

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



IN 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 only occurs when both copies of the gene have a change in the message, this change is called a **recessive 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 usually 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 copy 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**.

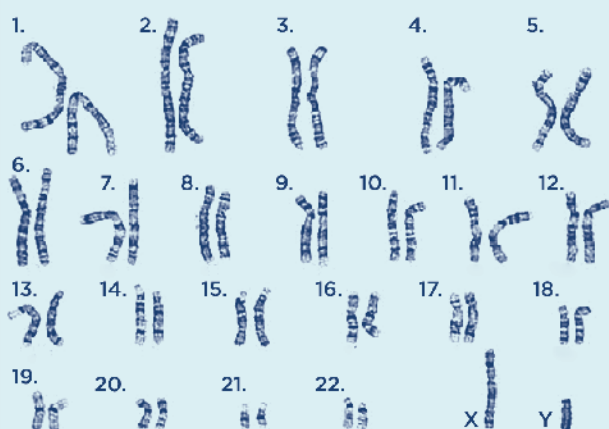
We all have a number of recessive gene variants which are hidden due to the fact that we have a backup working copy of the gene, and therefore enough of the right gene product is made.

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.

Figure 7.1:

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



A CLOSE LOOK AT AUTOSOMAL RECESSIVE INHERITANCE

This type of inheritance refers to the inheritance of a **recessive** variant on an autosome (one of the chromosomes numbered 1-22). See *Figure 7.1*.




There are two copies of every autosomal gene. Both copies of the gene send a message to the cells to produce a particular product such as a protein. People who have a variant on one gene copy, and a working copy of that gene on the other partner chromosome, are said to be **genetic carriers** for a particular condition.

Although only one of the gene copies is sending the right instructions to make the gene product, the cell can usually still work with this.

Genetic carriers for the great many autosomal recessive genetic conditions usually do not show any symptoms of the condition or develop related health problems.

Figure 7.2:

Autosomal recessive inheritance - the non-working copy of the gene is represented by 'r' and the working gene copy by 'R'. There are three possible ways this may show up in a person and this is the same if the person is a male or female.

- A.**  • Non-Carrier who does not have the condition (unaffected)
- This person has the gene pair 'RR'. This means that both copies of the gene are working and making the right gene product. They will not develop signs and symptoms of the genetic condition caused by this gene not working properly
 - When this person has a child, they will only pass on a working gene copy 'R' to each of their children.
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- B.**  • Genetic Carrier who does not have the condition (unaffected)
- This person has the gene pair 'Rr'. This means that one copy of the gene is working and making the right gene product however the other copy (r) is not working. They will generally not develop signs of the genetic condition because for this gene, you only need one working copy. This person is a genetic carrier of the genetic condition caused by this gene
 - When this person has a child, there is a 50% chance they will pass on a working 'R' gene copy to each of their children and a 50% chance they will pass on the gene variant, which is not working (r)
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- C.**  • Affected or more likely to develop an autosomal recessive condition
- This person has the gene pair 'rr'. This means that both copies of the gene are not working and they are unable to make any of the gene product. They will develop signs of the genetic condition caused by this gene. This person is said to be affected by the genetic condition caused by variants in this gene
 - If this person has a child, they will only pass on the gene variant which is not working (r)

If a person has both of their gene copies for a genetic condition containing a recessive variant, they do not have the ability to make enough gene product in the right way and will have symptoms of the genetic condition.

Therefore, for autosomal recessive conditions, having only one pathogenic variant does not usually cause a health problem.

You will only get symptoms of the genetic condition if both copies of your genes have a pathogenic variant (See *Figure 7.2A, B and C*).

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

Humans need two copies of each gene in order to have the right balance of DNA (except the sex chromosome genes).

One copy of each gene is passed to a child from their mother and the other from the father.

In recessive inheritance, the possibilities for a parent are shown by people in *Figure 7.2*.

When a baby is conceived, each parent passes on one copy of each of his or her genes to the baby. Therefore the baby is a 'mixture' of the genetic information from each of their parents.

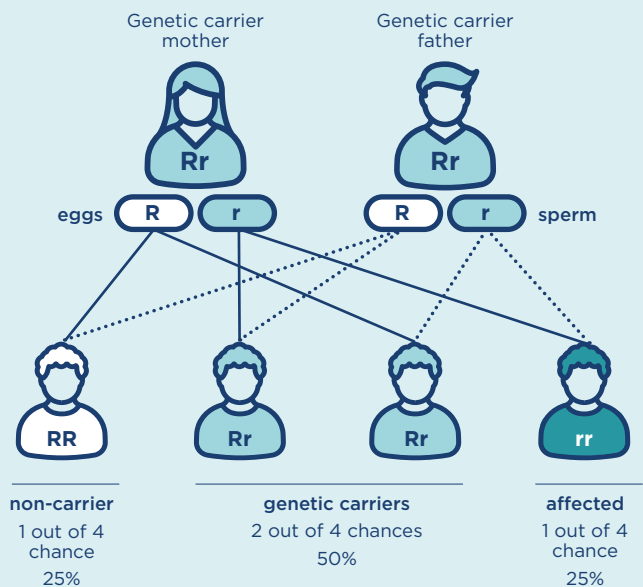
If both parents are genetic carriers for the same autosomal recessive condition

Both the mother and father would have the genetic make-up of the person in *Figure 7.2B*.

