Understanding chromosome disorders

Unique

11;22 Translocation

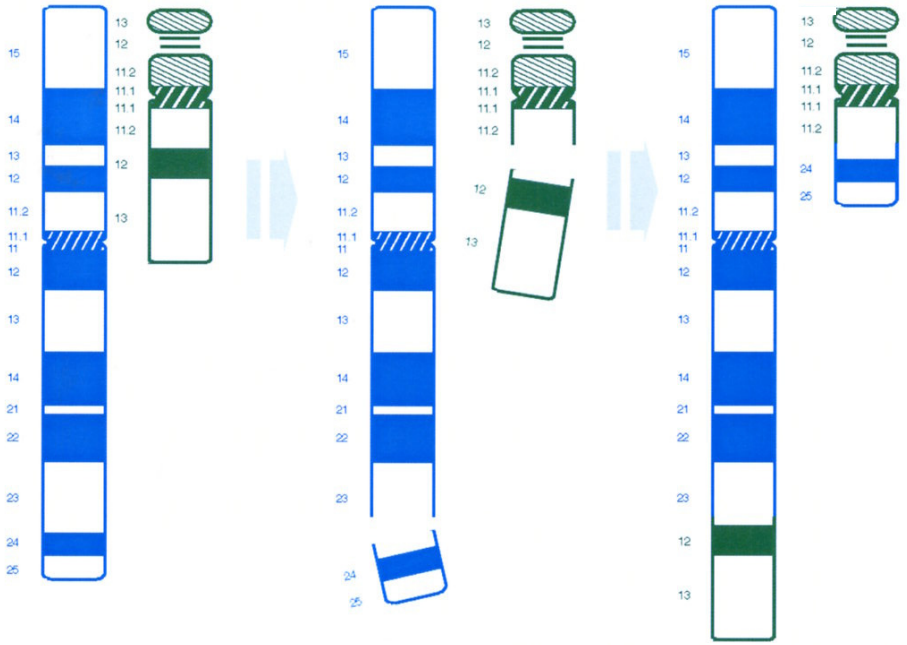
rarechromo.org

What is the 11;22 translocation?

In people with the 11;22 translocation two small pieces of two chromosomes have changed places. This usually makes no difference until they have children.

Our bodies are made of billions of cells. In each cell there is a set of structures called chromosomes. These chromosomes carry all the instructions (genes) for the cell to function. Genes are made up of the chemical called DNA. We generally have 23 pairs of chromosomes, so there are 46 chromosomes in a set. We inherit one chromosome from each pair from our father and one from our mother. Forty-four of the chromosomes are numbered from 1 to 22 approximately from the largest to the smallest. The other two chromosomes are the sex chromosomes that determine what sex we are, named XY for a male and XX for a female.

Sometimes a section from one chromosome changes places with a section from another chromosome. In people with the 11;22 translocation, the bottom bit of one chromosome 11 (a medium-sized chromosome) has transferred to chromosome 22 (a small chromosome) and the bottom bit of one chromosome 22 has moved to chromosome 11.



The 11;22 translocation: the bottom bit of one chromosome 11 changes places with the bottom bit of one chromosome 22

It is called a balanced translocation when the breaks in the chromosomes do not pass through a gene and no material appears to be gained or lost. Someone with a balanced translocation is called a carrier. They usually have no health or developmental problems, although they may have difficulties when they want to have children.
Unique also has a general guide to **Balanced Translocations**

Why has this happened?

Balanced translocations happen naturally. They can be new or they can be passed down in families from parent to child through the generations. Most people with an 11;22 translocation have inherited it from one of their parents. But even a family translocation was once a new one, though it may be generations back.

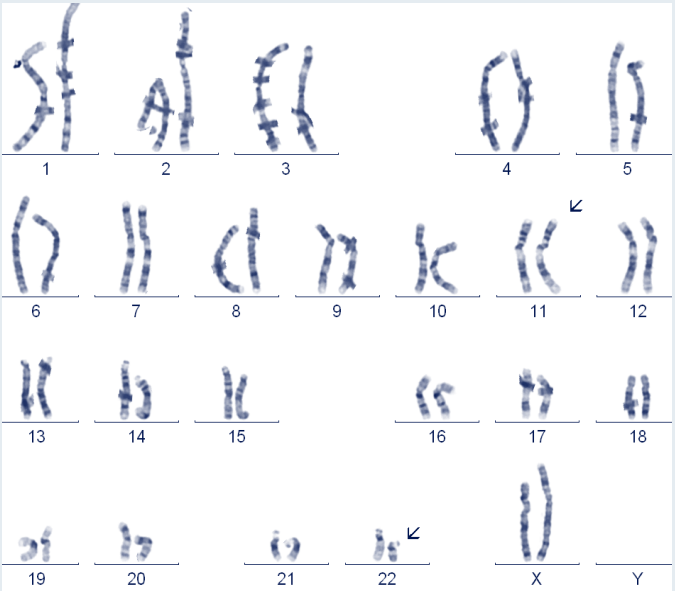
New translocations occur when sperm or egg cells are forming or just after fertilisation during the copying of the early cells that will become an embryo, then a fetus and then a baby. Studies suggest that the 11;22 translocation arises when egg or, much more commonly, sperm cells are forming.

