Naturopathic Approach to Alzheimer's Disease

by Dr. Farhang Khosh

Alzheimer's disease is perhaps the most important of all the degenerative diseases today because of its frequent occurrence and devastating nature. It is the most common cause of dementia in the elderly, with all that this implies in the way of distress for patients and families and economic loss in the form of the costs entailed in the long-term care of patients totally disabled by the disease. Historically, the term Alzheimer's disease was applied to progressive dementia coming on in late middle life but preceding the senile period, following the original description by Alois Alzheimer in 1907, in which the illness of a woman dying at the age of 55 was depicted clinically and pathologically.[1]

There are many different etiologies contributing to the pathogenesis, though this is a summary of the most important ones. The outstanding pathologic feature is death and disappearance of nerve cells in the cerebral cortex. This leads ultimately to extensive convolutional atrophy especially in the frontal, parietal, and medial temporal regions. There is a corresponding enlargement of the ventricular system, but this is usually not extreme. Two kinds of microscopic lesions are distinctive for the disease. The first, originally described by Alzheimer, consists of intraneuronal accumulations of filamentous material in the form of loops, coils, or tangled masses – referred to as Alzheimer neurofibrillary tangles. The neuropathologic evidence strongly suggests that these fibrillar masses are of major importance in bringing about the death of neurons. Neurofibrillary tangles and loss of synapses are the neuropathologic features most closely linked to dementia. The other histopathologic change that characterizes Alzheimer's disease is the presence of intracortical clusters of thickened neuronal processes, both axons and dendrites (collectively referred to as neurites), generally in the form of an irregular ring surrounding a spherical deposit of amyloid fibrils. These lesions, which had been recognized before Alzheimer's description of the neurofibrillary change, were termed senile plaques. Recent elucidation of their structure has led to their current designation as neuritic plaques. They have been shown to contain paired helical filaments identical to those found in the perinuclear cytoplasm of the diseased neurons. One form of plaque, the diffuse plaque, consists of amorphous amyloid without neurites.[2]

The amyloid peptide (ß or A4 peptide) gene is on chromosome 21, on which the familial Alzheimer's disease gene also has been localized in some families. A recent advance has been the finding that in a handful of families with familial Alzheimer's disease there are point mutations in the amyloid precursor protein. This observation suggests that Alzheimer's disease can be linked to a primary defect in amyloid production or processing, but most cases of familial and sporadic Alzheimer's disease do not have a clear cause.[2]

Biochemical studies show that choline acetyltransferase, the key enzyme required for the synthesis of acetylcholine, is decreased in the cerebral cortex in Alzheimer's disease. The major source of neocortical cholinergic innervation is a group of neurons situated in the basal part of the forebrain just beneath the corpus striatum – the nucleus basalis of Meynert. Careful neuropathologic investigations have shown that in Alzheimer's disease this nucleus is a site of major neuronal loss and of frequent Alzheimer neurofibrillary tangles. These studies suggest that impairment of cholingergic transmission may play a part in the clinical expression of the disease.[3]

The rule of neurotoxic chemicals such as Aluminum,[4] Mercury fillings,[5] and neurotoxic food additives such as MSG have been discussed in many articles to be the etiology of Alzheimer's disease.

Certain areas of the brain show greater vulnerability to glucose deprivation. They are the same temporal and parietal regions wherein the characteristic deficits in Alzheimer's disease (AD) are shown by PET and SPECT imaging studies.

Senile plaques and associated neurofibrillary tangles are probably the direct cause of Alzheimer's disease. The principal component of senile plaques is the beta amyloid of protein. There appears to be a reduction in essential fatty acids, with a corresponding increase in saturated fatty acids. This results in increased permeability of cellular membranes and a reduction in membrane fluidity. Consequently, the cellular membranes of Alzheimer's diseased brains might be penetrated by the enzyme that could cut the beta-amyloid precursor protein (ß-APP). This would release a large fragment of this protein into the extracellular space with the beta-amyloid section intact. Essential fatty acid deficiency will also reduce prostaglandins. Another pathogenesis of Alzheimer's disease is said to be deficiency of essential fatty acids which results in prostaglandin reduction.[6]

