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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 a person may cause a chromosomal condition that affects growth, development and health
- Chromosomal changes can be inherited from a parent
- Chromosomal changes can also occur when an egg cell or sperm cell is formed or during or shortly after conception
- Chromosomal conditions can be due to having:
 - Extra or fewer copies of the autosomes or the sex chromosomes; eg Down syndrome (3 copies of chromosome 21), Klinefelter syndrome (boys with XXY) and Turner syndrome (girls with only one copy of the X chromosome)
 - Extra or less of parts of individual chromosomes (duplications and deletions)
 - Chromosomes with structural abnormalities including forming rings or rearrangement of the material (translocations)
 - Both copies of a chromosome pair from one parent rather than a copy from each parent
- When the chromosomal change is only in some cells of the body rather than in all the cells, a person is 'mosaic' for the chromosomal change
- The impact of a chromosomal change will depend on
 - The type of change
 - The chromosomes (and therefore genes) affected by the change
 - The number and type of cells that contain the change
- The chance that a child will have a chromosomal change depends on the parents' family health history, the mother's age at the expected date of delivery and the type of change involved
- Testing in pregnancy is available to
 - Determine if the pregnancy is at risk for a chromosomal difference
 - Diagnose a chromosomal condition where indicated

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

Figure 6.1 is a photograph of the chromosomes arranged in order of size. These chromosomes must be from a male as there is only one X chromosome and one Y chromosome. *Figure 6.2* 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.

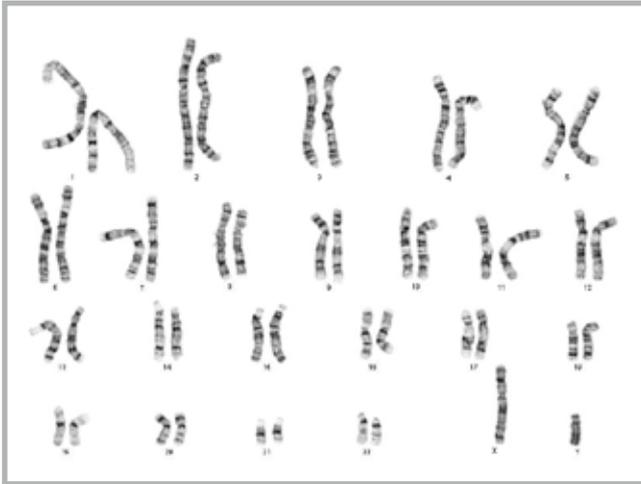


Figure 6.1: Picture (karyotype) of chromosomes from a male 46,XY (SEALS Genetics, Prince of Wales Hospital, Randwick).

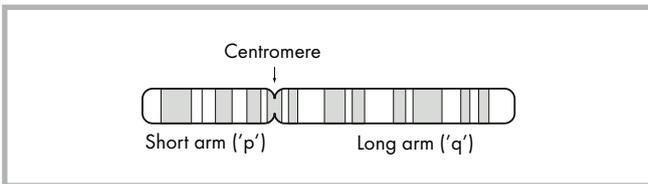


Figure 6.2: A diagrammatic representation of a chromosome showing the short ('p') and the long ('q') arms

Changes to chromosomes

A chromosomal 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.

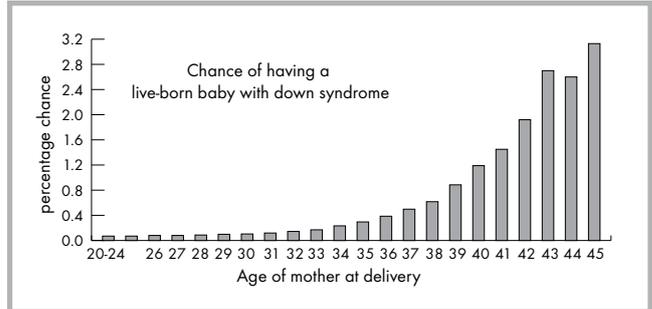
Chromosomal changes may be inherited from a parent. More commonly, chromosomal changes occur when the egg or sperm cells are forming or during or soon after conception: these occur for unknown reasons (spontaneous occurrence).

