimer's, genes almost certainly play a role in the disease. Someone with a parent who had the disease is more likely to have it, too.
- There is some evidence that people with high blood pressure and high cholesterol have a greater chance of getting Alzheimer's. More rarely, head injuries may be a reason, too -- the more severe they are, the greater the risk of Alzheimer's later in life.
- Scientists are still studying many of these theories, but it's clear that the biggest risks linked to Alzheimer's disease are being older and having Alzheimer's in your family.

ALZHEIMER'S STAGES

The progression of Alzheimer's can be broken down into three main stages:

1. preclinical, before symptoms appear
2. mild cognitive impairment, when symptoms are mild
3. dementia

In addition, the Alzheimer's Association describes seven stages along a continuum of cognitive decline, based on symptom severity.

Alzheimer's is a progressive disease, which means the symptoms will gradually worsen over time. Alzheimer's is broken down into seven stages:

- Stage 1. There are no symptoms at this stage but there might be an early diagnosis based on family history.
- Stage 2. The earliest symptoms appear, such as forgetfulness.
- Stage 3. Mild physical and mental impairments appear, such as reduced memory and concentration. These may only be noticeable by someone very close to the person.
- Stage 4. Alzheimer's is often diagnosed at this stage, but it's still considered mild. Memory loss and the inability to perform everyday tasks is evident.
- Stage 5. Moderate to severe symptoms require help from loved ones or caregivers.
- Stage 6. At this stage, a person with Alzheimer's may need help with basic tasks, such as eating and putting on clothes.
- Stage 7. This is the most severe and final stage of Alzheimer's. There may be a loss of speech and facial expressions.

ALZHEIMER'S FACTS

Although many people have heard of Alzheimer's disease, some aren't sure exactly what it is. Here are some facts about this condition:

- Alzheimer's disease is a chronic ongoing condition.
- Its symptoms come on gradually and the effects on the brain are degenerative, meaning they cause slow decline.
- There's no cure for Alzheimer's but treatment can help slow the progression of the disease and may improve quality of life.
- Anyone can get Alzheimer's disease but certain people are at higher risk for it. This includes people over age 65 and those with a family history of the condition.
- Alzheimer's and dementia isn't the same thing. Alzheimer's disease is a type of dementia.
- There's no single expected outcome for people with Alzheimer's. Some people live a long time with mild cognitive damage, while others experience a more rapid onset of symptoms and quicker disease progression.

Dementia vs. Alzheimer's

The terms "dementia" and "Alzheimer's" are sometimes used interchangeably. However, these two conditions aren't the same. Alzheimer's is a type of dementia.

Dementia is a broader term for conditions with symptoms relating to memory loss such as forgetfulness and confusion. Dementia includes more specific conditions, such as Alzheimer's disease, Parkinson's disease, traumatic brain injury, and others, which can cause these symptoms.

ALZHEIMER'S DISEASE RISK FACTORS

Experts haven't determined a single cause of Alzheimer's disease but they have identified certain risk factors, including:

- Age. Most people who develop Alzheimer's disease are 65 years of age or older.
- Family history. If you have an immediate family member who has developed the condition, you're more likely to get it.
- Genetics. Certain genes have been linked to Alzheimer's disease.

Having one or more of these risk factors doesn't mean that you'll develop Alzheimer's disease. It simply raises your risk level.

ALZHEIMER'S AND GENETICS

While there's no one identifiable cause of Alzheimer's, genetics may play a key role. One gene in particular is of interest to researchers. Apolipoprotein E (APOE) is a gene that's been linked to the onset of Alzheimer's symptoms in older adults.

Blood tests can determine if you have this gene, which increases your risk of developing Alzheimer's. Keep in mind that even if someone has this gene, they may not get Alzheimer's.

The opposite is also true: Someone may still get Alzheimer's even if they don't have the gene. There's no way to tell for sure whether someone will develop Alzheimer's.

DIAGNOSING ALZHEIMER'S DISEASE

The only definitive way to diagnose someone with Alzheimer's disease is to examine their brain tissue after death. But your doctor can use other examinations and tests to assess your mental abilities, diagnose dementia, and rule out other conditions.

They'll likely start by taking a medical history. They may ask about you're:

- symptoms
- family medical history
- other current or past health conditions
- current or past medications
- diet, alcohol intake, or other lifestyle habits

From there, your doctor will likely do several tests to help determine if you have Alzheimer's disease.

