

Support and Information



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Robertsonian Translocations

The image on page 2 comes from Scriven PN (1998) Communicating chromosome rearrangements and their outcomes using simple computer-generated color ideograms. *Genetic Testing* 2(1): 71-74

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Robertsonian translocations

A Robertsonian translocation is an unusual type of chromosome rearrangement caused by two particular chromosomes joining together. Out of every 1,000 newborn babies, one has a Robertsonian translocation.

The phrase Robertsonian translocation is too long for normal conversation and many people shorten it to **rob**.

When the translocation is **balanced**, the person with it is called a **Robertsonian translocation carrier**. As carriers are healthy and have a normal lifespan, many never discover about their unusual chromosome rearrangement. In fact, the translocation can be passed down in families for many generations without anyone discovering.

An **unbalanced** Robertsonian translocation may come to light after a baby is born with a chromosome disorder. Most babies with unbalanced Robertsonian translocations have parents with normal chromosomes. A minority of babies have one parent who is a Robertsonian translocation carrier.

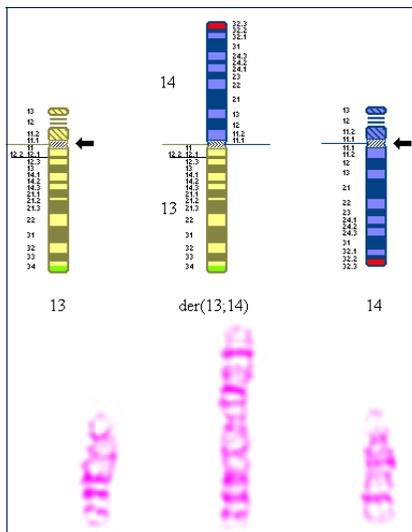
What are chromosomes?

Chromosomes are the microscopically small structures in the nucleus of the body's cells that carry genes. These genes are the instructions that tell our bodies how to develop and work properly. We have 46 chromosomes in all, 23 inherited from our father and 23 from our mother.

Each chromosome has a short arm and a long arm. Five of the 23 chromosomes have a very small short arm that contains no unique genes; these are chromosome 13, 14, 15, 21 and 22. Technically, they are called acrocentric chromosomes.

In a Robertsonian translocation, two of the five acrocentric chromosomes have broken at the beginning of the short arm near the point where it meets the long arm. The long arms have then fused together. This chromosome then consists of two long arms but no short arms.

The short arms are lost but as all the genes on a short arm are available on the short arms of other acrocentric chromosomes, a Robertsonian translocation carrier will have no health problems due to their chromosome rearrangement. However, while other people usually have 46 chromosomes, Robertsonian translocation carriers have 45. In this leaflet we also call the chromosome with the Robertsonian translocation a fused chromosome.

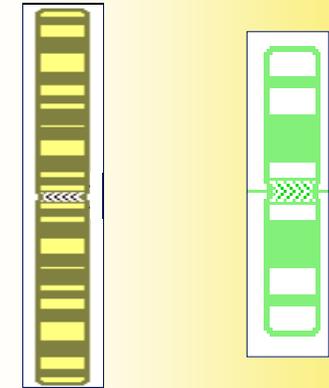


One person in 1,300 has a rob chromosome made up of the long arms of 13 and 14

Image courtesy Guy's & St Thomas' Cytogenetics Dept.

Same-chromosome translocations

There is a group of carriers whose translocation chromosome consists of the two long arms of the same chromosome – 13;13, 14;14, 15;15, 21;21 or 22;22. These carriers will always produce eggs or sperm with unbalanced chromosomes – either with two copies of the chromosome or with none. This means that they can never achieve a normal full-term pregnancy. For these couples, egg or sperm donation can offer the hope of pregnancy.



15;15 **21;21**
Same-chromosome translocations

How does a Robertsonian translocation happen?

The great majority of Robertsonian translocations very likely arise when the eggs (or more rarely sperm) are forming. In the case of eggs, this means that the process started when the mother of the first person in the family with a Robertsonian translocation was herself a three or four-month-old fetus in her mother's womb. Many families wonder what they did wrong to cause this. In reality, chromosomes break and rejoin as a natural part of evolution and as a parent you cannot control this. No environmental, dietary or lifestyle factors are known to cause Robertsonian translocations, so there is nothing you did before you were pregnant or during pregnancy that caused this and nothing you could have done to prevent it.

