

## Important points

- Down syndrome is the most common chromosomal condition affecting newborn babies
- Characteristics may include intellectual delay, distinct facial features, problems with the heart and digestive tract
- Down syndrome is due to one of the following:
  - An additional copy of chromosome 21 (*trisomy 21*) in all of the cells of the body (about 95% of cases)
  - An additional copy of chromosome 21 in some of the cells of the body (*mosaic trisomy 21*-about 1% of cases)
  - A chromosomal *translocation* involving chromosome 21 (about 4% of cases)
- The chance for having a child with Down syndrome due to trisomy 21 increases with the mother's age
  - If a woman has had a child with *trisomy 21* there may be a small additional increase in risk over her age risk for having another child with the condition
- The translocation type of Down syndrome can run in families (inherited)
- Screening and diagnostic testing (where indicated) for Down syndrome is available in pregnancy

## What is Down syndrome?

In 1866, a physician named John Langdon Down who worked with people with intellectual disabilities, observed that a number of his patients were so similar in appearance that they might easily be mistaken to be brothers and sisters. In a classic description, he recorded that these individuals possessed a broad, flat face, a thick tongue and a small nose and were intellectually impaired to a variable degree.

About 1 in every 1000 babies in Australia is born with Down syndrome, and it affects people of all ethnic backgrounds.

A syndrome is a condition distinguished by a number of features that may occur together. At birth, many babies with Down syndrome will have one or all of the following features:

- Low muscle tone (a floppy baby)
- A face that appears flatter with eyes slanting upward
- Small ears and a wider neck than usual
- A crease across the palm of the hand and a gap between the first and second toes ('sandal-gap' sign)
- Children with Down syndrome vary considerably between individuals but may have a variety of health problems including those which affect the heart, digestive system and general development
- It is very unlikely that any one child with Down syndrome will have all of the features commonly associated with the syndrome

While intellectual disability is a feature of the syndrome, those with the condition will develop and learn throughout life, but at a slower pace than usual. Early intervention programs are very effective in maximising the potential of children with Down syndrome.

## Chromosomes

In each human cell, except the egg and sperm cells, there are 46 chromosomes, made up of 23 pairs. The chromosome pairs are numbered according to their size from 1-22 and there are two sex chromosomes; two X chromosomes in females and an X and a Y in males (see Genetics Fact Sheet 1).

When egg and sperm cells are formed, the chromosome pairs separate so that there is only one of each pair in these cells i.e. 23 chromosomes instead of 46. A baby is conceived when the egg from the mother and the sperm from the father come together.

The baby would then have two copies of each chromosome (46 chromosomes in total) just like the parents. One copy of each chromosome would have come from the mother and one copy from the father.

Sometimes, when the egg and sperm are forming, a mistake occurs so that the chromosome pairs do not separate in an ordered fashion. The result is an egg or sperm cell that has only 22 chromosomes while others have 24 chromosomes.

If an egg or sperm carrying 24 chromosomes combines with an egg or sperm carrying the usual 23 chromosomes, the result would be an individual with cells in which there are 47 chromosomes instead of the usual 46 (*Figure 28.1*).

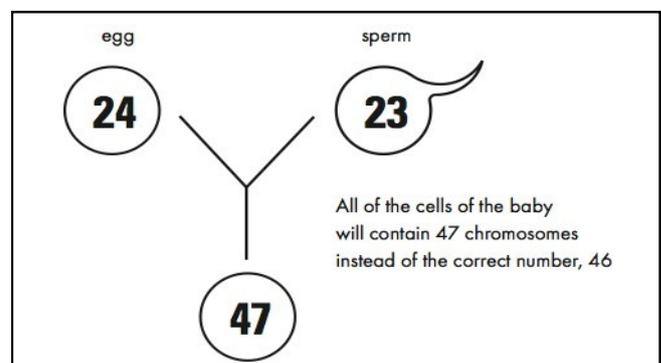
- There would be three copies of a particular chromosome in the cells rather than two (see Genetics Fact Sheet 6). This is called **trisomy**.

## The chromosome pattern in Down syndrome

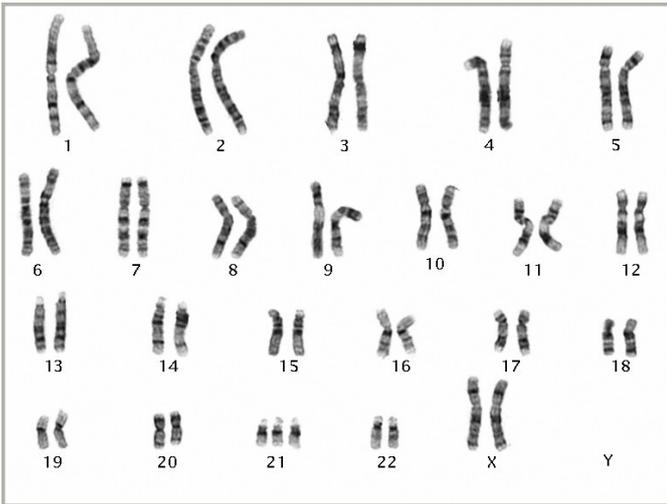
The presence of the extra copy of chromosome 21 causes the intellectual and physical characteristics of Down syndrome.

**In 95% of all cases of Down syndrome**, the extra copy of chromosome 21 is present in all the cells of the baby and in these cases the condition is referred to as trisomy 21. *Figure 28.2* is a picture (karyotype) of the chromosomes from a female with trisomy 21.

