Fact sheet **04**

CHROMOSOME CHANGES

Genes are made up of DNA and are packaged on chromosomes. It is important that the chromosomes are balanced in the cells of our body for the right amount of DNA 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 usually only 23 single chromosomes (one from each pair)
- Having more or less chromosome material present in the cells of a person may lead to a health or developmental condition
- 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 code for our bodies to grow, develop and work properly.

Cytogenetics is the 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 usually 46 chromosomes. Chromosomes are found in pairs and each pair varies in size. Therefore there are 23 pairs of chromosomes, one of each pair being inherited from each parent.

- There are 22 numbered chromosomes roughly ordered 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 typically 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 typically 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 make unique banding patterns. These patterns allow the laboratory to check the size and structure of the chromosomes.

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Figure 4.1:
At conception, the sperm and egg combine

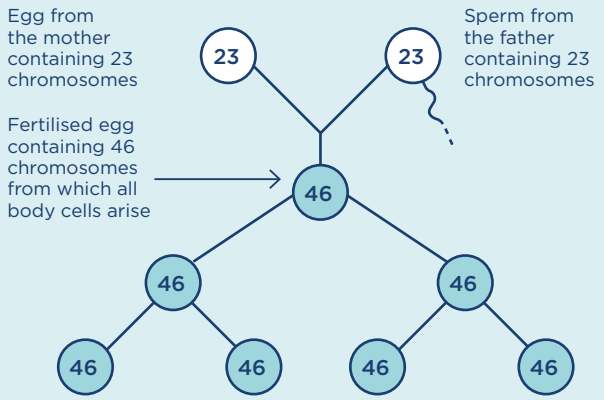
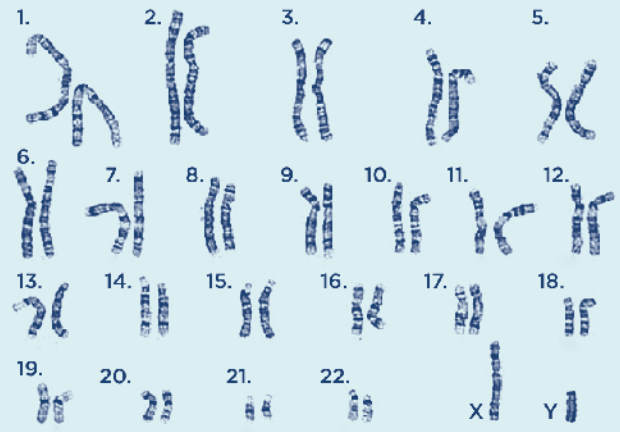


Figure 4.2 shows a banded chromosome karyotype from a male where each chromosome has been numbered from roughly the largest (chromosome number 1) to the smallest (chromosome number 22) and arranged in pairs.

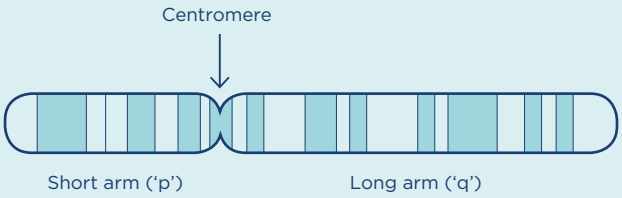
We know these chromosomes are from a male because of the X and a Y.

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



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

Figure 4.3:
A diagram of a chromosome showing how the centromere divides it into a short arm, called the 'p' arm, and a long arm, called the 'q' arm.



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

A chromosome condition happens when a person has a change in the number, size or structure of one or more chromosomes.

The change in the amount of material or arrangement of the chromosome(s) in the cells may result in conditions involving growth, development and/or how the body systems work.

Chromosome changes may be inherited from a parent or can happen for the first time in a baby for unknown reasons (happens spontaneously). When some chromosome conditions happen for the first time, the chromosomes were unbalanced in the egg or sperm cells that made the baby. Changes may also happen after a baby is conceived.

TYPES OF CHROMOSOME CHANGES

1. Changes in the number of chromosomes in the cell

Having extra or missing a 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, mistakes can happen in the way that chromosome pairs separate, 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 (early developing baby) with too few or too many chromosomes e.g. 47 or 45 instead of the usual 46.

