



Review Article

## Alzheimer's Disease: Know The Risk Factors

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### ABSTRACT

Alzheimer's disease (AD) is a chronic progressive neurodegenerative disorder characterized by a loss of brain function, an inability to care for one's self and, eventually death is a growing problem as the population ages. Worldwide, about 35 million people are thought to suffer from the disease, including nearly 6 million cases in the United States. The global prevalence of dementia has been estimated to be as high as 24 million, and is predicted to double every 20 years until at least 2040. Alzheimer's disease is not considered a normal part of aging. It happens over a period of time. In a person with Alzheimer's disease, neurofibrillary tangles and plaques develop causing both structural and chemical problems in the brain.

It has been estimated that up to half the cases of Alzheimer's disease worldwide may be the result of seven key modifiable risk factors: diabetes, high blood pressure, obesity, depression, cognitive inactivity or low educational attainment, and physical inactivity. Risk factors that are less firmly established include smoking, excessive alcohol consumption and drug abuse. Nearly every risk factor discussed in the article cannot be changed: Age, genetics, and sex are inevitable, but maintaining a healthy life style may reduce the risk of developing AD. An increasing amount of evidence suggests that lifestyle factors such as diet/nutrition, exercise, intellectual activity, and social engagement can affect someone's Alzheimer's risk.

**Keywords:** Alzheimer's disease, risk factors, age, diet, physical exercise

### INTRODUCTION

As dementia is getting more common worldwide <sup>[1]</sup> researchers have highlighted some important factors that affect our risk of developing different types of dementia. <sup>[2-8]</sup> Some risk factors can be changed like lowering blood pressure; other risk factors cannot be changed like genetic makeup.

Alzheimer's disease appears to disconnect areas of the brain that normally work together. Symptoms include difficulty remembering things, making decisions and

performing everyday activities. Risk factors on their own are not causes of a disease. Scientists believe that Alzheimer's disease is caused when there are too many risk factors, and they overwhelm the brain's natural self-repair mechanisms. This reduces the brain's ability to maintain healthy nerve cells. Risk factors suggest an increased chance but not a certainty that the disease will develop. Similarly, having little or no exposure to known risk factors does not necessarily protect a person from developing Alzheimer's disease. It is important to

identify the risk factors for Alzheimer's disease so that people can make lifestyle choices that help reduce the risk of developing the disease.

### **Age**

The risk of developing Alzheimer's disease increases with age. It is possible to develop dementia early in life, but the risk of developing it increase significantly as one gets older. <sup>[9-11]</sup> This increased risk may be due to factors associated with aging, such as higher blood pressure, an increased incidence of some heart diseases, changes to nerve cells, DNA and cell structure, the weakening of natural repair systems.

### **Family history and genetics**

Scientists have been aware for some time that the genes inherited from our parents may partly determine whether one will develop specific diseases. The role of genetics in the development of dementia is still not fully understood, but researchers have made some important advances in recent years.

### **Familial Alzheimer's disease (FAD)**

Early-onset familial AD is usually caused by autosomal dominant mutations in the genes for amyloid precursor protein (APP), presenilin 1 and presenilin 2. This form of AD accounts for approximately 2–5% of all AD cases. <sup>[1]</sup> First-degree relatives of patients with AD are at higher lifetime risk of developing the disease than the rest of the population. <sup>[2]</sup> A very small percentage of people with Alzheimer's disease (5-7%) have Familial Alzheimer's disease or FAD (formerly known as "early onset Alzheimer's disease"). At some point in their family history certain genes mutated and developed the abnormal characteristics that cause FAD. These inherited genes have a powerful influence: if one parent has FAD, each child has a 50 % risk of inheriting the disease, and with two parents with FAD, all of their children will go on to develop Alzheimer's disease in adulthood. These inherited genes

differentiate FAD from the more common sporadic form of Alzheimer's disease, but the disease itself is identical.

### **Sporadic Alzheimer's disease**

The sporadic form of Alzheimer's disease, which used to be called "late onset Alzheimer's disease," was formerly assumed to have no family linkages. However, it's now known that a person with a direct relative (parent or sibling) with Alzheimer's disease has a three times greater risk of developing the disease than someone who does not. The risk increases further if both parents have the disease. So aside from the FAD-related genes there are Alzheimer's disease-related genetic factors shared by family members.

People with these genetic risk factors are not in the same high-risk category as people who have the genes responsible for FAD. In fact, the risk associated with any one of these genetic risk factors is lower than the risk associated with having a parent with the sporadic form of the disease.