At certain stages in the formation of sperm and egg cells, chromosomes, which are naturally dynamic, moving structures, become particularly active. It is most likely that chromosomes 11 and 22 break and rejoin then. As the chromosomes move around, parts of them come very close to each other and it's believed that if the parts that are very close contain similar stretches of DNA, they can break and rejoin incorrectly. At the points where chromosomes 11 and 22 break and rejoin there are sequences of DNA that are unusually fragile. During the high activity phase of chromosomes when sperm and egg cells are formed, these fragile spots on chromosomes 11 and 22 lie physically very close together, making a break and incorrect rejoining more likely.

Everything that is known about balanced translocations suggests that it is 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.

To find out whether your translocation is a new one or a family one, your geneticist will offer to check the chromosomes of other members of your family. A small blood sample is needed for the test.

Testing both your parents may be enough to find the answer is but if that is not possible, other family members may be invited for testing. It makes no difference if the 11;22 translocation comes from your mother or your father.



The chromosomes of a female - woman or girl - with the 11;22 translocation. The arrows show the translocated chromosomes

How common is the 11;22 translocation?

You are not alone. Translocations between chromosomes are not rare: approximately one person in 560 has one, making a total world population of over 12 million balanced translocation carriers. The 11;22 translocation is by far the most common of the translocations in which two pieces of chromosome swap places. Hundreds of families with this translocation have been reported in the scientific literature but many more go unreported. This suggests that there must be thousands and possibly tens of thousands of families with an 11;22 translocation. However, this can only be a guess.

Are the breakpoints the same in everyone with the 11;22 translocation?

It seems that the breakpoints are always the same in all families. Chromosome 11 breaks at a point known as q23.3 (*see diagram on page 2)* and chromosome 22 breaks at a point known as q11.2. Sometimes there tiny differences in the breakpoints.

Families originally diagnosed more than 10 or 15 years ago may have been told they have different breakpoints. Older ways of looking at chromosomes were much less precise than today's technologies and it almost always turns out that these families have the same breakpoints as the rest of the 11;22 translocation community.

Finding out that you have this translocation

You are most likely to find out that you have the 11;22 translocation when you have a chromosome test in one of these situations:

- after having a baby with Emanuel syndrome. Emanuel syndrome is also known as derivative 22 syndrome; der(22)t(11;22) syndrome; or partial 11/22 trisomy
- when you are investigated for repeated miscarriages or infertility
- when a relative has the 11;22 translocation and you are tested as part of the wider family.

When you find out that you have the 11;22 translocation, you may feel any, or all, of these emotions.

Isolation You are set apart from other people who have 'normal' chromosomes. In fact, there are millions of people around the world who have a balanced translocation. There are support groups for people with unusual chromosome arrangements and they act as self-help communities. Some of the support groups for the 11;22 translocation are:

Chromosome 22 Central

Unique

Chromosome Disorder Outreach

The contact details for these organisations are on the back page of this guide.

Guilt that something that you or someone else in your family did caused the translocation or made it more likely. In fact, nothing in people's environment or lifestyle is known to cause this translocation. It is no more than a chance event that has occurred in an entirely natural process.

Fear or uncertainty that it will affect your children. It *is* possible that future pregnancies will be affected by the translocation. But once you know that you are a carrier, you will be able to manage the risk.

Results of the chromosome test

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

46 = The total number of chromosomes in your cells
XX or XY = The two sex chromosomes, XX for females; XY for 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 family one, inherited from the mother
pat = The translocation is a family one, inherited from the father
de novo = The parents' chromosomes have been checked and no rearrangement found involving chromosomes 11 and 22. The translocation is very unlikely to be inherited.

Having children when you have the 11;22 translocation

There are a number of possible outcomes when a couple with an 11;22 translocation tries for a baby.

Depending which partner carries the 11;22 translocation, if the sperm or egg has a chromosome imbalance, it may not lead to a recognised pregnancy. If this occurs repeatedly, the couple may appear to have fertility problems.

If a pregnancy is established with a chromosome imbalance, it may miscarry, usually early in the pregnancy.

Apparent fertility problems and miscarriages can happen to anyone, but they are more common when one partner carries the 11;22 translocation.

There are three possible outcomes if the pregnancy continues and a baby is born. He or she will either have normal chromosomes, or the 11;22 translocation, or a chromosome imbalance that causes a condition known as Emanuel syndrome.

