



Understanding Chromosome & Gene Disorders

Unbalanced Translocations

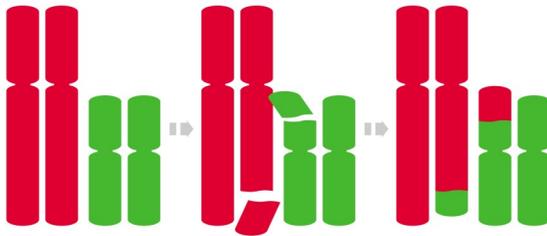


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What is a translocation?

Our bodies are made of billions of cells. In most cells is a set of structures called chromosomes that carry all of the instructions (genes) for the body to function. We generally have 23 pairs of chromosomes and inherit one in each pair from each parent. Sometimes a section from one chromosome of a particular pair changes places with a section from a chromosome of another pair (a [translocation](#)).

When the two breaks do not disrupt a gene and there is no gain or loss of material, it is called a [balanced translocation](#). Someone with a balanced translocation (a carrier) usually has no health or developmental problems, although they may sometimes have difficulties when they want to have children. *See [Unique's guide to balanced translocations](#).*



A balanced translocation

On the left are two pairs of normal chromosomes. The ends of one chromosome in each pair change places (middle).

This results in a balanced translocation (right). This is a reciprocal translocation.

What is an unbalanced translocation?

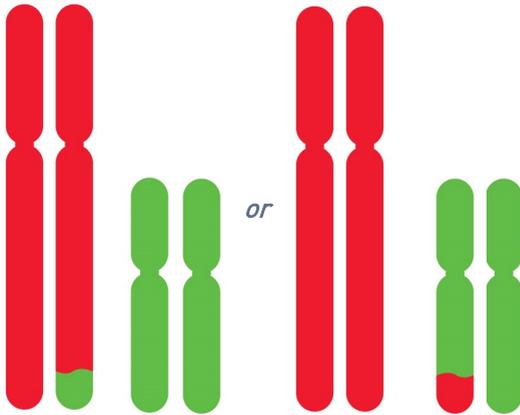
Sometimes a translocation is [unbalanced](#). In [reciprocal unbalanced translocations](#) there is loss of a part of one chromosome and/or a gain of part of one chromosome.

In [Robertsonian unbalanced translocations \(rob\)](#) there is loss of one whole chromosome and/or gain of another whole chromosome. *See [Unique's guide to Robertsonian translocations to find out about unbalanced Robertsonian translocations](#).*

When a section of genetic material from one chromosome of a particular pair inserts into a chromosome from another pair this is called an [insertional translocation](#). Insertional translocations can be balanced or unbalanced. *See [Unique's guide to balanced insertional translocations](#).* In an [unbalanced insertional translocation](#) there would only be a loss of part of one chromosome or a gain of part of one chromosome, but never both.

Translocations can also be a bit more complicated and involve more than two chromosome pairs, such as three or four way translocations.

When a translocation is unbalanced, significant genes are likely to be missing ([deleted](#)) and/or present as an extra copy ([duplicated](#)). An



Examples of unbalanced translocations involving two pairs of chromosomes

On the left there is a duplication of some of the genetic material of one chromosome (green) and a deletion of some of the genetic material of the other chromosome (red) and vice versa in the diagram on the right. Contrast this situation with the diagram on page 2, depicting a balanced translocation, where there is no gain or loss of genetic material.

unbalanced translocation is therefore likely to cause significant health and/or developmental problems in the affected person.

An individual usually finds out that they or their child have an unbalanced translocation following investigations for health and/or developmental problems. Sometimes an unbalanced translocation is found in a baby during pregnancy following prenatal diagnosis. Others have a blood test as part of family investigations.

“ We found out about our son’s unbalanced translocation following genetic testing as a result of his cleft palate, which was diagnosed shortly after birth. Further tests revealed that I - his mother - carried a balanced translocation. ”

When they do find out, there are likely to be a range of questions about what the future holds for them or their child. This guide answers the most common questions that *Unique* members have asked. Of course, it doesn’t replace your consultation with your genetics centre; your genetic counsellor or geneticist is the best person to answer your questions about your personal situation.

