Genes are made up of DNA and are packaged on chromosomes. It is important that the chromosome balance in the cells of our body is correct in order for the correct amount of DNA and genes to be present.

**In summary**

- **In the cells of the body, there are usually 23 pairs of chromosomes making a total of 46**
- **In the female egg cells and the male sperm cells there are only 23 single chromosomes**
- **If there is more or less chromosome material present in the cells of an individual, a health or developmental problem may occur**
- **Chromosome changes can include variations in the number, size and structure of one or more chromosomes**

## CHROMOSOMES IN THE BODY

Chromosomes are long strands of DNA found in the cells of the body. DNA contains genes that provide the coded information for our bodies to grow, develop and function.

***CYTOGENETICS* is the scientific study of chromosomes**
***KARYOTYPE* refers to the number and type of chromosomes seen in a person's cells**

In each human cell, except the egg and sperm cells, there are 46 chromosomes. Chromosomes are found in pairs and each pair varies in size. Thus there are 23 pairs of chromosomes, one of each pair being inherited from each parent.

- There are 22 numbered chromosomes from the largest to the smallest: i.e. 1-22. These are called **autosomes**
- There are also two **sex chromosomes**, called X and Y

In females, cells in the body have 46 chromosomes (44 autosomes plus two copies of the X chromosome). They are said to have a 46,XX karyotype. Eggs (female reproductive cells) are different as they only contain half of the chromosomes (23 made up of 22 numbered chromosomes and an X chromosome).

In males, cells in the body have 46 chromosomes (44 autosomes plus an X and a Y chromosome). They are said to have a 46,XY karyotype.

Sperm (male reproductive cells) are different as they only contain half of the chromosomes (23 made up of 22 numbered chromosomes and an X chromosome or a Y chromosome).

When the egg and sperm join at conception, the baby will have 46 chromosomes in its cells, just like the parents (see *Figure 4.1*).

In a genetic testing laboratory, the chromosomes may be coloured (stained) with special dyes to produce distinctive banding patterns. These patterns allow the laboratory to check the size and structure of the chromosomes.

