



Alzheimer's Disease: History, Stages, Diagnosis and Its Future

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Alzheimer's is a brain disease in which brain cells responsible for memory loss and other intellectual functions starts to die. It can also be said that there is a loss of connections in nerve cells of brain. Although scientists have not yet found out the main underlying cause of this disease, there are several other factors that have been studied which leads to alzheimer's. Some of them include tangling of TAU protein, plaques formed by amyloid, shrinkage in brain tissue etc. It is the 6th leading cause of death in US and 3rd in older people. It was discovered by a psychiatrist Alzheimer's, who researched on a patient Auguste D. He noticed dementia, aggressiveness and some other mental illness in her and then studied her brain after her death. Alzheimer's is asymptomatic in early stages, that is why we cannot start the treatment in early stage. The disease can be identified once a person start getting symptoms. But until then the damage has already begun and progressed. We do not have a cure for this disease yet. It can only be delayed by treating the symptoms and by therapy. But the scientists are carrying out different clinical trials such as detangling of TAU protein etc to make this disease fully curable.

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1. INTRODUCTION

During the past decade, a conceptual shift occurred in the field of Alzheimer's disease (AD) considering the disease as a continuum. Thanks to evolving biomarker research and substantial discoveries, it is now possible to identify the disease even at the preclinical stage before the occurrence of the first clinical symptoms. This preclinical stage of AD has become a major research focus as the field postulates that early intervention may offer the best chance of therapeutic success [1-6]. To date, very little evidence is established on this "silent" stage of the disease. A clarification is needed about the definitions and lexicon, the limits, the natural history, the markers of progression, and the ethical consequence of detecting the disease at this asymptomatic stage. This article is aimed at addressing all the different issues by providing for each of them an updated review of the literature and evidence, with practical recommendations [7].

2. HISTORY

Alzheimer's was a young scientist who wanted to understand the relation between brain diseases and mental illness. He was committed to mental health care. A woman named Auguste D was a 50 year old patient suffering with memory problem along with other symptoms like aggressiveness, fearfulness, and constant behavioral changes. She met Alzheimer but was not treated by him. She died a year later and this was when Alzheimer went to work at another hospital. After her death her brain was sent to Alzheimer to examine. What he found to his surprise was that her brain tissue was shrunk and tangles of TAU and amyloid plaques in her brain. It was also found that tangles and plaques of proteins were found in older people having dementia. Thus it was discovered that the tangles and plaques are not only found in Alzheimer's patient but also patients with different mental illness which leads to dementia. Dementia was categorised as senile and presenile dementia. As Auguste D was not an elderly woman, her illness was considered presenile, and those who were old were considered senile. In 2011, it was found that Alzheimer's was not only a disease with dementia due to tangles in brain but it was also a pathological process that develops into a clinical

disease. Several different hypothesis were made to find the cause of this illness. In 1970s scientists made a hypothesis known as "cholinergic hypothesis" of Alzheimer's [8]. This theory attributed that in Alzheimer's there is a deficiency of certain neurotransmitter acetylcholine in brain. To prevent this cholinesterase inhibitors were developed that stopped the destruction of acetylcholine. This method was approved by FDA and still valid in current world. Another theory was of amyloid plaques, which confirmed that beta-amyloid protein formed tangles in blood vessels and were found in patients of Alzheimer's. Soon it was identified as an important component of plaques and was linked to a gene which was located on 21st chromosome. TAU protein involvement was another research that was done. In this there are abnormalities in tau protein. They are present in neurons. In normal TAU protein microtubules are present whose function is to help transport nutrients and other substances from one nerve cell to another. These TAU proteins starts to get tangled which lead to abnormalities [9].

3. STAGES [10]

3.1 Initial Stage/Mild Stage

This stage is asymptomatic. The only symptoms that can be seen are wandering, getting lost in thoughts and small behavioral changes. But by this time the damage has already started.

3.2 Moderate Stage

This stage is also known as pre dementia phase because there is mild cognitive impairment or mild neurological disorder. It can be seen that in this stage there is damage in areas of brain controlling sensory, reasoning, language and conscious thoughts. Memory loss and confusion can also be seen in some cases in this stage.

3.3 Severe Stage

This stage has major neurocognitive disorder. There are major changes in cognitive behavior. Tissue gets severely shrunk and the neurons cannot communicate. Patients at this stage has major dementias and sometimes hallucinations. Changes in brain occurs way before there is a cognitive problem in a patient. This is the preclinical stage in which we are not able to see

any symptoms but toxic changes in brain starts to occur. These toxic changes gradually increases. They can be deposition of plaques or any other protein deposition.

These problems start affecting our hippocampus, entorhinal complex and other parts of brain that are essential in forming memories and in intellectual thinking.

Slowly the neurons die and in the last stage the brain has shrunken.

4. SIGNS AND SYMPTOMS [11]

- a) Mild cognitive impairment
- b) Problems with smell
- c) Difficulty in movements
- d) Patient starts having visions
- e) Forgetting conversations
- f) Troubles in handling day to day activities
- g) Low energy
- h) Depression
- i) Hallucination

5. TREATMENT [12]

Alzheimer's cannot be treated by any drug. We can only treat the symptoms but cannot cure it fully. The treatments can only prolong the death or severity of disease, that is we can only delay memory loss and not cure it.