How will an unbalanced translocation affect my child?

As with other chromosome disorders, having an extra piece and/or missing piece of genetic material may affect the development and intellectual abilities of a child and can be associated with a range of other individual features and health problems.

The effects can be variable and depend on a range of factors, including exactly which parts of which chromosomes are involved, the genes affected

and what those genes do. This is because some parts of a particular chromosome(s) are more important than other parts.

Unbalanced translocations are thought to account for approximately 1% of cases of developmental delay and intellectual disability (Weckselblatt 2015).

Why did it happen? Where did it start?

Sometimes a child can be born with an unbalanced translocation even though both parents' chromosomes are normal. The unbalanced translocation has arisen as a "new event" (*de novo*, dn) when the sperm or egg cells are forming or just after fertilisation during the copying of the early cells that will become an embryo, then a fetus and then a baby. Sometimes they can be inherited from a parent who has the balanced form of the same translocation or, very occasionally, the same unbalanced translocation.

Your geneticist will offer to test you or other members of your family to find out whether the translocation is a new one or a family one. A small blood sample is needed for the test. Testing you or both your parents may be enough but if that is not possible, other family members may also be invited for testing.

Why me? Is it my fault?

If you've been told you or your child has an unbalanced translocation, you may wonder 'Why me?'. Remember that there is nothing you can blame yourself for or feel guilty about.

Everything that is known about unbalanced translocations suggests that it is down to chance whether you have one or not. No environmental, diet, workplace or lifestyle factors are known to cause them. They affect men and women from all types of background and all income and ethnic groups. They are not your fault and they are not the fault of anyone else in your family. Some people with a balanced translocation who have pregnancies or children with unbalanced translocations feel guilty. Some people who inherit an unbalanced translocation find that the parent who passed it on feels guilty. There is absolutely no reason to do so.

How common are unbalanced translocations?

It is difficult to say. Any chromosome can make a swap with any other chromosome, anywhere along its length. This is what makes most specific translocations extremely rare, even unique. However, some translocations are found repeatedly, including those involving the short (p) arms of chromosomes 4 and 8, which may be balanced or unbalanced ([see *Unique's guide to 4p;8p translocation*](#)). *Unique* produces guides to a range of duplications and deletions affecting each chromosome; these can

occasionally be used together to give you a bit more information on the implications for a child with a specific unbalanced translocation.

How common is a particular unbalanced translocation?

Many translocations are so unusual that we can't estimate how common they are and many may be unique. Whatever your translocation, your geneticist will research the medical literature to see if other families have been reported, although these may only be the tip of the iceberg (there may be other families with the translocation who have never been identified). Occasionally, a genetic service or *Unique* may have other families with a particular translocation, or they may know of people who have either the duplication or the deletion that is involved. To find out if this is the case for your translocation, ask your geneticist and *Unique*.