How unusual is it to be a Robertsonian carrier?

Although one person in 1,000 is a Robertsonian carrier, some combinations of the five acrocentric chromosomes are much more common than others.

Robertsonian translocation	Approximately how common are carriers?
13;14	1 : 1,300
14;21	1 : 12,500
14;15	1 : 20,000
13;13, 13;15, 13;22, 14;22	1 : 50,000
13;21, 15;22	1 : 100,000
15;21, 21;21, 21;22	1 : 200,000

What are the risks of having more than one affected pregnancy or child?

This depends chiefly on whether either parent is a Robertsonian translocation carrier. If neither parent is a carrier, it is extremely unlikely that another baby will be conceived with an unbalanced Robertsonian translocation. If the mother is a carrier and her translocation chromosome includes 21, there is an appreciable risk of having another affected pregnancy. For other carriers, the risk is low.

If one parent is a Robertsonian translocation carrier

Mother has 13;21, 14;21, 15;21 or 21;22	10-15% risk of a baby with translocation Down's.
Mother has 13;14, 13;15, 13;21 or 13;22	1% chance of having a baby with trisomy 13.
Mother has 14;15, 14;22 or 15;22	Almost certainly no risk of having a baby with a trisomy, but possible risk of miscarriage or UPD.
Father with any Robertsonian combination	Low risk, below 1%, of any child being affected.

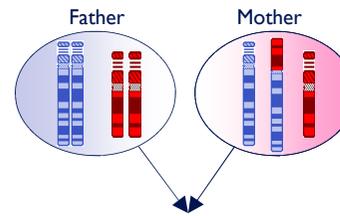
For carriers, what are the risks of pregnancy loss?

Generally speaking, Robertsonian translocation carriers do have an increased risk of pregnancy loss. While a few babies with trisomy 13 or 21 will survive, those with trisomy 14, 15 or 22 usually miscarry in the first twelve weeks. It has been suggested that certain Robertsonian translocation carriers are particularly prone to pregnancy loss. If you are a carrier and have repeated pregnancy losses, you should be able to discuss your options with your genetics service.

What are the chances of a couple with fertility problems having a child?

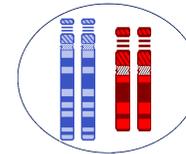
Most couples where one partner is a Robertsonian translocation carrier do not have fertility problems but if they do, it is possible to help by using assisted reproduction. In carrier men, 10 to 15% of the sperm may be chromosomally unbalanced and in addition it is thought that the translocation chromosome may block the creation of sperm. As even men with low sperm counts do produce some sperm, it should still be possible to achieve pregnancy using intracytoplasmic sperm injection (ICSI). In countries where this is permitted, pre-implantation genetic diagnosis (PGD) may also be offered to ensure that implanted embryos are chromosomally balanced. If you have had more than one affected pregnancy or have had repeated miscarriages caused by unbalanced chromosomes, this is an option to consider.

Why does being a Robertsonian carrier matter?



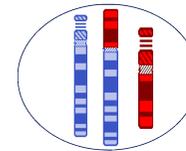
A balanced Robertsonian translocation only matters when a couple tries for a baby. When one parent is a Robertsonian translocation carrier there are four possible outcomes. The most common outcomes are **1** and **2**. In the examples on this page, the mother is a Robertsonian 14;21 carrier. The father has two separate 14s and two separate 21s.

1 A normal pregnancy and baby



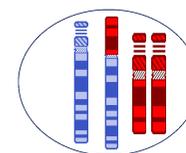
The baby does not inherit the fused chromosome and has a normal make-up of 46 separate chromosomes.

2 A normal pregnancy and baby but the baby is a carrier



The baby inherits the fused chromosome but, like their carrier parent, is expected to grow and develop normally.

3 A baby or a pregnancy with a chromosome disorder



Occasionally a baby will be born with a chromosome disorder. **Translocation Down's syndrome** is the most common and can occur when the long arm of chromosome 21 forms part of the fused chromosome. This and other disorders are described on pages 4 and 5.

