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# Alzheimer’s Disease: The Most Common Form of Dementia

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Abstract

Alzheimer's is a progressive disease, where dementia symptoms gradually worsen over a number of years. In its early stages, memory loss is mild, but with late-stage Alzheimer's, individuals lose the ability to carry on a conversation and respond to their environment. Alzheimer's is the sixth leading cause of death in the United States. Those with Alzheimer's live an average of eight years after their symptoms become noticeable to others, but survival can range from four to 20 years, depending on age and other health conditions. In this paper, I will discuss the risk factors/contributing factors, the role of genetics and epigenetics, pathophysiology of the disease, the role of the immune system, major treatments and complications of Alzheimer’s Disease.

Alzheimer’s Disease: The Most Common Form of Dementia

Alzheimer’s is a progressive, declining brain disease that gradually destroys memory and thinking skills. The decline in memory or other skills are severe enough to disrupt a person's ability to perform simple, everyday functions. Ultimately, this disorder destroys the ability of language skills, motor function, and resulting in death. According to the National Institute of Health, “More than 5.5 million Americans, most of them age 65 or older, may have dementia caused by Alzheimer’s. Alzheimer’s disease is currently ranked as the sixth leading cause of death in the United States, but recent estimates indicate that the disorder may rank third, just behind heart disease and cancer, as a cause of death for older people (nia.nih.gov,2019).”

**Risk Factors/Contributing Factors**

Just like any bodily system, our brains change with age. However, serious memory loss, confusion and other major changes is a sign our brains cells are failing. There are many risk factors for Alzheimer’s: such as, genetics, lifestyle behaviors and environmental exposures.

The greatest risk factors for Alzheimer’s Disease are “Age and family history. Other proposed risk factors include, diabetes, hypertension, hyperlipidemia, obesity, smoking, depression, low educational attainment, female gender, estrogen deficient at the time of menopause, physical inactivity, head trauma, high cholesterol levels, oxidative stress and neuroinflammation (McCance, Huether. pg. 520).” These risk factors contribute to Alzheimer’s disease and are considered mainly lifestyle behaviors and environmental factors. However, I feel that the two greatest risk factors for Alzheimer’s disease are any form of head trauma (environmental) and having the APOE4 allele (genetic).

**Genetics and Epigenetics**

“A mutation is an inherited alteration of genetic material. Genes, the basic units of inheritance, are composed of DNA and are located on the chromosomes. The most important constituent of DNA is the four types of nitrogenous bases. Labeled A, C, G and T. The DNA bases code for amino acids, which in turn make up protein (McCance, Huether.pg.157).” Mutation of certain genes seem to be the cause of most early onset Alzheimer’s. “Mutation of any three genes which affect amyloid-B deposition. Two of these genes, PSEN-1 and PSEN-2’s protein products are involved in the cleavage of the amyloid-B precursor protein (APP). When APP is not cleaved normally, a long form of it accumulates excessively and is deposited in the brain. With late onset form of Alzheimer’s, an important risk factor is the allelic variation of apolipoprotein E (APOE). APOE has three major alleles: e2, e3, e4. Studies have shown persons with the e4 allele are 2 to 5 times likely to develop Alzheimer’s. And persons with 2 copies of this gene are 5 to 10 times more likely to develop Alzheimer’s (McCance, Huether. pg.174).” Women are at a higher risk for developing Alzheimer’s than men. Any family history of Alzheimer’s could be a genetic component to development. One study suggest “A new mutation with PSEN1/G209A can be a pathogenic variant in an early onset Alzheimer’s patient (An, Bagyinszky, et al. 2016).” It is suggested that, “This mutation did not exist in any of the Alzheimer’s mutation databases, and it could be a new causative mutation for early onset Alzheimer’s (An, Bagyinszky, et al. 2016).”

**Lifestyle Behaviors**

 Cardiovascular issues such as heart disease, high blood pressure, myocardial infarct, and stroke are associated risk factors for the development of Alzheimer’s. Diabetes, high intake of saturated fats and a sedentary lifestyle are also linked with cognitive decline.

**Environmental Factors**

Traumatic brain injury is a major factor in the development of Alzheimer’s. Viruses and bacteria that cause illness such as HIV and Syphilis**,** andtoxins such as alcohol and cigarette smoke increase a person’s risk for development.