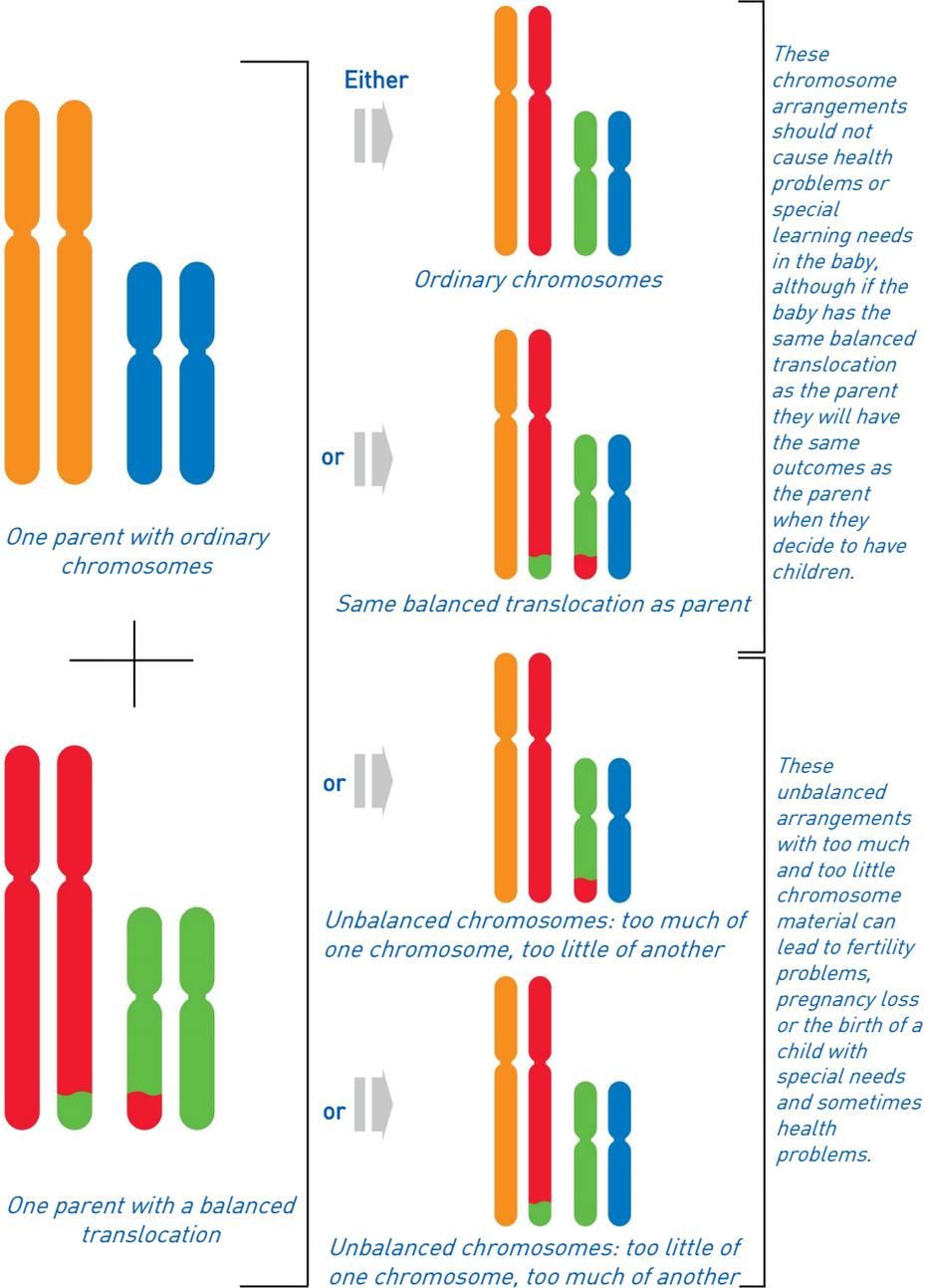
An unbalanced translocation is found in the baby during pregnancy

Sometimes a baby is found to have an unbalanced translocation during invasive testing such as chorionic villus sampling (CVS) or amniocentesis. An unbalanced translocation may cause miscarriage or serious problems in the growth and development of the baby. The mother should be offered high-level ultrasound scans to look for any physical abnormalities. Couples should also have very early access to genetic counselling to identify possible problems. A genetic counsellor or doctor will be able to explain more about the translocation and implications for the baby. They will also offer the parents chromosome tests to check whether the unbalanced translocation has been inherited from either parent. There are three possible results:

- 1 One parent will have a balanced translocation from which the unbalanced translocation derived. When one parent carries a balanced translocation, the couple's other or future children may have either normal chromosomes, the balanced translocation or the unbalanced translocation (see diagram on page 6 to see how this can happen). *Please refer to Unique's guide to balanced translocations for all further information about balanced translocations and the implications for families and for future pregnancies. (We would strongly advise you to be referred to your local Clinical Genetic Service to discuss this further.)*
- 2 Both parents have normal chromosomes meaning the baby's translocation has arisen out of the blue as a new event. When the unbalanced translocation is *de novo* the couple are very UNLIKELY to have another baby with an unbalanced translocation in subsequent pregnancies.

