Inform Network Support

Rare Chromosome Disorder Support Group,
The Stables, Station Rd West, Oxted, Surrey. RH8 9EE
Tel: +44(0)1883 723356
info@rarechromo.org | www.rarechromo.org
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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!

There is a closed Facebook group for families affected by balanced chromosome translocations at www.facebook.com/groups/35507179052

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. It was originally compiled by *Unique* in collaboration with Professor Maj Hultén BSc, PhD, MD, FRCPath, formerly Professor of Reproductive Genetics, University of Warwick, UK, in 2009. An update was carried out in 2022/23 by Falak Arshad (Genetic Counsellor) and Unique (CA).

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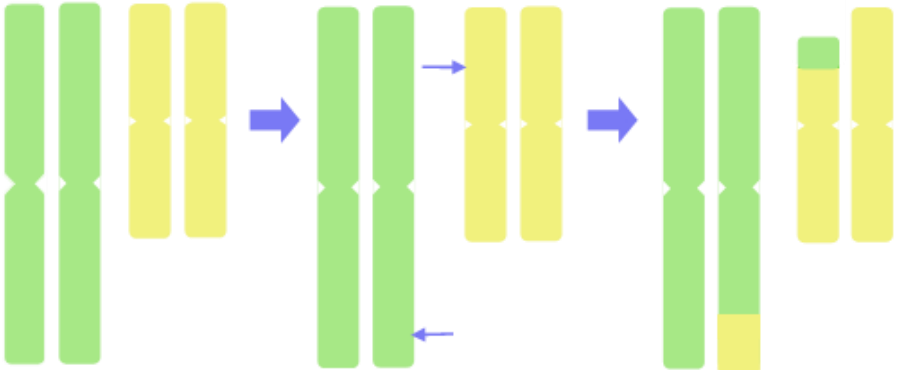
Understanding Chromosome & Gene Disorders

Balanced Translocations

What is a balanced translocation?

Our bodies are made of trillions of cells. Most cells contain our genetic information which makes us who we are. To fit all the genetic information into our cells, it is packaged in structures called chromosomes that carry the instructions (genes) for the cell to function. We generally have 23 pairs of chromosomes and inherit one of each pair from each biological parent.

Sometimes a section from one chromosome of a particular pair swaps places with a section from a chromosome of another pair. The end of this specific section is referred to as a break point (see below for an illustration of this). When the break points do not impact a specific gene, and there is no gain or loss of chromosome material, is called a balanced translocation. A balanced translocation carrier usually has no health or developmental concerns, although they may sometimes experience difficulty when they want to expand their family and have children.



1. Two pairs of normal chromosomes

2. The ends of two chromosomes, one from each pair, change places with each other (break points marked by arrows)

3. This leads to a balanced translocation. This is called a reciprocal translocation

Most balanced translocation carriers do not know that their chromosomes are any different to anyone else's. Some people find out about the balanced translocation following investigations as their biological child requires special support or has health concerns caused by a chromosome disorder. Some people may have repeated miscarriages or other fertility issues. Others may have a blood test as part of family investigations, whilst some find out by chance when they have a chromosome test for other reasons. Occasionally a balanced translocation is found in a baby during an ongoing pregnancy. We talk about this scenario on page 14.

Notes

A balanced translocation is found in the baby during pregnancy

Occasionally a baby is found to have a balanced translocation at chorionic villus sampling or at amniocentesis. First the parents' chromosomes should be checked to see if the translocation is inherited. If it is inherited, and the parent has no problems from the translocation, it is unlikely that the baby will have any problems either.

If both parents have normal chromosomes, the baby's translocation is a new one (*de novo*). There is a chance that the chromosome breaks have disrupted important genes or that the break points are not as clean as they appear. The mother should be offered high-level ultrasound scans to look for any physical anomalies. Couples should also have very early access to genetic counselling to identify any possible issues.

It is sometimes helpful to analyse the chromosomes again using a sensitive molecular or DNA technology that will show whether particular genes have been left out, added in or disrupted at the break points.

Unlike these people, most of the 14 million people with a balanced translocation have no idea that they have an unusual chromosome arrangement.

When they do find out, they may have different questions about what this means and what the future holds for them and their family. This guide answers the most common questions that *Unique* members have asked. This does not replace information or recommendations you receive from your consultation with your clinician or clinical genetics service. Your genetic counsellor or geneticist is the best person to answer your questions about your personal situation.

Why did it happen? Where did it start?