When two carriers of a recessive gene variant in the same gene have a baby, each parent has a chance of passing on either the gene variant (non-working copy of the gene) or the working copy of the gene to their baby.

Figure 7.3:

Autosomal recessive inheritance when both parents are unaffected genetic carriers for the condition. The non-working copy of the gene containing a recessive variant is represented by 'r'; the working copy of the gene by 'R'.



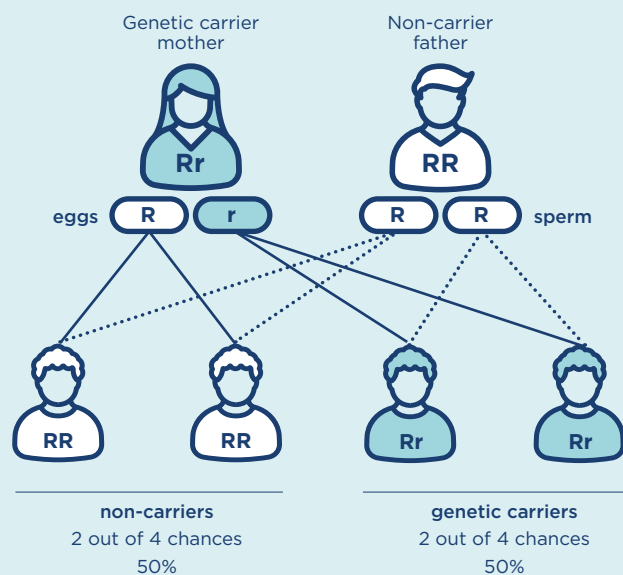
As shown in *Figure 7.3*, where the gene containing a recessive variant is represented by 'r' and the working copy by 'R', there are four possible ways the genetic information may be passed on in each pregnancy.

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

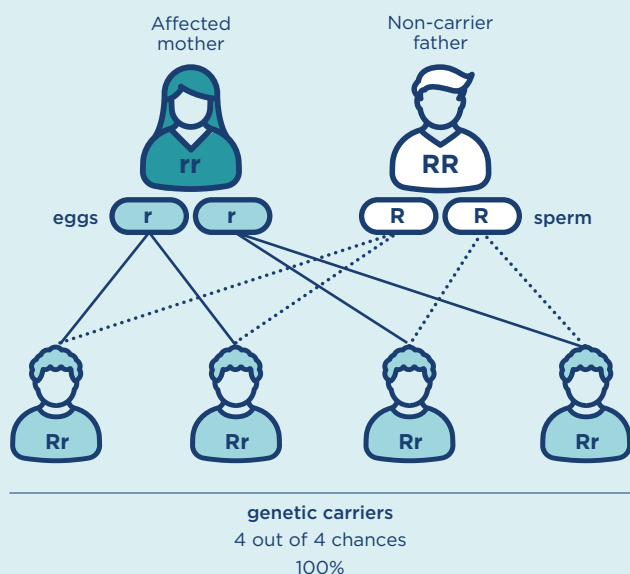
- 1 in 4 (25%) chance that they will have a child who inherits **both copies of the recessive gene variant** from them. In this case, no working gene product will be made and their child will have the condition caused by variation in this gene
- 1 in 4 (25%) chance that their child will inherit **both copies of the working gene** and will not have the condition and is not a genetic carrier
- 1 chance in 2 (2 in 4 or 50% chance) that their child will inherit **the recessive gene variant as well as the working copy of the gene** from them and the child will be an unaffected genetic carrier of the condition, just like the parents.

Figure 7.4:

Autosomal recessive inheritance when only one of the parents is an unaffected genetic carrier of the condition. The non-working copy of the gene with a recessive variant is shown as 'r'; the working copy of the gene by 'R'.

**Figure 7.5:**

Autosomal recessive inheritance when one of the parents has the condition or is more likely to develop the condition, and the other parent is an unaffected non-carrier of the condition. The non-working copy of the gene containing a recessive variant is shown as 'r'; the working copy of the gene by 'R'.



If one parent is a genetic carrier of the autosomal recessive gene variant

One parent would have the genetic make-up of the person in *Figure 7.2A* and the other would have the genetic make-up of the person in *Figure 7.2B*.

The possibilities for each pregnancy are the same whether it is the mother who is a genetic carrier (as in *Figure 7.4*) or the father.

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

- No chance that the couple will have a baby affected with the genetic condition caused by this particular gene
- 1 chance in 2 (2 in 4 or 50% chance) that they will have a child who inherits **both copies of the working gene** from them. In this case, the child will not have the condition
- 1 chance in 2 (2 in 4 or 50% chance) that their child will inherit the **recessive gene variant and the working copy of the gene** from them and will be an unaffected genetic carrier of the condition.

