Genes and dementia
Introduction

This information is for anyone who wants to know more about the link between genes and dementia. This includes people living with dementia, their carers, friends, and families.

The booklet gives an overview of what genes are and how they are involved in the different diseases that cause dementia, along with information on genetic testing and current research.

The information here does not replace advice that doctors, pharmacists, or nurses may give you. If you are worried about your health, including memory and thinking problems, speak with your doctor as soon as possible.

The booklet was updated in September 2022 and is due to be reviewed in October 2024. It was written by Alzheimer’s Research UK’s Information Services team with input from lay and expert reviewers. Please get in touch using the contact details below if you’d like a version with references or in a different format.

If you have questions about dementia or dementia research you can contact the Dementia Research Infoline call 0300 111 5 111 email infoline@alzheimersresearchuk.org Or write to us using the address on the back page.
What is dementia?

The word dementia describes a group of symptoms including memory loss, confusion, mood changes and difficulty with day-to-day tasks.

There are a number of different causes of dementia, including Alzheimer’s disease, vascular dementia, dementia with Lewy bodies and frontotemporal dementia. Alzheimer’s is the most common cause of dementia, accounting for around two in every three cases.

For more detailed information on dementia, ask for our leaflet ‘All about dementia’ or talk to your doctor.

What role do our genes play in dementia?

As dementia is so common, many of us will have a relative living with the condition – but this does not mean we will develop it too.

Dementia is caused by diseases that affect the brain, such as Alzheimer’s disease. The likelihood of developing one of these diseases will usually depend on a complex mix of factors like our age, medical history, and lifestyle, as well as our genes. Most cases of dementia are not directly caused by genes we inherit from our parents.
What are genes?

Genes determine our traits, such as our eye colour and height. In some cases, they can determine whether we will develop a disease or not. They are “passed on” or inherited from our parents.

Every cell in our body contains thousands of genes. Each gene is a portion of DNA ‘code’, which holds the information our cells need to make a specific protein. These proteins are the building blocks of life. They make up our tissues and organs, and many have specific functions, like carrying messages between our nerve cells.

Risk genes

The DNA code in our genes naturally varies from person to person. Often this variation has no effect on us, but sometimes the DNA code can contain differences that slightly alter the protein made by a particular gene, causing it to work differently. This can lead to changes in processes in our cells, which may increase (or sometimes decrease) our likelihood of developing a disease. These are known as risk genes.

If we inherit risk genes from our parents, this does not mean we will definitely get dementia. This is because a person’s risk of developing dementia is a combination of their age, genes, lifestyle, and environment. We cannot change our age or genes, but some research has found that even if you carry a risk gene, there are still things you can do to reduce your risk.

Faulty genes

In very rare cases, a person may inherit a gene that does not work properly from one of their parents. This faulty gene, sometimes called a mutated gene, can cause a person to develop a disease no matter what other risk factors they have. Rare types of Alzheimer’s disease, and some cases of frontotemporal dementia, can be caused by faulty genes and are passed down from an affected parent. Someone who carries one of these rare mutations is extremely likely to develop the disease during their lifetime. Around one in 100 cases of dementia are caused by inherited faulty genes.

You can find out how to reduce your risk of developing dementia by asking us for ‘Reducing your risk of dementia’ information. Contact details can be found on the back of this booklet.
Genes and Alzheimer’s disease

Late onset Alzheimer’s disease
Late onset Alzheimer’s disease affects people over the age of 65. It is the most common type of Alzheimer’s (causing 19 out of 20 cases) and evidence suggests it is caused by a combination of risk factors including age and lifestyle.

Our genetics also play a part, since people often inherit one or more risk genes that make the disease more likely (but not certain).

To date, scientists have found versions of over 75 different genes that are associated with an altered risk of developing Alzheimer’s disease. However, having one of these versions may only have a small effect on our overall risk. There is still a lot to be understood about these genes and their role in the development of late onset Alzheimer’s.

The best understood risk gene, with the largest effect on Alzheimer’s risk, is called APOE. This gene makes a protein that helps keep our brain cells healthy. There are three different versions of it – APOE2, APOE3 and APOE4 – and everyone carries two copies of it - one from each parent.

