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

In summary

- **Genes contain the instructions for growth and development. Some gene changes make the gene faulty so that the message is not read correctly or is not read at all by the cell. A variation in a gene that makes it faulty is called a *mutation***
- **If a genetic condition only occurs when both copies of the gene are changed, this is called a *recessive mutation***
- **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 remain healthy. The gene sends 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. 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. Genes are sections of DNA that code for the proteins our body needs to function. A variation in a gene that creates a fault is called a **pathogenic variant** or **mutation**.

A mutation in a gene will affect the body differently depending on how much it changes the resulting protein, how critical that protein is to the body and how much of that protein is needed in the body.

If a DNA change occurs in only one of the pair of genes and this causes a health condition, it is called a **dominant mutation**.

If a health condition only occurs when both copies of the gene are changed, this is called a **recessive mutation**.

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

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

An X-**linked** gene is located on the X or Y chromosome and affects males and female differently.

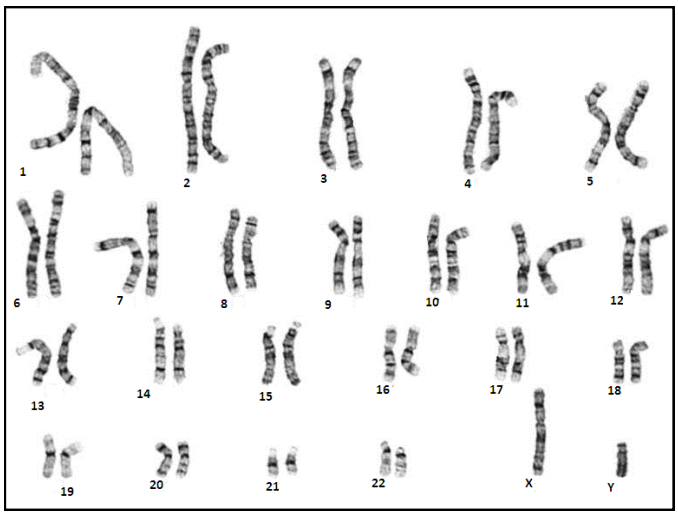

Figure 7.1: *Chromosome picture (karyotype) from a male 46,XY.*

A CLOSE LOOK AT AUTOSOMAL RECESSIVE INHERITANCE

This type of inheritance refers to the inheritance of a **recessive** gene mutation 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. Individuals who have a mutation on one gene, and a working copy of that gene on the other partner chromosome, are said to be **genetic carriers** of the mutation for a particular condition.

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

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

If a person has both of their genes for a genetic condition containing a recessive mutation, they do not have the ability to make the correct gene product and will have symptoms of the genetic condition.

Therefore, for autosomal recessive conditions, having one gene mutation does not usually cause a health problem.

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

Figure 7.2: *Where an autosomal recessive gene mutation is represented by 'r' and the working gene copy by 'R', There are three possible combinations a person could have. This is regardless of whether the person is a male or female.*

A		• Unaffected Non-Carrier • This person has the gene pair RR. This means that both copies of the gene are working and producing the correct gene product. They will not develop symptoms of the genetic condition caused by this gene • When this person has a child, they will only pass on a working R gene to each of their children
B		• Unaffected Genetic Carrier • This person has the gene pair Rr. This means that one copy of the gene is working and producing the correct gene product however the other copy (r) is not working. They will not develop symptoms of the genetic condition because for this gene, you only need one working copy. This person is a genetic carrier for 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 to each of their children and a 50% chance they will pass on the gene mutation which is not working (r)
C		• Affected or predisposed to 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 produce any of the gene product. They will develop symptoms of the genetic condition caused by this gene. This person is said to be affected by the genetic condition caused by this gene • If this person has a child, they will only pass on the gene mutation which is not working (r)

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

Humans need TWO copies of each gene in order to have the correct balance of DNA (with the exception of the sex chromosome genes).

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

The possible gene combinations a parent may have for a recessive gene are represented by the individuals 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 his/her parents*.

If both parents are genetic carriers for the same autosomal recessive gene mutation