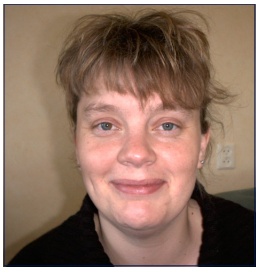
Studies of families with the 11;22 translocation have shown that it is most likely that a child will either have normal chromosomes or the balanced 11;22 translocation, as in the table below. The chance of each outcome is for *each* pregnancy.

	Mother has 11;22	Father has 11;22
Child is unaffected and has normal chromosomes	~ 40%	~ 55%
Child inherits balanced 11; 22 translocation	~ 55%	~ 41%
Child is born with Emanuel syndrome	~ 6%	2-5%

Unique also has a guide to **Emanuel syndrome**

Mother and daughter with 11;22 translocation

Women with the 11;22 translocation



The 11;22 translocation is often found in families going back for generations, suggesting that fertility in women carriers is not seriously affected. In each pregnancy, a woman with the 11;22 translocation has a one-in-three risk of losing it to miscarriage, usually before she even knows she is pregnant. This occurs because there is so much excess or missing chromosome material that it isn't possible for the embryo to survive to become a fetus or a baby. There is also a possibility of ~ 6 per cent of having a baby with Emanuel syndrome.

Men with the 11;22 translocation

Studies show that around a quarter of the millions of sperm produced by a man with the 11;22 translocation either have normal chromosomes or have the 11;22 translocation. The chromosomes in the remaining sperm contain too much or too little material from chromosomes 11 and 22 and any egg that they fertilise will result in a pregnancy that usually miscarries. In each pregnancy where the male partner has the 11;22 translocation, there is a small but real possibility of ~ 2-5 per cent of a baby with Emanuel syndrome being born.

How soon can you find out about the baby's chromosomes when you're pregnant?

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 (afterbirth). You will usually be given the results in three days to two weeks. The test itself may make it slightly (about one 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 at amniocentesis. A fine needle removes fluid from the water surrounding the fetus in the uterus. This is performed at about 16 weeks of pregnancy and you will usually have confirmation of the baby's chromosome make-up in 10-14 days. 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.

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 full picture of how a baby with unbalanced chromosomes such as Emanuel syndrome is affected can only be drawn after birth.

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.

What are my options?

If these tests give an abnormal result, you will have the choice of continuing the pregnancy and preparing yourselves for the birth of a child with Emanuel syndrome or terminating the pregnancy. Before reaching any decision, you should be offered a chance to talk over the implications with your genetics department. You can also consult any of the voluntary support groups listed on the back page to find out more about families' personal experiences. Many *Unique* members have faced decisions about having a child with special needs or terminating a pregnancy.

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 diagnosis; Egg or sperm donation; Adoption
For more detail on these choices, look at *Unique*'s guide to **Balanced translocations**

If I have the 11;22 translocation, are any other genetic disorders likely to be more common in my family?

No, there is nothing to suggest that having the 11;22 translocation makes any other genetic disorders more common.

Can the 11;22 translocation affect the carrier's health or development?

People with the 11;22 translocation are healthy, develop normally and are only different from other people when it comes to having children.

A possibility has been highlighted that women who are11;22 translocation carriers might run a higher risk of developing breast cancer before the menopause than the general population. This is not certain and is being studied at the moment. Given that breast cancer is common, and the 11;22 translocation is also not rare, the association between the two may be no more than chance. Until studies clarify this one way or the other, 11;22 translocation carriers are recommended to discuss it with their geneticist or genetic counsellor. If they have a family history of breast cancer, they may wish to be regularly screened themselves.

Could I have a baby with the family 11;22 translocation, but whose development or health is affected?

This is very unlikely. The 11;22 translocation is generally stable. The more people there are in your family with the balanced translocation and no special needs, the more confident you can be. If a child who has inherited the 11;22 translocation from a developmentally normal parent has problems with development, learning or health, it is assumed that the translocation is not the cause of the problems.

If you nonetheless want this investigated, the first step is to discuss it with your geneticist or genetic counsellor. They can investigate further and may start by re-examining the breakpoints in chromosomes 11 and 22 using the new sensitive technique of array CGH.

Very occasionally, it turns out that a translocation thought to be balanced in fact includes an unbalanced element too tiny to be seen under a microscope. In this extremely rare situation, the carrier may have some special needs.

Support and Information

Rare Chromosome Disorder Support Group,
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info@rarechromo.org | www.rarechromo.org

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 Please help us to help you!

Chromosome 22 Central
c/o Murney Rinholm
7108 Partinwood Drive, Fuquay-Varina, North Carolina, 27526 U.S.A.
Email: usinfo@c22c.org
or
info@c22c.org
www.c22c.org

Chromosome Disorder Outreach
info@chromodisorder.org
www.chromodisorder.org

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. It was compiled by Unique and reviewed by Dr Melissa Carter, clinical geneticist, The Hospital for Sick Children, Toronto, Canada and by Unique's chief medical advisor, Professor Maj Hultén BSc PhD MD FRCPath, Professor of Reproductive Genetics, University of Warwick, UK. 2009 (PM)

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