

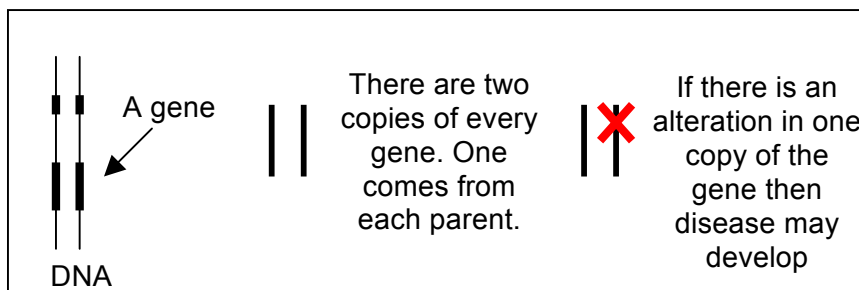
Genes, Inheritance and Genetic Testing

Our body is made up of millions of cells. There are many different types of cells, including brain cells, liver cells and heart cells, to name a few. Each cell contains around 22,000 different genes (the 'genetic recipes') that enable the cells to work correctly and determine features such as the colour of our eyes and whether we are tall or short.

The genes are packaged up into small parcels called chromosomes (the 'genetic recipe books' of the cell). These 46 chromosomes are grouped into 23 pairs, one of each pair coming from a person's mum and the other from their dad. The chromosome pairs are numbered from 1 to 22, with the 23rd pair, known as the sex chromosomes. There are two different sex chromosomes, called the X chromosome and the Y chromosome and they determine whether we are male or female. A female has two of each of the chromosomes 1 to 22 and two X sex chromosomes. A male has two of each of the chromosomes 1 to 22, and one X and one Y sex chromosome.

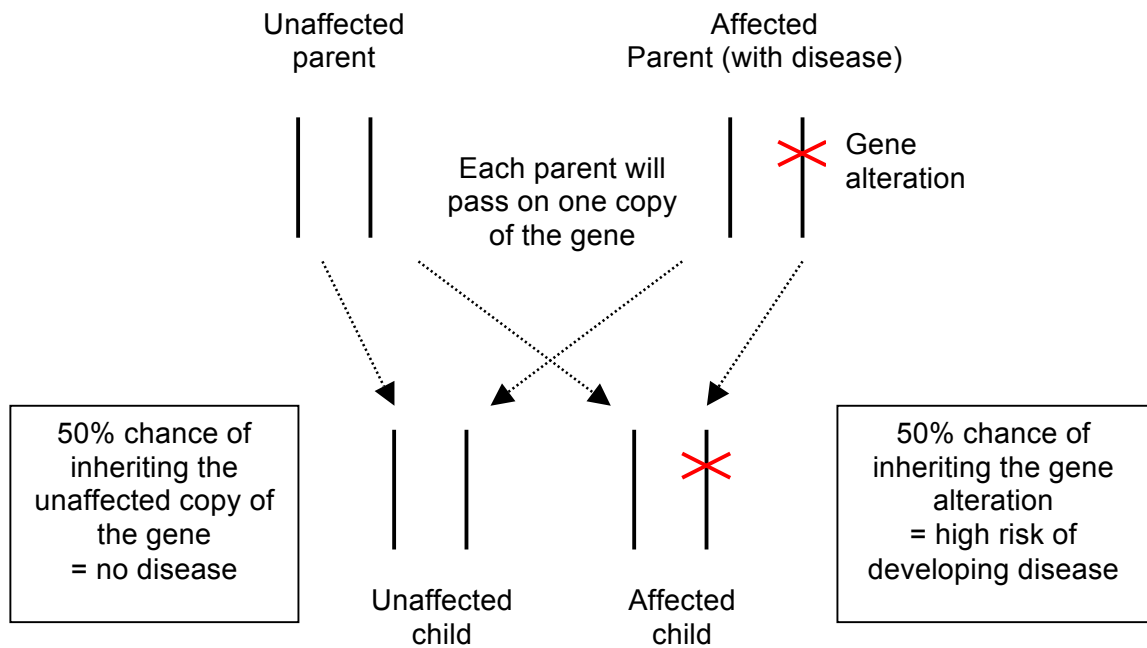
You can imagine a chromosome as a ball of wool that you can stretch out into one long strand of genetic code called DNA. The DNA is spelt out by a 4-letter alphabet or code. The complete DNA code is 3 billion letters long. Along the strand of DNA are regions called genes. As there are two copies of every chromosome, there are also two copies of every gene (one from each parent). Each gene is unique, based on the order of the letters that spell it out.

