

Important points

- In each human cell, except the egg and sperm cells, there are 46 paired chromosomes of varying size
- One chromosome of each pair is inherited from each parent
- The *autosomes* are chromosomes numbered 1-22 (largest to smallest)
- The two sex *chromosomes* are called X and Y
- Egg cells contain 23 chromosomes, made up of 22 autosomes and an X
- Sperm cells contain 23 chromosomes, made up of 22 autosomes and an X or a Y
- When the egg and sperm join at conception, the baby will have 46 chromosomes in its cells, just like the parents
- Changes in the number, size or structure of chromosomes in the cells of an individual may cause a chromosomal condition that affects growth, development and health
- A particular type of chromosomal structural change is called a translocation. There are two different types of translocations:
 - Reciprocal translocation - material is exchanged between any of the chromosomes and involves pieces of any size
 - Robertsonian translocation - material is exchanged between chromosomes 13, 14, 15, 21 and 22
- Where there does not appear to have been any loss or gain of chromosome material, the translocation is described as **'balanced'**
- An **'unbalanced'** translocation means that an individual has more or less chromosomal material than usual
- A parent who carries a 'balanced' translocation may not have any problem with their growth, development and health but, depending on the chromosomes involved, they may experience reproductive problems such as infertility, miscarriage and having a child with an 'unbalanced' chromosomal complement
 - Generally, when a mother is a carrier of a 'balanced' Robertsonian translocation between chromosomes 14 and 21, there is a substantial risk of the child having Down syndrome of the translocation type
- If a child has the same 'balanced' chromosomal translocation in their cells as their parent, the child is unlikely to be affected by the chromosomal rearrangement
- Diagnostic testing is available in pregnancy where one parent carries a 'balanced' chromosomal rearrangement

Chromosomes in the human cell

Chromosomes are long strands of DNA found in all the cells of the body as described in Genetics Fact Sheet 1. The chromosomes contain genes that provide the coded information for our bodies to grow, develop and function. The scientific study of chromosomes is known as 'cytogenetics'.

In each human cell, except the egg and sperm cells, there are 46 chromosomes. The 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.

- Scientists have numbered 22 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

Egg cells contain 23 chromosomes, made up of 22 autosomes and an X chromosome. Sperm cells contain 23 chromosomes, made up of 22 autosomes and either an X 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 Genetics Fact Sheet 1).

The chromosomes in more detail

When the cells are dividing to form new cells, the chromosomes appear as rod-shaped structures that can be seen when using a microscope.

Figure 7.1 is a photograph of the chromosomes arranged in this order of size. These chromosomes must be from a male as there is only one X chromosome and one Y chromosome.

Figure 7.2 is a diagrammatic representation of a chromosome, showing that a centromere divides it into two 'arms': the short arm, called the 'p' arm, and a long arm called the 'q' arm.

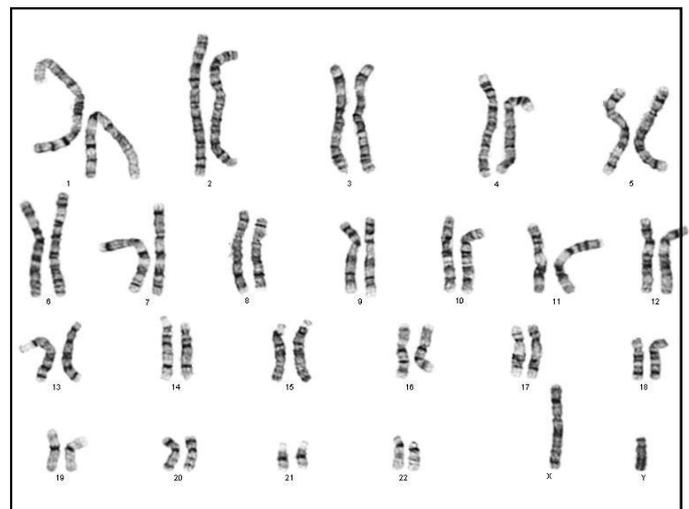


Figure 7.1: Normal chromosomal picture (karyotype) from a male 46,XY. Source: (SEALS Genetics, Prince of Wales Hospital, Randwick).