People who inherit one copy of APOE4 (roughly one in four people) are around three times more likely to develop late onset Alzheimer’s disease. About one in 50 people inherit two copies of APOE4 – one from each parent. They may be more than eight times more likely to develop Alzheimer’s. However, due to other contributing factors, such as age and lifestyle, people who inherit APOE4 – from one or both parents - still may never develop the disease.

Late onset Alzheimer’s is not directly inherited through faulty genes.

Is genetic testing available?
Genetic tests can be used to tell whether someone has inherited a gene linked to a particular disease, and to estimate their chances of developing that disease later in life. Genetic testing for Alzheimer’s disease risk genes is not available on the NHS. This is because most of the genes discovered so far only have a relatively small effect on someone’s overall risk of developing late onset Alzheimer’s disease, and many people who inherit these genes will not develop it. Equally, people who do not have risk genes may still develop the disease.
Young onset Alzheimer’s disease

Around one in 20 people with Alzheimer’s disease are diagnosed with the condition at a younger age, usually in their 50s or early 60s. For many cases of young onset Alzheimer’s, the cause is still unclear but is likely due to a complex interaction of genes and lifestyle.

A very small number of young onset Alzheimer’s cases are caused by a faulty gene passed down in families. This is called ‘familial’ Alzheimer’s disease (FAD) or ‘young onset inherited’ Alzheimer’s. It usually affects many members of the same family at every generation, typically in their 30s, 40s or 50s. The faulty gene is passed down directly from a parent who has the disease to their child, it does not skip generations.

So far three genes have been linked to ‘young onset inherited’ Alzheimer’s disease. These genes are called:
- amyloid precursor protein (APP)
- presenilin 1 (PSEN1)
- presenilin 2 (PSEN2).

These genes are involved when cells produce a protein called amyloid. If the gene is faulty, it causes an abnormal build-up of amyloid in the brain, which forms clumps or ‘plaques’ which damage brain cells and are part of how Alzheimer’s disease develops.

People who carry one of these faulty genes will develop Alzheimer’s, and their children have a 50% (one in two) chance of inheriting the gene and developing the disease too. It is important to stress that faulty versions of these genes are very rare and only account for 1% (one in 100) cases of the disease.

The Familial Alzheimer’s Disease (FAD) Support Group helps families affected by mutations in the PSEN1, PSEN2 or APP genes. More information can be found at www.raredementiasupport.org/familial-alzheimers-disease
You can also email contact@raredementiasupport.org or call on 0203 325 0828.
Genes and frontotemporal dementia

Frontotemporal dementia (FTD), sometimes called Pick’s disease, is a rarer type of dementia mostly affecting people under the age of 65 years.

The symptoms of FTD can be quite varied but include changes to behaviour, communication and language. There are different types of FTD that have different underlying causes.

To find out more information about FTD, please ask us for ‘What is frontotemporal dementia?’. Contact and order details can be found on the back of this booklet.

Some people with FTD have a family history and the condition may be inherited in some of these families. In a particular form called ‘behavioural variant’ FTD, a third to half of people affected may have a family history. This figure is thought to be much lower for other types of FTD.

Overall, around one in 10 cases of FTD are thought to be caused by a faulty gene passed down in families. Several genes have been found that causes these inherited types of FTD, including:

- **MAPT (tau)**
- **GRN (progranulin)**
- **C9ORF72**

Mutations in the MAPT gene can cause the protein it makes, called tau, to behave abnormally, forming toxic clumps that can damage brain cells. Researchers are less certain about how mutations in GRN (progranulin) and C9ORF72 cause the disease.

The C9ORF72 gene can cause people to develop motor neurone disease, FTD or both conditions and may affect members of the same family differently.

In cases of FTD that are not caused by these faulty genes, researchers are still studying which risk factors might be involved in the development of the disease.
Genes and other dementias

Vascular dementia
Vascular dementia is caused when blood flow to the brain is reduced, damaging nerve cells. This can happen as a result of a stroke or damage to blood vessels deep in the brain. The majority of cases of vascular dementia are not caused by faulty genes.

However, there are risk genes that affect a person’s chances of having a stroke, heart disease, high blood pressure or high cholesterol – which can all contribute to vascular dementia. But age and lifestyle factors - such as smoking, lack of exercise, drinking alcohol over the recommended limits, and an unhealthy diet - can also increase someone’s risk.

There are rare genetic disorders that can cause vascular dementia by damaging blood vessels in the brain. One is called CADASIL (which stands for ‘cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy’) which can be passed down through families. CADASIL only affects around one thousand people in the UK.