Balanced translocations occur by chance naturally. They are part of the natural evolution of species, including humans. Translocations can be new (*de novo* (dn)) or they can be passed down in families from parent to child through the generations (although even a family translocation was once a new one, though the family member it first arose in may be generations back). Translocations can occur when sperm or egg cells are forming or just after fertilisation (when the sperm and egg fuse together).

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

Why me? Is it my fault?

If you have been told you have a balanced translocation, you may wonder 'Why me?' Remember, a *de novo* translocation probably arose when the egg or sperm cell, that was destined to create you, was formed. At the very latest, it arose in the earliest days of your mother's pregnancy. Everything that is known about balanced translocations suggests that it occurs by chance. 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. Some people with a balanced translocation may feel guilty. Some people who inherit a translocation find that the parent who passed it on feels guilty. Given that this occurs by chance, it is not a choice of an individual(s) and is no one's fault.

> "Whenever I tell someone that I have a 'chromosome disorder' I feel like I'm telling them that I'm seriously ill."

> "I just tell people that I have a problem that means I'm automatically in the high-risk group for screening in pregnancy."

How common are balanced translocations?

Around one person in 560 has a balanced translocation, so as a group they are not at all rare (Gupta 2019). In the world, there are around 14 million balanced translocation carriers. In 2022, *Unique* had over 1300 member families with either a new or familial balanced translocation.

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, a few balanced translocations are found repeatedly. One is a translocation between chromosome 11 and chromosome 22 and is known as the 11;22 translocation. Another is a translocation between the short arms of chromosomes 4 and 8. *Unique* has published separate information guides for these translocations.

Chromosome test results

Your geneticist or genetic counsellor will very likely give you your karyotype, which is a way of describing what your chromosomes look like under a microscope. It is likely to read similarly to this:

46,XX or XY,t(11;22)(q23;q11.2)

46: The total number of chromosomes in your cells tested

XX or XY: The two sex chromosomes, XX for biological females XY for biological males

t(11;22): There is a reciprocal translocation between chromosomes 11 and 22

(q23;q11.2): The breakpoint in chromosome 11 is in band q23. The breakpoint in chromosome 22 is in band q11.2

At the end of the karyotype, you may see one of these words:

mat: The translocation is a familial one, inherited from the mother

pat: The translocation is a familial one, inherited from the father

de novo (dn): The parents' chromosomes have been checked and no rearrangement found involving chromosomes 11 and 22. The translocation is very unlikely to be inherited but rather happened for the first time in the person being tested.

How common is my particular balanced translocation?

Many translocations are so unusual that we can't estimate how common they are. Whatever your translocation, your geneticist/genetic counsellor may be able to research the scientific literature to identify whether other families with the same translocation have been reported, although these may be only the tip of the iceberg. It is quite likely that there will be other families with the translocation who have never been identified. Sometimes a genetic service does have other families with a particular translocation and

Your children: More questions

Your other children

Your other children can have their chromosomes tested once they are old enough to decide that they want to know. If you feel strongly that you want to know their chromosome status, but they are still too young to decide for themselves, talk it over with your genetics service. The guidance about when it is best to test and tell is flexible and intended to be in families' best interests.

If your child is developing as expected, it is most likely that they will either have normal chromosomes or the familial balanced translocation. A child with the familial balanced translocation can expect to be unaffected by it until they have children of their own.

When and how should we tell a child about their balanced translocation?

Unique has a separate information guide to telling children about having a balanced translocation.

We have one child with special needs. If we have another child with special needs, will they be affected in the same way?

If you have another child with unbalanced chromosomes, it is very likely that they will have special needs. But their needs will not necessarily be exactly the same as their brother or sister's. Depending on your translocation, they may have a different unbalanced chromosome make-up, or they may have the same make-up as your older child. Even if the two children 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.

Will my balanced translocation affect my health?

For the great majority of the millions of people with a balanced translocation there is no effect on their own health. For any child who inherits the familial balanced translocation there should also be no health problems caused by the translocation. Balanced translocations do not usually have any effect on health or development because in the great majority of cases the points in the genome where chromosomes have broken and re-joined do not disrupt the smooth-running of the genes.

Can a balanced translocation be cured?

No, it can't. But a balanced translocation is very unlikely to cause any problems until the carrier wants to have biological children.

Egg or sperm donation

Couples may consider egg or sperm donation if they are not successful in having an unaffected child. Donated sperm or eggs can come from someone you know or be supplied by a clinic. Donated sperm can be given using intrauterine insemination (IUI) following a woman's natural cycle or after stimulating ovulation with medication. Donated eggs can be combined with the partner's sperm and left to grow following fertilisation. Once the recipient's womb has been prepared with hormones, the embryo is usually transferred into the womb.

Adoption

Some families choose to adopt children.