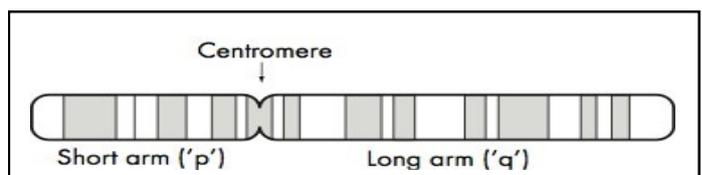


Figure 7.2: A diagrammatic representation of a chromosome showing the short ('p') and the long ('q') arms

Changes to chromosomes

A chromosome condition occurs when an individual is affected by a change in the number, size or structure of his or her chromosomes. This change in the amount or arrangement of the genetic information 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. More commonly, chromosome changes occur when the egg or sperm cells are forming or during or soon after the baby's conception: these occur for unknown reasons (spontaneous occurrence).

- Genetics Fact Sheet 6 discusses changes that can occur in chromosome **number**, **size** and **structure**.

This Fact Sheet describes in more detail a particular type of chromosome structural change called a **translocation**.

Chromosome translocations

Translocation (*trans* = across; *location* = place) is the term used to describe a rearrangement of chromosome material involving two or more chromosomes. There are two different types of translocations:

- Reciprocal translocation - material is exchanged between two chromosomes
- Robertsonian translocation - involves exchange between chromosomes 13, 14, 15, 21 and 22

Types of chromosome translocations

a. Reciprocal translocations

Reciprocal translocations are the most common type of translocation

- About 1 in 930 people in the general population have a reciprocal translocation

These translocations can occur between any of the chromosomes and involve pieces of any size.

The translocation arises when an exchange of chromosome material takes place between two different chromosomes; for example, where there is an exchange of material between chromosomes number 1 and number 9 (Figure 7.3). Pieces of each of these chromosomes have changed places.

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

b. Robertsonian translocations

Robertsonian translocations, named after an American cytogeneticist, are relatively common

- About 1 in 1000 people in the general population have a Robertsonian translocation

Robertsonian translocations only involve exchanges between chromosome numbers 13, 14, 15, 21 and 22.

- These chromosomes are different from the other chromosomes as their centromeres lie very near the tip of the chromosome, giving a chromosome with a long arm and a very tiny short arm (*acrocentric chromosomes*)

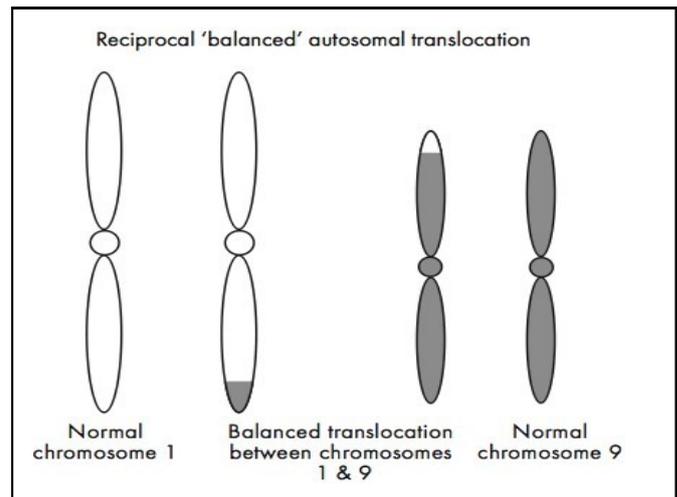


Figure 7.3: A person with this chromosome arrangement has a **'balanced' translocation** with the equivalent of two chromosomes each of numbers 1 and 9.

