

Important points

- Some changes in genes stop the gene working properly: the gene is said to be faulty (mutated)
- There are two copies of every gene located on an autosome (one of the chromosomes numbered 1-22). Both copies of the gene send a message to the cells to produce a particular product such as a protein
- Where the impact of having a faulty gene copy on one chromosome and a working gene copy on the partner chromosome is such that the cell cannot work properly, the mutation making the gene faulty is described as **dominant**
- People who have one faulty gene copy on one chromosome, and a working copy of that gene on the other partner chromosome, are said to be 'carriers' of the faulty gene for a particular condition
- Carrying a dominant faulty autosomal gene means that a person is either affected by the condition at birth or will be affected in later life, or is predisposed to develop the condition i.e. at increased risk. They may never develop the condition unless other environmental factors are present to 'trigger' the condition
- Autosomal dominant inheritance refers to the pattern of inheritance of a condition directly or indirectly due to a dominant faulty gene located on an autosome
- When one parent is a carrier of an autosomal dominant faulty gene, there is 1 chance in 2, or 50% chance, in every pregnancy that their child will be affected by, or predisposed to developing the condition. So there is an equal chance that they will neither be affected nor predisposed to developing the condition
- Where both parents are carriers of an autosomal dominant faulty gene, there is 1 chance in 4, in every pregnancy, that their child will receive the faulty gene copy from both parents and be more severely affected by the condition
- Where neither parent is a carrier of a dominant faulty gene and they have a child affected by a condition known to be due to autosomal dominant inheritance, the condition will most likely be due to a new or spontaneous change in that gene. Rarely, the parent will have the mutation in some of their egg or sperm cells
- Conditions that follow a pattern of autosomal dominant inheritance usually affect men and women equally and include Huntington disease, familial hypercholesterolaemia and inherited predisposition to bowel, breast and ovarian cancers
- Genetic testing to determine if an unaffected person is a carrier of a dominant faulty gene condition (presymptomatic or predictive genetic testing) is only appropriate if there is a family history of the condition
- Testing in pregnancy where a child is at risk for inheriting an autosomal dominant condition, may be available
- Contact the local genetic counselling service for information regarding the appropriateness and availability of presymptomatic, predictive and prenatal genetic testing

Our genes, located on our chromosomes in our cells, provide the information for the growth, development and function of our bodies. When the information in a gene is changed, there is a different message sent to the cells. A change to the genetic code that causes the gene not to work properly is called a **mutation**: the gene is described as faulty (see Genetics Fact Sheet 1).

A faulty (mutated) gene may directly cause a genetic condition (see Genetics Fact Sheets 2, 4 & 5). Having a faulty gene however, may also be beneficial as described in Genetics Fact Sheets 4 & 34.

Inheritance patterns in families of conditions due to faulty genes

The inheritance pattern depends on whether the

- Faulty gene is located on one of the chromosomes numbered 1-22 called an *autosome* or on the X chromosome which is one of the *sex chromosomes* (see Genetics Fact Sheet 1)
- Change to the genetic code that makes the gene faulty is 'recessive' or 'dominant' (see Genetics Fact Sheets 4 & 5)

The four most common patterns of inheritance of genetic conditions due to a change in a single gene in families are therefore described as:

- Autosomal recessive
- Autosomal dominant
- X-linked recessive
- X-linked dominant

This Fact Sheet discusses autosomal dominant inheritance. See Genetics Fact Sheets 8 & 10 for information about the other traditional patterns of inheritance.

The inheritance of autosomal dominant faulty genes

This type of inheritance usually refers to the inheritance in families of a 'dominant' change (mutation) in a gene that is located on an autosome (one of the numbered chromosomes). There are some genes however, located on the end of the short arms of both the X and Y chromosomes that are called 'pseudo-autosomal' genes and the information in this Fact Sheet will be equally applicable to the inheritance of dominant changes in these genes. See Genetics Fact Sheet 5 for a discussion of 'dominant' changes that make the gene faulty.

There are two copies of every autosomal gene. Both copies of the gene send a message to the cells to produce a particular product such as a protein. If the information in one of the copies of the gene has been changed so that it is faulty, the gene will not

