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Prevention of Alzheimer disease

The roles of nutrition and primary care

Abstract: Risk factors for developing Alzheimer disease include hypercholesterolemia, hypertension, obesity, and diabetes. Due to lack of effective treatments for Alzheimer disease, nutrition and primary prevention becomes important.

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Complaining of low back pain and depression, Mr. J (a middle-aged man) walks into the clinic to establish a primary care home. He leaves with a diagnosis of depression, obesity, low back pain, and hypercholesterolemia. His new primary care provider offers guidance on following a low-cholesterol/low-fat diet and prescribes an antidepressant and an analgesic for the low back pain.

Years later, in his seventies, Mr. J is still obese, sees a pain management provider for chronic back pain (managed with an opioid analgesic), and takes numerous medications for his comorbid conditions, including hypertension, type 2 diabetes mellitus, and hypercholesterolemia. Mr. J's wife accompanies him to the visit and reports recent deterioration in his memory, concentration, and mood. Mr. J leaves the clinic with the diagnosis of dementia and possibly Alzheimer disease (AD), for which his provider prescribes donepezil.

While in his early eighties, Mr. J lives in a long-term care facility. His type 2 diabetes mellitus, hypercholesterolemia, and hypertension remain

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well controlled, but he is unable to recognize his wife or children. The progressive nature of his AD has led to urinary and fecal incontinence, an inability to walk, and dependence upon staff for all of his activities of daily living. Finally, unable to remember how to swallow, Mr. J develops aspiration pneumonia and dies.

Prevalence of AD

Every 67 seconds, someone is diagnosed with AD, which translates to an estimated 5.3 million Americans in 2015.[1,2] Prevalence of AD is projected to total nearly 13.8 million Americans age 65 and older by 2050.[2] AD is the sixth leading cause of death in the United States. With the aging of the baby boomer generation and longer life expectancies, the impact on quality of life, cost of healthcare, and funding for research must be addressed.

Currently, the five million Americans living with AD are mostly older adults in their prime retirement years. It leads to significant disability and reduced quality of life, taking away their ability to recognize family and friends, care for themselves, and live independently. The lack of ability to care for oneself or live independently places a significant burden on caregivers. Much of this care is provided by unpaid family members and friends. "In 2014, family and friends provided 17.9 billion hours of unpaid care to those with AD, care valued at $217.7 billion."[2] This high-stress emotional care takes a devastating toll on the health of these care providers, leading to an increase in $9.7 billion additional healthcare costs for those caring for those afflicted with this disease.[2]

There currently is no cure for AD—only a possible slowing of its progression with pharmaceuticals.

In addition to the human toll, the economic toll of AD is great. According to the *Alzheimer's Disease Facts and Figures* (2015), direct costs associated with AD in 2015 will reach $226 billion.[2] Average per person Medicaid spending for older adults with dementia including AD is 19 times higher than the average per person Medicaid spending for all other older adults. In addition, the average per person Medicare spending for older adults with dementia including AD is three times higher than the average older adult without dementia.[2]

Primary prevention improves quality of life and is often cost-effective. Health-related behavior, including diet, impacts a person's risk, incidence, and ability to cope with chronic disease. Immunization, education, and other healthy behaviors such as proper nutrition are accepted methods of preventing or reducing the risk of disease but are not often linked to the prevention or risk-reduction of AD, despite supporting evidence. Clinicians need to incorporate primary prevention strategies into clinical practice, offering suggestions for doing so. This article hopes to draw attention to the evidence linking nutrition to the prevention of AD. Nutrition has a role to play in AD prevention, and the primary care clinician's role in this implementation is pivotal.

Pathophysiology and clinical manifestations

AD is the most common neurodegenerative disorder affecting Americans.[4] AD is characterized by progressive cognitive and behavioral deficits accompanied by diffuse abnormalities in the brain.[4] Late Onset AD (LOAD) is the most common type, accounting for 97% of all cases.[4] Aging is the most significant risk factor for LOAD.[4]

The neuro-pathologic hallmarks of AD include amyloid plaques and neurofibrillary tangles, which accompany diffuse loss of neurons and synapses in the brain.[4] Three particular brain proteins are targeted indicators of brain neurotoxicity and AD development: amyloid precursor protein (APP), amyloid-beta (AB), and tau.[4] APP, as the name suggests, is a protein that regulates functions in the brain, and when metabolized in the brain, produces AB. This peptide forms the plaques found on the AD brain. AB is neurotoxic. This buildup of AB plaques begins a deteriorating cycle of brain tissue inflammation, decreased synapse transmission, and increased oxidative stress.[4]

The AB accumulation inhibits axonal transport causing build-up of tau protein and the second hallmark of AD: neurofibrillary tangles.[4] The tau protein that once stabilized neuronal transport continues to tangle, which progress to breakdown of pathways and cell death. AD is characterized by slow progressive decline in cognitive function. These symptoms progress at varying intervals and are usually described based on diagnostic criteria for AD (see *Diagnostic criteria for AD*).