"After six miscarriages, my husband and I decided to look at adoption. We are now proud parents of two beautiful (adopted) children and have never looked back. Adoption is a way of giving children a loving family who may not be so lucky otherwise. An unconceived child does not need to be created or yet have the right to live. A child who has been born does."

sometimes *Unique* does. To find out if there are other families with the same translocation as you, ask your geneticist and/or *Unique*.

Can we have children?

Most men and women with a balanced translocation can and do have children. There are usually four possible outcomes when a couple with a balanced translocation tries for a baby. These outcomes will be more or less likely, depending on your particular translocation. Your genetic counsellor or geneticist may be able to help by saying which outcomes are more likely for you.

1. a child with an ordinary chromosome pattern
2. a child with the same balanced translocation as the parent
3. failure to establish an ongoing pregnancy, or apparent fertility problems due to repeated pregnancies with unbalanced chromosomes
4. an ongoing pregnancy with unbalanced chromosomes which may not continue to term or may lead to the birth of a child with physical and/or learning problems associated with the specific chromosome change.

Some people wonder if having a balanced translocation makes other genetic disorders more likely in their children. There is no evidence at all of this.

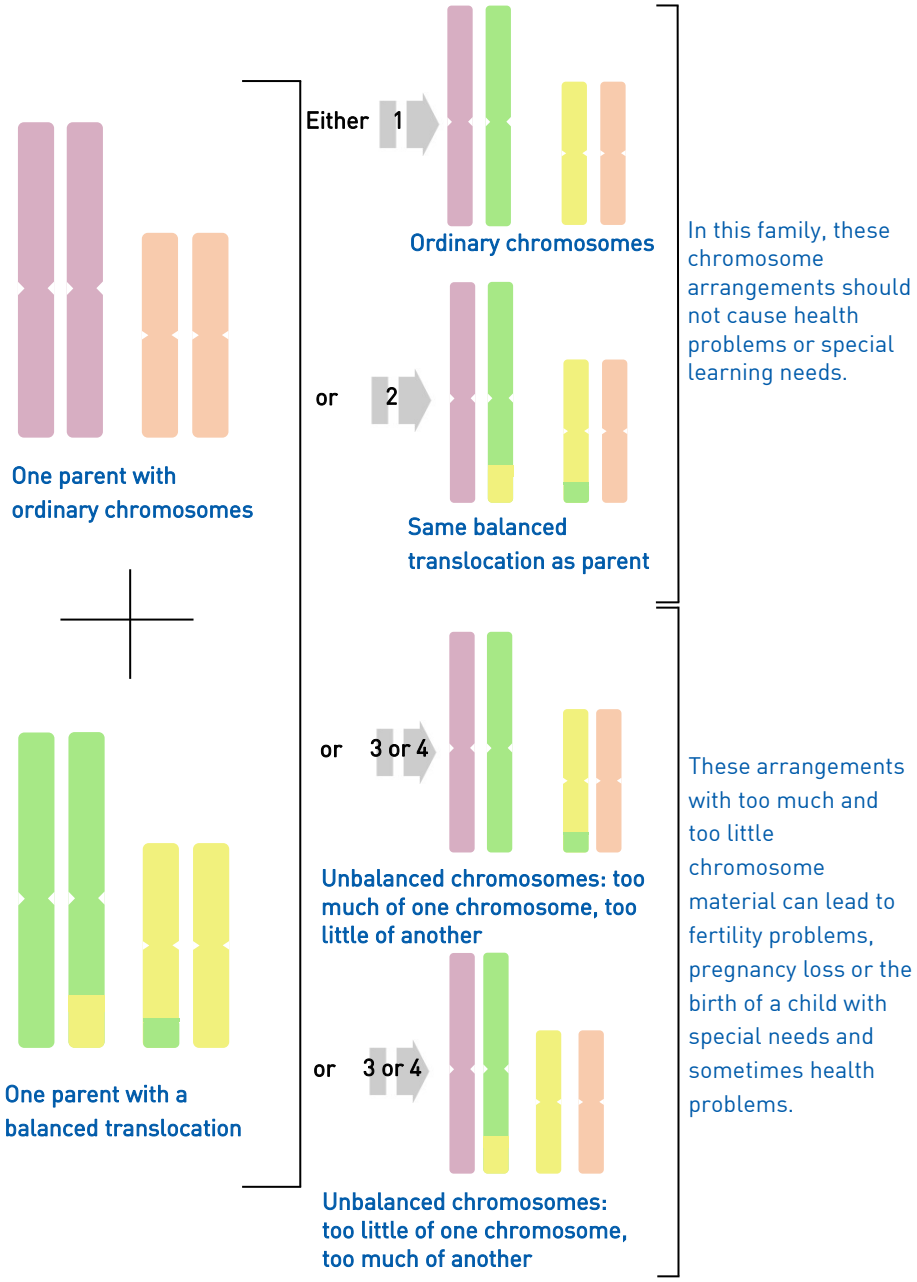
The mother has a balanced translocation, inherited from her father (behind). After two miscarriages and two pregnancies terminated due to chromosome imbalance, she has had a daughter with the family translocation.