**Decreasing the Risk**

There are no proven ways to prevent Alzheimer’s Disease. However, regular physical exercise can help lower the risk. Exercise increases blood flow to the brain cells which deliver oxygen rich blood. “Exercise also promotes changes in brain activation, and lessons the emotional anti-stress index (Effects of Therapeutic recreation on the Brain, 2015).” Eating a heart healthy diet can drastically decrease risk for stroke and heart attack. Consume whole grains, lean meats and plenty of fruit and vegetables. Consume plenty of Omega3 fats, increase folic acid intake along with B vitamins. Moderation is the key to drinking alcohol**.** If you smoke, stop. Smoking increases the risk for stroke and heart attack. Maintain a healthy weight; keep blood pressure, cholesterol and blood sugar levels within range. Also, keep your mind active. Activities such as walking, swimming, dancing, puzzles, word games and memory training decrease the risk for developing Alzheimer’s.

**Cellular Level and Body System**

**Pathophysiology**

Microscopic changes happen in the brain causing Alzheimer’s Disease. Neurofibrillary tangles, neuritic plaques, and vascular degeneration are classic findings in an autopsied brain of an AD patient. “Neurofibrillary tangles are long proteins called Amyloid-B precursor proteins (APP). Mutations of the genes, Presenilin 1 (PS1) and Presenilin 2 (PS2), keep these genes from cleaving the Amyloid-B precursor protein from the brain. When Amyloid-B is not cleaved properly, it accumulates excessively in the brain (McCance & Huether, 2019). “Neuritic plaques are composed of degenerating nerve terminals and are found mainly in the hippocampus. Deposited within these plaques, are significant amounts of a protein called beta-amyloid. These peptides tend to stick together and form the neuritic plaques. Abnormalities in neurotransmitters such as acetylcholine, norepinephrine, dopamine and serotonin occur. High levels of beta-amyloid protein are associated with decreased levels of acetylcholine. These abnormal levels reduce the amount of acetyltransferase in the hippocampus and interferes with cholinergic innervation to the cerebral cortex (Ignatavicius & Workman, 2014).” In turn, this results in impaired cognition and the ability of recent memory and to acquire new memories. Vascular degeneration occurs in normal aging brains but accounts for partial loss of the ability of neve cells to function correctly. “Cell deterioration can lead to hemorrhage, and this pathologic change contributes to the mortality associated with this disease (Ignatavicius & Workman, 2014).”

**Immune Response**

The immune system changes during an individual’s lifespan. These changes are influenced by many factors, such as environmental conditions, nutritional status, drugs, disease, and age. As the body ages, so does its immune function. Older adults have an increased risk for many different health issues. The immune system is not located in one particular area of the body. All immune system cells are made in the bone marrow but travel to different areas of the body to mature. The immune system is influenced by many systems. These systems include the GI system, the endocrine system and especially the nervous system.

Several theories and articles are written about the cause and effects of Alzheimer’s Disease, along with treatment and prevention. One article written in 2016, (that was very interesting) reveled the correlation between high levels of stress induced cortisol and high serum IgA levels. “Patients with mild AD produce more IgA in saliva than participants without the illness, which confirms the results obtained in other studies in which patients with AD have high serum IgA level. These results support the idea that patients with AD suffer from an immune alteration which could partly explain the pathogenesis of the disease which presents with great inflammation. This produces important changes in the organism that, at the same time, are related to changes in behavioral patterns, agitation, depression, and memory loss. Moreover, the IgA could be an interesting biomarker in the diagnosis of dementia. The level of IgA in patients with AD is really high compared with the reference values in healthy adults of the same age (well above 30 mg/dl). This indicates that, there is an obvious alteration of the immune system that could be related to the cortisol production mechanism. This could be explained because when stress is not chronic, the immune response decreases as a response to acute stress. Nonetheless, in patients with AD there is chronic stress which produces an inflammation that stimulates the immune system, hence the elevated IgA production as a consequence of the inflammatory nature of the disease (de la Rubia Orti, Sancho, et al. 2016).”

