

This fact sheet describes the interaction between our genes and the environment to bring about certain health problems. The combination of genetics and external factors is sometimes called multifactorial inheritance.

### In summary

- **Multifactorial inheritance refers to the pattern of inheritance of certain health problems caused by a combination of both genetic and other factors**
- **Genes contain the instructions for growth and development. Some gene changes make the gene faulty so that the message is not read correctly or is not read at all by the cell. A variation in a gene that makes it faulty is called a *mutation***
- **A person may be at an increased risk of developing a multifactorial health condition due to having a gene mutation, but unless other factors are also present, they may never develop symptoms of the condition.**

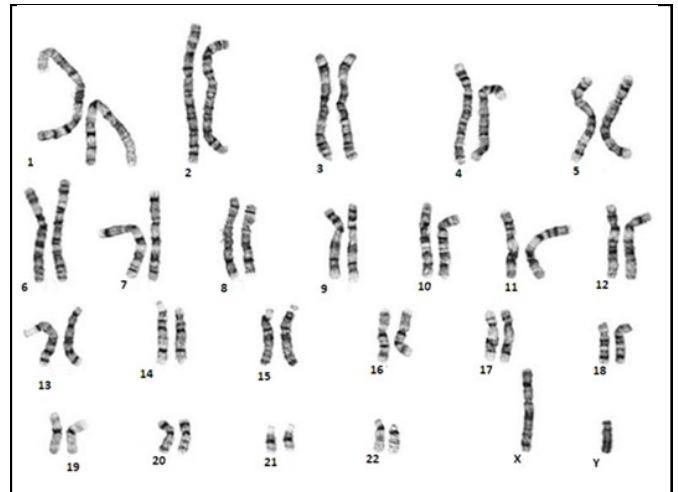
### CELLS, DNA AND GENES

Our bodies are made up of millions of cells. Each cell contains a complete copy of our genetic information or DNA. Our DNA contains the instructions for growth and development and is packaged into chromosomes that contain all our genes. A variation in a gene that creates a fault is called a **pathogenic variant** or **mutation**. Genes are sections of DNA that code for the proteins our body needs to function. A mutation in a gene will affect the body differently depending on how much it changes the resulting protein, how critical that protein is to the body and how much of that protein is needed in the body. *Figure 9.1* shows how chromosomes and therefore genes, come in pairs.

### A CLOSE LOOK AT MULTIFACTORIAL INHERITANCE

Multifactorial inheritance refers to the pattern of inheritance of certain conditions due to a combination of both genetic and other factors that may include internal factors such as ageing, and exposure to external environmental factors such as diet, lifestyle, and exposure to chemicals or other toxins (*Figure 11.2*)

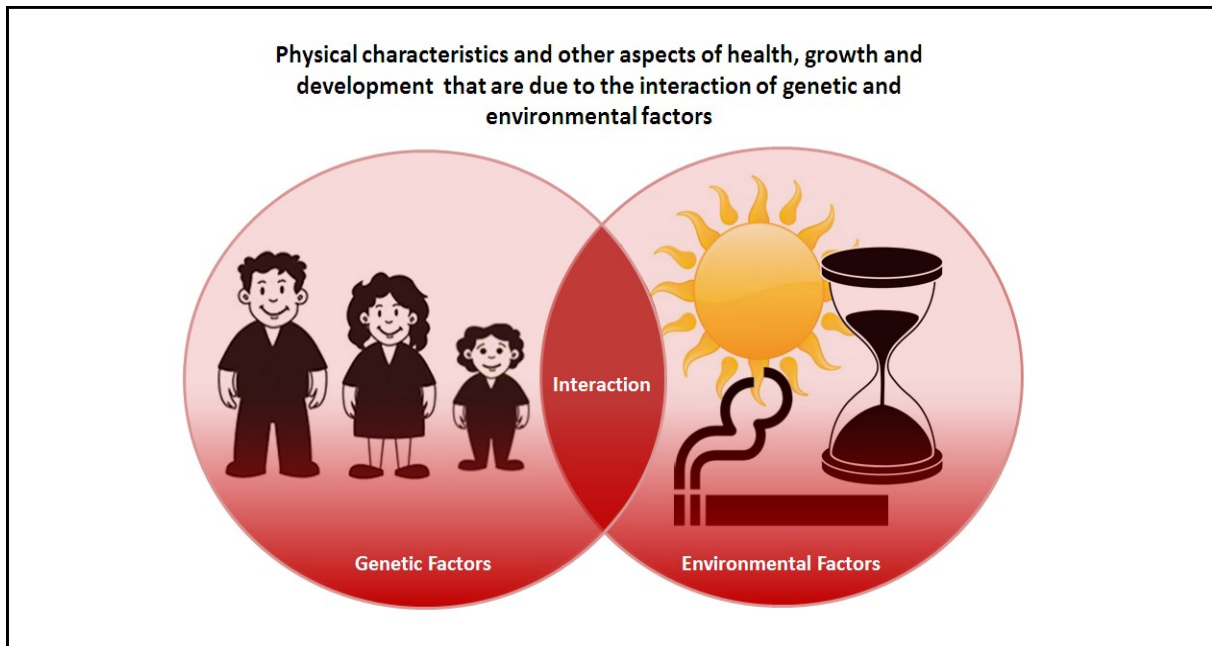
Multifactorial conditions do not always develop despite the presence of a genetic mutation which increases the person's risk.



