This fact sheet describes how genes affect our health when they follow a well understood pattern of genetic inheritance known as X-linked dominant inheritance.

In summary

- **Genes contain the instructions for growth and development. Some gene variations 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* or *pathogenic variant***
- **An X-linked dominant gene is a gene located on the X chromosome and affects males and females differently.**

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. The genes in our DNA provide the instructions for proteins, which are the building blocks of the cells that make up our body. There may be small variations in our genes that can affect how our bodies grow and develop.

Generally, these variations do not have any impact on our health and are called neutral variants or polymorphisms. Some gene variations 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 **pathogenic variant** or **mutation**.

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

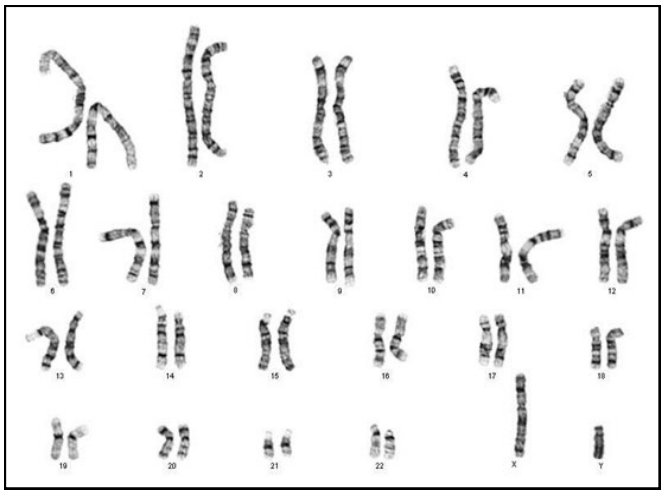


Figure 10.1: *Chromosome picture (karyotype) from a male 46,XY.*

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 females differently.

A CLOSE LOOK AT X-LINKED DOMINANT INHERITANCE

This type of inheritance refers to the inheritance of a gene mutation on the X chromosome. Males have one X chromosome and one Y chromosome whereas females have two copies of the X chromosome and no Y chromosome. Men will therefore only have one copy of each X chromosome gene whereas women will have two. *(*See *Figure 10.1).*

In women, despite the fact that each body cell has two X chromosomes, only one is used for making the gene product and the other X chromosome is switched off.

This switching off is known as **X-inactivation** and is thought to occur randomly so that in some of the woman's cells, one particular X will be inactivated and in another cell, that X will be active while the other copy of the X is switched off or inactive.

WHAT DOES IT MEAN IF YOU HAVE AN X-LINKED DOMINANT GENE MUTATION?

Mutations on the X chromosome are more commonly recessive.

This means that if there is a normal working copy of the same gene in each cell of a person, they will not usually show symptoms of the condition.

When a gene mutation is dominant however, the body cannot work normally with less than the usual amount of working gene product. The X-linked dominant mutation appears to override or dominate the unchanged information in the working copy of the gene. It is very rare for a woman to have a dominant gene mutation on both copies of her X chromosome.

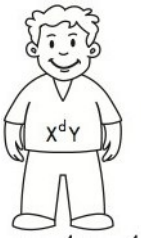
A		• This female has the gene pair Dd on her X chromosomes. This means that one copy of the gene is working (d) and producing the correct gene product however the other copy (D) is not working. • When this woman has a child, there is a 50% chance that she will pass on a working (d) gene to each of her children and a 50% chance that she will pass on the gene mutation which is not working (D). • They will themselves have the genetic condition caused by the X-linked dominant mutation because the (D) dominates the working copy of the gene and blocks the correct gene product from being used by the cells.
B		• This represents an unaffected female who has two working copies (dd) of the gene on her X chromosomes. • When this woman has a child, there is a 100% chance they will pass on the working copy of the gene if they have a sons and daughters.
C		• This represents an affected male who has an X-linked dominant gene on his X chromosome. There is no working copy of the gene and therefore he will not be making the correct gene product and will show symptoms of that particular condition. • When this man has a child, there is a 100% chance that he will pass on the gene mutation which is not working (D) if he has a daughter. If he has a son, he will not pass on the X chromosome, but rather the Y chromosome which means his sons will not have inherited the gene mutation from him.
D		• This represents an unaffected male who has a working copy of the gene on his X chromosome. His body cells can therefore make the correct gene product and will not show symptoms of that particular condition. • When this man has a child, there is a 100% chance that he will pass on the working copy of the gene if he has a daughter. If he has a son, he will not pass on the X chromosome, but rather the Y chromosome, which means his sons will not have inherited the gene mutation.