Having children: a family with a balanced translocation

Your geneticist can try to suggest which of these outcomes are more likely for your family. Parents contribute one chromosome from each pair.



3 Rarely, one parent will have the same unbalanced translocation as the baby, in which case the baby would be expected to have broadly similar health and development to the parent.

As a general rule, unbalanced translocations involving large genetic imbalances (missing and/or extra genetic material) are more likely to result in infertility or recurrent miscarriage, while those with small imbalances have the highest chance of the baby surviving the pregnancy to be born with health and/or developmental problems.

The diagram on page six shows the more common combinations of chromosomes that can occur in the baby when one parent carries a typical balanced translocation. However, sometimes the situation can be more complicated and other possible combinations may occur. For instance, the baby may receive an extra chromosome or they may be missing a chromosome. When this happens it is more likely to result in infertility or miscarriage due to the large amount of extra or missing chromosome material present. Your geneticist will be able to discuss this further with you.

There are, however, a few balanced reciprocal translocations that when carried by one parent more commonly give rise to babies with an extra chromosome in addition to the normal chromosome pairs, meaning the baby will have 47 chromosomes instead of the usual 46. One of these is a balanced translocation between chromosomes 11 and 22. When a parent carries this particular balanced chromosome combination, a situation may arise where when they try for a baby, the baby may carry an unbalanced translocation. This occurs because the baby inherits two normal chromosomes 11, two normal chromosomes 22 but also an *additional* chromosome, made up of some material from chromosome 11 and some material from chromosome 22, which has been inherited from the parent with the balanced translocation. The extra chromosome is known as a derivative 22 or der(22) chromosome. The carrier parent has passed on their normal chromosome 11 and chromosome 22 but also the derivative chromosome. As a result of the extra derivative chromosome, there will be three copies of some of the genes carried on chromosomes 11 and 22, instead of the usual two copies, which gives rise to Emanuel syndrome (*see Unique's* guide to [Emanuel syndrome](#)).

Parents with normal chromosomes - implications and options

Parents with normal chromosomes whose baby has an unbalanced translocation are very UNLIKELY to have another child with an unbalanced translocation. There will only be a slightly increased risk (around 1%) above general population risk, of a future baby or one of your other children having

an unbalanced translocation. This slightly increased chance in a future pregnancy is due to a few of one parent's egg or sperm cells alone carrying the same unbalanced translocation. This is called [confined germline mosaicism](#) or [confined gonadal mosaicism](#) and it means that very rarely even when both parents' chromosomes appear normal when their blood is tested, they go on to have more than one child with the unbalanced translocation. If your other child(ren) is developing normally, it is most likely that they will have normal chromosomes. If you are particularly concerned that any of your existing children has significant health and/or learning problems, you may wish to consider having their chromosomes checked to look for an unbalanced translocation. You would need to be referred to your local Clinical Genetic Service to discuss this testing.

In a future pregnancy couples can ask to have tests during pregnancy to check their baby's chromosomes for reassurance. These tests currently include CVS and amniocentesis. Please refer to *Unique's* leaflet '[Planning your next child](#)' for more detailed information about these tests. Couples interested in discussing the tests available during pregnancy are encouraged to contact their local Clinical Genetic Service for more information well ahead of a pregnancy.

One of the parents has the same unbalanced translocation as the baby - implications and options