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

For example, not all women who have a hereditary breast and ovarian cancer gene mutation will develop breast or ovarian cancer. The mutation alone is not completely **penetrant**.

The reason for this **incomplete penetrance** of the condition is most likely due to the interaction between the information in the gene mutation with the information in one or more other genes and with other **environmental** factors.



**Figure 11.2:** A diagrammatic representation of the interaction between genetic and environmental factors

**Table 11.1:** Multifactorial conditions: The conditions listed are some of the health problems in which genetics plays a role but is not always enough on its own to bring about symptoms

<b>Birth Defects:</b> cleft palate/lip, neural tube defects such as spina bifida	<b>Cancer:</b> bowel, breast, ovarian, bowel, melanoma and prostate
<b>Cardiovascular conditions:</b> high blood pressure, some causes of heart disease, high cholesterol	<b>Metabolic:</b> diabetes
<b>Neurological/psychiatric conditions:</b> Alzheimer disease in later life, schizophrenia, bipolar disorder	<b>Muscular/skeletal:</b> arthritis, rheumatic disorders, osteoporosis
<b>Skin conditions:</b> psoriasis, moles, eczema	<b>Respiratory:</b> asthma, allergies, emphysema

Some of the conditions listed in *Table 11.1* are well understood and there may be genetic testing available to determine whether a person has a gene mutation which predisposes them to developing the condition.

#### ARE MULTIFACTORIAL GENETIC CONDITIONS PASSED DOWN THROUGH THE FAMILY?

It may be possible to determine if you or other members of your family are at risk for developing a particular multifactorial condition by documenting your family health history in detail.

Some of the clues that there may be a multifactorial genetic condition in your family

include you and/or one or more blood relatives who have been affected by a condition, particularly at a younger than expected age.

Documenting the health history of family members (blood relatives) over several generations is important in determining if a condition is running in the family. Ask about the family history of on both your mother's and father's side of the family. It is important to note:

- How the individual is related to you
- The type condition they have or had
- The age of the individual when they were first diagnosed with the condition.

If there is a multifactorial genetic condition identified in a family, such as inherited breast and ovarian cancer, it may be possible for individuals to have genetic testing to determine whether they have the predisposing gene mutation.

It is important to remember though that for some people, despite having a gene mutation, breast and/or ovarian cancer will not develop unless other genes mutate over the person's lifetime. Possible triggers for other genes to mutate include factors in our internal and external environments as well as the impact of ageing.

Other conditions that run in the family may be due to exposure to the same environmental factor such as poor quality air or water or poor nutrition; e.g. having a number of family members who smoke can lead to exposure to toxins from passive smoking with its established health impact.

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

### **CAN SOME MULTIFACTORIAL GENETIC CONDITIONS BE PREVENTED?**

Multifactorial conditions involve an inherited genetic predisposition and one or more other triggers. An obvious preventive approach is to modify the known triggers in those individuals who are susceptible due to their family history or having a predisposing mutation.

For a few conditions, these triggers have been identified.

- A lack of the vitamin folate in a developing baby's environment has been linked to an increased chance that the baby will have a neural tube defect such as spina bifida. Supplementation by folate in women pre-pregnancy and in early pregnancy can significantly reduce the number of babies born with this condition
- High dietary cholesterol is a factor in increased risk for cardiovascular disease and obesity has also been linked to increased risk for diabetes type 2. Exercise and a healthy diet are an effective intervention.

This approach is only possible for those few conditions where the environmental trigger, or some of the triggers, have been identified.

It is clear that for many common and rare conditions such as those listed in *Table 9.1*, simply inheriting one or more gene mutations associated with a particular condition is not enough for that condition to develop.

The person's inherited genetic information may make them susceptible (predisposed) to the condition but if other steps do not occur during their life then the condition will never develop.

The field of cancer genetics has provided some clues as to how the pathway works for some cancers to develop and this may be the model for other multifactorial conditions.

### **Discuss your family history with your doctor**

Discuss your personal and family history with your GP if you are concerned that a condition is in your family.

### **Genetic counselling and risk management**

Some individuals with a strong family history of a certain condition may require referral by their GP to their local genetic counselling service. Their risk of developing the condition, based on their family history, can be estimated and discussed in more detail.

The genetic counselling team may be able to:

- Clarify their chance of developing a condition based on family history
- Answer any questions they have about their family history
- Discuss what medical check-ups are appropriate
- Discuss the limitations, potential benefits, disadvantages and appropriateness of genetic testing
- In some cases, preventive measures such as medication, diet or lifestyle changes may help.