### **ApoE4 gene**

Other genes also contribute to the pathogenesis of this mental disorder. <sup>[4]</sup> The apoE4 allele is the only proven genetic factor so far identified in the development of both the early- and late-onset forms of AD. This factor increases susceptibility to AD but it is neither necessary nor sufficient for the development of this disease. This gene is the most important genetic risk factor for the sporadic form of Alzheimer's disease. ApoE genes regulate the production of a protein that helps carry cholesterol and other fats in the blood to the cells of the body. Of the three variants of the apoE gene (apoE2, apoE3 and apoE4), the apoE4 variant is associated with an increased risk of Alzheimer's disease.

In our cells (except ova and sperm) all genes are paired, one being contributed by the father and one by the mother. If a person's pair of apoE genes includes one

apoE4 gene, her risk of developing Alzheimer's disease is increased. However, approximately half of all people with two apoE4 genes will develop Alzheimer's disease at age 65 or older. People with no apoE4 genes can still get the disease and people with two apoE4 genes will not necessarily get the disease.

#### ***Female gender/ Removal of the ovaries***

Twice as many women get Alzheimer's disease than men. <sup>[12]</sup> Hormonal changes are not the only factor contributing to the increased incidence of Alzheimer's disease in women. On average, women live longer than men and age is a risk factor. Women are also more prone to diabetes, which is also a risk factor, and recently, a gene was identified that occurs only in women, and appears to somewhat increase the risk for Alzheimer's disease.

There may also be a connection between removal of the ovaries and the risk of Alzheimer's disease. The removal of the ovaries triggers menopause, and removes the source of most of the body's estrogen. Estrogen may protect the brain from age-related changes that could lead to cognitive impairment and dementia. This finding is inconclusive and further research is needed.

#### ***Medical history***

Specific medical conditions can increase a person's risk of developing dementia. These include multiple sclerosis, Huntington's disease, Down's syndrome and HIV. <sup>[13-15]</sup> Conditions that affect the heart, arteries or blood circulation can particularly affect a person's risk of developing vascular dementia. These conditions include mid-life high blood pressure and high blood cholesterol levels, stroke, diabetes, and heart problems such as a heart attack or irregular heart rhythms. Mid-life obesity can also increase a person's risk of developing dementia in later life. People who suffer severe or repeated head injuries are at a three-to-four-fold increased risk of

developing dementia. It is possible that deposits that form in the brain as a result of the injury may be linked to the onset of dementia.

#### ***Cardiovascular disease***

All the risk factors for cardiovascular disease (such as high blood pressure and high cholesterol levels) are risk factors for both Alzheimer's disease and vascular dementia. Strokes and mini-strokes are well-accepted risk factors for Alzheimer's disease and for vascular dementia. Other risk factors for Alzheimer's disease include: inflammatory conditions (reflecting a possible immune system malfunction), a history of clinical depression, stress, and inadequate exercising of the brain. Also cardiovascular diseases including strokes are associated with an increased incidence of dementia and AD, with the highest risk of dementia in persons with peripheral artery disease, suggesting that extensive peripheral atherosclerosis is a risk factor for AD. <sup>[16-19]</sup>

#### ***Diabetes***

Type 2 ("Adult") diabetes has been a known risk factor for Alzheimer's disease. The two diseases are linked by cardiovascular disorders, which are associated with diabetes and are risk factors for Alzheimer's disease. In people with Alzheimer's disease the use of glucose in the brains is impaired, similar to the situation in the bodies of people with type 2 diabetes. Higher BMI in middle age is a risk factor for AD and other dementias. <sup>[20-23]</sup>

Earlier studies have shown that increased blood pressure in middle age, especially if uncontrolled, was associated with a higher risk of the later development of AD. <sup>[24-25]</sup> The presence of diabetes in middle age or a longer duration of diabetes may play a key role in the development of AD and other dementias. <sup>[26-31]</sup> Anti-diabetic drugs that target the brain are now being tested in people with Alzheimer's disease.