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

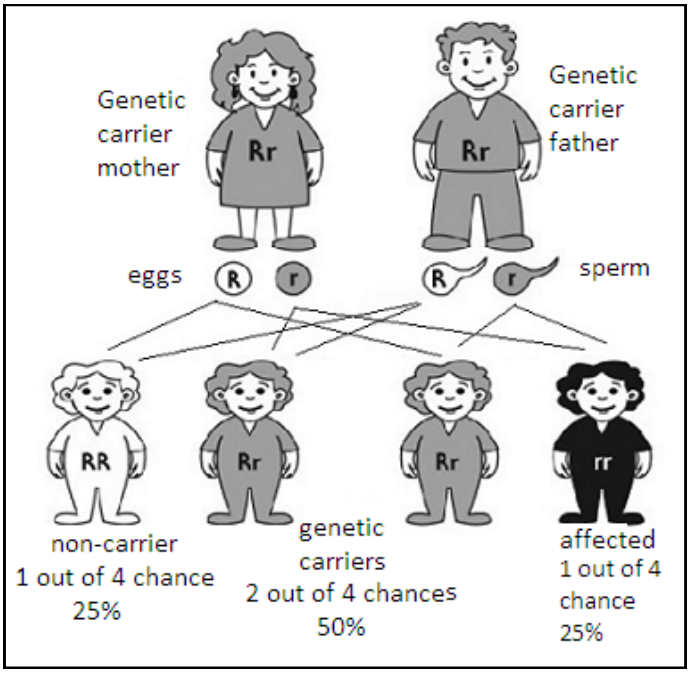

Figure 7.3: *Autosomal recessive inheritance when both parents are unaffected genetic carriers for the condition. The faulty copy of the gene containing a recessive mutation is represented by 'r'; the working copy of the gene by 'R'.*

When two carriers of the same recessive gene mutation have a baby, each parent has a chance of passing on either the gene mutation or the working copy of the gene to the baby.

As shown in *Figure 7.3*, where the gene containing a recessive mutation is represented by 'r' and the working copy by 'R', there are four possible combinations of the genetic information to be passed on in every pregnancy.

This means that in every pregnancy there is:

- 1 chance in 4 (25% chance) that they will have a child who inherits **both copies of the recessive gene mutation** from his/her parents. In this case, no working gene product will be produced and their child will be affected by the condition caused by this gene.
- 1 chance in 4 (25% chance) that their child will inherit **both copies of the working gene** and will be unaffected by the condition and not a genetic carrier.
- 1 chance in 2 (2 chances in 4 or 50% chance) that their child will inherit **the recessive gene mutation and the working copy of the gene** from the parents and he/she will be an unaffected genetic carrier of the condition, just like the parents.

If one parent is a genetic carrier for the autosomal recessive gene mutation

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

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 chances in 4 or 50% chance) that they will have a child who inherits **both copies of the working gene** from his/her parents. In this case, the child will be unaffected by the condition.
- 1 chance in 2 (2 chances in 4 or 50% chance) that their child will inherit the **recessive gene mutation and the working copy of the gene** from the parents and he/she will be an unaffected genetic carrier of the condition.

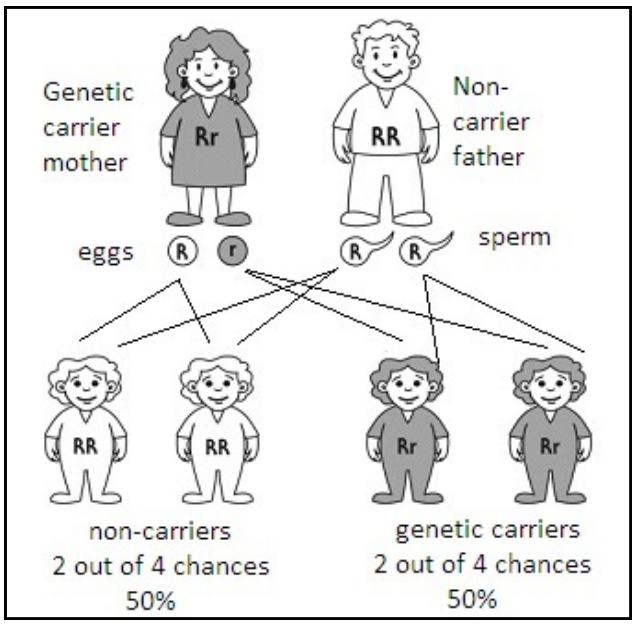

Figure 7.4: *Autosomal recessive inheritance when only one of the parents is an unaffected genetic carrier for the condition. The faulty copy of the gene containing a recessive mutation is represented by 'r'; the working copy of the gene by 'R'.*

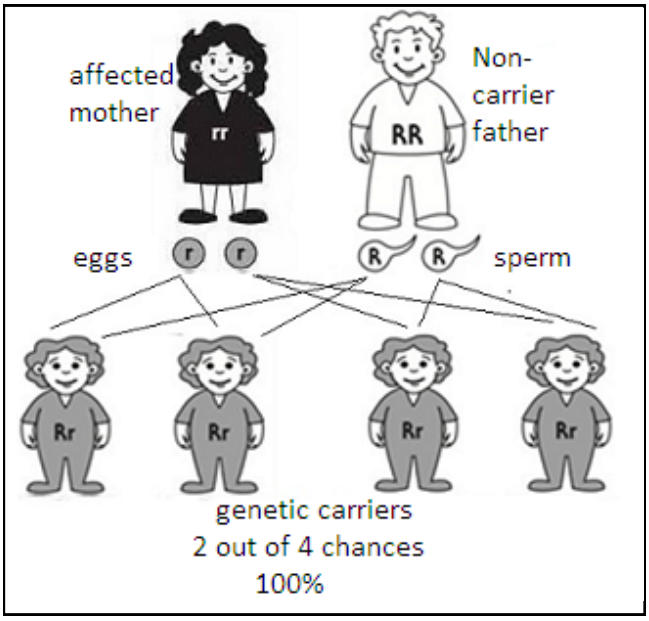

Figure 7.5: *Autosomal recessive inheritance when one of the parents is affected or predisposed to develop the condition and the other parent is an unaffected non-carrier for the condition. The faulty copy of the gene containing a recessive mutation is represented by 'r'; the working copy of the gene by 'R'.*

If one parent is a affected by the autosomal recessive condition

There are two possible scenarios:

i) 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

ii) 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 outcomes for each pregnancy are the same whether it is the mother who is affected (as in *Figure 7.5*) or the father.