Treatment

There currently is no cure for AD—only a possible slowing of its progression with pharmaceuticals. The current classes of drugs used today have only been found to slow progress on an average of 6 to 12 months from one stage of dementia to the next (see *Summary of current AD medications*).[1] Even with attempts to slow its progression, the larger task would be to reverse the damage from the

plaques and restore cognitive function. Current research is aimed at developing such drugs.

Risk factors. Risk factors for developing AD include age, genetics, hypercholesterolemia, hypertension, obesity, and diabetes mellitus. Due to the lack of effective treatments for AD and the high cost of this disease, primary prevention becomes of utmost importance. What if primary prevention of other chronic disease through lifestyle modification (such as diet, exercise) was also effective in prevention of this disabling cognitive disease? Would it not make sense that if primary care providers mitigated these risk factors it could reduce the incidence/occurrence or severity of AD? There are evidence-based findings that suggest such a link exists.

Hypercholesterolemia has been linked to increased production and deposition of AB, and reduced cholesterol levels have been shown to coincide with decreased AB production and deposition.[4]

Diabetes mellitus has been linked to development of AD as well. With AD, normal glucose metabolism within the brain is disrupted. Although the pathologic impairment is not completely understood, the abnormal insulin signaling that occurs with diabetes is linked to the disruption of tau protein breakdown that is found in AD.[5] This correlation continues to gain attention and link prevention of diabetes with prevention of AD.

Additionally, just as disrupted insulin regulation has linked diabetes mellitus to AD, disrupted plasma lipid function and arteriosclerotic cardiovascular disease (ASCVD) have been increasingly examined and linked to AD. Similar to the diabetes mellitus and AD association, evidence has shown that the same damaging properties of vascular disease on the peripheral and cardiac endothelium exist within the neurovascular system, causing damage to endothelial brain cells and astrocytes.[6] This association may not only link ASCVD to the development of AD but also to the progression of its course. Prevention of ASCVD that affects the sensitive and nonreplaceable neurons can be a primary prevention strategy to mitigate the risk of developing AD. Preventing disease and promoting health will likely give these patients more years of independent living.

These risk factors can be altered with nutritional strategies. Current practice guidelines for hypercholesterolemia, hypertension, ASCVD, obesity, and diabetes attribute a great deal of support for nutrition as part of disease prevention and treatment. In the next section, nutrition is examined more closely as a strategy for preventing AD and promoting health.

Nutrition

Evidence suggests that nutrition has a role to play in prevention by decreasing risk factors for developing AD.

Diagnostic criteria for AD

In 2011, the diagnostic criteria for AD were updated by the National Institute on Aging and the Alzheimer's Association workgroup on diagnostic guidelines for AD. The three revised phases include:

Preclinical phase
- Amyloid biomarkers are used to determine the presence of a pathophysiologic process before symptoms are manifested
- No symptoms or very subtle overt symptoms are present

Mild cognitive impairment
- Symptoms are present such as mild changes in memory, short term memory loss, misplacing objects
- Neuronal degeneration biomarkers are used to complement the diagnosis and determine the etiology of clinical findings

AD Dementia
- Cognitive and behavioral symptoms impair the patient's ability to function in daily life
- Neuronal degeneration biomarkers are used to help determine the disease progression.

Adapted from: Jack CR, Albert MS, Knopman DS, McKhann, GM, Sperling R A, Carrillo M C, Thies B, and Phelps CH. Introduction to the recommendations from the National Institute on Aging and the Alzheimer's Association workgroup on diagnostic guidelines for Alzheimer disease. 2011; *Alzheimer's and Dementia.* http://www.alz.org/documents_custom/intro_diagnostic_recommendations_alz_proof.pdf.