- This Fact Sheet discusses changes that can occur in chromosome **number**, **size** and **structure**
- Genetics Fact Sheet 7 describes in more detail a particular type of chromosomal structural change called a **translocation**

Changes in the number of chromosomes in the cell

Usually there are 23 pairs of chromosomes (46 in total) in all the body cells except the egg and sperm. Cytogeneticists describe this chromosome complement as **diploid**, meaning two sets of 23 chromosomes. The total number of chromosomes in the cells, and the description of the sex chromosomes present, is written in a shortened way. The chromosome complement of a female is written as 46,XX and a male as 46,XY.

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 happen 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).



Age of mother at delivery	Chance of having a live-born baby with Down syndrome	Age of mother at delivery	Chance of having a live-born baby with Down syndrome
20-24 years	1 in 1411	35 years	1 in 338
25 years	1 in 1383	36 years	1 in 259
26 years	1 in 1187	37 years	1 in 201
27 years	1 in 1235	38 years	1 in 162
28 years	1 in 1147	39 years	1 in 113
29 years	1 in 1002	40 years	1 in 84
30 years	1 in 959	41 years	1 in 69
31 years	1 in 837	42 years	1 in 52
32 years	1 in 695	43 years	1 in 37
33 years	1 in 589	44 years	1 in 38
34 years	1 in 430	45 years	1 in 32

Figure 6.3: Chance of having a live-born baby with Down syndrome (trisomy 21) according to the mother's age at the time of delivery of the baby. Source: Morris JK, Mutton DE, and Alberman E (2002). Revised estimates of maternal age specific live birth prevalence of Down syndrome. *Journal of Medical Screening*. 9,2-6.

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 eg 47 or 45 chromosomes instead of the usual 46.

(1) When there are more copies of particular chromosomes than usual:

There can be extra copies of the autosomes or the sex chromosomes.

a. Extra copy of an autosome (a numbered chromosome)

The most common example of a chromosomal condition due to an extra copy of an autosome is called **Down syndrome**. Individuals with this condition have three copies of chromosome 21, ie. 47 chromosomes in their cells instead of 46. As **trisomy** means 'three bodies', **Down syndrome** may also be called trisomy 21 (see Genetics Fact Sheet 28).

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



Figure 6.4: Chromosome picture (karyotype) from a baby with trisomy 18. Also called Edward syndrome (SEALS Genetics, Prince of Wales Hospital, Randwick).

The risk for having a baby with trisomy 21 increases with the mother's age, particularly when the mother's age at expected date of the delivery of the baby is at or more than 35 years. This is described as 'Advanced Maternal Age' (AMA) and the increasing risk is shown in Figure 6.3.

Other relatively common chromosomal conditions due to changes in the number of autosomes include:

- Trisomy 13 (three copies of chromosome number 13 instead of the usual two – see Genetics Fact Sheet 29)
- Trisomy 18 (three copies of chromosome number 18 – see Genetics Fact Sheet 30 and Figure 6.4)

Babies born with either of these chromosomal conditions in all the cells of their body have a range of severe disabilities and do not usually survive past infancy or early childhood.

Figure 6.5 shows that the risk for having a baby with any chromosomal abnormality, which includes trisomy 21, 18 or 13, increases with the mother's age.

b. Extra copy of a sex chromosome (an X or Y)

Having extra copies of either the X or Y chromosomes (the sex chromosomes) may also cause problems. An example is **Klinefelter syndrome**, where boys are born with two or more copies of the X chromosome in addition to a Y and is described as 47,XXY (Genetics Fact Sheet 31). Even though there are at least two copies of the X chromosome, the presence of a Y chromosome makes a person a male, regardless of the number of X chromosomes.

Other sex chromosomal conditions include triple X syndrome (girls with three copies of the X chromosome 47,XXX) and boys who have two copies of the Y chromosome (47,XYY syndrome).

