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ALZHEIMER'S DISEASE: A NEURODEGENERATIVE TYPE OF DEMENTIA

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Abstract

Alzheimer's disease (AD), the most common form of dementia, is a degenerative disorder of the brain that leads to memory loss. Alzheimer's disease is a neurological disorder in which the death of brain cells causes memory loss and cognitive decline. The disease starts mild and gets progressively worse. It first involves the parts of the brain that control thought, memory and language. People with AD may have trouble remembering things that happened recently or names of people they know. Dementia is a general term that describes a significant loss of intellectual abilities, including memory, the ability to reason, and other cognitive and behavioral changes that can interfere with daily life. While a number of health conditions can lead to dementia and related brain deterioration, the most common cause is Alzheimer's disease.

Keywords: *Alzheimer's disease, Dementia, Neurological disorder.*

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INTRODUCTION:

5 million people live with Alzheimer's disease (AD) in the USA, and it is forecasted that by the year 2025 there will be an average 50% increase in patients with AD [1]. AD is a principal cause of dementia in the aging population [2]. AD experienced patients symptoms including memory loss, cognitive alterations and behavioral changes [3, 4]. The dementia in AD patients are associated with neurodegeneration that is characterized primarily by synaptic injury [5-7] followed by neuronal loss [8]. This is accompanied by astrogliosis [9], microglial cell proliferation [10, 11] and the presence of neurofibrillary tangles composed of dystrophic neurites and hyperphosphorylated tau [5, 12-16]. Recent studies have uncovered evidence, suggesting that another component to the neurodegenerative process in AD might include the possibility of interference with the process of adult neurogenesis in the hippocampus [17, 18]. AD is normally founded in aged people and characterized by malfunctioning of different biochemical pathways. AD has been associated with a significant decrease in the amount of acetylcholine (ACh) by breaking down of ACh. ACh is a neurotransmitter that transmits signal in the synapse, after delivering signal ACh is hydrolyzed and given choline and acetyl group in a reaction catalyzed by the enzyme AChE and its pharmacological action is done primarily by acetyl cholinesterase (AChE) and secondary by butyrylcholinesterase (BChE). Over activity of AChE and BChE enzymes are responsible for the development of different neurological disorder like AD, Parkinson's disease etc [19].

Epidemiological studies have revealed that AD is the leading cause of dementia, accounting for about 50% of all cases worldwide [20]. Aging is the most obvious risk factor for developing AD. It was estimated that the age-associated prevalence rate of AD would be doubled every 5 years in the patients beyond 65 years of age [21]. Moreover aging, several other possible biological (such as genetic alterations and polymorphisms, and abnormal immune or inflammatory responses) and environmental factors (such as education, traumatic injury, oxidative stress, drugs, and hormone replacement) and the interactions among these factors have been considered to be contributors to a common pathway leading to AD [22, 23].

Dementia is a progressive, incurable illness. In patients with advanced dementia, the final year of life is characterized by a trajectory of persistently severe disability [24]. Stage 7 on the Global Deterioration Scale (ranging from 1 to 7, with higher stages indicating worse dementia) provides a useful description of the features of advanced dementia [25], including profound memory deficits (e.g., inability to recognize family members), minimal verbal abilities, inability to ambulate independently, inability to perform any activities of daily living, and urinary and fecal incontinence.

The clinical course of advanced dementia was described in the Choices, Attitudes, and Strategies for Care of Advanced Dementia at the End-of-Life (CASCADE) study, which prospectively followed 323 nursing home residents with this condition for 18 months. [26] The median survival was 1.3 years. The most common clinical complications were eating problems (86% of patients), febrile episodes (53% of patients), and pneumonia (41% of patients).

SYMPTOMS OF ALZHEIMER'S DISEASE:

Alzheimer's disease symptoms vary along with individuals. The most familiar primary symptom is a increasingly worsening ability to remember new information. This memory decline occurs because the first neurons to malfunction and die are usually neurons in brain regions involved in forming new memories. As neurons in other parts of the brain malfunction and die, individuals experience other difficulties. The common symptoms of Alzheimer's: Memory loss that disrupts daily life, challenges in planning or solving problems, difficulty completing familiar tasks at home, at work or at leisure, confusion with time or place, trouble understanding visual images and spatial relationships, new problems with words in speaking or writing.