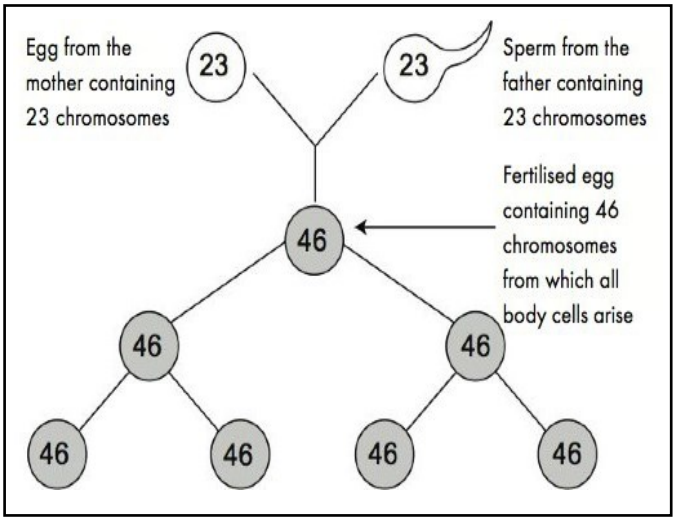


***Figure 4.1:*** *At conception the sperm and egg combine*

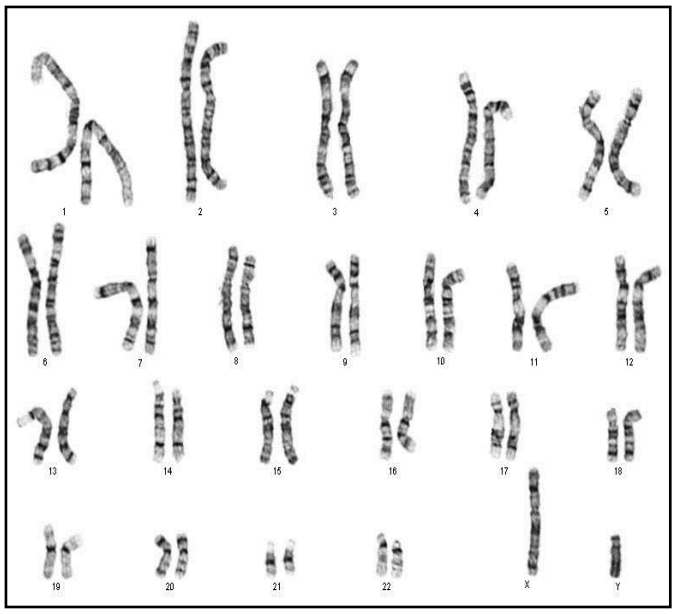

***Figure 4.2:*** *Chromosome picture (karyotype) from a male 46,XY.*

*Figure 4.2* shows a banded chromosome karyotype from a male where each chromosome has been numbered from the largest (chromosome number 1) to the smallest (chromosome number 22) and arranged in pairs in order of size.

We know these chromosomes are from a male because of the X and a Y.

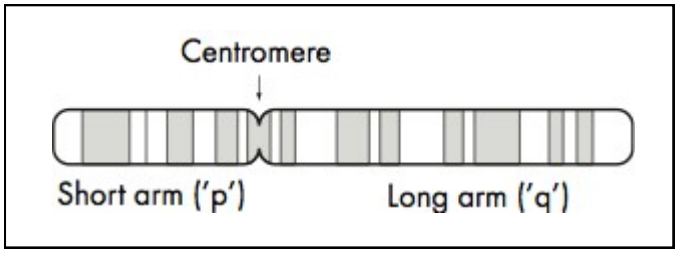


***Figure 4.3*** is a diagram of a chromosome showing how the centromere divides it in to a short arm, called the `p' arm, and a long arm called the `q' arm.

At one point along their length, each chromosome has a constriction, called the **centromere**. The centromere divides the chromosome in to two sections or **arms**. Numbering the chromosomes and labelling their arms allows scientists to pin point important sections of chromosomes.

The total number of chromosomes in the cells, and the description of the sex chromosomes present, is written in a shortened way. Female is written as 46,XX and male as 46,XY.

A chromosome condition occurs when an individual is affected by a change in the number, size or structure of one or more chromosomes.

The change in the amount or arrangement of the chromosome/s in the cells may result in problems in growth, development and/or functioning of the body systems.

Chromosome changes may be inherited from a parent or can occur for the first time in a baby for unknown reasons (spontaneous occurrence). When a chromosome condition occurs for the first time, it is thought that the chromosomes became unbalanced when the egg or sperm cells which made that baby were forming. Changes may also occur after a baby is conceived.

## TYPES OF CHROMOSOME CHANGES

### 1. Changes in the number of chromosomes in the cell

***Having extra or missing chromosome/s***

During the formation of the egg or sperm, the chromosome pairs usually separate so that each egg or sperm cell contains only one copy of each of the 23 pairs of chromosomes. Sometimes, errors can occur in the separation of the chromosome pairs when the eggs or sperm are forming.

The result is that some of the eggs or sperm may have either an extra chromosome (24 chromosomes) or a loss of a chromosome (22 chromosomes).

When a sperm or egg that contain the usual 23 chromosomes combine at conception with an egg or sperm containing a changed chromosome number, the result is an embryo with too few or too many chromosomes e.g. 47 or 45 chromosomes instead of the usual 46.

The most common example of a chromosomal condition due to an **extra** copy of a chromosome is called **Down syndrome**.

Individuals with this condition usually have three copies of chromosome number 21, i.e. 47 chromosomes in their cells instead of 46. As **trisomy** means *three bodies*, **Down syndrome** may also be called trisomy 21.

