

## Alzheimer's Disease and Risk Factors

### What are risk factors?

Many diseases have specific causes, for example, a virus causes measles. However, for many chronic disorders (long-lasting conditions such as Alzheimer's disease), the causes remain uncertain. In their search for answers, scientists look for factors that appear to be linked to the development of a disease. These are "risk factors"—if they are present, there is an increased chance, but not a certainty, that the disease will develop. **It is important to note that risk factors are not necessarily causes of the disease.**

Risk factors are characteristics of the person, their lifestyle and environment that contribute to the likelihood of getting the disease. They can include family background, work history or exposure to a substance or product. Some risk factors can be modified (for example, lowering blood pressure); other risk factors cannot be modified (for example, one's age or family history).

### How are risk factors determined?

Two types of studies are used to determine risk factors. One approach is to study people who already have the disease (such as Alzheimer's disease) and compare them with persons without the disease, who are otherwise similar in age, gender and other characteristics. This is known as a *case-control study*. Information is gathered on their personal and family characteristics, as well as on past exposures that may have occurred through lifestyle and work. Risk factors that are more frequent in the diseased than the non-diseased group can be identified. This method was used in the first analysis of risk factors for Alzheimer's disease from the Canadian Study of Health and Aging (CSHA)<sup>1</sup>.

The second approach is to monitor a group of healthy people over a long period of time. This is known as a *cohort study*. From this group, people who have a particular characteristic or who were exposed to a particular substance are compared to those without the characteristic or exposure to detect any difference in the rate at which the two groups develop a disease. Lifestyle factors (such as diet) as well as family and work histories are examined in those with the disease and those without the disease. Factors known to be associated with a specific disease are of particular interest. In this way, characteristics and exposures that are associated with the occurrence of the disease can be identified. This approach was used in the second analysis of risk factors for Alzheimer's disease from the CSHA (CSHA-2)<sup>2</sup>.

Data from CSHA-2 have been published identifying new areas of reduced risk for Alzheimer's disease. These preliminary findings are important because they indicate lifestyle choices that can be made that would help protect against Alzheimer's disease.

### What are the risk factors associated with Alzheimer's Disease?

#### Age

Age is the most important risk factor. As we age, our body's self-repair abilities become less efficient. This change occurs in the brain at different rates in different people. The CSHA provides evidence to support age as a risk factor. The following chart shows the older you become, the higher the risk for Alzheimer's disease.

1 in 20 Canadians over age 65 is affected by Alzheimer's disease

- 1 in 100 between ages 65-74
- 1 in 14 between ages 75-84
- 1 in 4 over age 85<sup>3</sup>

## Family History

We know that the majority of cases of Alzheimer's disease in people over the age of 65 are of the sporadic (or "late onset") form, suggesting that the disease has no family link. However, about seven per cent of the Alzheimer population have "Familial" (FAD) or "early onset" Alzheimer's disease. FAD is identical to the sporadic form but it occurs largely due to the inheritance of certain genes which at some point in the family's history "mutated" from having normal to abnormal characteristics. In FAD, this means that if a parent is affected, each child has a 50 per cent chance of inheriting the disease gene and those children will go on to develop Alzheimer's disease in adulthood.

Please refer to [Alzheimer's Disease and Heredity](#) for more information.

### • ApoE Gene

Apart from the mutated genes responsible for FAD, the most important genetic risk factor for both the familial and sporadic forms of Alzheimer's disease is the apoE4 gene. The apoE4 gene is not, however, an abnormal gene.

Everyone has a double set of genes, one from each parent. ApoE4 is one variant of the apoE gene, the others being the benign apoE2 and apoE3 genes. If a person's pair of apoE genes includes one apoE4, they have three times the normal risk of developing Alzheimer's disease, but if they carry two apoE4 genes the risk increases to ten times. However, people with no apoE4 genes can still get Alzheimer's disease and people with two apoE4 genes will not necessarily get the disease. Although the genes are there from birth, they can't cause Alzheimer's disease on their own. The brain has to reach a certain critical age for the disease to occur.

Researchers are actively looking for evidence of other quite normal genes that predispose one to Alzheimer's disease, but it seems unlikely that these still to be discovered genes will be as important a risk as the apoE4 one.

## Diabetes

It has been known for some time that type 2 (adult) diabetes is a risk factor for Alzheimer's disease. It was generally assumed that this was because the blood vessel and heart disorders associated with diabetes are also risk factors for Alzheimer's disease. It is also known that the utilization of glucose is impaired in the brains of people with Alzheimer's disease, somewhat resembling the situation in the bodies of people with diabetes. New research tells us that the impairment in the Alzheimer brain may be because the brain is in a sort of diabetic state, even though the person may not be diabetic in the ordinary sense. It seems that in the brain of a person with Alzheimer's disease, either the production of insulin in the brain is reduced for some reason or the brain cells are becoming insensitive to insulin.

