**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 missing segments of individual chromosomes (duplications and deletions).
  - Structural abnormalities including where chromosomes have become ring-shaped or the material has been rearranged (translocations).
  - Inheriting 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 their cells, a person is said to be ‘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.
- Testing can be done in a child or adult that looks at changes in the number or structure of their chromosomes to determine if the change is associated with the condition under investigation.
- Testing looks for variations in the number of copies of very small segments of the DNA in each chromosome (copy number variants).

**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.

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. The numbered chromosomes 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.*

**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.
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).

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

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 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 (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.
Changes to chromosomes—number, size and structure

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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:

- 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 to see if the person has a change in their chromosome number or structure?

Testing can be done on a sample that is usually obtained from a blood test. Previously, the chromosomes from the white blood cells were examined under a microscope and a picture (karyotype) was generated as shown in Figure 6.1: Very small chromosomal changes such as missing or extra segments (deletions and duplications) were however missed.

New technologies are now being used that enables these small changes to be seen and so a karyotype is not usually the test that is done today. These techniques look at individual segments of each chromosome. Usually there would be two copies of each segment. The DNA making up the extra or missing copies of the segments (copy number variant) found are then further examined to determine if they are likely to be associated with the condition under investigation. See http://www.genetics.edu.au for further information about this test (Microarray testing for extra or missing segments of DNA).

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. Samples of tissue from the baby are obtained using two types of tests: CVS (chorionic villus sampling) or amniocentesis. However, 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). 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