|  |  |
| --- | --- |
|  | **ABSTRACT**  Alzheimer's disease (AD) is a progressive degenerative disorder that afflicts 3 to 4 million people. It is the leading cause of dementia. Although the exact cause of the disease is not certain, studies have found that probable risk factors include age and family history. Symptoms of AD are loss of memory and retardation of basic cognitive and motor functions. Although there is presently no cure for this disease, the fourth largest killer in the United States, its symptoms may be diminished and degeneration may be slowed through treatment.  source: "An Overview of Alzheimer's Disease and Related Dementias" from Alzheimer's Assoc.  Alzheimer's disease, the most common cause of senile dementia, has many different names. These include the obvious Alzheimer's disease, and the less obvious: Alzheimer's dementia, presenile dementia, dementia presenilis, primary neurological degeneration, primary senile dementia, primary degenerative dementia, dementia of the Alzheimer's type, senile dementia of the Alzheimer's type (SDAT). 3  The German neurologist and psychiatrist that first described the the disease in 1901 was Alois Alzheimer. For his accomplishment, the disease was named after him. The features that he described and are present in all Alzheimer's patients, are tangles in the neuron fibrils and plaques on the brain. Neurofibrilary tangles are nerve filaments that clump together and create thick masses on neurons and the plaques are aggregations of the protein amyloid that also accumulate on the neurons. These plaques decrease the levels of the neurotransmitter acetylcholine, which is involved with motor functions, and, thus, impairs these functions. 4, 7  Neuritic Plaques  source: http://www.uokhsc.edu  The risk factors that have been established for the disease are genetics, the age, and the environment of a person. None of the factors have been established as absolute facts, but scientific research seems to support these hypotheses. The risk factors depend upon which category of AD each person's case falls into. the two major types include familial (one or more relatives have the disease), or sporadic (no other family member is known to have the disease). 1  The familial category includes the genetic risk factor. Due to inheritance and the genes that have been given a person from their parents, some people are more susceptible to the disease than others. Through extensive Alzheimer's research, scientists have been able to identify that there are certain genes that are vulnerable to mutations that may cause the onset of the disease. These genes are located on chromosomes 21, 14, and 1. There also exist chromosomes that simply contain genetic risk factors for the disease: chromosomes 19, 12, 6, and 17. 2  Early-onset Alzheimer's, which constitutes less than 5% of all cases, is usually associated with mutations on chromosomes 21, 14, and 1. At the same location as the gene for Down syndrome (which is a result of nondisjunction), there is the gene that codes for the protein amyloid precursor protein (APP). Mutations at this gene cause an increase in the production of beta-amyloid proteins (Aß proteins), which leads to the formation of the characteristic plaques on the brain's nerve cells. This mutation usually causes an earlier age of onset -- affecting people as young as 30 years old. Mutations similar to this happen on chromosomes 14 and 1, causing an over-production of the Aß proteins, which occur in all mutations causing Alzheimer's. 2  The genes on chromosomes 19, 12, 6, and 17 all can cause either early or late-onset of the disease. About half of patients with late-onset of AD have a mutation on chromosome 19. The gene associated with the disease on chromosome 19 codes for apolipoprotein E (ApoE), which is associated with the binding of the Aß peptides. The three alleles of ApoE are e-2, e-3, and e-4. The greatest risk of developing the disease (as well as the earliest onset) lies with the e-4 allele, since it is associated with an increase in plaques. E-3 alleles present average risk, and the e-2 allele presents an even lesser risk. Therefore, a person that has either one or two e-4 alleles, as opposed to two e-2 alleles, runs a greater risk of developing AD. 2, 7, 8  Although less understood than chromosome 19, the genes on chromosomes 12, 6, and 17 also affect the Aß deposits on the brain. The gene on chromosome 12 is associated with both early and late-onset of AD, depending upon which allele is present. The gene on chromosome 6 will cause early onset, and the gene on chromosome 17 is involved in the processing of APP. 2, 6  A theory that can basically summarizes all of the different genetic causes of Alzheimer's is the amyloid cascade hypothesis. It states that the amyloid cascade is a series of mutations, nerve cell death, and Aß production, which is hypothesized to cause AD. 2  Along with genetic risk factors, there also seem to exist some environmental factors leading to the development of Alzheimer's. This conclusion was made due to the fact that only about half of identical twins develop the disease, suggesting that only one of two people with basically the same genetic makeup might develop the disease. Also, if both twins are diagnosed, the age of onset can vary by about 15 years, again leading to outside factors. One such factor is traumatic head injuries. Although he is not diagnosed with Alzheimer's, boxer Mohammed Ali, has a type of dementia that came as a result of so many blows to the head. In addition to head trauma, it has been theorized that AD can be caused by metal exposure. This is because it has been found that AD patients have higher levels of metal, especially aluminum, in their brains. This has led researchers to believe that deodorants, antacids, and aluminum cookware could be causing Alzheimer's. Yet, although this does cause nervous tissue damage, studies have failed to conclude it as a cause. Thus, more environmental factors are being considered in the search for the exact causes of the disease. 