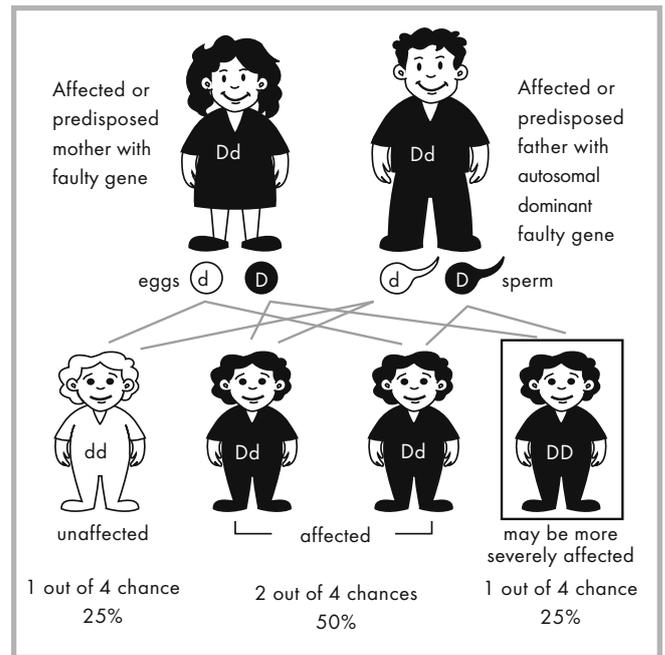
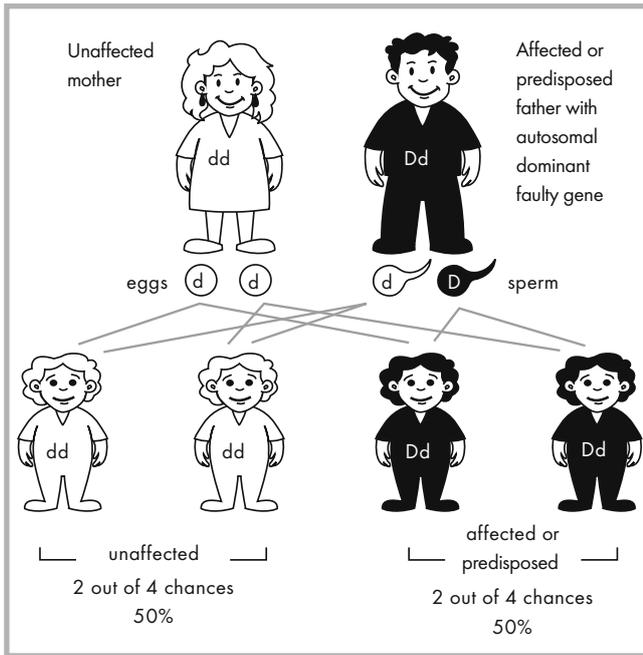


Figure 9.1: Autosomal dominant inheritance when one parent carries the autosomal dominant faulty gene copy. The autosomal dominant faulty gene copy is represented by 'D'; the working copy of the gene by 'd'.

Figure 9.2: Autosomal dominant inheritance when both parents carry the autosomal dominant faulty gene copy. The autosomal dominant faulty gene copy is represented by 'D'; the working copy of the gene by 'd'.

function properly. The cell will however still have instructions to produce a gene product from the working copy of the gene. Since the message from the faulty gene will lead to an abnormal or incorrect amount of the gene product, there will be less than the usual amount of the working gene product available.

In some cases, this amount of gene product from one working gene copy will not be enough for the body to work or grow normally and the person will be affected by a condition due to the faulty gene. Therefore, though one copy of the gene contains the information for the working gene product, the faulty gene is causing a problem for that individual. The faulty gene copy is thus dominant over the working gene copy.

For some conditions, carrying a dominant change in one of their autosomal gene copies means that a person:

- Will be directly affected by the condition, at birth or in later life (see Genetics Fact Sheets 38 & 44)
- Is predisposed to develop the condition, i.e. at increased risk. They may never develop the condition unless other environmental factors are present to 'trigger' the condition (see Genetics Fact Sheets 48 & 49)

What happens if one of the parents has a condition due to an autosomal dominant faulty gene?

When a baby is conceived, each parent has passed on one copy of each of his or her genes to the baby. Therefore, the baby is a 'mixture' of the genetic information from each of his/her parents. When one of the parents is affected by, or predisposed to developing a condition due to an autosomal dominant mutation, he/she will pass on to a child either the working, or the faulty copy, of the gene.

As shown in *Figure 9.1*, where the autosomal dominant faulty gene copy is represented by 'D' and the working copy by 'd', there are four possible combinations of the genetic information that is passed on by the parents, in every pregnancy. There is a 1 in 2 chance that the autosomal dominant faulty gene will be passed on to the child by the affected or predisposed parent. The other parent can only pass on working copies of the gene.

This means that **in every pregnancy** there is:

- 1 chance in 2 (ie. 2 chances in 4) or 50% chance that their child will inherit **the faulty copy of the gene and the working gene copy**, and will therefore be affected by, or at increased risk for developing the condition (predisposed)
- 1 chance in 2 (ie. an equal chance) or 50% that their child will inherit **both working copies of the gene**: the working copy of the gene from his/her affected or predisposed parent as well as a working copy from his/her unaffected parent. In this case, the child will not be affected by or predisposed to the condition and cannot pass on the faulty gene that causes or contributes to the condition to any of his/her children

While *Figure 9.1* shows the father as the parent carrying the autosomal dominant faulty gene, the same situation would arise if it was the mother.

Conditions that are due to autosomal dominant faulty genes usually affect men and women equally.

What happens if both parents have a condition due to an autosomal dominant faulty gene?

As shown in *Figure 9.2*, where the autosomal dominant faulty gene copy is represented by 'D' and the working copy by 'd', there are also four possible combinations of the genetic information that is

passed on by the parents, in every pregnancy. There is 1 chance in 2 that each parent will pass on the faulty copy of the gene. There is also 1 chance in 2 that each parent will pass on the working gene copy.

