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Important points

- Genetic conditions include many of the health or developmental problems seen at birth, in childhood, adolescence or adulthood
- They include rare and common conditions and make a significant contribution to the problems in growth, development and health experienced by humans
- Some conditions are directly due to a change in the genetic information in one or more genes. Others are due to an interaction between a change in the genetic information and other factors which can either affect the expression of a gene or cause changes to the information in other genes during the person's lifetime
- Certain population groups are more at risk for developing particular genetic conditions than others
- For some genetic conditions, when a family member is affected or at risk, genetic testing may be available and appropriate
- It is currently not possible to cure a genetic condition
- For some genetic conditions there is no treatment but more treatments are being developed each year
- For other conditions it may be possible to implement preventive and early detection strategies to limit or stop the symptoms developing
- Current information and support is available from genetic counselling
- Support groups also provide information about the day to day living with a particular genetic condition and an understanding and empathic ear

Genetic conditions include many of the health, growth or developmental problems seen at birth. Others may not be noticed until childhood, adolescence or adulthood.

There are over 6,000 known conditions which affect growth, development and health that are due to a change in just one of the 20,000 or so gene pairs in the human cell (see Genetics Fact Sheets 1 & 4).

There are over a hundred syndromes known to be due to a chromosomal change (see Genetics Fact Sheets 6 & 7).

There is a growing number of genetic conditions identified due to an interaction between a genetic susceptibility (predisposition), environmental factors or other influences on the expression of the genes (*epigenetics*), many of which cause common health problems. (see Genetics Fact Sheet 11).

Examples of genetic conditions

Genetic conditions include rare and common conditions. *Table 2.1* provides some details about a range of genetic conditions. Genetic testing may be available for these conditions for either diagnosis or risk estimation as appropriate. The cost of such testing should be discussed with the local genetic counselling service.

Support groups in Australia and New Zealand for many of these conditions have been formed (see Section I).

Genetic conditions in Australia

- About 50% of the Australian population will, during their lifetime, be adversely affected by a condition with a genetic basis
- In the first twenty five years of life about 5% of the Australasian population will be affected by an illness, impairment or disability either wholly or partly due to their inherited information

- About 30% of patients in paediatric hospitals have a genetic component to their illness
- At least 28% of all infant deaths result from genetic factors
- At least 50% of all miscarriages are caused by chromosomal abnormalities

Some population groups are more at risk for developing particular genetic conditions than others

A number of genetic conditions occur more frequently in some population groups and in people with a particular ancestry (see *Table 2.1*). A Genetics Fact Sheet provides more information for almost all of the conditions listed.

What causes genetic conditions?

There are four possible causes of genetic conditions.

(a) A change in the genetic code of genes

There are two copies of the genes, one on each of the chromosome pairs located in the nucleus of the cell. Genes are also located in the mitochondria. Changes to the genetic code in one or both copies of one or more genes found in the nucleus or mitochondria of a cell can be inherited from a parent.

A change can also occur either during the formation of the egg or sperm or during or soon after conception (See Genetics Fact Sheets 1, 4 & 5). If the change is in the genes in the egg or sperm cells, the changed gene can be passed on to a child and the condition resulting now 'runs in the family'. The pattern of inheritance of the condition resulting from the changed gene(s) depends on the chromosomal location of the changed gene(s) in the nucleus or the mitochondria of the cell and the type of gene change (see Genetics Fact Sheets 8, 9, 10 & 12).

Table 2.1 Genetic conditions occur more frequently in some population groups and in people with a particular ancestry.

Ethnic or cultural background	Condition and Genetics Fact Sheet reference
Ashkenazi Jewish (Central and Northern European Jewish)	Cystic fibrosis (33)
	Canavan disease (35)
	Familial breast and ovarian cancer predisposition (48)
	Familial dysautonomia (35)
	Fanconi anaemia (35)
	Tay-Sachs disease (35)
Northern European (includes UK)	Cystic fibrosis (33)
	Hereditary haemochromatosis (36)
Middle Eastern, Southern European, Indian Sub-continent, Central and South East Asian and African	β – Thalassaemia (34)
Chinese, South East Asian (also Southern European, Middle Eastern, Indian Subcontinent, African, the Pacific Islands and Maori)	α – Thalassaemia (34)
African (also Middle Eastern, Southern European, Indian Subcontinent, South American and the Caribbean)	Sickle cell disease (34)
Lebanese (Christian), Dutch descent (cf Afrikaans), French Canadian	Familial hypercholesterolaemia (53)
Middle-Eastern, Mediterranean, African, South East Asian, African and New Guinea	Glucose – 6 –phosphate dehydrogenase (G6PD) deficiency

- Conditions that directly result from changes in genes located in the nucleus include cystic fibrosis, thalassaemia, Tay-Sachs disease, haemophilia and Huntington disease (See Genetics Fact Sheets 33, 34, 35, 40 & 44).
- Conditions that result from changes to mitochondrial genes include those that affect organs such as the heart, kidney and other muscles (See Genetics Fact Sheet 12).

