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Alzheimer Disease –Etiology, Pathophysiology and Treatment: An Overview

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ABSTRACT

Alzheimer diseases were first described by German physician Dr. Alois Alzheimer in 1906, an Alzheimer disease is also known as neurodegenerative or aging disorder. Presently AD is categorized by psychopharmacological drugs. Alzheimer disease is a type of disorder where neurons are continuously degrade timely and said to be neuronal degenerative disorder. Through this nerve cells are progressively dead i.e. occurrence of nerve disorder. General, symptoms of Alzheimer disease in daily life, and people they unable to recall or remember the things and activities that they have seen in daily routine. Alzheimer disease is associated by loss of synapses and neurons, which result in cognitive deficits.

Key words: Alzheimer's disease, rivastigmine, dementia, etc.

INTRODUCTION

Alzheimer disease is a progressive impairment of membranes and cognitive functions and ultimate decline of memory loss. Alzheimer disease is caused by the development of senile plaques, which is responsible for neuronal destruction and accumulation of Beta Amyloid and synovial tangles formation (fig1) [1]. These tangles are also helping in the destruction of normal neuron. Because these tangles tigers the inflammation in the brain and progressively this inflammation is caused by neuronal atrophy, which is responsible for the death of nerve cell (fig1-2). When sufficient amount nerve cells are died which is converted into neuronal destruction [2, 3]. The formation of these tangles in senile plaque may also destruct neurons. And they also inhibit the neuronal transmission of those particular neurons. Basically, those neurons are called as cholinergic neurons which are affected by Alzheimer disease.

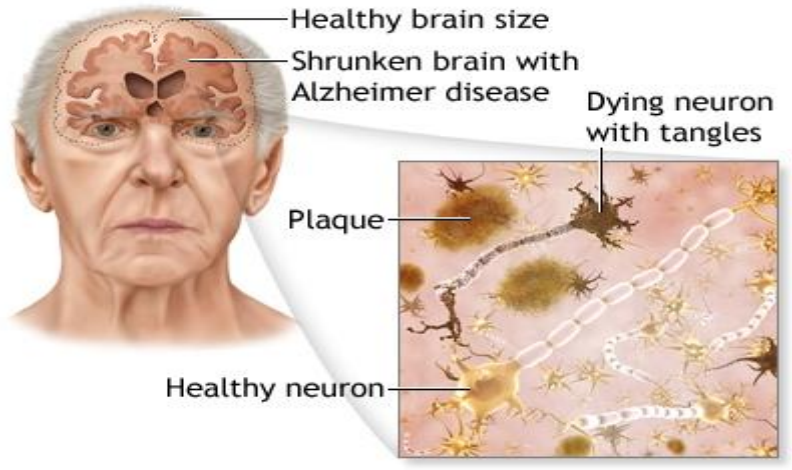

Figure 1: Age changing Alzheimer disease destruction in nervous system and comparison of healthy brain and shrunken brain with Alzheimer disease (1, 2).

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Etiology

Basic etiology of Alzheimer disease (fig.2) is destruction of nerve especially cholinergic nerves. Due, destruction of these cholinergic nerves there is also decrease the level of acetylcholine (3, 4).

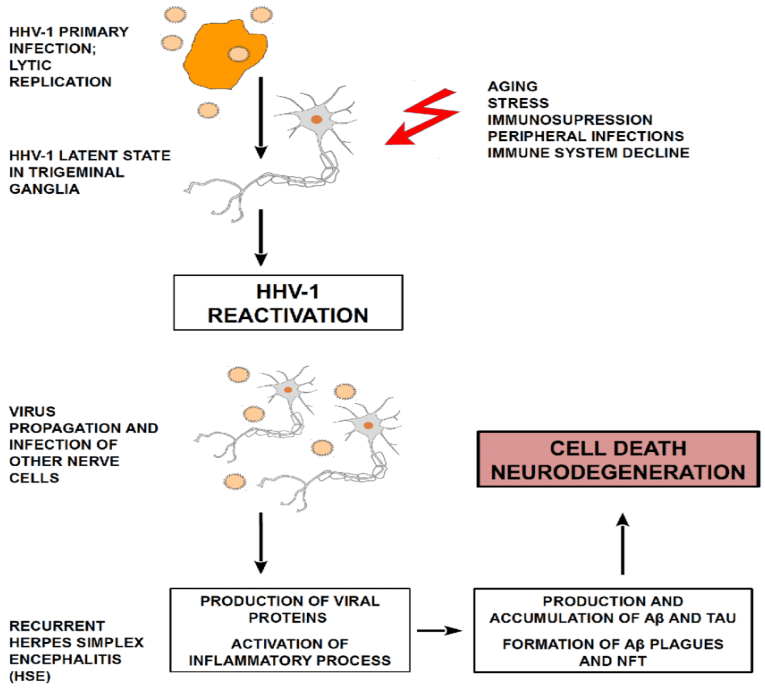

Figure 2: Infectious Etiology of Alzheimer disease (5)

Vascular Etiology: Alzheimer disease patient in addition to carrying regions such as plaque and tangles very frequently harbor sub-vascular region (fig. 3).