#### ***Head injury/ Mild cognitive impairment***

Most clinicians accepted brain injuries at any age, especially repeated concussions, as risk factors for the later development of Alzheimer's disease. [32]

In mild cognitive impairment (MCI), there is a level of cognitive and/or memory impairment beyond that expected for normal aging but not advanced enough to be called "dementia" or "Alzheimer's disease." Up to 85 per cent of people with MCI, who are often in their early forties or fifties, will develop Alzheimer's disease within ten years. Therefore, MCI is an important risk factor for the disease. Researchers now know that the abnormal changes in the brain characteristic of Alzheimer's disease can begin to appear in people diagnosed with MCI twenty or more years before there are signs of dementia. Brain imaging may make it possible to detect the most at-risk individuals with MCI, and research to this end is ongoing.

#### ***Low levels of formal education***

Lower education is tied to increased risk of dementia and AD. [33-35] Several studies have shown that people with less than six years of formal education may have a higher risk of developing Alzheimer's disease. It was thought that the brain stimulation from learning provides a protective effect for the brain. New studies show that it may be that factors often associated with low educational background, such as unhealthy lifestyle, account for the risk, rather than low educational level itself. Although the reason is not clearly understood, some studies have shown that low education levels can be related to an increased risk for Alzheimer's disease.

#### ***Diet***

Diet can affect a person's risk of developing many types of illness, including dementia. A healthy and balanced diet that enables a person to maintain a normal body weight is likely to reduce the likelihood of developing high blood pressure or heart

disease, both of which put a person at greater risk of developing dementia.

Too much saturated fat can cause narrowing of the arteries, making heart attack or stroke more likely and heart attacks, stroke and vascular disease increase a person's risk of developing vascular dementia. [36] Fresh fruit and vegetables contain many vitamins and antioxidants, which may prevent heart disease and protect the brain. A number of research studies have shown that the polyunsaturated fatty acids found in oily fish might also help to protect the heart and blood vessels and lower the risk of developing dementia. [37-38]

#### ***Smoking***

Smoking has an extremely harmful effect on the heart, lungs and vascular system, including the blood vessels in the brain. This increases the risk of developing vascular dementia. More recent epidemiological research has shown that smoking is a significant risk factor for Alzheimer's disease, with smokers almost twice as likely to develop the disease as non-smokers. [39-43]

#### ***Alcohol***

People who drink excessive amounts of alcohol over a long period of time increase their risk of developing a form of dementia. [44] However, it has been suggested that moderate amounts of red wine, which contains antioxidants, might help to protect the brain against dementia and keep the heart and vascular system healthy. The risk of developing dementia and AD was reduced in light and moderate alcohol consumers but can cause brain atrophy. In heavy consumers, alcohol is shown to damage the brain. [45-48]

#### ***Physical exercise***

A good level of physical health helps to protect against many conditions, including dementia. Regular physical exercise helps to keep the body, especially heart and vascular system healthy. This

helps to reduce a person's risk of developing vascular dementia, which is caused by problems with the circulation of blood to and around the brain. Substantial evidence exists to confirm that regular and moderate exercise is a potent disease prevention and health promotion resource for the elderly.

Regular physical exercise leads to delay in onset of dementia and AD in the elderly without cognitive impairment. It has also been reported that low-intensity physical activity such as walking may lower the risk of dementia and cognitive impairment. [49-51]

### ***Environmental toxins***

Some researchers suspect that increased exposure to certain substances such as aluminum may make a person more susceptible to Alzheimer's disease. [52] Trace levels of many metals are present in the brain. Aluminum is the metal that has been most often studied in this context, and that has received the most publicity. Aluminium is extremely common within the environment, and exists in many different chemical forms, so exposure is very difficult to measure. Other metals, such as copper and zinc, may be important in the way that key proteins are processed in the brain. Most researchers no longer regard aluminum as a risk factor for Alzheimer's disease. Some researchers are still examining whether some people are at risk because their bodies have difficulty handling foods containing the metals copper, iron, and aluminum.

### ***Reducing the risk***

Although genes play an important role in the development of Alzheimer's disease, a healthy lifestyle may help us reduce the risk. A healthy lifestyle includes healthy eating, maintaining a healthy weight, taking part in regular physical activity (which can be quite modest), maintaining normal blood pressure and cholesterol levels and participating in activities that involve socializing and

stimulating brain activity. [53] Avoid obesity and weight gain by eating healthy and taking exercise. Being physically active for at least 30 minutes, five times a week - not only will this help reduce your risk of dementia but also your risk of heart disease and diabetes.

## **CONCLUSION**

Alzheimer's disease represents an important public health issues, especially in old age. There's no proof that lifestyle prevents Alzheimer's disease. Still, there is no downside to eating healthy and staying physically and mentally active.

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