4, 8  The prevalence of Alzheimer's Disease has been increasing, and now affects about 4 million people in the United States. It is responsible for about 100,000 deaths per year. This makes it the number four killer in adults behind heart disease, cancer and stroke. The risk involved in having the disease increases with age, for about five percent of people over age 65 are affected, whereas about fifty percent of the population over 85 have it. 1, 5, 6  The Multi-Institutional Research in Alzheimer's Genetic Epidemiology (MIRAGE) project has proven that sex and race also have effect on the risk of developing the disease. It has been found that women have a higher risk of developing the disease than do men, as do Hispanics and African Americans over whites. The statistics that they have put out are that "by age 93 women's risk is 13 percent higher than men's" and that "by age 90 African Americans were four times more likely to develop the disease, and Hispanics were twice as likely to get it". The graph below demonstrates that, because it is projected that, by the year 2050, nearly 15 percent of the population over 65 could be affected by the disease, the number of AD victims could rise to about 14 million people. 8, 9  source: http://www.uokhsc.edu  Initial symptoms of the disease are quite often dismissed as old age setting in on a person. These symptoms include depression, memory loss, lack of energy, difficulties with vision and language skills, loss of simple motor abilities, and emotional irritability or moodiness. Yet, although these symptoms all hint toward the effects of the disease, the most commonly associated symptom is memory loss. The person will first forget long term memories, then will proceed to lose his or her short term memory. This could get to the point where the patient does not even remember his or her own name. 1, 4  Because Alzheimer's Disease is a type of dementia, it is hard to differentiate between it and other degenerative diseases. Therefore, researchers have developed three different diagnostic groupings for the disease: probable, possible, and definite. In order to use the criteria given out by the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) for these three groupings, the patient usually must have impaired memory and some sort of psychological disturbance. The criteria are as follows: 1) memory impairment, language problems, impaired ability to perform motor activities, impaired recognition abilities, and loss in ability to plan and organize; 2) problems in everyday life as a result of decline from previous level of functioning; 3) problems in 1 worsen as time goes on; 4) problems in 1 are not the result of any other disease or substance; 5) problems in 1 are not associated with delirium; 6) problems in 1 are not caused by another mental illness (schizophrenia). 6, 8  Probable AD, according to the NINCDS (National Institute of Neurological and Communicative Disorders and Stroke) and the ADRDA (Alzheimer's Disease and Related Disorders Association), can be established by a standard test produced for diagnosing Alzheimer's disease, such as the Mini-Mental State Examination (MMSE) and Blessed Dementia Scale, or neuropsychological tests. The MMSE is a thirty item test that tests different areas that Alzheimer's patients would be deficient in. It is not perfect and can be wrong at times, yet helps to evaluate at what level the patient is on. In addition to taking these tests, the patient must have not suffered loss of consciousness, have difficulty understanding things, progressively lose memory abilities, be between the ages of 40 and 90, and have no other dysfunction that could be causing the disorder. These criteria are bout 90 percent accurate. Yet, the Alzheimer's association has added that the best "diagnostic tools" are interviews and clinical assessment. 6, 8  Possible AD has only three components to its criteria. They are that there exists an unexplained dementia syndrome, a second possible cause to the condition (although it may not be suspected as the cause), and progressive psychological decline with no knowledge of the cause. 8  Definite AD can only be tested by the autopsy or biopsy. The way that the disorder is assessed is by the presence of the Aß plaques and the neurofibrillary tangles mentioned earlier. 6  Because the only way to be assured that a patient has Alzheimer's disease is when they are dead, researchers have developed many tests that suggest probable or possible AD. In addition to the diagnostic criteria put out by the DSM-IV and NINCDS/ADRDA, screening tests, lumbar procedures, and brain imaging can be  used. 8  Screening tests are mainly used to rule out other causes for the patient's state. Included in these tests are blood cell count, a series of blood tests, liver function tests, tests for STDs, hormone level and vitamin tests, as well as screening for the presence of heavy metals. 6  Lumbar procedures test for the levels of certain proteins in the brain fluid. Because people with AD usually have higher than normal levels of the Aß protein, due to the presence of the plaques on the brain, tests that measure its level suggest the disease. 