If one parent has the autosomal recessive condition

There are two possibilities:

- One parent would have the genetic make-up of the person in *Figure 7.2A* (non-carrier) and the other would have the genetic make-up of the person in *Figure 7.2C* or
- One parent would have the genetic make-up of the person in *Figure 7.2B* (unaffected genetic carrier) and the other would have the genetic make-up of the person in *Figure 7.2C*.

For scenario i) the possibilities for each pregnancy are the same whether it is the mother who has the condition (as in *Figure 7.5*) or the father.

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

- 4 in 4 (100%) chance that they will have a child who inherits the recessive gene variant and the working copy of the gene from them, and the child will be an unaffected genetic carrier of the condition.

For scenario ii) the possibilities for each pregnancy are the same whether it is the mother who has the condition (as in *Figure 7.6*) or the father.

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 copies of the recessive gene variant** from them. The child will therefore have the condition or is more likely to develop the condition
- 1 chance in 2 (2 in 4 or 50% chance) that they will have a child who inherits the **recessive gene variant and the working copy of the gene** from them and the child will be an unaffected genetic carrier of the condition.

If both parents have the autosomal recessive condition

Both the mother and father would have the genetic make-up of the person in *Figure 7.2C*.

This means that in every pregnancy there is:

- 4 in 4 (100%) chance that they will have a child who inherits **two copies of the recessive gene variant** from their parents.
- Each child will have the condition or is more likely to develop the condition, just as the parents have the condition or are more likely to develop the condition.

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

The most common conditions that are caused by an autosomal recessive gene variant are cystic fibrosis, thalassaemia, haemochromatosis and Tay-Sachs disease.

Figure 7.6:

Autosomal recessive inheritance when one of the parents has the condition or is more likely to develop the condition and the other parent is an unaffected genetic carrier of the condition. The non-working copy of the gene containing a recessive variant is represented by 'r'; the working copy of the gene by 'R'.

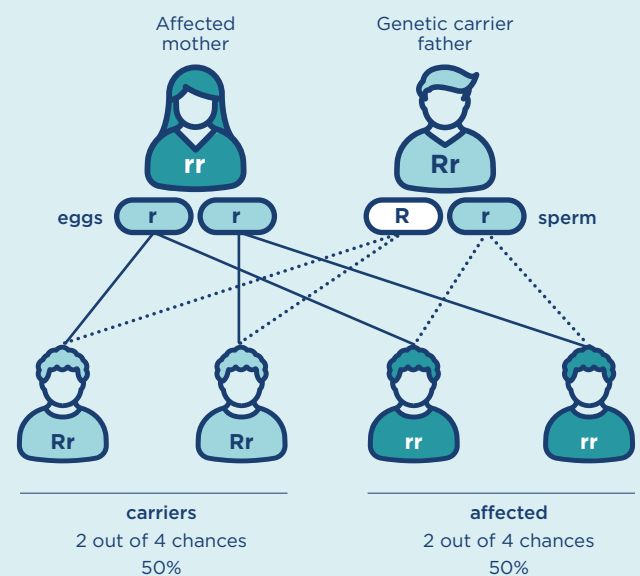
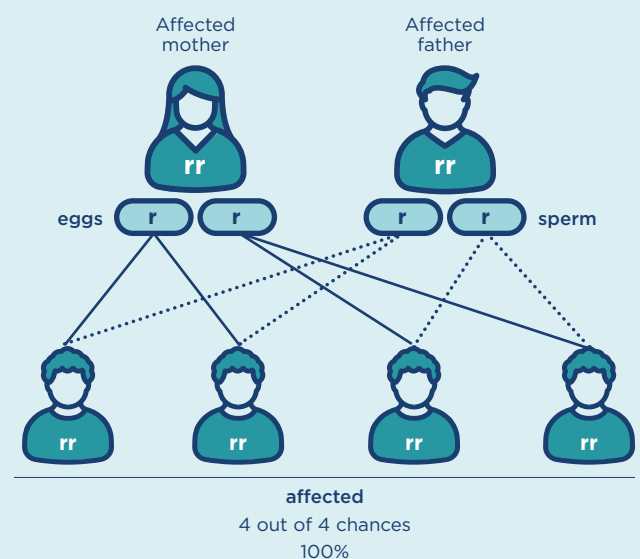


Figure 7.7:

Autosomal recessive inheritance when both parents have the condition or are more likely to develop the condition. Their children are all expected to have the condition or have a higher chance of developing it.



Usually genetic carriers of autosomal recessive genetic conditions do not show any symptoms of the condition and do not develop health problems due to being a genetic carrier. It is possible, however, to test a person to determine whether they are a carrier of certain recessive variants (e.g. reproductive genetic carrier screening).

Indications that someone may be a genetic carrier of an autosomal recessive variant include:

- Having family members known to have a condition that follows an autosomal recessive pattern of inheritance
- Coming from a certain ethnic or cultural background where a condition may be more common, and therefore the chance of a person from these population groups being a carrier is higher than in others.