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## Down Syndrome

Almost all individuals with Down syndrome over the age of 40 have changes to brain cells typical of Alzheimer's disease. Alzheimer's disease usually develops when these individuals are in their 50s or 60s.<sup>4</sup>

Please refer to the Alzheimer Society's Information Sheet on [Alzheimer's Disease and Down Syndrome](#) for more information.

## Mild Cognitive Impairment (MCI)

In MCI, there is a level of cognitive and/or memory impairment beyond that expected for normal aging but not sufficiently advanced to be called "dementia" or "Alzheimer's disease". It is estimated that 85% of people with MCI will develop Alzheimer's disease within ten years, making MCI an important risk factor for the disease. As researchers believe that abnormal changes in the brain may begin as early as 5-10 years before there are signs of Alzheimer's disease, brain imaging may make it possible to detect the most at-risk individuals with MCI. Research into the progression of MCI is ongoing.

## Head Injury

Brain injuries, especially repeated concussions, are risk factors for the later development of Alzheimer's disease.

## Low Levels of Formal Education

Several studies have shown that people who have less than six years of formal education appear to have a higher risk of developing Alzheimer's disease. Education as a protective factor requires more study to determine whether it is education itself that makes a difference or other factors related to it (e.g., low income level).

## Aluminum

Most researchers no longer regard aluminium as a risk factor for Alzheimer's disease. However, some researchers are still examining whether some people are at risk because their bodies have difficulties in handling foods containing the metals copper, iron, and aluminium.

## Menopause in Women

Twice as many women get Alzheimer's disease than men. This is partly due to their living longer than men on average, partly because women are more prone than men to get diabetes, but also in large part because in post-menopausal women there is a decline of the important hormone estrogen. For many years, estrogen has been prescribed to relieve symptoms of menopause. Despite a recent large-scale clinical study on women which recommended discontinuation of Hormone Replacement Therapy (HRT) because it was both ineffective and had potentially dangerous side effects, a number of clinical researchers continue to regard it as worthy of further study. Any decision regarding the use of HRT should be made in consultation with a physician.

## Other Risk Factors

In addition to the risk factors described above, all of the following have been documented as risk factors for Alzheimer's disease: chronic inflammatory conditions (such as certain forms of arthritis), a history of episodes of clinical depression, strokes or "ministrokes", high cholesterol, high blood pressure, stress, inadequate exercising of the brain and obesity. Risk factors that are less firmly established include

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smoking, excessive alcohol consumption and taking drugs of abuse.

## Reducing the risk

Living a healthy lifestyle may help reduce one's overall risk of developing Alzheimer's disease. A healthy lifestyle includes healthy eating, maintaining a healthy weight, taking part in regular physical activity, maintaining normal blood pressure and cholesterol levels and participating in activities that involve socializing and stimulating brain activity. In studies of identical twins (who share the same genes) it was found that about 60% of the overall risk for sporadic Alzheimer's disease comes from lifestyle and not genetics. For more information on reducing your risk, see the Healthy Brain section.

## What is our current understanding of risk factors?

In general, scientists today believe that Alzheimer's disease is caused when the combined effects of various risk factors cross a certain "threshold" and overwhelm the natural self-repair mechanisms in the brain, thus reducing the brain's ability to maintain healthy nerve cells.

It is important to remember that exposure to any or even to all of the known risk factors does not mean that a person will develop Alzheimer's disease. Similarly, having little or no exposure to known risk factors does not necessarily protect a person from developing Alzheimer's disease. Further research is the key to helping us deepen our understanding of the role of risk factors in developing Alzheimer's disease.

## Need further information?

For more information on risk factors, download the following PDF file:

- [A Report on Alzheimer Disease and Current Research](#) by Dr. Jack Diamond, Scientific Director, Alzheimer Society of Canada, November 2006 (23 pages). Sheets are available from your local Alzheimer Society.

## References:

1. *Canadian Study of Health and Aging: Risk factors for Alzheimer's Disease in Canada*. Neurology 1994; 44:2073-2080.
2. *Risk Factors for Alzheimer's Disease: A Prospective Analysis from the Canadian Study of Health and Aging*, American Journal of Epidemiology 2002; Vol. 156, No. 5, 445-453.
3. *Canadian Study of Health and Aging Working Group. Canadian Study of Health and Aging: study methods and prevalence of dementia*. Canadian Medical Association Journal 1994; 150:899-913, and personal communication, CSHA.
4. *Preventing Dementia*, S.E. Black, C. Patterson, J. Feightner, The Canadian Journal of Neurological Sciences 2001; 28: Suppl. 1—S56-S66.

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