The karyotype to describe the chromosome change in Down syndrome is 47,XX+21 if the person with Down syndrome is female and 47,XY+21 would describe a male with Down syndrome.

Having extra copies of either the X or Y chromosomes (the sex chromosomes) may also cause health or developmental problems. An example is **Klinefelter syndrome**, where boys are born with two or more copies of the X chromosome in addition to a Y. Klinefelter syndrome is represented by 47,XXY. All people with Klinefelter syndrome will be male due to the presence of a Y chromosome.

Having an entire numbered chromosome **missing** is very rare and will usually lead to pregnancy loss or a baby who is not alive for long after birth.

It is possible however to have one X chromosome missing and have a condition called **Turner syndrome**. Girls with Turner syndrome have only one copy of the X chromosome instead of the usual two copies i.e. 45 chromosomes in their cells instead of 46. This is represented by 45,X. All people with Turner syndrome will be female due to the absence of a Y chromosome.

***Having an extra full set of chromosomes***

Sometimes babies are conceived with three copies of every chromosome instead of the usual two and have a total of 69 chromosomes in each cell instead of 46. This situation is described as triploidy and usually leads to pregnancy loss or a baby who is not alive for long after birth.

**2. Changes in chromosome size and structure**

Sometimes the structure of one or more chromosome is rearranged leading to a gain or loss of genetic information. These changes can occur during the formation of the egg and sperm, during or shortly after conception or they can be inherited from a parent.

***Deletions (loss of genetic material)***

A small part of a chromosome may be lost (deleted). If the missing material contains important information for the body's development and growth, a genetic condition may result.

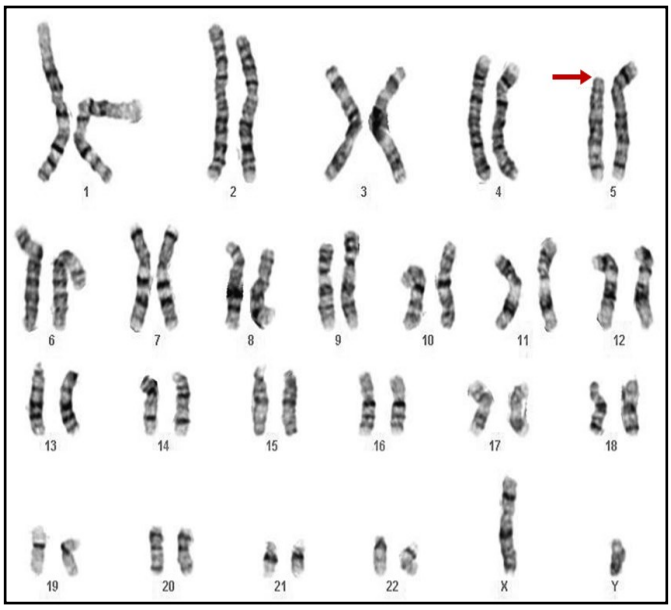


***Figure 4.4:*** *Chromosome picture (karyotype) from a male with 5p- syndrome.*

Deletions can occur anywhere along the length of any chromosome. One example of a deletion syndrome is 5p- syndrome. In this condition, a small part of the short (p) arm of chromosome 5 has been deleted, causing a range of health problems (*Figure 4.4*)

***Duplications (gain of genetic material)***

A small part of a chromosome may be gained (duplicated) along its length. This results in an increase in the number of genes present and may result in a problem with health, development or growth. Duplications can occur anywhere along the length of any chromosome.

***Inversions and rings***

Sometimes the chromosomes twist in on themselves, i.e. become inverted or join at the ends to form a ring instead of the usual rod shape. This may result in the loss of some genetic material. Also, the change in structure may cause problems when the chromosomes divide to form the egg or sperm.

If a parent has a chromosomal re-arrangement like an inversion or a ring, the child may receive an imbalance of chromosomal material, which may result in a problem with health, development or growth.