Clinical Appearance

The onset of Alzheimer's disease is insidious and subtle, with changes most noticeable first in memory for recent happenings and in other aspects of mental activity. Psychiatric disturbances such as depression, anxiety, or odd, unpredictable quirks of behavior, delusions, and hallucinations may be silent features in the early stages. Progression is usually slow and gradual, and unless other medical conditions supervene, it may smolder on for 10 or more years. In the milder case, including those of the senile period, the noteworthy features are those of simple dementia. More unusual disorders of thought and intellect, including aphasia, apraxic disturbances, and abnormalities of space perception, may be seen, especially in the presenile group. Exceptionally, and only in the advanced stages of the disease, extrapyramidal signs appear; the patient walks in a shuffling manner with short steps, and there is a generalized stiffness of the musculature with slowness and awkwardness of all movements. In some patients, sudden jerky contractions of various muscles (myoclonus) may occur in the presence of otherwise typical Alzheimer's disease, but this is unusual and should immediately raise the suspicion of Creutzfeldt-Jakob disease. Terminally, the patient may become nearly decorticate, losing all ability to perceive, think, speak or move.[2]

Relevant labs, Special tests and Imaging

CBC, chemistry panel, thyroid function studies, folate and B12 levels, VDRL, UA, EKG, EEG, CSF, Head CT/MRI and PET.[7]

Differential Diagnosis[8]

1. Vascular dementia
2. Multi-infarct dementia
3. Dementia associated with Parkinson's
4. Creutzfeldt-Jakob disease
5. End-stage multiple sclerosis
6. Brain tumor
7. Subdural hematoma
8. Progressive multifocal leukoencephalopathy
9. Metabolic dementia (hypothyroidism)
10. Drug reactions
11. Alcoholism and other addictions
12. Dementia pugilistica
13. Depression
14. Toxicity from liver or kidney failure
15. Vitamin and other nutritional deficiencies

Treatment

There are many treatment approaches that have been suggested for Alzheimer's disease. In this paper, I will emphasize those treatments that have been clinically proven effective. This is by no means the only available treatment.

1. **Acetyl-Carnitine**: L-carnitine is required for mitochondrial transport of long-chain fatty acids for ß-oxidation. Carnitine naturally occurs in the diet, particularly in animal products, and can be made from the essential amino acids lysine and methionine. Carnitine is produced in the liver and the kidney and requires several other nutrients, including vitamin C, niacin, vitamin B6 and iron, for its synthesis. Recently a multicenter trial giving acetyl-carnitine at 2 gms per day for one year affected the progression of cognitive and functional impairment in Alzheimer's disease. This was a placebo, double-blind trial. The 2 gm doses were well tolerated. Acetyl-L-carnitine induces acetyl-carnitine release in the striatum and hippocampus. Acetyl-carnitine also increases membrane cytoskeletal protein-protein interactions.[9]

2. **Anti-oxidants such as Vitamin A** (5,000-20,000 I.U. a day), **E** (2,000-3,000 I.U. a day), **C** (500-3,000 mg a day), **Selenium** (400 mcg a day) and **Carotenoids**: In one study the results showed that both Alzheimer's and multi-infarct dementia patients had significantly lower levels of vitamins E and beta-carotene than controls. Vitamin A was significantly reduced only in Alzheimer's disease patients. Since vitamins A, E and beta-carotene act as antioxidants, reduced levels could result in increased degeneration of the nervous system, exacerbating the dementia. It would be interesting to see if lipid-soluble vitamin supplements alter the rate of the progression of the dementia.[10]

3. **Zinc** (15-60 mg a day): The hippocampus is the area of the brain with the highest zinc concentration. Studies show that chronic neuroleptic medication increases amyloid induced production of NFT (neurofibrillary tangles), while zinc compounds can inhibit amyloid-induced production of neuronal paired-helical filaments. Preliminary trials with zinc aspartate have shown promise.[11]