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

People with this condition usually have three whole copies of chromosome number 21, i.e. a total of 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 a health or developmental condition. 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. 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 will not survive 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 pair, i.e. 45 chromosomes in their cells instead of 46. This is represented by 45,X. 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 is described as triploidy and usually leads to loss of the pregnancy or a baby who will not survive long after birth.

2. Changes in chromosome size and structure

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

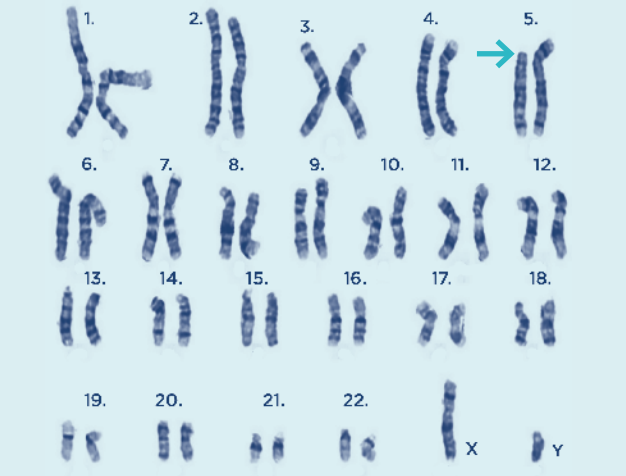
The main types of changes include:

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.

Deletions can happen 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 and developmental conditions (*Figure 4.4*).

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



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 condition involving health, development or growth. Duplications can happen 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 shape may cause problems when the chromosomes divide to form the egg or sperm.

If a parent has a chromosome re-arrangement like an inversion or a ring, the child may receive an imbalance of chromosome material, which may result in a condition affecting 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 called **uniparental disomy**.

Although the child will still have two copies of the chromosome with all the genes, a health condition may still sometimes happen. This is because some genes on certain chromosome pairs are switched on or off correctly, if one copy comes from the father and the other from the mother.

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 when there is a different chromosome makeup in different cells of the body.

Some people with a chromosome condition have some cells in the body with the right number and structure and other cells with a chromosome change.

Just as mosaic tiles on a floor have a mixture of colours and patterns, someone who is mosaic for a chromosome change will have a mixture of cells in their body.

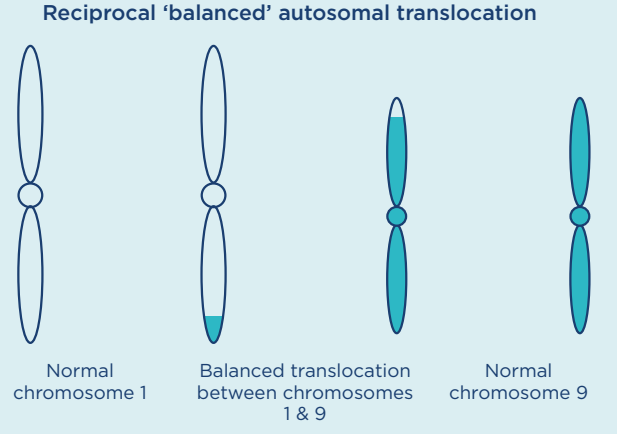
Translocations

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 happen when material is swapped between two chromosomes. The swap may not interrupt any important information in the DNA and therefore may not affect the person's own health or development. Sometimes, however, the translocation may interrupt an important DNA message which may lead to some health or developmental conditions. These translocations can involve any of the chromosomes and are nearly always spontaneous. In other words they happen when the egg or sperm is formed, 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.

Figure 4.5:
A person with this chromosome rearrangement has a 'balanced' translocation with the equivalent of two copies of chromosomes 1 and 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 chance 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 on one of each of their chromosomes from each chromosome pair (see *Figure 4.1*).

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

Once fertilisation happens and the other parent passes on their intact 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 conditions. It is difficult to predict exactly how this might affect someone. If there is someone else known to have the exact same chromosome change, this may help with understanding what may be likely for health, growth and development.

