

This fact sheet talks about how our genes and the environment work together to cause certain health conditions. The mixture of genetics and other reasons why a health condition happens is sometimes called multifactorial inheritance.



IN SUMMARY

- Multifactorial inheritance refers to the pattern of inheritance for health conditions caused by both genetic and other factors
- Genes contain the instructions for growth and development. Some gene variations may mean that the gene does not work properly or works in a different way that is harmful. A variation in a gene that causes a health or developmental condition is called a **pathogenic variant** or **mutation**
- A person may have an increased chance of developing a multifactorial health condition due to having a gene variant, but unless other causes are also present, they may never develop symptoms of the condition.

Since the chromosomes come in pairs, there are also two copies of each of the genes. The exception to this rule applies to the genes carried on the sex chromosomes called X and Y.

The genes in our DNA provide the instructions for proteins, which are the building blocks of the cells that make up our body. Although we all have variation in our genes, sometimes this can affect how our bodies grow and develop. Generally, DNA variations that have no impact on our health are called **benign variants** or **polymorphisms**. These variants tend to be more common in people. Less commonly, variations can change the gene so that it sends a different message. These changes may mean that the gene does not work properly or works in a different way that is harmful. A variation in a gene that causes a health or developmental condition is called a **pathogenic variant** or **mutation**.

CHROMOSOMES, GENES AND DNA

In all the cells of our body, our genes are found on chromosomes (long strings of genes). We have many thousands of genes that provide information for our body to grow, develop and stay healthy. The gene sends messages to the cell to make important chemical products such as proteins.

There are usually 46 chromosomes in each cell that are arranged into 23 pairs. One of each pair is passed on to us from our mother and the other from our father. 22 of these chromosome pairs are numbered. These numbered pairs are known as the autosomal chromosomes. The 23rd pair is made up of the sex chromosomes called X and Y. Typically males have an X and a Y chromosome and females have two copies of the X chromosome.

Figure 11.1:

Chromosome picture (karyotype) from a male 46,XY.

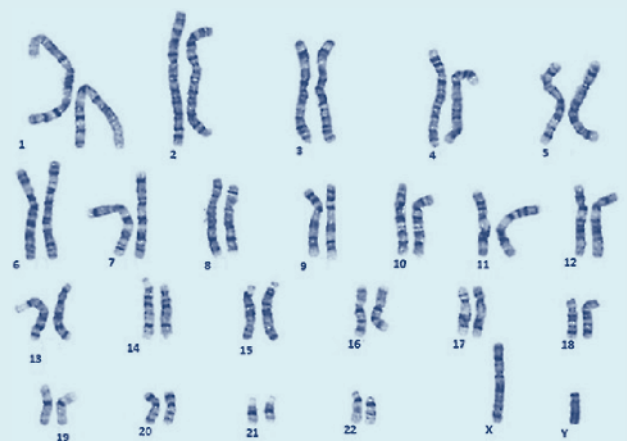
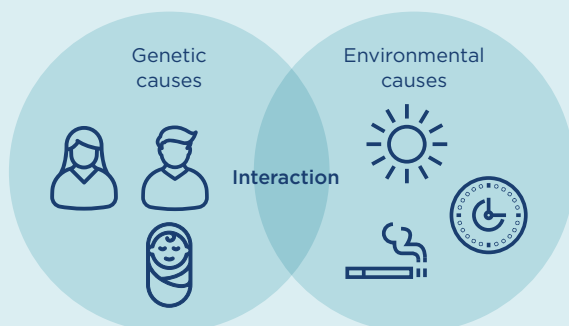


Figure 11.2:

A representation of how genetic and environmental causes work together in multifactorial health conditions



A CLOSE LOOK AT MULTIFACTORIAL INHERITANCE

Multifactorial inheritance refers to the pattern of inheritance for health conditions caused by both genetic and other factors. Causes (in addition to genetic or inherited ones) may include ageing, diet, lifestyle, and contact with chemicals or other toxins (Figure 11.2)

Multifactorial conditions do not always develop, even when there is a genetic variant that increases a person's chance of developing a health condition.

Figure 11.1: Chromosome picture (karyotype) from a male 46,XY.

For example, not all women who have an inherited breast and ovarian cancer gene variant will develop breast or ovarian cancer. The variant is not completely **penetrant**.