If there is a genetic error or 'spelling mistake' in one of these genes it may lead to the development of a condition or disease. The technical name for a genetic spelling mistake is mutation. Less technical names for a mutation include genetic change, genetic variant and genetic alteration.



We all have a number of genetic alterations in our genes. Usually these genetic alterations do not cause problems because there is a second 'good' copy of the gene, which is able to do the job on its own. However, sometimes a genetic alteration in one copy of a gene 'dominates' over the other 'good' copy of the gene, and this may lead to problems. **This is known as dominant inheritance.** Most inherited cardiac conditions are inherited in this way.

If a person has a dominantly inherited genetic change, there is a 1 in 2 (50%) chance of passing the genetic change to their own child and a 1 in 2 (50%) chance of not passing the genetic change to their own child. This is illustrated in the diagram below.



Occasionally a person may have a genetic alteration that has not been inherited from one of their parents. Instead, the genetic change is new in either the egg or sperm that made them. In this situation (a new mutation) the person's brothers and sisters are unlikely to develop the condition. However the new genetic change can be passed down to that person's children (a 1 in 2 or 50% chance for each child).

It is important to remember that we cannot control the genes we inherit from our parents and the genes we pass to our children – this is a matter of chance.

Further information about DNA, genes and chromosomes, and how genetic alterations are passed from a parent to a child can be found on the web site for the Centre for Genetics Education (NSW Health) at <http://www.genetics.edu.au/factsheet>

Inherited heart conditions

Most inherited heart conditions show wide variability in symptoms among family members. This means one person in a family may have severe symptoms while another from the same family may only have very mild or no symptoms.

Genetic Testing

Genetic testing is now available for some of the inherited heart conditions. It is commonly used for hypertrophic cardiomyopathy (HCM) and Long QT syndrome.

Genetic testing is a two-step process. Firstly, a genetic alteration must be identified in a family member who definitely has the condition. This is called a "mutation search".

A mutation search is a process that can be likened to looking for a spelling mistake in a series of large recipe books. Each of the inherited heart conditions can be caused by a genetic alteration in one of a number of different genetic recipes and each family will have their own unique genetic change. This means that two families with the same inherited heart condition are likely to have a different gene

alteration, in a different recipe, in a different recipe book. In more technical terms we say that two families with the same inherited heart condition are likely to have a different gene alteration, in a different gene, on a different chromosome.

This is why a mutation search can be a difficult and expensive task. It is possible for a member of a family to undergo a mutation search and for no genetic alteration to be found. This does not mean that a genetic alteration does not exist; just that it is likely to be present in a gene we have not yet discovered and/or tested. Further research will help improve the speed of testing and will increase the mutation pick-up rates in families.

If a gene alteration is identified and found to be the cause of disease in your family, we can then offer other family members a genetic test for that specific genetic alteration. This type of test is called a predictive genetic test.

This is a much faster test, as it involves looking for the presence or absence of the family gene alteration because the laboratory knows exactly which genetic alteration to look for and exactly which gene to test. This type of test can determine if a family member is likely to develop the same heart condition at some time in the future. It cannot predict when the heart condition will develop or how severe it will be.

Deciding to have a predictive genetic test is a very personal decision. Thinking about the consequences of the possible results can help with making this decision. It is recommended that all persons undergoing genetic testing see a genetic counsellor to discuss these issues.

An ABNORMAL or POSITIVE result means that a person does carry the genetic change responsible for the condition in their family. They are at risk of developing the condition in the future and their children have a 1 in 2 (50%) chance that they will inherit the same genetic change. A NORMAL or NEGATIVE result means that a person does not carry the genetic change responsible for the condition in their family and will not develop the heart condition. In addition, they cannot pass the genetic change to their children.

Genetic testing services

Prior to having a mutation search or a predictive genetic test, it is important to receive genetic counselling, ideally from experts in cardiac genetics. Your GP can refer you to such clinics but you can also contact them directly for advice and to discuss genetic testing in your family (see Contact details). For more information about genetic testing in your family, contact the nearest cardiac genetic clinic (see the Contacts sheet).

For more information

To find out more about genetic heart conditions and the latest research news, please visit the Australian Genetic Heart Disease Registry at www.heartregistry.org.au or the Cardiac Inherited Diseases Group (New Zealand) at www.cidg.org