Figure 10.2: *Where an X-linked dominant gene mutation is represented by 'D' and the working gene copy by 'd', There are several possible combinations a person could have and depending on whether they are male or female, the effect of the genetic combination will differ*

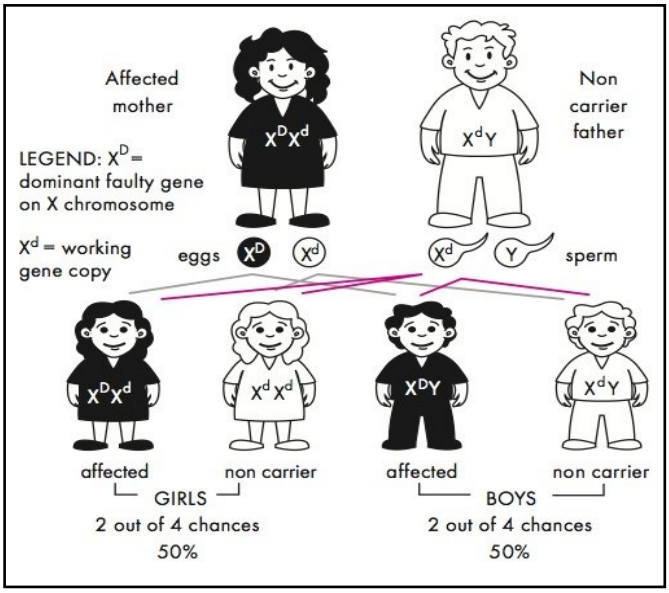


Figure 10.3: *X-Linked dominant inheritance where the mother carries the faulty X-linked dominant gene and is affected. The faulty copy of the X-linked gene is represented by 'D', the working copy by 'd'.*

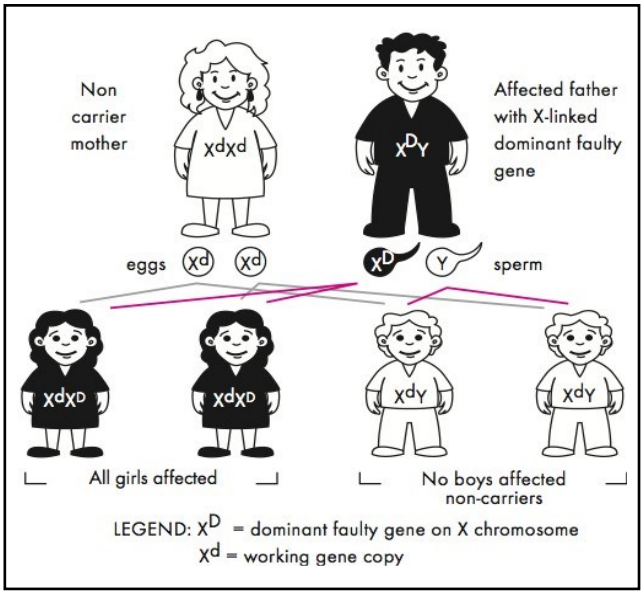


Figure 10.4: *X-linked dominant inheritance where the father carries the faulty X-linked dominant gene and is affected. The faulty copy of the X-linked gene is represented by 'D', the working copy by 'd'.*

HOW ARE X-LINKED DOMINANT GENE MUTATIONS PASSED DOWN THROUGH THE FAMILY?

If the mother is affected by a condition caused by an X-linked dominant gene mutation

When the mother is affected by a condition caused by an X-linked dominant gene mutation (as in *Figure 10.2A)*, there are four possible combinations of the genetic information the child can receive from the parents (*Figure 10.3*).

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

- 1 chance in 2 (2 chances in 4 or 50% chance) that both their **sons** and **daughters** will inherit **the X-linked dominant gene mutation** from the mother and be affected by the condition. Either no working gene product will be made or not the right amount of the gene product will be able to be made by the cells
- 1 chance in 2 (2 chances in 4 or 50% chance) that both their **sons** and **daughters** will inherit the working copy of the gene ('d') from the mother and will not be affected by the condition.

If the father is affected by a condition caused by an X-linked dominant gene mutation

When the father is affected by a condition caused by an X-linked dominant gene mutation (as in *Figure 10.2C)*.

He will pass on the X-linked dominant gene mutation (on the X chromosome) to all his daughters and his Y chromosome to all his sons. The unaffected mother will only give working copies of the gene to her children. There are four possible combinations of the genetic information the child can receive from the parents (*Figure 10.4*).

For such a couple this means that in every pregnancy:

- None of their **sons** can inherit the X-linked dominant gene mutation since the son only inherits the Y chromosome from the father. They will inherit the **working gene copy** from their mother. None of their sons will have the condition
- All of their **daughters** will inherit the **working gene copy** from their mother **and the X-linked dominant gene mutation** from their father. All of their daughters will have the condition.

WHAT GENETIC CONDITIONS ARE CAUSED BY AN X-LINKED DOMINANT GENE MUTATION?

There are very few conditions that have been shown to follow a pattern of X-linked dominant inheritance. Rett syndrome, which is a condition that causes physical and intellectual disability, is one example.