CAUSES OF ALZHEIMER'S DISEASE:

Development of Alzheimer disease is related to 2 abnormal proteins in the brain called β-amyloid and tau**,** which are toxic to nerve cells (neurons) in the brain. The buildup of these proteins in neurons eventually leads to neuron death, worsened brain function, and symptoms of dementia. Like all types of dementia, Alzheimer's is caused by brain cell death. It is a neurodegenerative disease, which means there is progressive brain cell death that happens over a course of time. Dementia is a term used to describe a decline in mental abilities including memory, language, and logical thinking. The total brain size shrinks with Alzheimer's - the tissue has progressively fewer nerve cells and connections. While they cannot be seen or tested in the living brain affected by Alzheimer's disease, autopsy will always show tiny inclusions in the nerve tissue, called plaques and tangles [27, 28]. Plaques are found between the dying cells in the brain - from

the build-up of a protein called beta-amyloid (you may hear the term "amyloid plaques"). The tangles are within the brain neurons - from a disintegration of another protein, called tau. The exact trigger for Alzheimer disease is unknown. It tends to run in families, meaning there is a genetic component. More than 30 genes have been identified that may be involved in Alzheimer disease. Three genes have been found to be passed down from parent to child in a "dominant" manner, with about half of children of an affected parent also eventually developing Alzheimer disease. A small percentage of Alzheimer's cases (an estimated 1 percent or less) develop as a result of mutations to any of three specific genes. A genetic mutation is an abnormal change in the sequence of chemical pairs that make up genes.

RISK FACTORS FOR ALZHEIMER'S DISEASE:

With the exception of the rare cases of Alzheimer's disease caused by genetic mutations, experts believe that Alzheimer's, like other common chronic diseases, develops as a result of multiple factors rather than a single cause. The greatest risk factor for Alzheimer's disease is age. Most people with Alzheimer's disease are diagnosed at age 65 or older. People younger than 65 can also develop the disease, although this is much more rare. Another strong risk factor is family history**.** Those who have a parent, brother, sister or child with Alzheimer's is more likely to develop the disease. The risk increases if more than one family member has the illness. When diseases tend to run in families, either heredity (genetics) or environmental factors, or both, may play a role. Having a certain gene (the apolipoprotein E or APOE gene) puts a person, depending on their specific genetics, at three to eight times more risk than a person without the gene.

TREATMENT OF ALZHEIMER'S DISEASE:

Pharmacologic intervention for Alzheimer's disease is only palliative and provides modest short-term benefit. None of the currently available therapeutic agents have been shown to alter the underlying neurodegenerative process. Current therapies are aimed at either improving cholinergic transmission within the CNS or preventing excitotoxic actions resulting from overstimulation of N-methyl-D-aspartic acid (NMDA)-glutamate receptors in selected brain areas. It is postulated that inhibition of acetylcholinesterase (AChE) within the CNS will improve cholinergic transmission, at least at those neurons that are still functioning. Currently, four reversible AChE inhibitors are approved for the treatment of mild to moderate Alzheimer's disease. Stimulation of glutamate receptors in the CNS appears to be critical for the formation of certain memories; however, overstimulation of glutamate receptors, particularly of the NMDA type, has been shown to result in excitotoxic effects on neurons and is suggested as a mechanism for neurodegenerative or apoptotic (programmed cell death) processes. Binding of glutamate to the NMDA receptor assists in the opening of an associated ion channel that allows Na^+ and, particularly, Ca^{2+} to enter the neuron. Unfortunately, excess intracellular Ca^{2+} can activate a number of processes that ultimately damage neurons and lead to apoptosis. Antagonists of the NMDA-glutamate receptor are often neuroprotective, preventing the loss of neurons following ischemic and other injuries.

REFERENCES:

1. Hebert L.E., Scherr P.A., Bienias J.L., Bennett D.A., Evans D.A. State-specific projections through 2025 of Alzheimer disease prevalence. Neurology.2004;62:1645
2. Ashford J.W. APOE genotype effects on Alzheimer's disease onset and epidemiology. J. Mol. Neurosci. 2004;23:157–165.
3. Katzman R. Alzheimer's disease. N. Engl. J. Med. 1986;314:964–973
4. Budson A.E., Price B.H. Memory dysfunction. N. Engl. J. Med. 2005;352:692–699.
5. Terry R., Hansen L., Masliah E. Structural basis of the cognitive alterations in Alzheimer disease. In: Terry R., Katzman R., editors. Alzheimer Disease. New York: Raven Press; 1994. pp. 179–196.
6. Masliah E., Mallory M., Alford M., DeTeresa R., Iwai A., Saitoh T. Molecular mechanisms of synaptic disconnection in Alzheimer's disease. In: Hyman B., Duyckaerts C., Christen Y., editors. Connections, Cognition and Alzheimer's Disease. Berlin: Springer; 1997. pp. 121–140.
7. DeKosky S., Scheff S. Synapse loss in frontal cortex biopsies in Alzheimer's disease: correlation with cognitive severity. Ann. Neurol. 1990;27:457–464.
8. Terry R., Peck A., DeTeresa R., Schechter R., Horoupian D. Some morphometric aspects of the brain in senile dementia of the Alzheimer type. Ann. Neurol. 1981;10:184–192.
9. Beach T., Walker R., McGeer E. Patterns of gliosis in Alzheimer's disease and aging cerebrum. Glia. 1989;2:420–436.
10. Rogers J., Luber-Narod J., Styren S., Civin W. Expression of immune system-associated antigens by