ALZHEIMER'S TESTS

There's no definitive test for Alzheimer's disease. However, your doctor will likely do several tests to determine your diagnosis. These can be mental, physical, neurological, and imaging tests.

Your doctor may start with a mental status test. This can help them assess your short-term memory, long-term memory, and orientation to place and time. For example, they may ask you:

- what day it is
- who the president is
- to remember and recall a short list of words

Next, they'll likely conduct a physical exam. For example, they may check your blood pressure, assess your heart rate, and take your temperature. In some cases, they may collect urine or blood samples for testing in a laboratory.

Your doctor may also conduct a neurological exam to rule out other possible diagnoses, such as an acute medical issue, such as infection or stroke. During this exam, they will check your reflexes, muscle tone, and speech.

Your doctor may also order brain-imaging studies. These studies, which will create pictures of your brain, can include:

- Magnetic resonance imaging (MRI). MRIs can help pick up key markers, such as inflammation, bleeding, and structural issues.
- Computed tomography (CT) scan. CT scans take X-ray images which can help your doctor look for abnormal characteristics in your brain.
- Positron emission tomography (PET) scan. PET scan images can help your doctor detect plaque buildup. Plaque is a protein substance related to Alzheimer's symptoms.

ALZHEIMER'S MEDICATION

There's no known cure for Alzheimer's disease. However, your doctor can recommend medications and other treatments to help ease your symptoms and delay the progression of the disease for as long as possible.

For early to moderate Alzheimer's, your doctor may prescribe medications such as donepezil (Aricept) or rivastigmine (Exelon). These drugs can help maintain high levels of acetylcholine in your brain. This is a

type of neurotransmitter that can help aid your memory.

To treat moderate to severe Alzheimer's, your doctor may prescribe donepezil (Aricept) or memantine (Namenda). Memantine can help block the effects of excess glutamate. Glutamate is a brain chemical that's released in higher amounts in Alzheimer's disease and damages brain cells.

Your doctor may also recommend antidepressants, antianxiety medications, or antipsychotics to help treat symptoms related to Alzheimer's. These symptoms include:

- depression
- restlessness
- aggression
- agitation
- hallucinations

OTHER ALZHEIMER'S TREATMENTS

In addition to medication, lifestyle changes may help you manage your condition. For example, your doctor might develop strategies to help you or your loved one:

- focus on tasks
- limit confusion
- avoid confrontation
- get enough rest every day
- stay calm

Some people believe that vitamin E can help prevent decline in mental abilities, but studies indicate that more research is needed. Be sure to ask your doctor before taking vitamin E or any other supplements. It can interfere with some of the medications used to treat Alzheimer's disease.

PREVENTING ALZHEIMER'S

Just as there's no known cure for Alzheimer's, there are no foolproof preventive measures. However, researchers are focusing on overall healthy lifestyle habits as ways of preventing cognitive decline.

The following measures may help:

- Quit smoking.
- Exercise regularly.
- Try cognitive training exercises.
- Eat a plant-based diet.
- Consume more antioxidants.
- Maintain an active social life.

DRUG THERAPY

No disease-modifying drugs are available for Alzheimer's disease, but some options may reduce the symptoms and help improve quality of life.

Cholinesterase inhibitors that are approved for symptomatic relief in the U.S. include:

- Donepezil (Aricept)
- Rivastigmine (Exelon)
- Tacrine (Cognex)

A different kind of drug, memantine (Namenda), an NMDA receptor antagonist, may also be used, alone or in combination with a cholinesterase inhibitor.

CONCLUSION

The use of any measure for the clinical assessment of dementia, whether in people with learning disabilities or in the 'normal' population carries with it limitations. Informed knowledge of these limitations allows use scientific choices which enable us to tailor our neuropsychological battery or adopt alternative measures.

Ultimately, there may be a compromise because of these limitations; however, scientific understanding has given us a better picture of the course of dementia than ever before. With the advancement of technology, such as MRI and fMRI, and PET and SPET scans, used in conjunction with neuropsychological tests administered at key time points including follow-ups, the clinician is better placed to make a more reliable diagnosis and prognosis than in the past. It is hope that this will also enlighten service providers in widening access to people with learning disabilities who also have dementia.

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