(2) When there are fewer copies of particular chromosomes than usual:

In most cases, the loss of a whole chromosome is incompatible with life and will result in miscarriage or stillbirth. The loss, however, of the X or Y chromosome results in the condition called **monosomy X** (monosomy means 'one body').

- This condition is also called Turner syndrome. Girls born with

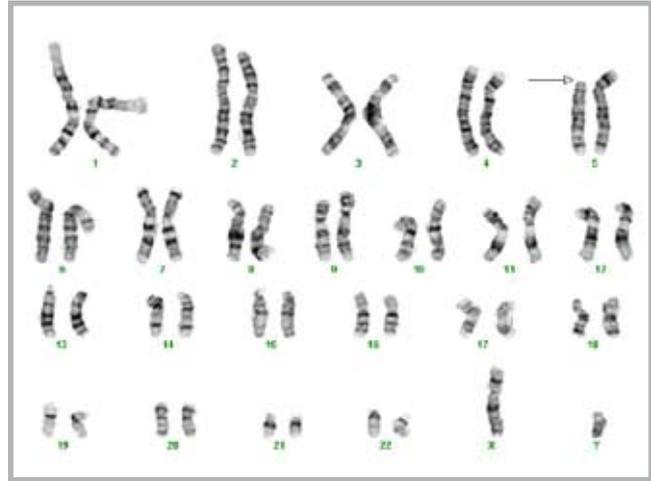


Figure 6.6: Chromosome picture (karyotype) from a baby with 5p- syndrome (SEALS Genetics, Prince of Wales Hospital, Randwick).

Turner syndrome have only one copy of the X chromosome instead of the usual two copies ie. 45 chromosomes in their cells instead of 46 (45,X) - see Genetics Fact Sheet 32.

(3) When there are extra copies of all of the 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 is incompatible with life.

Changes in chromosome size and structure

Sometimes the structure of individual chromosome(s) is changed so that the chromosomal material is broken and rearranged in some way or chromosomes gain or lose material. These structural changes can occur during the formation of the egg and sperm, during or shortly after conception or they can be inherited from a parent.

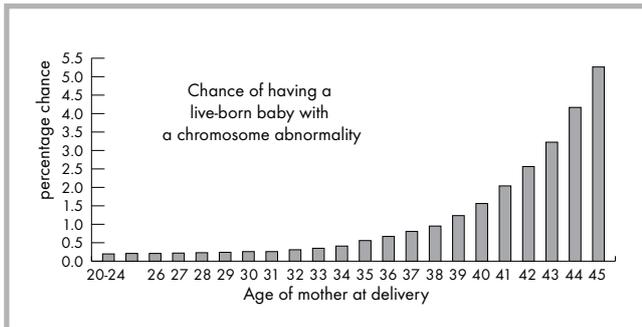
a. Translocations

Sometimes, a piece of one autosome or sex chromosome is broken off and becomes attached to another different autosome or sex chromosome. More detailed information about translocations can be found in Genetics Fact Sheet 7.

b. Deletions (loss of chromosomal material)

A small part of a chromosome may be lost (deleted). If the missing material contains important information for the body's development and function, a genetic condition may result. Large deletions are usually incompatible with life. Deletions may occur anywhere along the length of any chromosome.

Figure 6.6 is a photograph of the chromosomes from a child with 5p- syndrome. A small part of the short ('p') arm of chromosome 5 has been deleted, causing a range of disabilities including a characteristic high pitched mewing or cat cry in infancy.



Age of mother at delivery	Chance of having a live-born baby with a chromosomal abnormality	Age of mother at delivery	Chance of having a live-born baby with a chromosomal abnormality
20-24 years	1 in 506	35 years	1 in 179
25 years	1 in 476	36 years	1 in 149
26 years	1 in 476	37 years	1 in 124
27 years	1 in 455	38 years	1 in 105
28 years	1 in 435	39 years	1 in 81
29 years	1 in 417	40 years	1 in 64
30 years	1 in 385	41 years	1 in 49
31 years	1 in 385	42 years	1 in 39
32 years	1 in 323	43 years	1 in 31
33 years	1 in 286	44 years	1 in 24
34 years	1 in 244	45 years	1 in 19

Figure 6.5: Chance of having a live-born baby with any chromosomal abnormality according to the mother's age at delivery. Source: Hook EB (1981). Rates of chromosomal abnormalities. Obs Gyn 58, 282-285.

c. Duplications (gain of chromosomal 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.

d. 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. The result may be that during the formation of the ring some genetic material may be lost. Also the chromosome 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 cause problems in their physical and/or intellectual development.

e. When a child inherits both copies of a pair of their chromosomes from only one parent (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 cases, however, 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 situation is referred to as **uniparental disomy**.

