Fact sheet **08**

AUTOSOMAL DOMINANT INHERITANCE

This fact sheet explains how genes affect our health when they follow a well understood pattern of genetic inheritance known as autosomal dominant inheritance.

SUMMARY

- Genes contain the instructions for growth and development. Some gene variations may mean that the gene does not work properly or works in a different way that is harmful. A variation in a gene that causes a health or developmental condition is called a **pathogenic variant** or **mutation**
- If a genetic condition happens when only one copy of the gene has a variation, this is called a **dominant variant**
- An autosomal gene is a gene located on a numbered chromosome and usually affects males and females in the same way.

CHROMOSOMES, GENES AND DNA

In all the cells of our body, our genes are found on chromosomes (long strings of genes). We have many thousands of genes that provide information for our body to grow, develop and stay healthy. The genes send messages to the cell to make important chemical products such as proteins.

There are typically 46 chromosomes in each cell that are arranged into 23 pairs. One of each pair is passed on to us from our mother and the other from our father. 22 of these chromosome pairs are numbered. These numbered pairs are known as the autosomal chromosomes. The 23rd pair is made up of the sex chromosomes called X and Y. Typically males have an X and a Y chromosome and females have two copies of the X chromosome.

Since the chromosomes come in pairs, there are also two copies of each of the genes. The exception to this rule applies to the genes carried on the sex chromosomes called X and Y.

The genes in our DNA provide the instructions for proteins, which are the building blocks of the cells that make up our body. Although we all have variation in our genes, sometimes this can affect how our bodies grow and develop. Generally, DNA variations that have no impact on our health are called **benign variants** or **polymorphisms**. These variants tend to be more common in people. Less commonly, variations can change the gene so that it sends a different message. These changes may mean that the gene does not work properly or works in a different way that is harmful. A variation in a gene that causes a health or developmental condition is called a **pathogenic variant** or **mutation**.

If a DNA change occurs in only one of the pair of genes and this causes a health condition, it is called a **dominant variant**. If a health condition only occurs when both copies of the gene are changed, this is called a **recessive variant**.

An **autosomal** gene is a gene located on a numbered chromosome and usually influences males and females in the same way.

An **X-linked** gene is located on the X chromosome and generally influences males and females differently.

A CLOSE LOOK AT AUTOSOMAL DOMINANT INHERITANCE

This type of inheritance refers to the inheritance of a **dominant** gene variant on an autosome (one of the chromosomes numbered 1-22). See *Figure 8.1*.

There are usually two copies of every autosomal gene in each of our cells. Both copies of the gene send a message to the cells to produce a particular product such as a protein.

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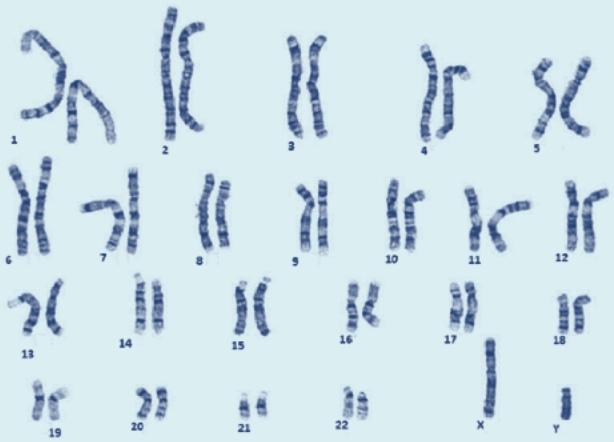
People with a dominant variant on one gene copy, and a working copy of that gene on the other partner chromosome, will have that condition even though the working copy is there.

Figure 8.1:
Chromosome picture (karyotype) from a male 46,XY.



Therefore although one of the gene copies is sending the right instructions to make the gene product, the other copy with the dominant variant is not sending the right message and overrides the action of the working gene copy.

WHAT DOES IT MEAN IF YOU HAVE AN AUTOSOMAL DOMINANT GENE VARIANT?

If a person has an autosomal dominant gene variant, they cannot make enough of the right gene product and will have signs and symptoms of the genetic condition from birth, or be more likely to develop the condition later in life (depending on the gene involved).

HOW ARE AUTOSOMAL DOMINANT GENE VARIANTS PASSED DOWN THROUGH THE FAMILY?

We need two copies of each gene to have the right balance of DNA (except the sex-chromosome genes).

Figure 8.2:
Where an autosomal dominant gene variant is represented by 'D' and the working gene copy by 'd', there are usually two different ways these may exist in a person and this is the same if the person is a male or female.

A.

- Affected by, or more likely to develop a genetic condition
- This person has the gene pair 'Dd'. This means that one copy of the gene is working and making the right gene product, however, the other copy (D) is not working. They may develop symptoms of the genetic condition because for this gene, you need both copies to be working
- When this person has a child, there is a 50% chance they will pass on a working 'd' gene copy to each of their children and a 50% chance they will pass on the copy of the gene that is not working (D)

B.

- Unaffected person
- This person has the gene pair 'dd'. This means that both copies of the gene are working and they are able to make the gene product. They will not develop symptoms of the genetic condition caused by variants in this gene
- When this person has a child, they will only pass on the working gene copy (d). A rarer possibility is that an unaffected person has a child with a new (called *de novo*) condition *(Figure 8.4)*

Figure 8.3:
Autosomal dominant inheritance - when one parent has the autosomal dominant non-working gene copy. The non-working gene copy with an autosomal dominant variant is shown as 'D'; the working copy of the gene by'd'.