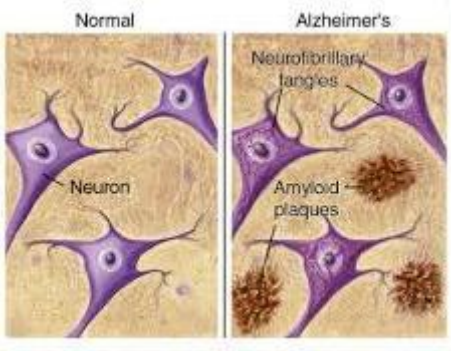

Figure 3: Etiology of Alzheimer disease (a) normal brain (b) region carries plaque and neurofibrillary tangles (1, 2).

Causes

The most seen able cause (Table 1) is dementia which declines the thinking behavior and social activity skills by which the person will not able to function independently (3). The premature signs of Alzheimer disease are forgetting events and conversation or personality disorder (4, 5).Patient will develop several impairments and lost the ability to carry out daily routine tasks (5,6)

In earlier stages its medication may temporary improve symptoms slow the rate of decline. But as in Alzheimer stage increase its complications may also increase acute loss of brain function like; dehydration, malnutrition or infection at the end results in cell death (7-9).

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Table 1: Alzheimer's Disease Causes

Causes	
Neuro-chemical factors	Acetylcholine, Somatostatin, Substance P, Norepinephrine.
Environmental factor	Cigarette smoking, Certain Infection, Metals or Industrial toxins.

Diagnosis

The main components to diagnosis of Alzheimer Disease are:

- Self-Reporting regarding symptoms too family members either friend can provide symptoms and their impact on daily routine (10).
- Diagnosis Alzheimer on the basis of asses, memory and thinking skills (11).
- Clinical test and imaging test also helps them to understand the causes, stage or define the characteristic of mental illness (12).
- Actually Alzheimer diseases can be diagnosed after death, when microscopic examination or autopsy of brain done. This will helps to reveals the characteristic plaque and tangles (13-15).

Dementia

It is a group of co-occurring signs and symptoms which include memory, language, reasoning, decision making attention (16).

In person it can be recognized by change in personality, emotional regulation and social behavior that occurs which can interfere with social activities and relationships or daily routine activity (17, 18).

There are several causes of dementia such as depression, nutritional deficiency, space occupying lesions and excess addiction of any substance or activities (fig.4). Certain class of medications is also promotes it in older adult's examples: Anti-cholinergic, analgesic, sedative etc (19).

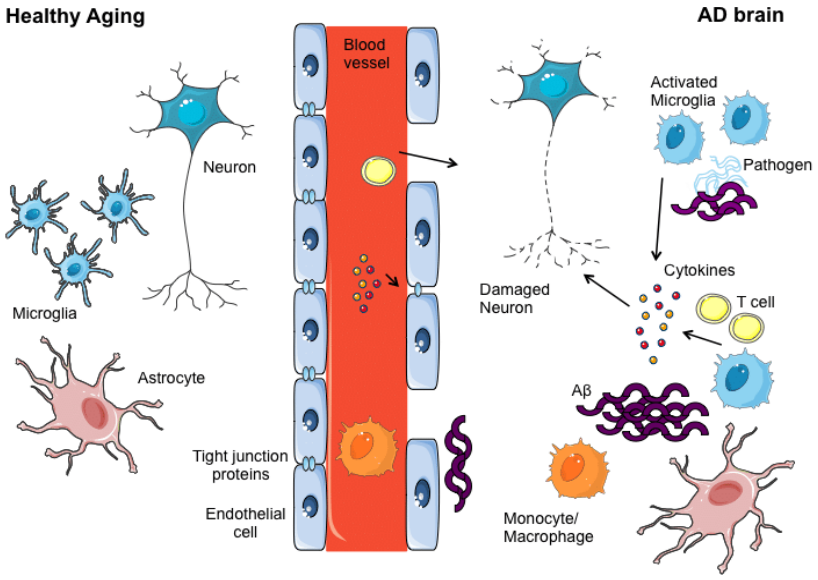

Figure 4: Impact of infection on Alzheimer Disease or Dementia (2)

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Pathophysiology

Mainly 4 changes in the brain structure define Alzheimer Disease (20)

- Cortical atrophy
- Degradation of cholinergic and other neurons
- Presence of neuro-fibrillary tangles (NFT's)

Beta Amyloid protein and apolipoprotein E are two proteins that contribute to the genesis of the NFT's and NP's (Table 2) which are considered the signature lesions of Alzheimer Disease (1, 2).