Summary of current AD medications[1]

Acetylcholinesterase inhibitors

(Slows the breakdown of acetylcholine, a neurotransmitter in the brain that is decreased in AD)

- **Donepezil:** Indicated for mild-to-moderate disease and moderate-to-severe disease to slow progression during all stages of disease—by slowing acetylcholine breakdown, helps to temporarily improve thinking and memory
- **Rivastigmine:** Indicated for mild-to-moderate disease (oral form), mild, moderate, and severe disease (transdermal system) to slow progression
- **Galantamine:** Indicated for mild-to-moderate disease to slow progression

N-methyl-D-aspartate receptor antagonist

(Regulates glutamate, a neurotransmitter in the brain associated with learning and memory)

- **Memantine:** Indicated for moderate-to-severe disease used alone or in combination to slow progression of more advanced decline

Diet and nutrition can serve as tools in the prevention of AD by providing protective benefits to the brain that help preserve cognition and memory through mitigation of ASCVD risk factors and reduction of AB production/deposition. Prevention through nutrition occurs in a multifaceted array of nutritional components, including vitamin deficiency prevention, oxidative stress prevention, and vascular and neuronal protection and preservation.

Research findings strongly supports diets rich in Omega 3 fatty acids, specifically high intake of oily fish, to prevent AD.[7] A diet that is high in fresh fruits and vegetables is also thought to combat AD and other chronic diseases. Specific foods, vitamins, and mineral supplements have been researched and are found to be associated with a reduced risk of AD as well (see *Summary of nutritional sources and proposed benefits for AD prevention*). The majority of data suggest that a combination of nutrition strategies, rather than a single method, may offer the most substantial preventive benefit.[8]

The Mediterranean diet encompasses intake of all the above listed nutritional categories and has substantial supportive evidence associated with its decreased risk of AD.[12-16] The diet has also been linked to decreased risk of mortality in AD as well as decreased risk of mortality from heart disease and cancer and the incidence of Parkinson disease.[14,15] The more strict the adherence to the diet, the more substantial the preventive association.[16]

Summary of nutritional sources and proposed benefits for AD prevention[7,9-13]

Fish

Omega-3 fatty acids – Resists free radicals, decreases oxidative stress and inflammation

Docosahexaenoic acid (DHA) – Higher levels of DHA in blood have been associated with up to a 50% reduced risk of AD

Grapes

Phytochemicals – Prevents oxidative stress. Additionally, phytochemicals help decrease low-density lipoprotein cholesterol and blood lipids, lower cardiovascular disease risk, and may potentially clear beta-amyloid proteins from the brain

Fresh fruits and vegetables

Phytochemicals – Prevention of oxidative stress. Benefits are from pure food sources specifically, with dietary supplements not shown to have same preventive properties

Green leafy vegetables, citrus fruits, whole grains, and liver

Folic acid – Decreases homocysteine levels preventing cell damage and death

Vitamins

Vitamins A and C – Prevention of oxidative stress, reduction of free radicals at the cellular level

Mediterranean diet

Micro- and macronutrients – Offers neuro-protection to prevent cognitive impairment

Antioxidant-rich foods and n-3 polyunsaturated fatty acids – Associated with prevention of cognitive decline

Implications for practice

Nurse practitioners (NPs) are in a position to promote preventive measures. Perhaps educating patients is not as large a task as motivating them to implement the dietary changes. Traditional ways of telling patients what to do are not always effective, and new studies show techniques such as "health coaching" have helped improve outcomes and reduce costs.[17] Taking the perspective of a "health coach" by partnering rather than dictating and creating awareness of primary prevention nutrition strategies can reduce risk factors for AD. Improved overall health, reduced cost/healthcare burden, and longevity/quality of life are additional benefits of reduced risk of AD. Primary prevention of AD through nutrition is a valid and worthy topic among patients and providers.

- Awareness first: A discussion about the relevance of primary prevention of AD should be initiated
- A health coach should be considered
- The perspective of a partner in health is advised
- Clinicians should not give up on patients, and nonadherence should not be considered a failure to produce change
- Clinicians should lead by example...personal examples on altering nutrition and reducing risk factors should be provided.

Case scenario revised

A middle-aged man walks into the clinic to establish a medical home. He complains of low back pain and depression. He is diagnosed with depression, obesity, low back pain, and hypercholesterolemia. His healthcare provider discusses current risk factors for chronic disease, including AD, and offers supportive recommendations on primary prevention with referral to a health coach. Fast forward to his early seventies, where he is active, healthy, enjoying his retirement with his wife, and enjoys volunteering at a long-term care facility providing care for patients with AD.

Primary prevention is key

Prevalence of AD is on the rise. Chronic disease can alter quality of life significantly, and AD is no different. No cure exists. Primary prevention is the key. Change is the challenge, and it goes beyond recommending a dietary change: it involves a holistic and integrative approach to behavioral and nutritional awareness by both patient and provider. NPs, as trusted primary healthcare providers, are fortunate to have the opportunity to significantly impact the quality of life of those who entrust them.

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