The mother has a balanced translocation. Both children were born with unbalanced chromosomes and sadly the daughter, five years old here, died.

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.



between countries, and it is not available for chromosome translocations in all fertility clinics. Success rates also vary. Some people find it emotionally demanding and counselling and support are vital before and throughout the process. If you want to find out more about your options for PGT-SR, ask first for a referral to a genetics centre or you can contact a fertility clinic.

Intracytoplasmic sperm injection (ICSI)/ In Vitro Fertilisation (IVF)

Where there are concerns over sperm quality or if other fertilisation methods have previously been attempted and not thought to be successful, the doctor, or specialists in fertility treatment and reproductive research called embryologists, may recommend a process called ICSI. Here, embryologists look at a semen sample under a microscope to identify the most active, healthy sperm cells which can then be injected directly into each of the mother's egg(s) to fertilise them. If you are recommended to consider IVF, this involves sperm being released near the eggs to swim towards and fertilise them, rather than being injected directly into them.

These procedures can be combined with PGT-SR to ensure that only embryos with normal or balanced chromosomes are transferred to the womb (see below). PGT-SR cannot tell the difference between embryos with normal chromosomes or those carrying a balanced translocation.

PGT-SR process

This process involves the collection or sperm and eggs. Following the egg collection, eggs will either be mixed with sperm using IVF or injected with a single sperm cell each using ICSI, as outlined above. ICSI/IVF are considered the fertilisation process. The eggs that have fertilised will then be left to grow in the laboratory until day 5/6 (blastocyst stage). At this stage, the embryologist will then review the development and quality of the embryo(s) to identify if they are suitable for a biopsy.

The biopsy takes around 5-10 cells from the part of the embryo that would eventually develop into the placenta. The cells are sent to the genetic laboratory to conduct PGT-SR to ensure only embryo(s) without the unbalanced translocation are transferred, the remainder of the embryo is frozen and kept at your fertility clinic.

When the results are returned to a patient, if there is a suitable embryo for a transfer that has either normal or balanced chromosomes, the clinic will then support a patient in arranging a frozen embryo transfer of an embryo to the womb. If patients would like to consider confirmatory testing that the embryo does not have the unbalanced translocation in an ongoing pregnancy, they may consider a CVS or an amniocentesis during an ongoing pregnancy.

A child with unbalanced chromosomes is very likely to have special needs.

A fetal anomaly scan can help to show if the baby is likely to have major health concerns by revealing structural anomalies 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. There is a test that you may be offered from around 9 weeks of a pregnancy called non-invasive prenatal testing (NIPT). This involves a blood sample being taken from the mother, since during a pregnancy some of the genetic information from the pregnancy is floating in the mother's blood stream. Scientists will analyse this sample and provide you with a high risk or low risk of the pregnancy having unbalanced chromosomes. You may then be offered a CVS or amniocentesis to confirm the result if you receive a high risk NIPT test.

You should have the opportunity to talk over what is involved in these tests with your midwife or obstetric doctor and they should refer you to a genetic counsellor or geneticist if you want more information about any abnormal results.

If these tests give an abnormal result, you will usually have the choice of continuing the pregnancy and preparing yourselves for the birth of a child with special needs or ending the pregnancy. Many *Unique* members have faced these decisions.

> "Terminating the pregnancy was an agonising decision for my husband and me but it was easier knowing that other couples have made the same decision."

Other reproductive choices

You may want to look at other reproductive choices. What is available and whether you have to pay depends on what country you live in but can include the following options.

Pre-implantation Genetic Testing for Chromosomal Structural Rearrangements (PGT-SR)

PGT-SR gives an individual/couple the opportunity to select an embryo without an unbalanced translocation that can be placed back in the womb.

The procedure uses *assisted reproduction* techniques, which involves checking the chromosomes of 5- to 6-day-old embryos (blastocysts) and only transferring an embryo with normal or balanced chromosomes to the womb. The method used at the moment does not distinguish between embryos with normal chromosomes and those with a balanced translocation.