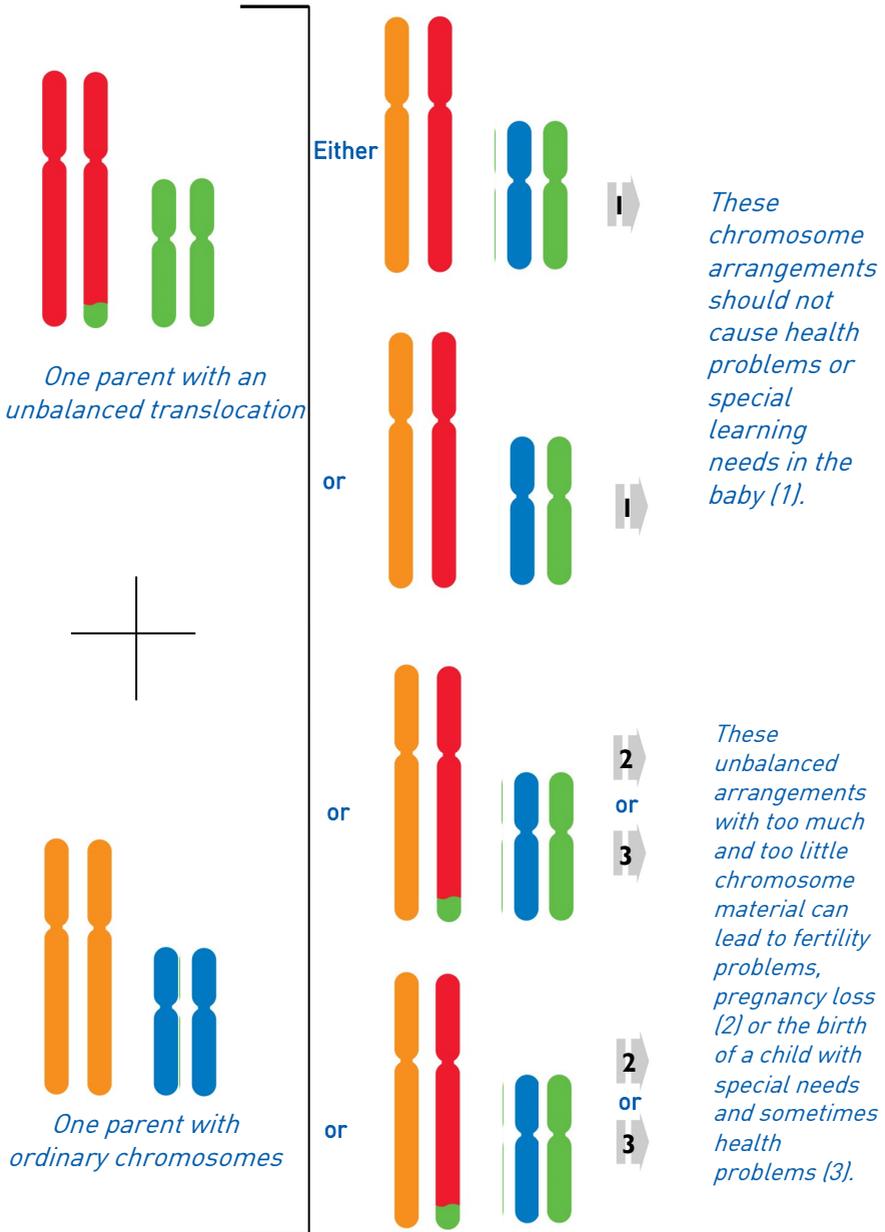
If a parent has the same unbalanced translocation as their baby, the baby would be expected to be affected in a broadly similar way to the parent, although the effects of the unbalanced translocation can be milder or more severe. Even when two people have the same chromosome make-up, the effects of having unbalanced chromosomes can vary quite a lot - just as brothers and sisters with ordinary chromosomes are different from each other.

There would in theory be a 50% (1 in 2) chance of a future baby or one of your other children having inherited normal chromosomes and therefore having NO health and/or development problems relating to the translocation ([see diagram on page 9](#)).

There would in theory be a 50% (1 in 2) chance of a future baby or one of your other children having inherited the unbalanced translocation. If your other child(ren) is developing normally, it is most likely that they will have normal chromosomes. If you were concerned that any of your existing children had the same unbalanced translocation you may want to ask for those children to be referred to your local Clinical Genetic Service to discuss chromosome testing.

Having children when one parent has an unbalanced translocation

Your geneticist can try to suggest which of these outcomes are more likely for your family. Parents contribute one chromosome from each pair.