Table 2: Differential Features Between NTFs and NPs

Neuro Fibrillary Tangles (NTFs)	**Neuritic Plaque (NPs)**
These are present in normal brain mainly hippocampus amygdale cerebral cortex	They are extra cellular lesions present in the brain and cerebral vasculature.
These are located intra-cellularly within the cytoplasm of neurons	Plaque are compressed of core of beta Amyloid proteins surrounded by axon and dendrite projections of neuron
These are comprised of paired neuro-filaments adopting a helical shape which appears like tiny flame filling the neuronal cell bodies. Its presence disturbs the cell structure and its functions and finally causes cell death.	They interfere with neural transmission pathway.

Degeneration of cholinergic neuro transmission:

Cholinergic neurotransmission are presents in hippocampus amygdale which are associated with higher learning memory (2). In Alzheimer Disease it leads to blockade of cholinergic neuro transmission (3)

Other neuro transmitter abnormalities

In Alzheimer disease, while mono-amine oxidase type b (MAO-B) activity is increased sterotonergic neuron of raphal nuclei and nor adrenergic cells of the clocus cerulus are lost (4, 5).

In glutamate pathways other abnormalities are also appears which is a major neuro transmitters in the cortex and hippocampus (6).

Tests

Several tests are performed by diagnostic to sure about AD. Dr. will perform a physical test to examine over all neural health on testing the following: (7, 8)

1. Reflexes
2. Muscle tone and strength
3. Ability to get up from a chair and walk across to room
4. Sense of sight and hearing
5. Coordination
6. Balance
7. Psychological status or neurological psychological testing

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Doctor's may perform a short mental status test to check out their memory, thinking skills; psychological function as compared with other people has similar age and education. These tests play an important role to tract the ongoing symptoms in the future (9).

Brain imaging

Image of brain (Fig.5) is used to identify abnormalities related to condition other than AD like strokes, trauma or tumors they cause cognitive changes (14). It includes the following:

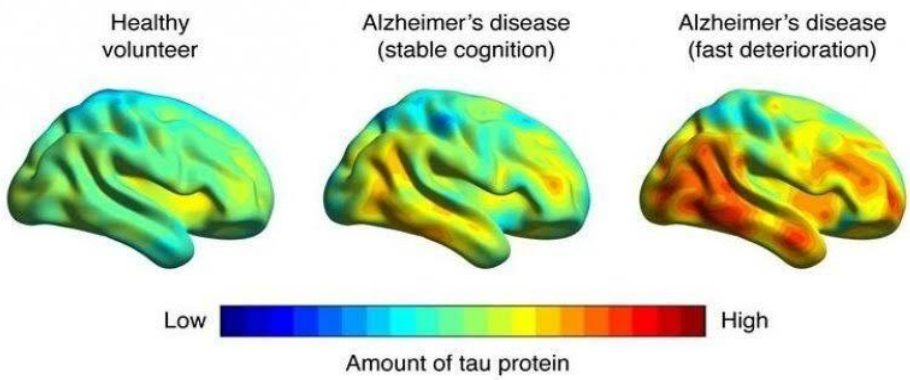

Figure 5: Comparison of Alzheimer Disease with healthy brain or Diseased caused brain (7, 14).

Magnetic Resonance Imaging (MRI)

Resonance Imaging(Fig. 6) uses radio waves and a strong magnetic field to construct detail images of brain to find out other situations like brain shrinkage etc (10).

Figure 6: MRI repot of brain shrinkage in Alzheimer Disease timely (11, 12).

Computerized Tomography

CT scan (Fig. 7) is specialized x-ray technology produce across narrow images of the brain to find out tumors, stokes and head injuries (11).

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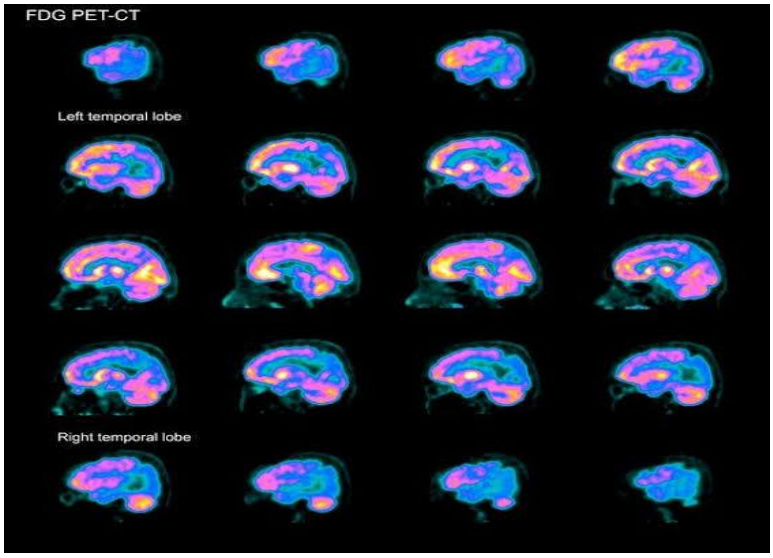

Figure 7: CT scan report of Alzheimer Disease across sectional images of brain (12).