### *Uniparental disomy*

Usually a child will inherit one copy of each pair of chromosomes from their mother and one copy from their father. In some individuals, both copies of one of the chromosomes come from either their mother or their father, i.e. both copies of a pair of chromosomes have come from the one parent. This is referred to as **uniparental disomy**.
In this situation, despite the fact that the child will still have two copies of the chromosome with all its genes, a health problem may occur. This is because some genes require there to be one copy from the father and one from the mother in order to function normally.

### *Mosaicism*

Most individuals have the same chromosome number and structure in all the cells in their body, whether they are blood cells, skin cells or muscle cells. **Mosaicism** refers to a situation where there are different chromosome amounts in different cells of the body.

Some people with a chromosomal condition have some cells in the body with the right number and structure and other cells with a chromosomal change. Just as mosaic tiles on a floor have a mixture of patterns, someone who is mosaic for a chromosomal change will have a mixture of cells in their body.

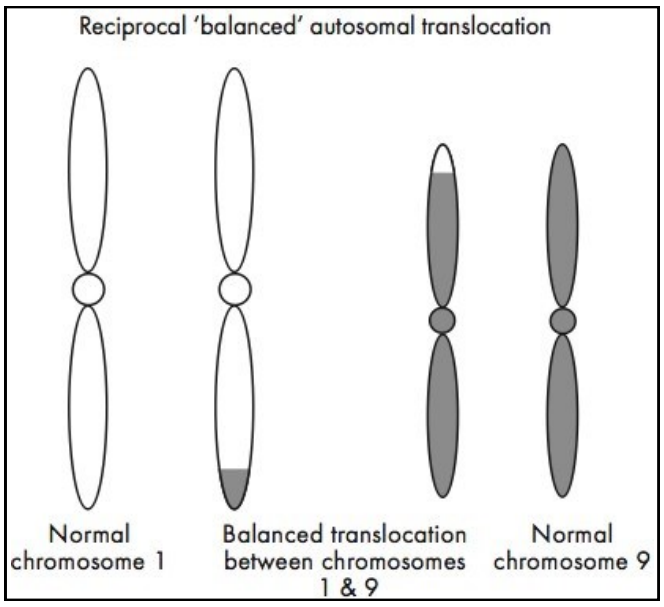


***Figure 4.5:*** *A person with this chromosome rearrangement has a 'balanced' translocation with the equivalent of two chromosomes each of numbers 1 and 9.*

The proportions of chromosomally changed and normal cells can be quite variable and may also vary between the cells of different body tissues.

For instance, someone who is mosaic for trisomy 21 may have the chromosome change in 60% of their skin cells and in only 5% of their blood cells.

### *Translocations*

Translocation is the term used to describe a rearrangement of chromosome material involving two or more chromosomes. There are two different types of translocations **reciprocal** translocations and **Robertsonian** translocations.

- Reciprocal translocations occur when material is exchanged between two chromosomes. The exchange may not interrupt any important information in the DNA and therefore will not affect the person's own health or development. In some instances however, the translocation may interrupt an important DNA message which may lead to some health or developmental problems. These trans-locations can involve any of the chromosomes and are nearly always spontaneous, i.e. they occur during the formation of the egg or sperm or during or shortly after conception.

An example of a reciprocal translocation can be seen in *Figure 4.5*. The chromosomes represented in this figure show that there is an exchange of material between chromosome number 1 and number 9.

In this case, where there does not appear to have been any loss or gain of chromosome material, the translocation is described as **balanced.**

If a parent has a balanced reciprocal translocation, there is a risk that the chromosomes in the eggs or sperm they create could pass on the incorrect amount of DNA information.

This is because when eggs and sperm are formed, a parent only passes down one of each of their chromosomes (see *Figure 4.1*).

