

This fact sheet describes neurofibromatosis type 2 and includes a discussion of the symptoms, causes and available testing.

### In summary

- Neurofibromatosis type 2 (NF2) is a genetic condition that is characterised by the development of non-cancerous tumours (called schwannomas) on the nerves that control hearing and balance (*auditory and vestibular nerves*).
- NF2 is caused by mutations in the *NF2* gene on chromosome 22 and is inherited in an autosomal dominant fashion.
- Approximately 50% of the people with NF2 are the first in their family to have the condition due to a spontaneous mutation in the gene.

### WHAT IS NEUROFIBROMATOSIS TYPE 2?

Neurofibromatosis type 2 (NF2) affects around 1 in 33,000-40,000 people worldwide.

NF2 is characterised by the development of non-cancerous tumours (called *schwannomas*) on the nerves that control hearing and balance (*auditory and vestibular nerves*). The tumours usually develop in late adolescence but some people do not develop problems until their 40's and 50's. In the majority of people, the schwannomas develop on both sides (*bilateral*) but not necessarily at the same time, so that there may be hearing loss of different degrees in both ears. For others, schwannomas develop on only one side (*unilateral*) and other nerves may be affected by different types of tumours that impact on the control of swallowing, speech, eye movements and facial sensations. Tumours may also occur in the central nervous system: the brain and spinal cord.

In about 50% of cases, the person with NF2 is the first person in the family to have the condition.

- NF2 in this person is caused by a new mutation occurred in one *NF2* gene copy during the formation of the egg cell or sperm cell from which they arose, or during or shortly after conception
- These changes are called 'spontaneous mutations' and the condition is described as occurring sporadically
- That person will then be able to pass on the faulty *NF2* gene copy to his/her children.

If the spontaneous mutation has occurred shortly after conception, when the cells of the embryo have already started to divide, not all of the person's cells may contain the mutation. The person is said to be 'mosaic' for the *NF2* mutation. Mosaicism means that a person has a mixture of cells with different genetic information.

- People who are mosaic may have a milder form of the condition and may only develop tumours on one side of their body
- The *NF2* mutation may not be in all of their eggs or sperm so the chance of passing the condition on to a child will be less than 50%.

***Despite sharing the same name with neurofibromatosis type 1 (NF1), they are separate conditions with different genes and symptoms involved.***

## WHAT CAUSES NEUROFIBROMATOSIS TYPE 2?

The *NF2* gene codes for a protein (called merlin) and is found on chromosome 22. *NF2* has a role in 'tumour protection' in the body by stopping tumour growth. Everyone has two copies of the *NF2* gene; one on each copy of chromosome 22. People with NF2 have a mutation in one copy of the *NF2* gene and the other copy on the partner chromosome is working.

Our body is made up of millions of cells, and in each cell there are instructions, called genes, that make all the necessary structural components and chemicals for the body to function. These genes are packaged onto little long strands known as chromosomes.

We all have 46 chromosomes arranged into 23 pairs. One copy of each pair is inherited from our mother and the other from our father. The first 22 chromosome pairs are numbered and are known as autosomal chromosomes. The 23rd pair is made up of the sex chromosomes called X and Y. Males have an X and a Y chromosome and females have two copies of the X chromosome.

Sometimes, a gene may have a variation in the instruction that causes the gene to no longer function properly. This variation is called a **mutation** or **pathogenic variant**, and means that the product produced by the gene, called a protein, is impaired or even absent.

Gene mutations may be inherited from a parent, or occur for the first time in an individual. Once you have a gene mutation however, it may be passed on to future generations. This is referred to as genetic inheritance.

## HOW IS NF2 INHERITED?

In about 50% of cases, neurofibromatosis type 2 is inherited from an affected parent.