To find out more about vascular dementia, you can ask for our booklet ‘What is vascular dementia?’.

Dementia with Lewy bodies
Dementia with Lewy bodies (DLB) is caused by a build-up of abnormal proteins called Lewy bodies in the brain. It can have symptoms similar to those seen in people with Parkinson’s disease.

Age is currently the biggest known risk factor for DLB, although research is underway to find out whether genes may also play a role. To find out more about dementia with Lewy bodies, you can ask for our booklet ‘What is dementia with Lewy bodies?’.

Dementia and Down syndrome
People with Down syndrome are born with an extra piece of DNA in all their cells. This means they have an extra copy of the APP (amyloid precursor protein) gene. This leads to the build-up of amyloid plaques in the brain, which play a role in the development of Alzheimer’s disease.

While not everyone with Down syndrome will go on to develop symptoms of Alzheimer’s, most people with the condition over the age of 40 will have amyloid build-up in their brains. It is estimated that about half of people with Down syndrome develop symptoms like memory loss, usually in their 50s and 60s.

To find out more about Down syndrome and dementia you can contact Down’s Syndrome Association helpline on 0333 121 2300, or visit their website www.downs-syndrome.org.uk
Information about genetic testing

Having a test to look for a faulty gene that causes dementia is only appropriate for a very small number of people. This is because inherited dementia is rare.

If you are worried that you have a strong history family of young onset Alzheimer’s disease or frontotemporal dementia, you can speak to your doctor about this.

Deciding to take a genetic test to see if you have an inherited type of dementia is a big decision and needs very careful thought.

Some people may not wish to know if they carry a faulty gene that causes dementia. Others may feel it would help them and their families to plan for the future.

It is also worth bearing in mind that not all mutations that cause dementia have been identified, meaning that some families may have many affected members, but no mutation can be found. Therefore, a negative test result cannot always rule out a genetic cause of a disease.

If a test is appropriate, your doctor should be able to refer you to a genetic counsellor or specialist.

This could be a cognitive neurologist or memory clinic psychiatrist. They will discuss with you the pros and cons of taking a test and what will be involved. They will also tell you where the results will be kept, who they will be shared with, and what the next steps would be.

For people found to have a genetic mutation that causes dementia, these discussions will also cover the options available if you are considering starting a family.

Within one family, any blood relative who may be at risk of inherited dementia can be offered genetic counselling.

Several months of genetic counselling are required before someone can undergo genetic testing. This allows time to discuss what a potential test result may mean, considering things like finances, insurance, and family planning. Genetic testing is not the right decision for everyone, and you can still choose to decline testing after a period of genetic counselling.

To find out more about genetic testing and what support is available you can visit the Rare Dementia Support website at www.raredementiasupport.org, or contact them on 0203 325 0828.
How can I reduce my risk of dementia?

For the majority of people, genes are only one factor that affects their risk of dementia. There are many other factors involved, such as age and lifestyle. While we cannot change our age or genes, research has suggested that up to 40% of all cases of dementia could be prevented through lifestyle changes.

There are steps we can take that may help lower our risk of dementia:

- Don’t smoke
- Control high blood pressure
- Drink fewer than 14 units of alcohol per week
- Eat a healthy balanced diet
- Maintain a healthy weight
- Keep cholesterol at a healthy level
- Keep active and exercise regularly

For more information about how you can reduce your risk of dementia, contact us for our free booklet ‘Reducing your risk of dementia’, or speak to your doctor.

Research into genetics

Alzheimer’s Research UK has funded more than £10.2 million of pioneering projects focussed on understanding the genetic basis of dementia.

Discovering new genes and understanding how they work provides vital clues about the cause of diseases like Alzheimer’s, taking researchers closer to developing new treatments.

Our researchers have already discovered over 75 risk genes for diseases like Alzheimer’s. We are helping them to build on these discoveries to develop effective new treatments for these diseases.

Through research we will bring about breakthroughs that will change lives. Thanks to the generosity of our supporters, we will continue to fund many more studies into the genetics of dementia.
Alzheimer’s Research UK is the UK’s leading dementia research charity dedicated to making life-changing breakthroughs in diagnosis, prevention, treatment and cure.

We provide free dementia health information, like this booklet and others. If you would like to view, download or order any of our other booklets please details below.

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