MANAGEMENT OF ALZHEIMER'S DISEASE

Pharmacological Approach

Drugs which are used for dementia and cerebral disorder in Alzheimer Disease

The indications of cognition enhancer are as follows:

- Alzheimer Disease or multiple infarct dementia
- Mild cognitive impairment and episodic memory lapses
- Mentally retard children, learning defects, attention deficit disorder or personality disorder
- Sequel of head injury or brain surgery

Drugs used for the treatment of Alzheimer Disease (12, 13)

Cholinergic Activators

- Rivastigmine
- Donepezil
- Galantamine
- Tacrine

Glutamate Antagonists (NMDA)

- Memantine

Miscellaneous Drugs

- Piracetam
- Dihydroergotoxine
- Pyritinol
- Citicoline
- Piribedil
- Ginkgo biloba

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Individual drug

Rivastigmine

Carbamate derivative of physostigmine which inhibits or bloke both acetylcholine-esterase and butyrylcholine- esterase (14).

Rivastigmine is extremely lipid soluble and enters in the brain or cross blood brain barrier (BBB). Plasma t ½ of Rivastigmine is about 2 hours (15).Rivastigmine is specify in conservative or chronic case of Alzheimer Disease (16, 17). Transdermal patches are also available for the prescribed patient dose to adequate release of Rivastigmine as 9.5 mg or 13.3 mg per 24 hours (18)

Donepezil

It may have Cerebro-selective and reversible anti-ACE producer measurable improvement in several cognitive as well. And activities of daily living score in Alzheimer Disease (19). It is beneficial to elevate the level of Ach in cortex like as in surviving neuron projection from basal forebrain to cerebral cortex or hippocampus. T½ of Donepezil is prolonged it considered formerly daily at bed time. It has distinctive advantage over Rivastigmine and Galantamine (20).

Galantamine

Natural alkaloid selectively blockade of cerebral acetylcholine-esterase and havesome direct action at nicotinic receptor. The adverse effect of Galantamine is nausea, vomiting, stomach pain, extreme tiredness (1, 2).

Memantine

Memantine is well absorbed tolerated anti-Ach used in Alzheimer Disease have some side effect like headache, dizziness, constipation. Memantine is used for other type of dementia (3).

Pyritinol (Pyrithioxine)

Mechanism of action: Pyritinol helps to increase the choline uptake into neurons and also increase the level of acetylcholine. It is successful precursor of dopamine which is one of the neurotransmitter mood-booster in brain (4, 5).It is used in contraction and memory defects. Also used in organic brain syndrome.

Piribedil

This dopaminergic agonist helps to improve the memory, contraction and tinnitus in elderly cause by cerebral circulatory insufficiency. It also has been reported in Parkinsonism.

Citicoline

This procures from choline and cytidine which involve over the synthesis of lecithin. Citicoline have to treat the cerebral function by increases blood flow in the brain or increase cerebral metabolism (6, 7).

Ginkgo biloba

The Dried extract or isolated from of Chinese plant which contains several mixtures of ginkgoflavone glycoside (e.g. ginkgolide B) and some PAF (platelet activating factor) antagonistic action (8).Ginkgo biloba is well treated cerebral deterioration in cerebrovascular insufficiency and it has been promotes a diversification of cognitive or behavioral disorder (9, 10).Adverse effect is upper g.i.t symptoms and increased risk of bleeding.

CONCLUSION

Now a day's few convenient diagnostic studies shows that the clinical evaluation are more sufficient diagnosis of Alzheimer Disease. Pathological, include bodily fluids with good specificity.Several medications are prescribed like cholinesterase inhibitor or Cerebro-active and Memantine drugs by doctor or physician to improve the memory and alertness without changing life expectancy of Alzheimer Disease dementia. In daily life style, people may change their daily diet, routine exercise to intervention with results shows low risk of Alzheimer Disease.According to, pathology features associated with Alzheimer Disease Amyloid β and protein tangles are present target to treatment of Alzheimer Disease for higher success in comparative study. Although, proper/sufficient has been evidence helps to earlier recognition of Alzheimer Disease. Pathophysiology of Alzheimer's for the better lead and for early and more definitive treatment for large scale result.

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