4. **Improve mitochondrial function**: Mutated mitochondrial DNA is associated with cellular dysfunction in close association with the brains of Alzheimer's patients. By improving mitochondrial function with vitamins B2, menadione (vitamin K) and coenzyme Q10, the function of SDAT (senile dementia of the Alzheimer type) patients may be temporarily improved by enhancing some impaired neurons and slowing mitochondrial decline. Coenzyme Q10, sodium ferrous citrate, and vitamin B6 have shown a benefit in improving mental function.[12]

5. **Vitamin B12**: Studies evaluated relationship between Vitamin B12 and dementia in Alzheimer's disease. The deficiency of Vitamin B12 is prevalent in Alzheimer's patients and must be screened.[13]

6. **Estrogen**: Epidemiological study suggests that estrogen protects women against Alzheimer's disease. Women using estrogen replacement therapy were 40% less likely to have Alzheimer's disease and related dementias compared to women not on estrogens.[14]

7. **Thiamine**: Activities of thiamine-dependent enzymes (pyruvate dehydrogenase (PDHC), alpha-ketoglutarate dehydrogenase (α-KGDH), and transketolase (TK)) were measured in autopsied samples of temporal cortex from six patients with Alzheimer's disease and from eight age-matched control subjects who were free from neurological or psychiatric diseases. Significant decreases in PDHC, decreases were by 70%; α-KGDH, decreased by 70%; and TK, decreased by 52%; were observed in brain tissue from patients with Alzheimer's.[15]

8. **NADH**: In one study all patients showed improvement in cognitive and functional capacity. The mechanism of action of NADH is believed to be an increased synthesis of neurotransmitters, particularly dopamine and norepinephrine, in the brain; NADH is also believed to increase intracellular energy production.[16] ➤

Alzheimer's

9. **Botanicals:**

a. *Huperizia serata*, a Chinese tea contains Huperzine A and this increases acetylcholine levels in the brain. Thereby improves cognitive function.[17,21]

b. *Lycorus radiata* (shisuan), a Chinese herb, contains the alkaloids lycorine, lycoramine, lycoreine, and galanthamine. Both lycoramine and galanthamine have been shown to be reversible cholinesterase inhibitors.[17]

c. *Macleaya cordata* (boluohui), a Chinese herb, contains several alkaloids including sanguinarine, chelerythine, protopine, and allocryptopine. Sanguinarine inhibits cholinesterase.[17]

d. *Coptis chinensis* (huanglian), a Chinese herb, contains berberine alkaloids, mainly berberine, but also coptisine, worenine, palmatine, and columbamine. Berberine is a cholinesterase inhibitor.[17]

e. *Berberis species* (sankezhen), a Chinese herb, also contains berberine and palmatine that have a strong anticholinesterase activity.[17]

f. *Securinega suffruticosa* (yiyiqiu), a Chinese herb, contains many alkaloids, mainly securinine and its derivatives. Securinine is a CNS stimulant that antagonizes the inhibitory action of meprobamate. Securinine inhibits cholinesterase activity.[17]

g. *Solanum nigrum* (longkui), a Chinese herb, contains solanine, salasodine. Solanine has a strong anticholinesterase action.[17]

h. *Physostigma venenosum* from the calabar bean blocks the action of acetylcholinesterase.[18]

i. *Pilocarpus jaborandi* contains pilocarpine that has a M1 mimetic activity, which can affect the M1 receptor site and take the place of acetylcholine in neurotransmission in the Nucleus basalis of Maynard.[18]

j. *Hawthorne berry, Blueberry, Elderberry, Red and Black grapes* improve the integrity of blood vessel walls via anthocyanins.[18]

k. *Ginkgo / Gotu kola / Zizyphus jujube* improves memory.[16]

l. *Ginkgo biloba / Salvia officinalis / Melissa officinalis*, ginkgo contains the ginkgolides which have antioxidant, neuroprotective and cholinergic activities relevant to Alzheimer's disease mechanisms. The therapeutic efficacy of Ginkgo extracts in Alzheimer's disease in placebo controlled clinical trials is reportedly similar to currently prescribed drugs such as tacrine or donepezil and, importantly, undesirable side effects of Ginkgo are minimal. Old European reference books, such as those on medicinal herbs, document a variety of other plants such as *Salvia officinalis* (sage) and *Melissa officinalis* (balm) with memory-improving properties, and cholinergic activities have recently been identified in extracts of these plants.[19]

m. *Periwinkle / Hydrocotyle asiatica* increases cerebral circulation and function.[20]

