

Alzheimer's disease - latest research

Alzheimer's disease is the most common form of dementia in the elderly. It is a progressive and eventually fatal disease of the brain. It impairs higher brain functions such as memory, thinking and personality. Current research is looking at causes, treatment and possible prevention of Alzheimer's disease.

Alzheimer's disease is most commonly sporadic, affecting one in 25 Australians aged 60 years and over. However, rare genetic mutations can cause an inherited form of the disease.

Alzheimer's disease causes changes in the brain

Brain cells or neurones 'talk' to each other through connections called synapses. In Alzheimer's disease, these connections are broken and ultimately disappear in the parts of the brain where thinking occurs.

Research has found that people with Alzheimer's disease have damaged brain cells, called 'tangles', and deposits between the cells, called 'amyloid plaques'. These plaques are mostly made up of a protein called beta amyloid or 'A-beta'. A build-up of this otherwise normal protein is thought to cause the damage.

The beta amyloid protein can damage brain cells in different ways, including:

- Converting oxygen into hydrogen peroxide – a form of bleach – which then oxidises or corrodes brain cells
- Signalling to brain cells to self destruct
- Interfering with the normal transmission of messages between brain cells, particularly the parts of the brain with memory and reasoning.

Researchers are trying to work out why this build-up of amyloid plaques occurs in some people and not others. They are also trying to find ways to reduce or abolish the toxic effects of this protein.

Established risk factors for Alzheimer's

The cause or causes of Alzheimer's disease are not known. However, some risk factors have been identified. Well-established risk factors for Alzheimer's include:

- **Age** – the risk of developing Alzheimer's doubles for every five years over age 65. For people aged 70–74 years, there is a 1 in 30 chance, compared to a 1 in 3 chance for people aged 90 to 94 years.
- **Genetic history** – early-onset Alzheimer's is a very rare form of the disease that can occur in people between the ages of 30 and 60. In the 1980s, researchers found that changes in certain genes cause early-onset Alzheimer's. A person has a one in two chance of developing early-onset Alzheimer's if one parent has any of these genetic mutations.
- **Genetic conditions** – many people with Down syndrome over the age of 40 will develop Alzheimer's disease at a relatively early age. This is most likely due to an accelerated build up of amyloid linked to the presence of an extra copy of the amyloid precursor protein gene, the 'parent' molecule of beta amyloid.

Possible risk factors

Other risk factors for Alzheimer's have been suggested, but not all have been proven. Some possible risk factors include:

- **Head injury** – especially more severe head injuries
- **Head size** – people with a smaller head may be at a higher risk of Alzheimer’s disease
- **Vascular risk factors** – factors that affect the vascular (blood vessel) system may also increase the risk of Alzheimer’s; these may include things such as smoking, hypertension and diabetes
- **Diet** – a diet high in saturated fats may increase risk.

Research into treatments

Research into Alzheimer’s is focused on four possible treatments, which are:

- **Increase the efficiency of the damaged nerve cells** – the drugs currently used are donepezil hydrochloride (Aricept) and memantine hydrochloride (Namenda, Ebixa). They bolster the efficiency of the nerve cells most affected by Alzheimer’s disease. However, the effects are short lived and don’t cure the disease.
- **Prevent production of beta amyloid proteins** – researchers are searching for molecules that inhibit processing of the ‘parent’ molecule of the beta amyloid protein, to reduce the production of the proteins.
- **Protect nerve cells from the damaging effects of hydrogen peroxide** – studies using vitamin E have shown small but significant improvements in function in one group of Alzheimer’s disease sufferers. Researchers are testing a range of antioxidants to see if they help protect nerve cells. Other research is aimed at preventing interactions with the metals copper, zinc and iron, which are needed for normal brain function, but can also cause the beta amyloid to become toxic.
- **Inhibit the build-up of beta amyloid proteins** – researchers believe that beta amyloid proteins may become toxic as they build up. If the accumulated proteins could be broken down, they may be less harmful.

Research into risk factors and prevention

Many areas are being researched as possible risk factors, which may help identify ways to delay or prevent the onset of Alzheimer’s disease. Areas of research include:

- Cholesterol
- High blood pressure
- Diabetes
- Gender and hormones
- Brain activity
- Physical activity
- Antioxidants and nutrition.

Cholesterol

Some research has suggested a connection between high blood cholesterol levels and a higher risk of Alzheimer’s. This caused researchers to ask whether drugs that lower blood cholesterol might also lower the risk of Alzheimer’s. The most common drugs used to lower blood cholesterol are called statins. However, clinical studies have not shown reduced risk of Alzheimer’s in long-term users of statins.

Other research has found that a high level of the amino acid homocysteine is associated with an increased risk of developing Alzheimer’s. High levels of homocysteine are known to increase the risk of heart disease.