According to another article in 2016, the use of activated immune cells could be the answer to reducing the risk for AD, and helping to decrease the effects current patients have with the disease. “Microbial prevalence suggests failing immune responses by immune gene variants against specific microbes. In fact, some immune gene variants have been detected significantly more often in Alzheimer patients. Failing immune responses can be corrected by activating [immune cells](https://www-sciencedirect-com.ezproxy.king.edu/topics/medicine-and-dentistry/immunocompetent-cell) outside the body (*in vitro*) for therapeutic injections. Activated immune cells digest and present microbial peptides better and differentiate naïve/resting immune cells to powerful [effector cells](https://www-sciencedirect-com.ezproxy.king.edu/topics/medicine-and-dentistry/effector-cell), which can be used for therapy. The patient’s activated immune cells can pass the [blood–brain barrier](https://www-sciencedirect-com.ezproxy.king.edu/topics/medicine-and-dentistry/blood-brain-barrier) and overcome chronic infections in the brain. Furthermore, activated immune cells can secrete a series of [neurotrophins](https://www-sciencedirect-com.ezproxy.king.edu/topics/medicine-and-dentistry/neurotrophin%22%20%5Co%20%22Learn%20more%20about%20Neurotrophin%20from%20ScienceDirect%27s%20AI-generated%20Topic%20Pages) for the restoration of neuronal circuits. Based on the encouraging results of [immunotherapy](https://www-sciencedirect-com.ezproxy.king.edu/topics/medicine-and-dentistry/immunotherapy) in a patient with late-onset AD, we hypothesize that therapy with the patient’s activated immune cells would safely benefit many Alzheimer’s Disease patients (Laumbacher, Fellerhoff, & Wank, 2016).”

**Treatments**

‘Neurofibrillary degeneration in the basal forebrain is believed to be the primary cause for the dysfunction and death of forebrain cholinergic neurons, giving rise to widespread presynaptic cholinergic denervation. Cholinesterase inhibitors increase the availability of acetylcholine at synapses in the brain. They are one of the few drug therapies that have been proven clinically useful in the treatment of Alzheimer’s disease, thus validating the cholinergic system as an important therapeutic target in the disease (Hampel, Mesulam, et al., 2018).”

The main medications used for Alzheimer’s disease, according to Alzheimer’s Disease and Dementia (2019), the Food and Drug Administration (FDA) have approved Aricept (Donepezil), Razadyne (Galantamine), Exelon (Rivastigmine), Namenda (Memantine), and Namzaric (Memantine + Donepezil). These medications are classified as cholinesterase inhibitors. “Physical activity, which include walking, swimming, and dancing, not only increases muscle tone and strength, but also decreases the mental decline in AD (Ignatavicius & Workman, 2014).” Complementary treatments include the use of mineral replacement medication. “Coenzyme Q10, Coral calcium, Ginko Biloba, Omega 3 Fatty acid, Tramiprosate, and Huperzinea are just a few that are used to help with the slowing of the disease (Alzheimer’s Disease and Dementia, 2019).”

I feel that the compound medication Namzaric would be the best medication treatment for Alzheimer’s, along with physical and memory exercise. I honestly do not feel that any of these treatments are wrong. Alzheimer’s disease is a horrible disease, and anything that can be done to slow the process or stop it entirely, should be done.

**Complications**

As stated previously, Alzheimer’s disease is a horrific disease, which happens to an individual in stages. In the 1st stages of Alzheimer’s (early), the individual is still independent, social, and active. However, he/she has trouble remembering names, misplaces personal items, loss of social engagement, and a decreased sense of smell. In the moderate stage (middle), the individual has some noted cognitive impairment, disoriented to time, place and event, depressed and agitated, increasingly dependent with ADLs, incontinent, trouble sleeping and wandering. In the 3rd stage “(severe), the individual becomes completely incapacitated or bedridden, totally dependent in ADLs, motor and verbal skills are lost, general and focal neurologic deficits, and agnosia (Ignatavicius & Workman, 2014).” Neurologically the individual becomes wholly impaired and unaware of their environment. The body gradually begins wasting and loss of muscle tone and subcutaneous tissue is apparent.

**Summary**

In summary, Alzheimer's is a progressive disease, where dementia symptoms gradually worsen over a number of years. In its early stages, memory loss is mild, but with late-stage Alzheimer's, individuals lose the ability to carry on a conversation and respond to their environment.

As the immune system changes during a person’s lifespan, these changes are influenced by many factors, such as: environmental conditions, nutritional status, drugs, disease and age.

There is no cure for Alzheimer’s, but several things can be done to decrease the risk. Regular physical exercise can help lower the risk. Eating a heart healthy diet can drastically decrease risk for stroke and heart attack. Consuming whole grains, lean meats and plenty of fruit and vegetables, along with Omega3 fats, increase folic acid, and B vitamins can also help reduce the risk of developing AD.

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