cells of the human central nervous system: relationship to the pathology of Alzheimer's disease. Neurobiol. Aging. 1988;9:339–349.
11. Masliah E., Mallory M., Hansen L., Alford M., Albright T., Terry R., Shapiro P., Sundsmo M., Saitoh T. Immunoreactivity of CD45, a protein phosphotyrosine phosphatase, in Alzheimer disease. Acta Neuropathol. 1991; 83:12–20.
12. Trojanowski J.Q., Lee V.M. 'Fatal attractions' of proteins. A comprehensive hypothetical mechanism underlying Alzheimer's disease and other neurodegenerative disorders. Ann. N. Y. Acad. Sci. 2000;924:62–67.
13. Lee V.M., Goedert M., Trojanowski J.Q. Neurodegenerative tauopathies. Ann. Rev. Neurosci. 2001;24:1121–1159.
14. Iqbal K., Grundke-Iqbal I. Neurofibrillary pathology leads to synaptic loss and not the other way around in Alzheimer disease. J. Alzheimers Dis. 2002;4:235–238.
15. Mandelkow E., Mandelkow E. Tau in Alzheimer's disease. Trends Cell. Biol.1998;8:125–127.
16. Crews L., Rockenstein E., Masliah E. APP transgenic modeling of Alzheimer's disease: mechanisms of neurodegeneration and aberrant neurogenesis. Brain Struct. Funct. 2010;214:111–126.
17. Boekhoorn K., Joels M., Lucassen P.J. Increased proliferation reflects glial and vascular-associated changes, but not neurogenesis in the presenile Alzheimer hippocampus. Neurobiol. Dis. 2006;24:1–14.
18. Li B., Yamamori H., Tatebayashi Y., Shafit-Zagardo B., Tanimukai H., Chen S., Iqbal K., Grundke-Iqbal I. Failure of neuronal maturation in Alzheimer disease dentate gyrus. J. Neuropathol. Exp. Neurol. 2008;67:78–84.
19. Md. Moniruzzaman**,** Md. Asaduzzaman**,** Md. Sarwar Hossain**,** Jyotirmoy Sarker**,** S. M. Abdur Rahman**,** Mamunur Rashid and Md. Mosiqur Rahman**.** In vitro antioxidant and cholinesterase inhibitory activities of methanolic fruit extract of Phyllanthus acidus. BMC Complementary and Alternative Medicine 2015, **15**:403.
20. Mount C, Downton C: Alzheimer disease: progress or profit? Nat Med 2006, 12: 780-784.
21.Bachman DL, Wolf PA, Linn RT, Knoefel JE, Cobb JL, Belanger AJ, White LR, D'Agostino RB: Incidence of dementia and probable Alzheimer's disease in a general population: the Framingham Study. Neurology1993, 43: 515-519.
22. Hardy J: The Alzheimer family of diseases: many etiologies, one pathogenesis? Proc Natl Acad Sci USA 1997, 94: 2095-2097.
23. Small GW: The pathogenesis of Alzheimer's disease. J Clin Psychiatry 1998, 59(Suppl 9):7-14.
24. Gill TM, Gahbauer EA, Han L,Allore HG. Trajectories of disability in the last year of life. N Engl J Med2010;362:1173-1180
25. Reisberg B, Ferris SH, de Leon MJ,Crook T. The Global Deterioration Scale for assessment of primary degenerative dementia. Am J Psychiatry 1982; 139:1136-1139.
26. Mitchell SL, Teno JM, Kiely DK, et al. The clinical course of advanced dementia. N Engl J Med2009;361:1529-1538
27. National Institute of Neurological Disorders and Stroke. Dementia: hope through research, Bethesda, MD: Office of Communications and Public Liaison, National Institute of Neurological Disorders and Stroke, US National Institutes of Health. Published online; version last updated June 26th, 2013, accessed November 1st, 2013.
28. Alzheimer's Association. The role of plaques and tangles Published online, accessed November 1st, 2013.