- The exchange involves loss of the short arms of two chromosomes and fusion of the remaining two long arms at their centromeres
- The result is one long chromosome that consists of two long arms of either
 - The same numbered chromosome
 - Two different chromosomes and containing either one or both centromeres

This means there is a loss of the short arm of the chromosomes involved. The loss of the genes that are located there, however, seems to have little or no effect on the health of the individual carrying a Robertsonian translocation

Figure 7.4 is a diagrammatic representation of a Robertsonian translocation between chromosomes 13 and 15. Chromosomes 13 and 15 have joined together to produce one long chromosome.

Figure 7.5 is a picture of the chromosomes (karyotype) from an unaffected individual with a **'balanced'** Robertsonian translocation between chromosomes 21 and 14. One copy of chromosome 21 is attached to chromosome 14 so the individual has two copies of chromosome 14 and two copies chromosome 21 - a **'balanced'** chromosome complement, simply rearranged.

Robertsonian translocations can also occur between the two chromosomes of the same pair, e.g. a Robertsonian translocation where the two chromosomes 21 fuse so the person has 45 chromosomes in total but with all the genetic material present (**'balanced'**).

How do chromosome translocations occur?

It is not understood what leads to breakage and rearrangements between chromosomes.

Reciprocal translocations are nearly always spontaneous, i.e. they occur during the formation of the egg or sperm or during or shortly after conception. Therefore neither parent has the chromosome change. In some cases, however, one parent may have a **'balanced'** reciprocal translocation themselves that causes no problems for themselves but may cause problems in pregnancy or with the baby's chromosome make-up.

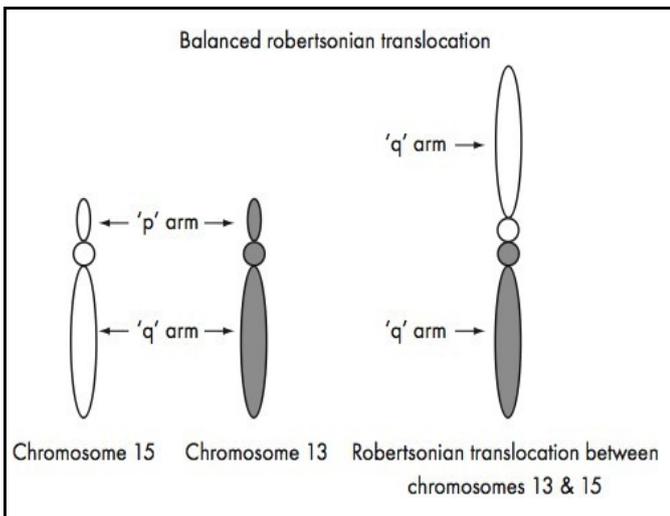


Figure 7.4: Robertsonian translocation between chromosomes 13 and 15, giving this individual the equivalent of two copies of chromosomes 13 and 15 re-arranged as one long chromosome.

Robertsonian translocations between the **same** two chromosomes are very rare and almost always occur as a spontaneous event, during the formation of the egg or sperm or during or shortly after conception. No other individual in the family would have a similar chromosome arrangement.

Robertsonian translocations between two **different** chromosomes are much more common and can be passed on through the generations as either 'balanced' or 'unbalanced' rearrangements (inherited). The most common of these is between chromosome 13 and chromosome 14 (around 33% of all Robertsonian translocations).

What is the impact of having a 'balanced' translocation?

a. 'Balanced' reciprocal translocation

The individual with a 'balanced' reciprocal translocation will usually have the correct amount of genetic information for normal development – simply rearranged differently from the usual.

- They are a 'translocation carrier'

When a parent is an unaffected carrier of a 'balanced' translocation:

- Their child may have the same 'balanced' chromosomal translocation in their cells as their parent and is also unlikely to be affected by the chromosome rearrangement
- Even though the parents themselves may not be affected, there is an increased chance that there will be reproductive consequences due to the child receiving an 'unbalanced' chromosome complement i.e the child has more or less chromosomal material than usual. For example:
 - one of the parents in a couple carries a 'balanced' translocation between chromosomes 1 and 9 as shown in Figure 7.3.
- This 'balanced' reciprocal translocation had no effect on the parent who is the translocation carrier as all the genetic information was present