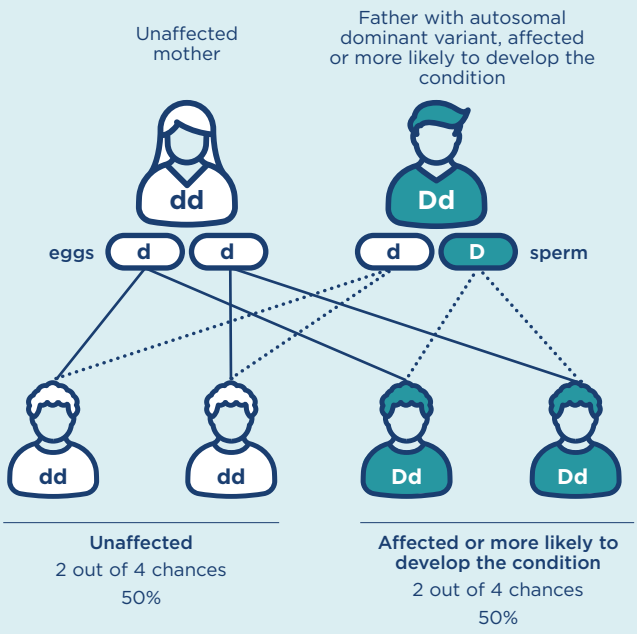
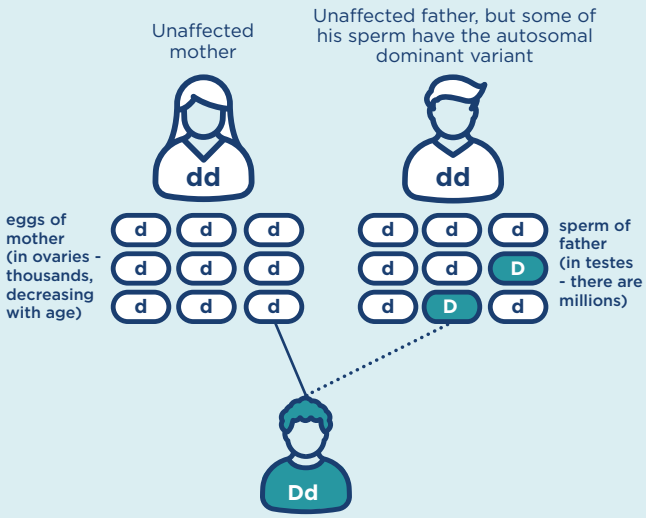


Figure 8.4:
De novo inheritance of an autosomal dominant condition. The variant is *de novo* (meaning *new- occurring for the first time*) in the child. Both parents are unaffected – they have the working gene copy, but **either the mother or the father** has some eggs or sperm with the variant. The non-working gene copy with an autosomal dominant variant is shown as 'D'; the working copy of the gene by 'd'



One copy of each gene is passed on to a child from their mother and the other from the father. In autosomal dominant inheritance the possibilities for a parent are shown by the people in *Figure 8.2*.

When one parent has an autosomal dominant gene variant

One parent would have the genetic make-up of the person in *Figure 8.2A* and the other would have the genetic make-up of the person in *Figure 8.2B.*

The possibilities for each pregnancy are the same whether it is the father who has the dominant gene variant (as in *Figure 8.3)* or the mother.

For such a couple this means that in every pregnancy there is:

- 1 chance in 2 (2 in 4 or 50% chance) that they will have a child who inherits **both working copies of the gene** from them. Therefore, the child will not have the condition
- 1 chance in 2 (2 in 4 or 50% chance) that they will have a child who inherits the **dominant gene variant on the non-working gene copy and a working gene copy** from them and will have the condition, or be more likely to develop the condition caused by the gene variant.

When neither parent has the autosomal dominant gene variant but they have a child with the gene variant. This is called *de novo* inheritance.

In this scenario (*Figure 8.4*), because neither parent has the condition, they both have the genetic make-up of the person in *Figure 8.2*B.

A *de novo* (meaning 'new') variant occurs in a child when the egg or sperm which formed the child had the variant. It is referred to as 'new' in the child because neither parent has the condition.

For such a couple this means that in every pregnancy after this there will be:

* A low chance of having a child with the same variant (often approximately 1%), but not zero. However, if one of the parents is mosaic for the variant (meaning they have a proportion of cells in their body with the variant) then there may be up to 50% chance in each pregnancy that the child will inherit the variant and will have, or be more likely to develop the condition. Mosaicism often goes undetected when the parent does not have any signs of the condition.

WHAT GENETIC CONDITIONS ARE CAUSED BY AN AUTOSOMAL DOMINANT GENE VARIANT?

A number of health conditions follow this pattern of inheritance in families. While some are obvious at birth, sometimes the symptoms do not appear until later in life. Neurofibromatosis type 1, achondroplasia, Huntington disease, inherited likelihood to develop breast, ovarian and bowel cancers and familial hypercholesterolaemia all follow a pattern of autosomal dominant inheritance.

You can find more about the underlined topics by following the links in the online version of this document. Go to https://www.genetics.edu.au/SitePages/Autosomal-dominant-inheritance.aspx for an online and downloadable copy.