In a future pregnancy, couples can ask to have tests before or during pregnancy to check the embryo or baby's chromosomes to see whether or not the baby has inherited the unbalanced translocation. These tests currently include pre-implantation genetic testing (PGT), CVS and amniocentesis. Please refer to Unique's leaflet '[Planning your next child](#)' for detailed information about these tests. Couples interested in discussing the tests available before or during pregnancy are encouraged to contact their local Clinical Genetic Service for more information well in advance of planning another pregnancy. Some couples may also consider egg or sperm donation or adoption. These options are also detailed in the *Unique* leaflet mentioned above.

Can someone with an unbalanced translocation have children?

For a person with an unbalanced translocation whose health and/or learning problems are compatible with being able to have children, there would be three possible outcomes during a pregnancy ([see diagram on page 9](#)):

- 1 A healthy child with an ordinary chromosome pattern who would be expected to have NO health and/or development problems relating to the translocation.
- 2 Possible difficulty getting pregnant or miscarriage(s), due to repeated pregnancies with the same unbalanced chromosomes as the parent with the unbalanced translocation.
- 3 An ongoing pregnancy with the same unbalanced chromosomes to the parent. Such a pregnancy may not continue to term or may lead to the birth of a child with broadly similar health and/or development problems to the parent.

As already mentioned, this means in theory there is overall a 50% (1 in 2) chance of having a baby with normal chromosomes who would be expected to be healthy. There is also in theory a 50% (1 in 2) chance of having a baby with the unbalanced translocation which may not survive the pregnancy (miscarriage) or may survive the pregnancy to be born with some health and/

“ [We told our son] about his unbalanced translocation when we attended a *Unique* family day, when he was about 12. There was a display about chromosome disorders and he showed an interest, so we took the opportunity to explain about his chromosomes. We kept the language simple due his learning disabilities and used humour to explain too (a sense of humour is a huge strength of his!). We described his unbalanced translocation as ‘mixed up chromosomes’, which he still uses to describe his chromosome disorder, five years later! ”

or learning problems. A baby inheriting the same unbalanced translocation as the parent would be most likely to survive the pregnancy, although the health problems could in theory be more serious, leading to miscarriage during pregnancy.

Could someone with an unbalanced translocation have a child with a balanced translocation?

No. It is only possible to have a child with either the ordinary, unaffected members of the pairs of chromosomes involved in the translocation or a child with the same unbalanced translocation (see diagram on page 9).

Considering testing in a future pregnancy

When you consider trying for another child (or before), ask your GP to refer you for a genetics appointment at your local Clinical Genetic Service. A genetic counsellor or doctor will be able to discuss in more detail with you what the implications are for having a baby, and will help you to decide whether or not you are interested in having any of the chromosome tests that may be available to you before or during pregnancy. If you are eligible and decide to have any of these tests, they will organise these for you. They can also arrange to give you the results and will be able to organise any necessary follow up support.

A fetal anomaly scan can help to show if the baby is likely to have major health concerns by revealing structural problems with the heart or other major organs. But a fuller picture of how a baby with unbalanced chromosomes is affected can only be drawn after birth.

Can an unbalanced translocation be cured?

No. An unbalanced translocation cannot be corrected; it is present for life. But a diagnosis means that appropriate monitoring can be put in place, while individual symptoms might be treatable or improved by appropriate therapies.

“ Although it’s a natural reaction as a parent, do not feel guilty or responsible for your child having an unbalanced translocation. Take everything moment by moment, day by day and try not to focus too much on the future, particularly whilst you’re adjusting to the news of the diagnosis and most likely trying to deal with all the health/learning needs of your child, whilst also becoming a parent. Time definitely heals and although life might be challenging raising a child with an unbalanced translocation, it can certainly be full of rewards, happiness and laughter. Over time, it becomes easier to accept and enjoy life as it is. ”

Support and Information



Understanding Chromosome & Gene Disorders

Rare Chromosome Disorder Support Group

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Join Unique for family links, information and support.

Unique is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation via our website at www.rarechromo.org/donate Please help us to help you!

Unique lists external message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. This guide was compiled by *Unique* (CA) in collaboration with Liz Kay MSc, Genetic Counsellor (GCRB 137), 2019.

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