This means that **in every pregnancy** there is

- 1 chance in 4 or 25% chance that their child will only inherit **working copies of the gene from both parents** and be unaffected by the condition, or not at increased risk
- 1 chance in 2 (2 chances in 4) or 50% chance that the child will inherit **the faulty gene copy and the working copy** and be affected at some time in their life or be at increased risk for the condition (predisposed)
- 1 chance in 4 or 25% chance that their child will inherit **the faulty gene copy from both parents**. In this case, they will usually be more severely affected at some time in their life, depending on the condition involved. Achondroplasia and familial hypercholesterolaemia (Genetics Fact Sheets 38 & 53) are examples of conditions that are more severe when a person has inherited both copies of the faulty gene involved

What if neither of the parents are affected by the condition due to the autosomal dominant faulty gene copy but they have a child affected with the condition?

A change in a copy of a gene can occur for the first time (a 'spontaneous' gene change), for unknown reasons, in a single egg cell, a single sperm cell, or during or shortly after conception.

Where the spontaneous change occurs in an autosomal gene copy and is dominant, the individual arising from the fertilised egg containing the faulty gene copy will be the first in the family to have the condition or be predisposed to developing it. Many genetic conditions that are due to dominant faulty genes are due to such new faulty genes occurring.

The risk for other family members having or developing a condition caused by the same new autosomal dominant faulty gene copy is low since it would require a change to occur in the same gene in another family member by chance. Since there are approximately 20,000 gene pairs, the likelihood of this occurring is very small.

The faulty gene copy will however now be in all the cells of the affected or predisposed individual and he/she will be able to pass on the faulty gene copy to his/her children (see Genetics Fact Sheet 4).

What if neither of the parents are affected by the condition due to the autosomal dominant faulty gene copy but they have several children affected with the condition?

In rare cases, the autosomal dominant faulty gene copy is in some of the egg or sperm cells (also called the 'germ' cells) of the father or mother and not in the other cells of their body. In these cases, the germ cells of one of these parents will be a mixture of cells containing the autosomal dominant faulty gene copy and cells containing the working copy of this gene. This situation is referred to as '**germ cell mosaicism**'.

Working out for parents the risk for passing the faulty gene on to their children where this non-traditional pattern of inheritance is present, is very complex (see Genetics Fact Sheet 13 for more information).

What types of conditions follow an autosomal dominant pattern of inheritance?

A number of conditions follow this pattern of inheritance in families. While some are obvious at birth, in other cases the symptoms do not appear until much later in life. Neurofibromatosis type 1, achondroplasia, Huntington disease, inherited predisposition to breast, ovarian and bowel cancers and familial hypercholesterolaemia all follow a pattern of autosomal dominant inheritance (see Genetics Fact Sheets 37, 38, 44, 47 & 53).

Is it possible to determine if a person is carrying an autosomal dominant faulty gene before any symptoms appear?

For a small, but growing number of conditions, it is now possible to test a person to determine whether they have a dominant change in one of their autosomal gene copies. In some cases, having a faulty gene copy means that the person will definitely develop the condition at some time in their life (if they live long enough). Such genetic testing is described as '**presymptomatic genetic testing**'. An example of this testing is described for Huntington disease in Genetics Fact Sheet 44.

For other conditions, such as determining inherited predisposition to breast cancer, the testing is described as '**predictive genetic testing**' because the presence of the faulty gene simply gives the person an increased risk for developing the condition, not certainty (see Genetics Fact Sheets 47 & 48).

Genetic counselling is very important in the provision of both presymptomatic and predictive genetic testing and should only be undertaken by a team of professionals who can address all the complex aspects of this type of genetic testing (see Genetics Fact Sheet 3).

Presymptomatic or predictive genetic testing is only appropriate where the person has some indication, such as a family history, that they are at risk for passing on a faulty gene or of developing the condition themselves.

Where the condition develops due to a new autosomal dominant faulty gene that occurred during the conception of that person, there would be no indication that the person has the faulty gene until the condition developed. It is not possible to check every gene in the body to see if it is faulty.

Contact the local genetic counselling service for information regarding the appropriateness and availability of genetic testing (see Genetics Fact Sheets 3 & 21).

What can be done if one or both parents are carriers of the same autosomal dominant faulty gene?

If one or both partners in a couple are genetic carriers for an autosomal dominant condition, they can find out information about the condition, their risk for having an affected child and

discuss their reproductive options with a genetic counsellor (see Genetics Fact Sheet 3).

Testing in pregnancy to determine the presence of the faulty gene may be possible. For more information about prenatal testing options, see Genetics Fact Sheet 17C.

Testing of the embryo in association with assisted reproductive technologies (ART) such as preimplantation genetic diagnosis (PGD) may also be possible (see Genetics Fact Sheet 18).

A discussion with a genetic counsellor will assist in enabling a couple to make an informed decision with the most up-to-date information.

Other Genetics Fact Sheets referred to in this Fact Sheet: 1, 2, 3, 4, 5, 8, 10, 13, 17C, 18, 21, 34, 37, 38, 44, 47, 48, 49, 53

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