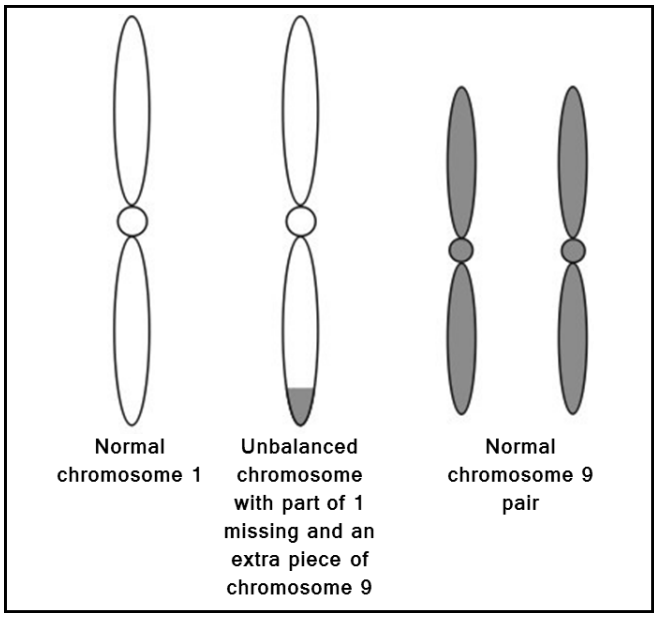


***Figure 4.6:*** *A person with an 'unbalanced' translocation between chromosome 1 and chromosome 9*

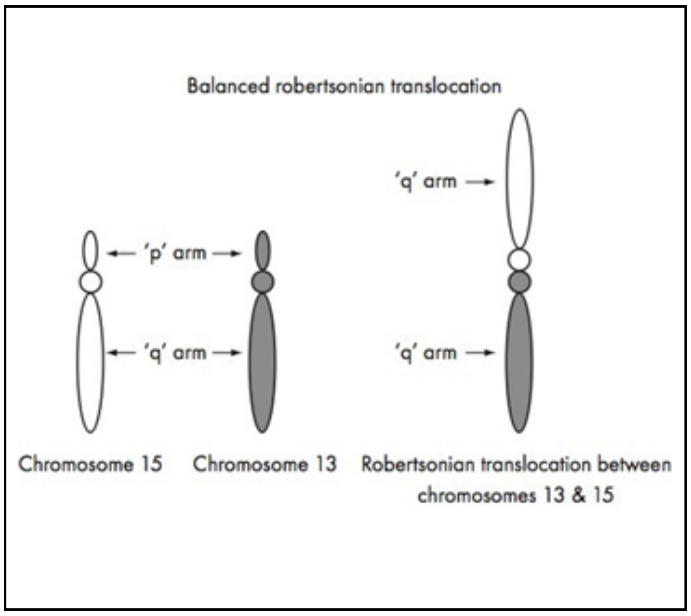


***Figure 4.7:*** *A Robertsonian translocation between chromosomes 13 and 15. Chromosomes 13 and 15 have joined together to produce one long chromosome*

In the situation shown in *Figure 4.5*, where the person has the balanced translocation themselves, an egg or sperm they produce (depending on whether they are female or male) could contain the **unbalanced** chromosome 1 and the **normal** chromosome 9.

Once fertilisation occurs and the other parent passes on their copy of chromosomes 1 and 9, the child will end up with an extra piece of chromosome 9 and the bottom of their chromosome 1 missing (see *Figure 4.6*)

Having extra or missing pieces of a chromosome may cause a number of health and developmental problems. It is difficult to predict the exact issues and severity unless there is already someone with the exact same chromosome changes.

For example, a child who has the same balanced translocation as their parent (who is healthy), would be expected to also have no health issues as a result of the same chromosome rearrangement.

When a child is the first member of a family to have a reciprocal translocation, it is not always possible to say that there will be no problem, even if it appears to be balanced.