The child will still have two copies of the chromosome with all its genes, and so this may not cause a problem for the child. For some genes carried on some chromosomes, normal cell function depends on having one gene copy inherited from each parent.

- In some cases both a maternal copy (copy from the mother) and a paternal copy (copy from the father) of some genes are required for normal function
- The genes on these parts of the chromosome are turned 'on' or 'off' depending on whether they are passed to the child through the egg (from the mother) or the sperm (from the father)

This system of switching genes on and off is called **epigenetics** and the genes are described as being **imprinted** (see Genetics Fact Sheet 15).

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 cells in other tissues like sperm (males) and eggs (females).

Commonly in **all** their cells:

- Females will have a chromosome complement of 46,XX
- Males will have 46,XY
- Individuals with Down syndrome will usually have an extra chromosome 21 (trisomy 21); 47, XX+21 or 47,XY+21

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
- 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 chromosomal change in 60% of their skin cells and in only 5% of their blood cells
- Individuals who have the chromosomal change in most of their cells are likely to be more severely affected by the resulting condition than those in whom only a small proportion of cells are chromosomally changed
- Individuals who are mosaic for a chromosomal change may not always have some cells with the correct chromosome number and structure: some have a mixture of cells with different unusual patterns

Mosaicism is one of the problem areas in the study of chromosomes because without studying the chromosomes of every cell in the body (which is impossible), we cannot always be certain that someone is not mosaic for the change.

Even in those cases where we know that mosaicism is present, we usually do not know what the pattern is like in different parts of the body; this makes it more difficult to predict how severely

affected an individual may be.

The impact of a chromosomal change

The impact of a chromosomal change will depend on:

- The type of change
- Which chromosome(s) and therefore gene (s) are affected by the change
- The number and type of cells that contain the change

In some cases, a change in chromosome number, size or structure will lead to a problem in growth, development or health. In other cases an individual can have a chromosomal change and not be aware of it at all until they try to have a child. At this point, a chromosomal change in one of the parents may be indicated if there is infertility or three or more miscarriages.

The estimation of risk that a child will have a chromosomal change depends on the:

- Parents' family health history
- Mother's age at the expected date of delivery
- Type of change

For example, where parents have a child with Down syndrome due to trisomy 21 (i.e. not associated with a translocation as detailed in Genetics Fact Sheet 7), the risk that they could have another child with Down syndrome is about 1 chance in 100 or 1% in every

pregnancy if the mother is under 35 years. When the mother is over 35 years, the risk will be higher and advice should be sought from a genetic counsellor (see Genetics Fact Sheets 3 & 28).

Can a test be done in pregnancy to see if the baby has a change in their chromosome number or structure?

Some screening tests can determine if the baby is at increased risk for having a change in chromosome number. These prenatal screening tests are discussed in Genetics Fact Sheet 17B.

Where the baby is at risk of having a chromosomal change in number or structure, testing is available to diagnose the chromosomal change. These tests, CVS (chorionic villus sampling) or amniocentesis, 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). Details of these tests can be found in Genetics Fact Sheet 17C.

Those couples who are at risk for having a child with a chromosomal 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, 7, 15, 17B, 17C, 18, 28, 29, 30, 31, 32

Information in this Fact Sheet is sourced from:

- Hook EB. (1981). Rates of chromosomal abnormalities. *Obs Gyn*, 58, 282-285.
- Gardner RJM and Sutherland G. (2004). *Chromosome abnormalities and genetic counselling*. 3rd ed. Oxford University Press. New York.
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