8  The last thing that is used to suggest diagnosis is brain imaging procedures. These procedures rule out other diseases that could be causing the symptoms that would suggest Alzheimer's disease. The MRI (magnetic resonance imagery) could rule out problems with blood vessels. In addition, these tests can indicate symptoms of AD. Computed tomographic (CT) scans can help to identify brain atrophy, which is present when a patient has the disease. Tests such as the single photon emission computed tomography (SPECT) and the positron emission tomography (PET) also indicate characteristics of Alzheimer's. 6  There is no cure for Alzheimer's disease. Therefore, any therapy that is being done is being used to lessen the effects and symptoms of the disease. In addition, because there is also no stopping the progression of the disease, the only thing that can be done is to try to slow its progression. This is what the various treatments of non-steroidal anti-inflammatory drugs, estrogen replacements, antioxidants, and acetylcholinesterase inhibitors are trying to accomplish. 4  Non-steroidal anti-inflammatory drugs (NSAIDS) could be used as a protection against Alzheimer's, due to the fact that people who regularly take them have developed the disease less often than those who have not. The reasoning behind this is that inflammation of the brain seems to promote the congregation of neurofibrillary tangles and Aß plaques. NSAIDS decrease inflammation all over the body, including the brain, causing this to be of lesser risk. Yet, they cause gastrointestinal bleeding, which causes more harm in the patient than they are worth. 8, 9  It has also been found that estrogen levels could be related to the higher level of women getting the disease. Studies have shown that increased levels of estrogen in women decrease the amount of Aß peptides, improve blood flow, and help certain brain structures to function. Thus, estrogen replacement therapy in postmenopausal women has been shown to slow the effects or prevent the disease. This therapy also has negative side effects, for it increases the risk of breast cancer by about 20 to 30 percent. 3, 8  Antioxidants are also believed to reduce symptoms of the disease. Some of the major antioxidants that are being used are vitamin E, Eldepryl, and vitamin C. They are believe to control damage to brain cells from free radicals (missing an electron). 3  Although all of these treatments seem to have positive and promising effects in the fight against Alzheimer's, the one that researchers are looking to for the most results are acetylcholinesterase (AChE) inhibitors. It was found that, in almost all cases of AD, the affected person had a lesser amount of acetylcholine (ACh) than normal people. Therefore, there had to be a way to either increase the level of ACh or inhibit the enzyme that breaks it down, AChE. Thus, the AChE inhibitors (drugs) inhibit AChE and stop it from breaking down ACh. The two acetylcholinesterase inhibitors that have been approved by the FDA are tacrine HCl (Cognex) and donepezil HCl (Aricept). 5, 6  Tacrine was the first out on the market, and did not fare too well. It only helped 10 to 30 percent of patients, for most cannot tolerate the high dosage required. Also, the drug produced side effects such as nausea, liver damage, and vomiting and cost about $4.75 per day, making it expensive and not worth the money for most patients. 5  Donepezil has been proven to be the drug of choice for most taking acetylcholinesterase inhibitors. It is taken once a day, does not cause liver damage, is better at inhibiting AChE, and costs about $4 a day. Although it only provides partial treatment for Alzheimer's, it is definitely safer, more convenient, and more cost effective than tacrine. 5  The prognosis for patients with Alzheimer's is presently not very promising. There is no cure for the disease and, although the various treatments may slow its effects, there is no way to stop its progressive deterioration of the brain and person. It will inevitably lead the patient to require 24 hour care, creating an emotional and financial burden on family members. Hopefully, in time, researchers will come up with a drug or treatment that could continue the path that present treatments are on and provide something that will be even more beneficiary. We believe that there will someday be a treatment that will make the disease almost insignificant, yet, might take decades to develop. 1  Although there are many drugs and advanced technology coming out for treating such diseases as Alzheimer's, sometimes the solution lies in much easier means of therapy. The Alzheimer's Association states that family members whose loved ones have been struck with any dementia should use the senses to stimulate the brain. This will keep the patient occupied and, hopefully, prevent further rapid deterioration. Thus, Alzheimer's disease should not be an exception. The reason, we believe, that sensory therapy would help out Alzheimer's patients, has to do with the Aß plaques and neurofibrillary tangles. If the brain is stimulated and constantly used in the areas that correspond to the senses, then less plaques and tangles should be present. This is because brain cells that are being used should not allow for as much buildup of materials (and, therefore, tangles) as would dormant tissue. Thus, it makes sense to attempt to keep the patients using their brains more than they usually would, especially in an area such as the senses to prevent this buildup. |

*This Web Site is Best viewed with 256 or more colors.*

*For More Information about Creekwatch, please contact Eric Thiel at* [*ethiel@pleasanton.k12.ca.us*](mailto:ethiel@pleasanton.k12.ca.us)