Unique has members who have used PGT-SR to have healthy children and are happy to share their experiences. The availability of PGT-SR varies widely

The father has a balanced translocation. This family had three miscarriages before having three children: two with the balanced translocation (daughter, left, and son) and one with ordinary chromosomes (daughter, right).

> "There is a balanced translocation in all generations of my family which doesn't have health implications for any of us.
> Out of three pregnancies, we have had a miscarriage of a baby with an unbalanced translocation, a child with a balanced translocation and a child with an unbalanced translocation who has special needs."

A child with the same balanced translocation as the parent: passing on a balanced translocation

Mothers and children with a family balanced translocation

If you or your partner pass on the balanced translocation to one of your children, they should not have any new health issues or special needs caused by it.

When your children begin considering their reproduction options, they will be essentially in the same position as you were: they can have children with ordinary chromosomes; children with the same balanced translocation as themself; fertility problems or pregnancies in which the baby has unbalanced chromosomes.

Any adult who has a balanced translocation can ask for an appointment with a clinical genetics service to find out what tests and services are available. It is important to note that with advances in science and healthcare, services and tests available may change over time.

> “We feel infinitely more prepared than we were to support our own daughter (who has a balanced translocation like Mum) when she starts to think about having her own family.”

Could I have a child with the familial balanced translocation, but who has special needs?

In a family with an inherited balanced translocation, it would be unusual to have a child with special needs caused by the familial translocation. The more people there are in your family with the same balanced translocation and no special needs, the more confident you can be.

Very occasionally, it turns out that a translocation thought to be balanced in fact includes an unbalanced element too tiny to be identified by that specific technology. New, more sensitive molecular ways of looking at chromosomes such as microarrays can help to detect tiny pieces of missing or extra chromosome material. In this extremely rare situation, the individual with the chromosome change may have some special needs.

Do men and women with a balanced translocation have fertility issues?

Most men and women with a balanced translocation are able to conceive naturally. It may however take longer for a pregnancy to be established because a proportion of their sperm or eggs have unbalanced chromosomes and any embryos created do not survive or lead to an ongoing pregnancy/ livebirth.

Miscarriage and pregnancy loss

Unfortunately, it is common to miscarry, often even before a woman knows she is pregnant. When someone discovers they are pregnant, there is a possibility that the pregnancy will result in miscarriage. Usually, no obvious reason is found - which is why clinicians do not normally investigate until after the second or third pregnancy loss or if several miscarriages have occurred consecutively.

When one member of the couple has a balanced translocation, the possibility of losing the pregnancy is increased. Miscarriages can occur in this situation because the developing foetus has unbalanced chromosomes - too much or too little chromosome material. The greater the imbalance, the more likely it

is that pregnancy will not be established in the first place or, if it is, it will be lost.

For each pregnancy, the possibilities are the same: a baby with “normal” or balanced chromosomes, or of a baby with unbalanced chromosomes.

Where there are repeated miscarriages without any successful pregnancies, it may be helpful to discuss this with a genetic counsellor or geneticist. Questions that couples may want answered include knowing whether a baby with unbalanced chromosomes can survive to birth, whether they may die soon after birth and if they survive how severely they will be affected mentally and physically. Where a familial balanced translocation has been inherited from a parent, this can be reassuring proof that it is possible to have a healthy child.

When a woman has a miscarriage, they may be invited to send the ‘products of conception’ for genetic testing. This is a hard decision to make at an emotionally challenging time but it can help to build up a picture of what is going on, and can also help to further genetic knowledge. It may be helpful to write down your thoughts whilst you decide how you would like to proceed if you find yourself in this position.

> “It was only coming to the *Unique* conference and meeting other people with balanced translocations that gave me the courage to try again for a pregnancy. I have now had nine miscarriages - and two healthy and very beautiful children!”

You’re pregnant: how soon can you find out about the baby’s chromosomes?

It is a good idea to talk to your healthcare team about what tests might be available.

The earliest test that will currently show your baby’s chromosome make-up during pregnancy is based on chorionic villus sampling (CVS) at about 11-13 weeks. A fine needle removes some tissue from the placenta. You will usually be given the results in three days to two weeks. The test itself may make it slightly (about 1 per cent) more likely that you will miscarry, and if this happens, it will occur within a few days of the test.

Your baby’s chromosomes can also be analysed from cells obtained by an amniocentesis. A fine needle removes fluid from the liquid surrounding the fetus in the uterus. This is performed from 16 weeks of pregnancy and you will usually have confirmation of the baby’s chromosome make-up in 10-14 days. An amniocentesis is associated with a slightly raised possibility of miscarriage of about 0.5 -1 per cent.

These tests can show whether your baby has too much or too little chromosome material but they cannot tell you how your baby will be affected.