This means that in every pregnancy there is:

- 4 chance in 4 (100% chance) that their child will inherit the **recessive gene mutation and the working copy of the gene** from the parents and he/she will be an unaffected genetic carrier of the condition.

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

This means that in every pregnancy, there is:

- 1 chance in 2 (2 chances in 4 or 50% chance) that they will have a child who inherits **both copies of the recessive gene mutation** from his/her parents. In this case, the child will be affected or predisposed to develop the condition
- 1 chance in 2 (2 chances in 4 or 50% chance) that their child will inherit the **recessive gene mutation and the working copy of the gene** from the parents and he/she will be an unaffected genetic carrier of the condition.

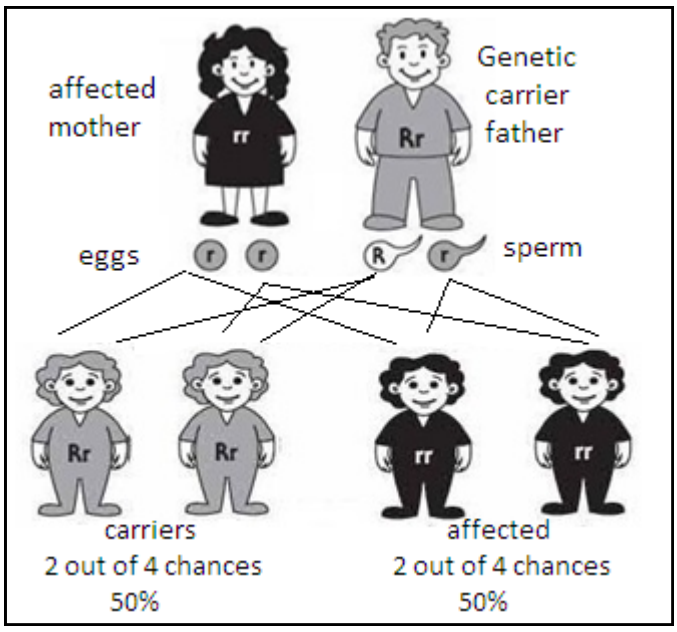

Figure 7.6: *Autosomal recessive inheritance when one of the parents is affected or predisposed to develop the condition and the other parent is an unaffected genetic carrier for the condition. The faulty copy of the gene containing a recessive mutation is represented by 'r'; the working copy of the gene by 'R'.*

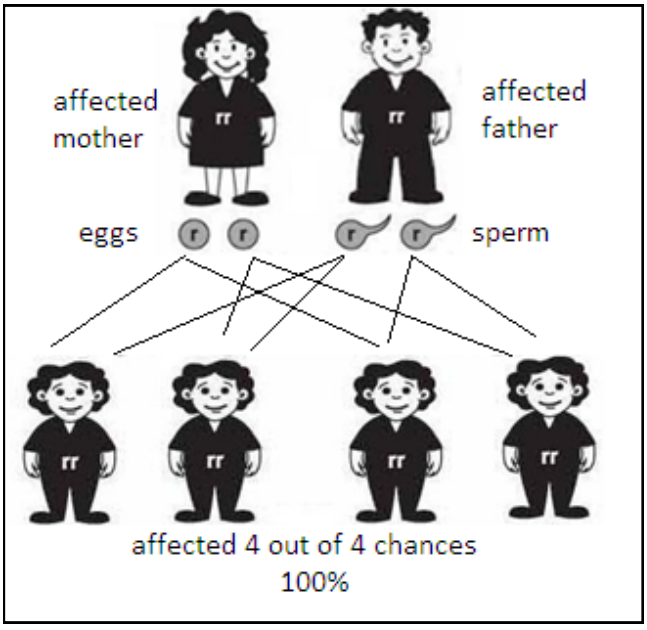

Figure 7.7: *Autosomal recessive inheritance when both parents are affected or predisposed to develop the condition.*

If both parents are affected by 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 chance in 4 (100% chance) that they will have a child who inherits **both copies of the recessive gene mutation** from his/her parents. like the parents
- Each child will be affected or predisposed to developing the condition, just parents are affected or predisposed to develop the condition.

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

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

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 an individual to determine whether they are a carrier of certain recessive mutations.

Indications that the individual may be a genetic carrier of an autosomal recessive mutation include:

- Having a family history of a condition that follows an autosomal recessive pattern of inheritance
- Where a condition is more common in people of certain ethnic or cultural backgrounds and therefore the chance of a person from these population groups being a carrier is much higher than in others.