High blood pressure

There may be a link between high blood pressure, other stroke risk factors and Alzheimer’s disease. High blood pressure and other stroke risk factors – age, diabetes and cardiovascular disease – can damage blood vessels in the brain and reduce the brain’s oxygen supply. The resulting ‘oxidative stress’ may accelerate the build-up of beta amyloid.

Diabetes

Studies show that diabetes is associated with several types of dementia including Alzheimer's and vascular dementia (a type of dementia associated with strokes). Alzheimer's and type 2 diabetes share several characteristics, including deposits of a damaging amyloid protein – in the brain for Alzheimer's and in the pancreas for type 2 diabetes. Scientists are learning more about the possible relationships between these two diseases.

Gender and hormones

It is known that women have a higher risk than men of developing Alzheimer's disease, even allowing for the longer average lifespan of women. Researchers are examining the effect of various hormones on the brain, including oestrogen.

Some studies have suggested that women who take oestrogen-based hormone replacement therapy (HRT) have a lower risk of developing Alzheimer's disease, while one recent study suggested a higher risk where oestrogen levels are low in the brain, not just in the blood. However, another study has shown that the risk of dementia does not reduce with oestrogen-only HRT, and increases slightly with combination oestrogen and progesterone therapy.

Brain activity

Keeping the brain active is associated with reduced risk of age-related Alzheimer's, but it is not yet clear why this is the case. Research is looking into:

- Mentally stimulating activities and how they might protect the brain. It is thought that these activities might help the brain become more adaptable and flexible in some areas of mental function so that it can compensate for declines in other areas.
- Reduced involvement in intellectual stimulation, which could reflect very early effects of the disease.
- Other lifestyle issues. People who regularly engage in mentally stimulating activities might have other lifestyle features that may protect them against Alzheimer's.

Physical activity

Research in animals and humans has shown that both physical and mental function improve with aerobic fitness. For example, some research has found that walking was particularly beneficial. In one study, a walking group became more physically fit than those who were assigned to a stretching and toning group. The walkers also showed greater improvements on tests of planning, scheduling and decision making.

Antioxidants and nutrition

Research is continuing into the role of nutrition and nutritional supplements in Alzheimer's disease. Areas of research include:

- **Antioxidants** – these may protect brain cells against the damaging effects of hydrogen peroxide as beta amyloid proteins break down. Vitamin E has shown some promise, but very high doses of vitamin E (above 1,000 units per day) can actually increase the risk of having a stroke. The herbal supplement ginkgo biloba is also being investigated for its antioxidant properties, but there is no evidence that it will cure or prevent Alzheimer's.
- **Fats in food** – a high intake of saturated fats increases the risk of diabetes, hypertension and other vascular conditions, which are thought to be associated with Alzheimer's. Research is investigating how diet interacts with Alzheimer's.
- **B-group vitamins** – people with low levels of folic acid (folate) or vitamin B12 appear to be at higher risk of Alzheimer's disease. A deficiency in either vitamin may allow an increase in the levels of an amino acid called homocysteine, which is known to be a risk factor for heart disease.
- **Sage** – the herb reputedly boosts memory. It has been shown that sage acts as a cholinesterase inhibitor, the same behaviour shown by three drugs licensed for Alzheimer's disease.
- **Aluminium** – there is no evidence that aluminium in the diet or environment increases the risk of Alzheimer's, but research is continuing.

Vitamins and herbal supplements can have powerful side effects and interact with other medication. Discuss taking any supplements with your doctor first.

Steps that may help prevent dementia and Alzheimer's disease

It is not possible to cure dementia. There is no proven way to prevent dementia, including Alzheimer's disease. However, research has shown that some measures may reduce the risk by either delaying or preventing the onset of dementia.

Many of these steps have proven health benefits for other conditions, even if they do not ultimately protect against Alzheimer's disease. Suggestions include:

- Avoid head injury – always wear a seatbelt and use protective headwear for sports.
- Monitor and lower cholesterol and homocysteine levels.
- Monitor and control high blood pressure.
- Control diabetes and maintain a healthy weight.
- Limit saturated fats in your diet.
- Enjoy a diet high in antioxidants from fruits and vegetables.
- Maintain adequate dietary vitamin E and consider supplements (not more than 400mg a day) on the advice of your doctor.
- Maintain adequate B12 and folic acid intake and consider supplements on the advice of your doctor.
- Enjoy a moderate alcohol intake if you drink alcohol.
- Maintain social and intellectual activities.
- Exercise regularly.
- Don't smoke.

Where to get help

- Your doctor
- National Dementia Helpline Tel. 1800 100 500
- The Mental Health Research Institute of Victoria Tel. (03) 9388 1633
- Your local community health service
- Your local council
- Aged Care Assessment Services (contact via DHS) Tel. (03) 9606 0000

Things to remember

- The cause of Alzheimer's disease is not known and there is no cure.
- Research has identified many risk factors for Alzheimer's disease.
- Activities that may prevent or delay Alzheimer's disease will also benefit your overall health.

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Mental Health Research Institute

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