4 Pregnancy loss or failure to establish a pregnancy

Many men who are Robertsonian carriers appear to have normal fertility, but the translocation can interfere with sperm production so some men have a very low sperm count.

If either partner produces sperm or eggs that do not have a balanced chromosome make-up, they are more likely to contribute to a pregnancy that leads to loss, either as a miscarriage - often before the pregnancy is recognised - or much more rarely as stillbirth.

A baby or a pregnancy with a chromosome disorder

Different chromosome disorders can occur. In all of them, the cause is:

either the unbalanced Robertsonian translocation has arisen as a one-off event and the parents have completely normal chromosomes. Geneticists call this *de novo*, meaning that it is not inherited. It is then extremely unlikely ever to happen again.

or one parent is a Robertsonian translocation carrier.



Photo courtesy Down's Syndrome Association

Translocation Down's syndrome

The Robertsonian translocation is unbalanced and the baby has three copies of the long arm of chromosome 21 instead of two. This causes a type of Down's syndrome called translocation Down's syndrome. The effects on the baby are exactly the same as when Down's syndrome is caused by having an extra entire chromosome 21.

A test of the parents' chromosomes will show why the baby has translocation Down's syndrome.

- In most families, both parents have normal chromosomes. The Robertsonian chromosome including an additional long arm of 21 fused together for the first time when the egg or sperm that went to make up the baby was created. This type of event is termed *de novo* and the risk of it happening again is very low indeed.
- In a smaller number of families, one parent is a Robertsonian translocation carrier. In almost every family, the mother is the carrier parent. She has passed on her translocation chromosome that includes the long arm of 21 as well as a normal chromosome 21. The baby has two long arms of chromosome 21 from the mother (remember: with 21, only the long arm matters) as well as a chromosome 21 from the father. With two 21s plus one long arm 21, Down's syndrome develops.



Beth Robbins lived for three months. Photo courtesy SFT UK

Translocation trisomy 13

If the fused chromosome includes the long arm of chromosome 13, there is a slight risk of having a baby with trisomy 13 (Patau syndrome). This syndrome causes such serious birth defects including congenital heart disease that only one baby in 10 survives to their first birthday. Sadly, those children who do survive have profound developmental delay.

Uniparental disomy (UPD) describes a collection of very varied chromosome disorders. In babies affected by Robertsonian translocations these disorders are extremely rare. They occur when the developing embryo has attempted to 'correct' a trisomy by disposing of the spare third copy of the chromosome. This can leave the baby with two copies of the chromosome from the same parent instead of the normal balance of one copy from each parent. If the corrected chromosome is 13, 21 or 22, it is unlikely to be important.

Chromosome 14

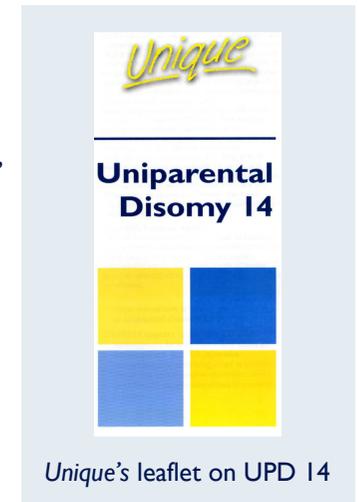
When the corrected chromosome is 14 and the baby inherits two chromosome 14s from the mother, typical features include a slight developmental delay, short stature, speech delay, feeding difficulties as a baby, early puberty, spinal curvature, high cholesterol levels, low muscle tone and hypermobile joints.

When the corrected chromosome is 14 and the baby inherits two chromosome 14s from the father, typical features include excess amniotic fluid in pregnancy, low birthweight, a narrow ribcage causing breathing problems, a hernia in the abdominal wall and moderate to severe learning difficulty. *Unique* publishes a leaflet on UPD14.

Chromosome 15

When the corrected chromosome is 15 and the baby inherits two chromosome 15s from the mother, the baby will have typical features of **Prader-Willi syndrome**, including overweight, short stature and learning difficulties.

When the corrected chromosome is 15 and the baby inherits two chromosome 15s from the father, the baby will have typical features of **Angelman syndrome**, including epilepsy, severe learning difficulties, an unsteady walk and a happy disposition.



Unique's leaflet on UPD 14

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