The reason for **incomplete penetrance** of the condition is most likely due to the mixture of information in the gene variant with the information in one or more other genes as well as other **environmental** causes.

Some of the health conditions and differences from birth listed in Table 11.1 are well understood and there may be genetic testing available to determine whether a person has a gene variant, which increases their chance of developing the condition.

Table 11.1:

Multifactorial conditions: This table shows a list of some of the health conditions where genetics plays a role, but is not always enough on its own to cause signs and symptoms

Birth differences:

cleft palate/lip, neural tube defects such as spina bifida

Cancer:

bowel, breast, ovarian, melanoma and prostate

Cardiovascular conditions:

high blood pressure, some causes of heart disease, high cholesterol

Metabolic:

diabetes

Neurological/psychiatric conditions:

Alzheimer's disease in later life, schizophrenia, bipolar disorder

Muscular/skeletal:

arthritis, rheumatic conditions, osteoporosis

Skin conditions:

psoriasis, moles, eczema

Respiratory:

asthma, allergies, emphysema

ARE MULTIFACTORIAL GENETIC CONDITIONS PASSED DOWN THROUGH THE FAMILY?

It may be possible to determine if you or members of your family have a higher chance of developing a particular multifactorial condition by noting your family health history.

Some of the clues that there may be a multifactorial health condition in your family include you and/or one or more family members related by blood who have been affected by a particular health condition, particularly at a younger than expected age.

Noting the health history of family members related by blood over several generations is important to work out if a condition is running in the family. Ask about the family health history on both your mother's and father's sides of the family. Questions to ask are:

- How is the person related to you?
- What type of condition do they have /had?
- At what age were they first diagnosed with the condition?

If there is a multifactorial condition in a family such as inherited breast and ovarian cancer, it may be possible for people to have genetic testing to work out if they have the gene variant causing a particular condition.

It is important to remember though that for some people, despite having a gene variant, breast and/or ovarian cancer will not develop unless other gene changes happen over the person's lifetime. A possible trigger for other genes to change over a lifetime may include the impact of ageing.

Other conditions that run in the family may be because of the same environmental cause rather than a genetic cause that is shared by family members. Examples of this include poor air or water quality or poor nutrition, or having a number of family members who smoke that can lead to contact with toxins from passive smoking.

In some cases, an environmental cause will be the only reason for a condition to run in a family; i.e. genetic causes may not be involved at all.

CAN SOME MULTIFACTORIAL GENETIC CONDITIONS BE PREVENTED?

Multifactorial conditions are often linked with one or more other triggers. A way to stop or lessen the impact of a multifactorial condition would be to control the known triggers in people who are more likely to develop signs and symptoms. This may be because of their family history or having a gene variant.

For a few conditions, these triggers have been identified.

- Not enough vitamin folate in a developing baby's environment has been linked to an increased chance that the baby may be born with a neural tube defect such as spina bifida. Adding folate in a woman's diet (for example by taking multivitamins that contain folate) both before pregnancy and in early pregnancy, can reduce the chance of having a baby with this condition
- High cholesterol in a person's diet can increase the chance for cardiovascular disease. Obesity has also been linked to an increased chance for a person to have diabetes type 2. Exercise and a healthy diet may be helpful in stopping or slowing the signs of these health concerns.

For many health conditions such as those listed in *Table 11.1*, simply inheriting one or more gene variants linked with a particular condition is not enough for that condition to develop.

The person's genetic makeup may make them more likely to develop a particular health condition, but other causes need to also be there, otherwise the condition may never develop.

The field of cancer genetics gives us some clues about what steps need to happen in the pathway to developing some cancers. This can help us to understand how other multifactorial conditions develop.

Discuss your family history with your doctor

Talk about your own health and family health history with your doctor if you are concerned that a condition runs in your family.

Genetic counselling and health management

Some people with a strong family history of a health condition may need a referral by their family doctor to see their local genetics service.

The genetic counselling team may be able to:

- Shed light on a person's chance of developing a condition based on family history
- Answer any questions a person may have about their family history
- Talk about helpful medical check-ups and screening
- Talk about when genetic testing may be useful
- Talk about ways of slowing or stopping symptoms from developing such as taking medication, or making changes to diet or lifestyle.