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References

1. Isselbacher, Braunwald, Wilson, Martin, Fauci, Kasper. *Harrison's Principles of Internal Medicine* 13th edition. 1994. McGraw-Hill, Inc., New York. Pg. 2270.
2. Isselbacher, Braunwald, Wilson, Martin, Fauci, Kasper. *Harrison's Principles of Internal Medicine* 13th edition. 1994. McGraw-Hill, Inc., New York. Pg. 2271.
3. Butterfield, A. Acetylcarnitine increases membrane cytoskeletal protein-protein interactions. 1993. *Life-Science*. Pgs. 297-303.
4. Woodruff, M. and Nonneman A. *Toxin-Induced Models of Neurologic Disorders*. 1994. Plenum Press. Pgs. 301-318.
5. Terry, RD., Katzman, R. and Bick, KL. Brain Trace Elements in Alzheimer's disease. *Alzheimer's Disease*. 1994. Raven Press. New York.
6. Newman, P. Could Diet be One of the Causal Factors of Alzheimer's Disease. *Medical Hypothesis*. 1992. Pgs.123-126.
7. Dambro, M. *Griffith's Five Minute Clinical Consult*. 1995. Williams & Wilkins, Baltimore, Maryland. Pg. 24.
8. Dambro, M. *Griffith's Five Minute Clinical Consult*. 1995. Williams & Wilkins, Baltimore, Maryland. Pg. 24.
9. Bowman, B. Acetyl-Carnitine and Alzheimer's Disease. *Nutrition Reviews*. 1992:50(5): Pgs. 142-144.
10. Zaman, C. Plasma concentrations of Vitamins A and E and Carotenoids in Alzheimer's Disease. *Age and Aging*. 1992:21: Pgs. 91-94.
11. Constantinidis, J. Treatment of Alzheimer's Disease by Zinc Compounds. *Drug Development Research*. 1992:27: Pgs. 1-14.
12. Harman, D. Free Radical Theory of Aging: A Hypothesis on Pathogenesis of Senile Dementia of the Alzheimer Type. *Age*. 1993:16: Pgs. 23-30.
13. Cunha, G., Rocha, L., Peixoto, M., Motta, F., Barbosa, T. Vitamin B12 deficiency and dementia. *Int. Psychogeriatr*. 1995: 7(1): Pgs. 65-8.
14. Johnson, R. Estrogen/Alzheimer's Link Found. *Medical Tribune*. 1993: Pg. 1,8.
15. Butterworth, F. and Besnard, M. Thiamine-dependent enzyme changes in temporal cortex of patients with Alzheimer's disease. *Metab-Brain-Dis*. 1990:5(4): Pgs. 179-84.
16. Birkmayer, JGD. Coenzyme nicotinamide adenine dinucleotide. New therapeutic approach for improved dementia of the Alzheimer type. *Ann Clin Lab Sci*. 1996:26: Pgs. 1-9.
17. Dharmananda, S. Traditional Chinese Specific Condition Review: Alzheimer's Disease. Protocol *Journal of Botanical Medicine*. 1996:2(1): Pgs. 114-116.
18. Mitchell, W. Naturopathic Specific Condition Review: Alzheimer's Disease. Protocol *Journal of Botanical Medicine*. 1996:2(1): Pgs. 107-110.
19. Perry EK, Pickering AT, Wang WW, Houghton PJ, Perry NS. Medicinal plants and Alzheimer's disease: from ethnobotany to phytotherapy. *J Pharm Pharmacol*. 1999 May;51(5): Pgs. 527-34.
20. Winston, D. Eclectic Specific Condition Review: Alzheimer's Disease. Protocol *Journal of Botanical Medicine*. 1996:2(1): Pg. 113.
21. Medical News & Perspective, Old Chinese herbal medicine used for Fever Yields New Alzheimer Drug Therapy. *Journal of American Medical Association*. 1997 March 12;277;776.