- The mistake in the distribution of the chromosomes occurred at the time of the production of the egg or sperm or at fertilisation, so that the extra chromosome 21 is in all the cells of the baby that arise from the fertilised egg (*Figure 28.1*).



**Figure 28.1:** When the egg has 24 chromosomes, and the sperm has the usual 23, the baby's cells will contain 47 chromosomes instead of 46.



**Figure 28.2:** Chromosome picture (karyotype) from a female with trisomy 21. In this cell, there are 47 chromosomes including three copies of chromosome 21 instead of the usual two. All her cells may contain the extra chromosome 21 copy or other cells in her body may have the correct chromosome number 46 (mosaic for trisomy 21) (source: SEALS Genetics, Prince of Wales Hospital, Randwick).

In about 1% of all cases of Down syndrome, the mistake in the distribution of chromosomes in cell division occurs shortly after fertilisation of the egg by the sperm, so that there is a mixture of cells with different chromosome patterns. This situation is called **mosaicism**.

- This means that some individuals who have Down syndrome have some of their body cells containing 47 chromosomes because of an extra copy of chromosome 21, while other cells in their body have the usual 46 chromosomes. These individuals are said to be **mosaic for trisomy 21**. They have the mosaic type of Down syndrome (see Genetics Fact Sheets 6 and 13)
- The number of cells that contain the extra copy of chromosome 21, and in which tissues or organs they occur, would have an effect on the severity and characteristics of the condition.

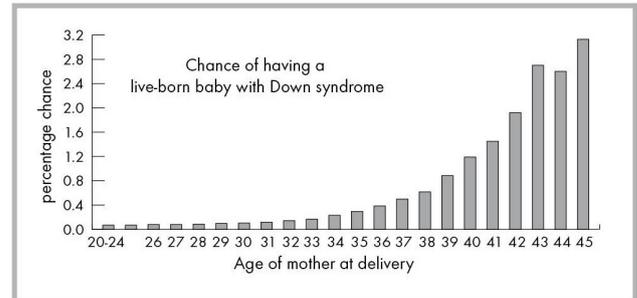
In about 4% of all cases of Down syndrome, the extra copy of chromosome 21 is attached (*translocated*) to another chromosome.

- This is called the **translocation type of Down syndrome** (see Genetics Fact Sheet 7) and is an inherited form of the condition.

### Can a baby with Down syndrome be cured?

There is no cure for a child born with this condition but many symptoms can be treated and special early intervention programs are enabling these individuals to develop to their potential.

A child with Down syndrome can usually do most things that any young child can do such as walking, talking, dressing and being toilet trained although they may do these things later than other children.



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 28.3:** 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. (Sources: 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).

### Who is at risk of having a child with Down syndrome?

In an individual with Down syndrome, the extra copy of chromosome 21 can come from either the egg or the sperm.

It has been shown, however, that as a woman gets older, her chance of having a child with Down syndrome increases, as shown in Figure 28.3. In particular, a woman who is 35 years or older at the time of delivery of her baby, has an increased chance of having a baby with Down syndrome.

### What is the chance that Down syndrome occurs more than once in a family?

Where there has been a previous child with Down syndrome or a close family history of Down syndrome, a discussion with a genetic counsellor can provide information about the chance of having another affected child, and the availability of testing (see Genetics Fact Sheet 3).

The chance that Down syndrome would occur twice or more in the same family depends on the genetic cause for Down syndrome.

- If a woman already has a child with trisomy 21 (an extra copy of chromosome 21 in all the cells), there may be a small additional increase in risk over her age risk
  - Overall, the risk of this happening again (recurrence risk) in a later pregnancy is about 1% (1 in 100) but may be slightly higher in older women
- If a woman has a child with mosaic trisomy 21, there is unlikely to be any additional risk over her age risk
- If a woman has a child with a translocation involving chromosome 21, there is an additional increase in risk over her age risk. The increase in risk depends on the type of translocation involved, whether or not it has been inherited from one of the parents, and if so, from which parent (mother or father)

## Can Down syndrome be diagnosed before the baby is born?

There may be a number of indications that there is an increased risk for the baby having Down syndrome including:

- The mother's age
- A family history of Down syndrome
- The results of a screening test for this condition in pregnancy

There are several prenatal screening and diagnostic tests that can be done during pregnancy to determine if the baby is at risk of having, or definitely has Down syndrome.

- Genetics Fact Sheet 17 provides a summary of the most common prenatal diagnostic and screening tests available
- The prenatal screening tests (which estimate risk of Down syndrome) are detailed in Genetics Fact Sheet 17B and the prenatal diagnostic tests in Genetics Fact Sheet 17C

In addition, preimplantation genetic diagnosis (PGD) allows for testing for Down syndrome on an embryo that has been created using assisted reproductive technology (ART) such as in vitro fertilisation (IVF). If the embryo does not have the condition, it is transferred to the uterus and allowed to develop normally (see Genetics Fact Sheet 18).

Any consideration of testing before or in pregnancy should only be made on an informed basis following counselling (see Genetics Fact Sheet 3).

## Current research into Down syndrome

Trisomy 21 is the single most common chromosomal condition and active research is ongoing. The whole of chromosome 21 has now been defined by DNA techniques and researchers are investigating the possibility of there being a 'critical region for Down syndrome' on the end of the long arm ('q' arm) of this chromosome.

**Other Genetics Fact Sheets referred to in this Fact Sheet: 1, 3, 6, 7, 13, 17, 17B, 17C, 18**