Some of the treatments are

- Medications like drugs that have been approved by FDA, one of which is donepezil. Others like Razadyne, Exelon are also used.
- Cholinesterase inhibitors:- This was the first tried treatment. This increases cell to cell communications by preserving chemical messengers which are limited in alzheimer's in brain. Although scientists are wholly sure about how these works.
- Memantine:- These helps in brain cell communications and slow down the process of degeneration of brain cells or tissues and thus eventually slow down the progression of disease from moderate stage to severe stage.
- Managing behavioral symptoms:- The symptoms of alzheimer's like aggression, wandering, laziness depression can be treated by some more comfortable ways. They involve creation of a supportive and happy environment. This can include:-

- i. Keeping medications secure and providing them with medications at proper time.
 - ii. Checking their small essential items like wallets and phones etc for them.
 - iii. Ensure they are in comfortable clothes and slippers.
 - iv. Removing extra and unnecessary furniture from the surroundings to avoid injuries.
 - v. Installing alarm sensors on doors and windows.
 - vi. Keeping photos around them so that they can remember their moments and loved ones.
 - vii. Installing handrails for easy walking.
- They can even be given some medicines so that they can rest properly. Like doctors sometime prescribe:-
 - i. Sleep aids- sometimes the hallucinations and delusions can make it difficult for the patient to sleep and take rest. At such situations they are given sleeping aids. They are not given often because they have their own side effects.
 - ii. Anti-depressants- these drugs are also not given regularly. They are give only when patient suffers from depression or anxiety or restlessness.
 - iii. Anti-psychotics- these are used when a patient can be seen hallucinating or in aggression. These drugs have side effects and sometimes can even lead to death. That is why they are not given often [9]
 - Some clinical trials have been done which suggests some chemicals and various herbs that might help prevent alzheimer's. They are not beneficial in treating the disease, they can only help in avoiding the risk of this disease happening. Some of them are:-
 - i. Vitamin E- It helps in delaying the progression of alzheimer's.
 - ii. Omega 3 fatty acids- this is found in fish. They help in lowering the risk of dementia.
 - iii. Curcumin- this is found in turmeric and its is anti-inflammatory.
 - Exercising regularly can also help in delaying degeneration of brain cells or even prevent this disease to occur.

- Nutritious diet is equally important to help us fight alzheimer's. we should keep ourselves hydrated.

6. DIAGNOSIS

There are several ways through which alzheimer's can be diagnosed. Although it does not have a specific test that can determine if a person has alzheimer's or not, but a set of tests help us to determine if a person is suffering with it or not. They can be:-

- Checking the muscle tone of patient. Checking their reflexes and muscle strength. Balance and coordination are also tested to get a more clearer perspective.
- Testings are done to check the menta state of the patient. These are the tests which checks memory and intellectual thinking. These can be a starting point to track the progression of disease.
- Later brain imaging is done which includes MRI, CT scan and PET scan. MRI involves radio waves and magnetic field to check the images and gives more detailed image of brain. Doctors identify shrinkage of brain through this scan. CT scans are slightly less appropriate to identify alzheimer's but can still be done to check tumors etc. PET scan can be one of the major way to diagnose alzheimer's. In this we can identify tangles, amyloid plaques and degeneration of tissue [13,1].

7. FUTURE OF ALZHEIMER'S [2]

Currently the treatment for alzheimer's is temporary. It does not cure the disease. Efforts are being taken to find a permanent cure for alzheimer's.

- Plaques are being targeted to find a cure. The main strategy is to prevent the beta amyloid plaques from happening by inducing drugs which are basically monoclonal drugs which mimics the antibodies of your body and reacts to formation of plaques. As per now no effect has been seen in moderate and severe Alzheimer. It might be effective in mild stage.
- Preventing the destruction of nerve cells and synapses can also be effective. The

beta amyloid protein interacts with fyn protein and destroys the synapses which inhibit the cell to cell interaction. Efforts are being taken to prevent this from happening.

- Scientists are trying to find a way to stop beta amyloid production in excess so that it prevent interaction with fyn protein and accumulation leading to plaque formation.
- Keeping TAU from tangling can be a major way to cure alzheimer. The aggregation inhibitors and vaccine are currently under clinical trials.

This is how scientists are working day and night to find a cure for alzheimer's. There are a lot of things that has to be discovered about alzheimer's. Maybe in coming future we might get a permanent cure. Till then we can support the alzheimer's patient with existing treatment and by being supportive.

8. CONCLUSION

Preventive factors should be critically considered as they may slow down or delay the evolution to a clinical AD. The major interest for identifying vascular and lifestyle modifiable risk factors is the possibility of impacting the onset of a clinical AD by advising and intervening subjects at risk. Since Alzheimer's disease is multifactorial, multicomponent therapies that address multiple risk factors at the same time may be required for optimal prevention. Several research, the majority of which were retrospective, have highlighted the importance of modifiable factors in delaying the clinical onset of AD in the last three decades.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely

no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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