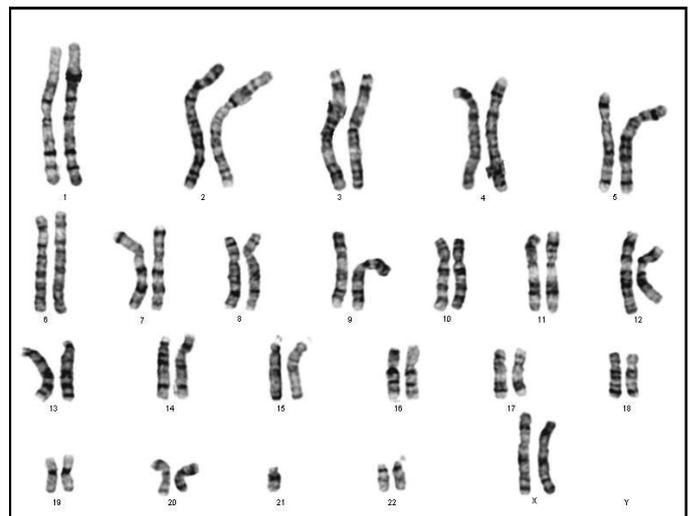


Figure 7.5: A picture (karyotype) of the chromosomes from a woman with a 'balanced' Robertsonian translocation between chromosomes 21 and 14. Source: (SEALS Genetics, Prince of Wales Hospital, Randwick).

- The child, however, (Figure 7.6) received a normal copy of chromosome 9 from each parent, one normal copy of chromosome 1 and the translocated chromosome 1 with additional chromosome 9 material - an 'unbalanced' translocation

Impact of the 'unbalanced' translocation in the child.

- The result is that the child has three copies of material from chromosome 9
- Depending on the information contained in the additional chromosome 9 material, the child may have a range of problems or not be affected at all
- The nature of these consequences depends on the particular chromosomes involved and the size of the translocated material
- It is not possible to outline all of these in this Fact Sheet. It is however, important for 'balanced' translocation 'carriers' and their partners to seek specialist genetic advice prior to conception (see Genetics Fact Sheet 3)

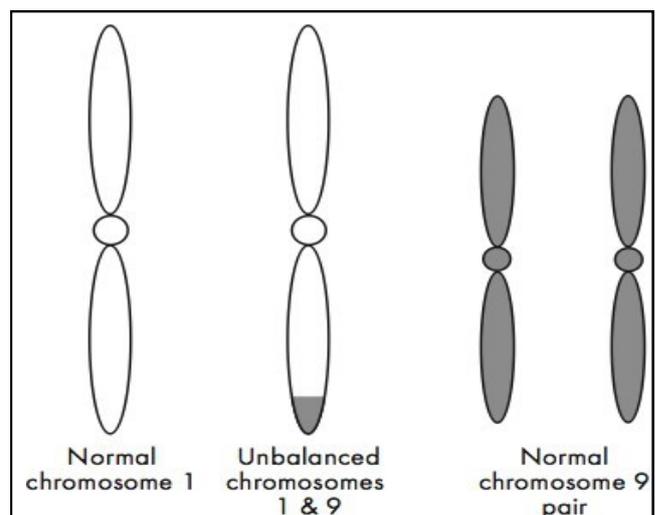


Figure 7.6: A diagrammatic representation of an 'unbalanced' autosomal translocation between chromosome 1 and chromosome 9 in a child where one parent has the 'balanced' translocation shown in Figure 7.3.

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

b. 'Balanced' Robertsonian translocations

'Balanced' Robertsonian translocations also generally do not result in physical or developmental problems for the 'carrier'.