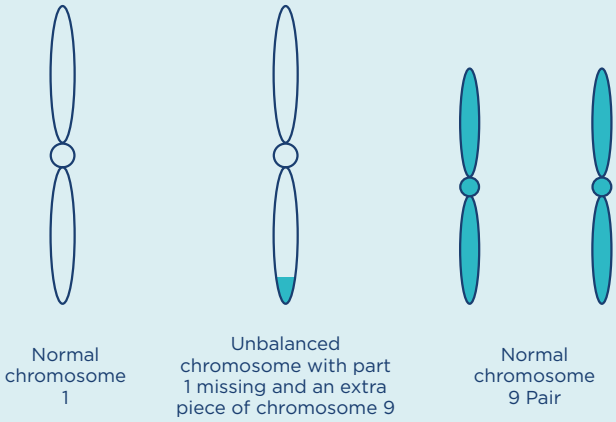
For example, a child who has the same balanced translocation as their parent (who is healthy), would be expected to also have no health issues as a result of the same chromosome rearrangement.

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 health condition, even if it looks balanced.

The points where the breaks happened in the chromosomes may interrupt an important gene so it no longer works properly. In this case, there may well be a health condition for the child.

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

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



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 happens when there is a loss of the short arms of two acrocentric chromosomes and the remaining two long arms join 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 joined chromosome may contain either one or both centromeres from the original chromosomes (see *Figure 4.7*).

Even though some of the short (p) arm is lost for the two chromosomes to join, this does not usually affect the health of a person with this since important chromosome material is usually not lost. In Figure 4.8, the chromosomes show a **balanced** Robertsonian translocation involving 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 of chromosome 21 - and is rearranged but essentially balanced.

If a parent has a balanced Robertsonian translocation, there is a chance that the chromosomes in the eggs or sperm they create could pass on the incorrect amount of DNA (see *Figure 4.1*).

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

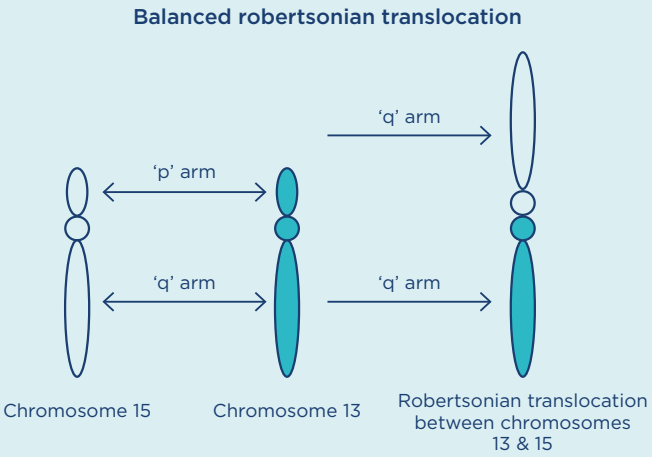
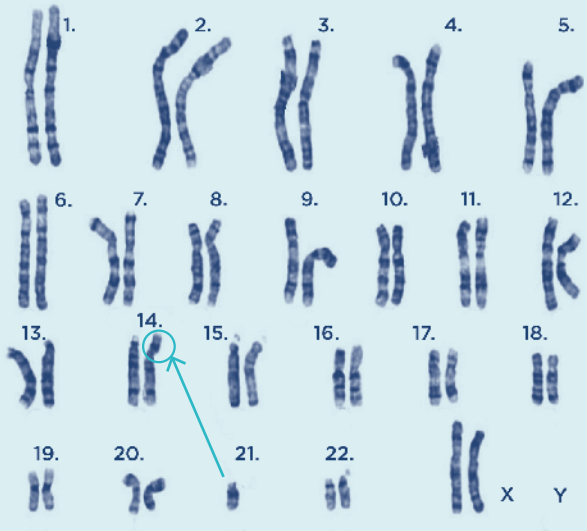


Figure 4.8:
A picture (karyotype) of the chromosomes from a woman with a `balanced' Robertsonian translocation involving chromosomes 21 and 14.



THE IMPACT OF A CHROMOSOME CHANGE

For all of the changes in chromosome structure mentioned above, it is important that accurate testing and discussion of results is arranged. The impact of a chromosome change may depend on:

- Which chromosome(s) are involved
- Which specific parts 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
- Whether an important part(s) of the chromosome is interrupted by the rearrangement.

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 a health condition. This is part of the discussion that may be important to have before falling pregnant, in order to be as informed as possible.

Options to help 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.