The points where the breaks occurred in the chromosomes may disrupt an important gene and impair its function. In this case, there may well be symptoms or a problem for the child.

Robertsonian translocations occur when material is exchanged only between chromosomes 13, 14, 15, 21 and 22.

These chromosomes are different from the other chromosomes as their centromere lies very near the tip of the chromosome, giving a very short (p) arm and a long (q) arm. They are referred to as **acrocentric chromosomes**.

A Robertsonian translocation occurs when there is a loss of the short arms of two acrocentric chromosomes and fusion of the remaining two long arms at their centromeres.

This results in one long chromosome that consists of two long arms of either the same numbered chromosome or two different acrocentric chromosomes. The fused chromosome may contain either one or both centromeres from the original chromosomes (see *Figure 4.7*).

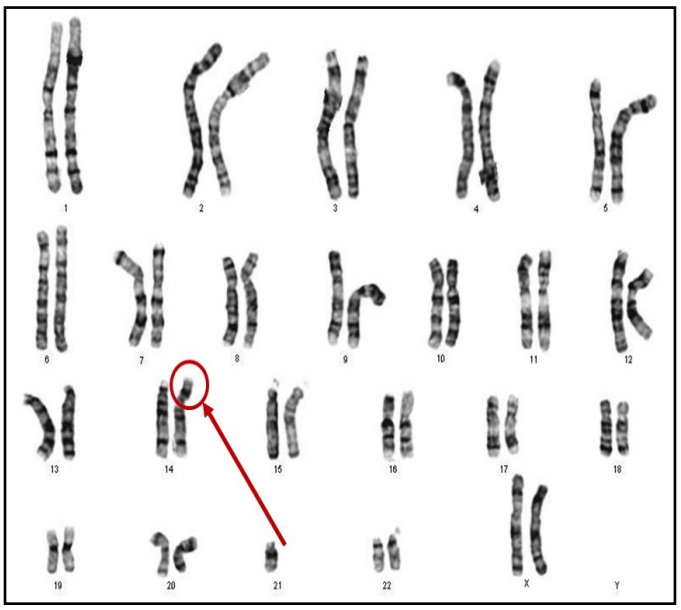

***Figure 4.8:*** *A picture (karyotype) of the chromosomes from a woman with a `balanced' Robertsonian translocation between chromosomes 21 and 14.*

Despite the fact that some of the short (p) arm is lost in order for the two chromosomes to fuse, there does not usually seem to be an effect on the health of that individual. This is provided that they have a total amount of balanced chromosome material in their cells.

In *Figure 4.8,* the chromosomes show a **balanced** Robertsonian translocation between chromosomes 21 and 14. One copy of chromosome 21 is attached to the top of chromosome 14.

This individual has two copies of chromosome 14 and two copies chromosome 21 - a balanced chromosome complement, simply rearranged.

If a parent has a balanced Robertsonian translocation, there is a risk that the chromosomes in the eggs or sperm they create could pass on the incorrect amount of DNA information.

This is because when eggs and sperm are formed, a parent only passes down one of each of their chromosomes (see *Figure 4.1*).

## THE IMPACT OF A CHROMOSOME CHANGE

For all of the changes in chromosome structure that are mentioned above, it is important that accurate testing and discussion of results is obtained from a genetic clinic. The impact of a chromosome change will depend on many factors including:

- Which chromosome/s are involved
- Which specific sections of the chromosome/s are involved
- Whether the change is balanced or not
- Whether the change is a new one in the family or passed down from a parent
- If all the cells in the body contain the change

If a parent has a balanced chromosome rearrangement, there is a chance that they may have a baby that inherits an unbalanced set of chromosomes which leads to health problems. This is part of the discussion that is important to have prior to falling pregnant in order to be as informed as possible.

Options to assist parents like these to have children with balanced chromosomes include testing before pregnancy, using assisted reproductive technology to fall pregnant and/or testing in the first few months of a pregnancy.