- Even though they themselves may not be affected, there is an increased chance that there will be reproductive consequences due to the child receiving an 'unbalanced' chromosomal complement
- The nature of these consequences depends on the particular chromosomes involved and the size of the translocated material
- It is not possible to outline all of these in this Fact Sheet. It is however, important for translocation 'carriers' and their partners to seek specialist genetic advice prior to conception (see Genetics Fact Sheet 3)

The result of having an 'unbalanced' translocation

a. Autosomal reciprocal translocations (translocation between the chromosomes numbered 1-22)

The major reproductive risks for couples where one partner has a 'balanced' autosomal reciprocal translocation are

- Miscarriage
 - The translocations seem to imply no risk to the baby, but a woman may have repeated miscarriages before attaining a pregnancy
- Having a child with an 'unbalanced' translocation
 - The chance that carrying a 'balanced' translocation will cause a genetic condition in their child due to receiving 'unbalanced' chromosomal material varies from less than 1% to up to 20% according to the specific chromosomes involved in the translocation

b. Translocations between an autosome and an X chromosome

Where a woman has a translocation between one of her autosomes and one of her X chromosomes, there is a high probability that she will be infertile.

If she is able to achieve a pregnancy, there is a high risk of the baby having problems due to the child inheriting an 'unbalanced' chromosome complement.

- The degree of severity of the problems will again depend on the specific autosome and breakpoints involved

A man who carries a translocation between one of his autosomes and his X chromosome is likely to be infertile.

c. Robertsonian translocations

Couples where one partner is the carrier of a Robertsonian translocation can experience repeated miscarriage and male infertility.

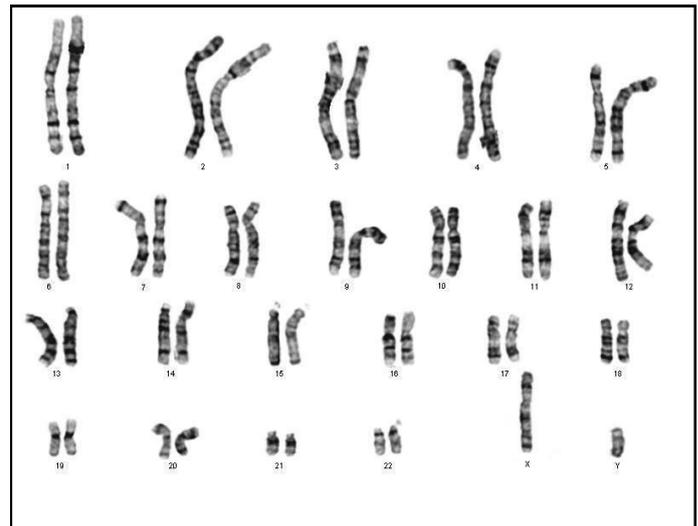


Figure 7.7: This male has Down syndrome of the translocation type due to having a total of three copies of chromosome 21: two individual copies and a third copy attached to chromosome 14.
Source: (SEALS Genetics, Prince of Wales Hospital, Randwick).

The risk of having a child with problems varies according to the specific chromosomes involved in the translocation.

- Generally, when a mother is a carrier of a 'balanced' Robertsonian translocation between chromosomes 14 and 21, there is a substantial risk of the child having Down syndrome of the translocation type (see Genetics Fact Sheet 28)

Figure 7.7 is a picture of the chromosomes from a male with Down syndrome of the translocation type. She has three copies of chromosome 21: two individual copies and a third copy attached to chromosome 14. This type of Down syndrome can't be inherited.

- The risk of having a child with a genetic condition for other Robertsonian translocations appears to be small

Testing in pregnancy to see if the baby has a chromosome translocation

Diagnostic testing is available in pregnancy where one partner carries a 'balanced' chromosomal rearrangement using either CVS (chorionic villus sampling) or amniocentesis (see Genetics Fact Sheet 17C). These tests are associated with a small risk to the pregnancy so should not be undertaken without appropriate genetic counselling and indication for having the testing (see Genetics Fact Sheet 3).

Those couples who are at risk for having a child with a chromosome change but who do not wish to undergo prenatal testing may be able to utilise the relatively new technology of preimplantation genetic diagnosis (PGD) discussed in Genetics Fact Sheet 18.

Other Genetics Fact Sheets referred to in this Fact Sheet: 1, 3, 6, 17C, 18, 28