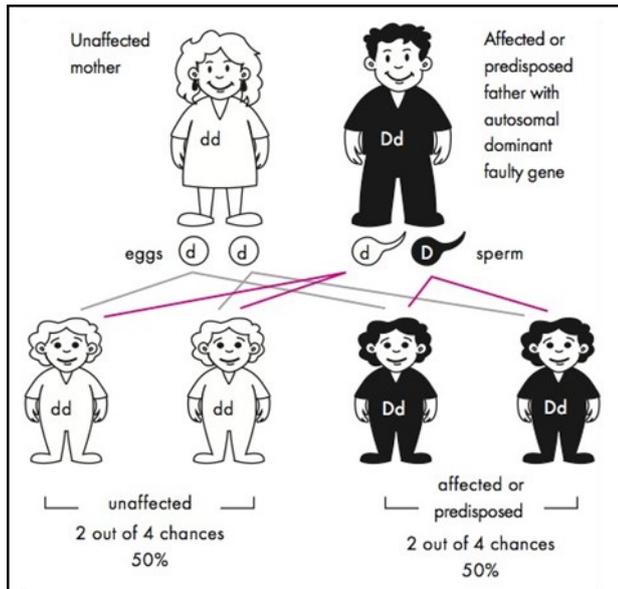
*NF2* follows a pattern called autosomal dominant inheritance in a family.

*NF2* is an autosomal gene as it is located on chromosome number 22. There are two copies of the gene in each cell and both copies of the gene normally send a message to the cells to produce the *NF2* protein. A person with NF2 will have one working copy of the *NF2* gene and one faulty copy in their cells, so there will be less than the usual amount of the protein produced. This means that certain processes in the body will not work as efficiently as they should. The faulty *NF2* gene copy is therefore described as being "dominant" since a person only needs one faulty copy to develop symptoms.

In *Figure 62.1*, the faulty *NF2* gene copy causing NF2 is represented by 'D' and the working copy by 'd'. When one of the parents has NF2 due to the faulty *NF2* gene copy, there are four possible combinations of the genetic information that is passed on by the parents.

This means that, **in every pregnancy**, there is

- A 1 chance in 2 (i.e. 2 chances in 4) or 50% chance that their child will inherit a copy of the faulty *NF2* gene and will therefore be affected by NF2 at some time in their life
- An equal chance (i.e. 1 chance in 2) or 50% that their child will inherit the working copy of the gene from his/her affected parent as well as a working copy from his/her unaffected parent. In this case, the child will not develop NF2 and cannot pass on the faulty *NF2* gene copy to any of his/her children.



**Figure 62.1:** Autosomal dominant inheritance when one parent has the faulty *NF2* gene copy. The faulty *NF2* gene copy is represented by 'D'; the working copy by 'd'.

While *Figure 62.1* shows the father as the parent carrying the faulty *NF2* gene, the same situation would arise if it was the mother. *NF2* usually affects men and women equally.

### IS THERE ANY TESTING AVAILABLE FOR NF2?

To diagnose *NF2*, a physical examination and tests to screen for hearing loss and the presence of *NF2* tumours is needed. Tests to diagnose *NF2* include:

- Audiometry
- CT scan
- MRI
- Balance tests
- Vision tests

As children of an individual with *NF2* have a 50% risk of having *NF2* themselves and developing *NF2*-related tumours, screening for tumours may start early in a child's life.

To offer genetic testing, a mutation in the *NF2* gene of a family member who has been diagnosed with *NF2* has to be identified.

- This testing is complex, time consuming and expensive and a mutation may not be found in the *NF2* gene even if it is present
- Once the mutation is identified, family members who are at up to 50% risk of having inherited the faulty gene, but who do not have any symptoms of the condition, can have 'presymptomatic' genetic testing
- Family members who have not inherited the *NF2* faulty gene copy do not need screening for the symptoms of *NF2* as they will not develop the condition.

Genetic counselling in conjunction with specialist familial cancer services may be useful in providing the most up-to-date information and advice about the availability and implications of genetic testing.

### Prenatal testing and PGD

If a mutation in the *NF2* gene has been identified in the family, genetic testing may be available during a pregnancy to determine whether the baby will be affected or unaffected with *NF2*. It may also be possible to undergo pre-implantation genetic diagnosis (PGD) screening for *NF2* on an embryo created using in vitro fertilisation (IVF). These options are best discussed and considered before pregnancy, when possible, in order to ensure all possible risks, benefits and outcomes to be explored.