(b) Chromosomal changes

Changes in the number or structure of chromosomes can be inherited from a parent who has the chromosomal change in their cells.

A change can also occur either during the formation of the egg or sperm, during or soon after conception (see Genetics Fact Sheets 6 & 7).

- Conditions resulting from chromosomal changes include Down syndrome, Klinefelter syndrome and Turner syndrome (see Genetics Fact Sheets 28, 31 & 32).

(c) Interaction between a change in the genetic code and other factors such as the environment or other genes (multifactorial inheritance)

A change to the genetic code may not directly impact growth, development or health but may make the person susceptible or predisposed to develop these problems. Onset of the condition requires additional factors to be present.

In the majority of cases the specific factors are unknown but include environmental factors such as diet, exposure to chemicals and other toxins and radiation and changes to the genetic code in

other genes in the cell that build up over a person’s lifetime as they age (see Figure 2.1 and Genetics Fact Sheets 11 & 47) .

- For example, the interaction between the vitamin folate and neural tube defects such as spina bifida is well established (see Genetics Fact Sheets 19 & 59).

(d) Modification of expression of the genes (epigenetics)

Normal processes in the cell control switching the genes on and off by ‘modifying’ the DNA. This process, called *epigenetics*, does not change the sequence of letters in the genetic code but stops the information being read by the cell.

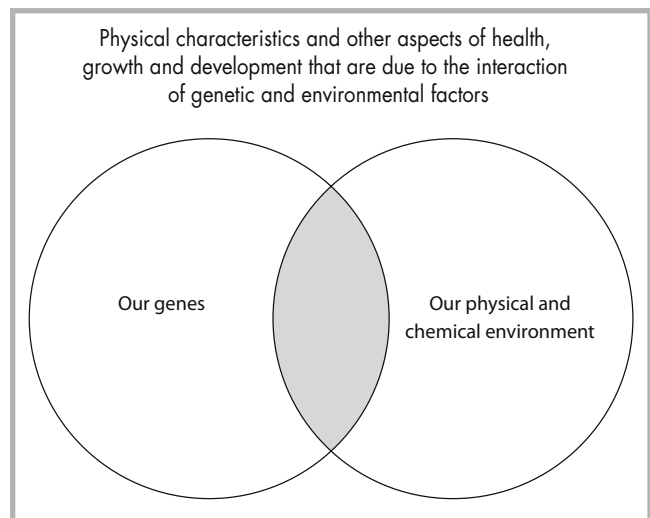


Figure 2.1: A diagrammatic representation of the interaction between genetic and environmental factors

Table 2.2. A list of the more common genetic conditions in Australia for which testing is available. The testing may look at the information in the gene or the gene product.

Condition and Genetics Fact Sheet Number (GFS) for further information	Number in population who are affected	Chromosome or Gene(s) involved	Symptoms and usual age of onset	Prevention/ surveillance for early detection	Treatment
Chromosomal conditions					
Down syndrome (GFS 28) – trisomy 21	1:660	Chromosome 21	A range of characteristic physical features and intellectual disability to varying degrees. Onset at birth.	None	Educational and behavioural support.
Klinefelter syndrome=XXY syndrome (GFS 31)	1:500-1,000 boys	Additional chromosome X in males	A range of physical characteristics due to the presence of one or more extra X chromosome(s) in males. Infertility. Specific learning disabilities usually present. Diagnosis often not made until puberty.	None	Educational and behavioural support.
Turner syndrome – 45,X syndrome(GFS 32)	1:2,000 girls	Loss of chromosome X in females	Short stature. Infertility. May be recognised at birth. Diagnosis often not made until puberty.	None	Educational and behavioural support.
Cancers					
Inherited susceptibility to breast cancer and ovarian cancer (GFS 48)	About 5% of all cases of breast and ovarian cancer	BRCA1, BRCA2	Cancer is a condition in which abnormal cell development occurs, causing destruction of healthy cells. Breast cancer is the commonest form of cancer occurring in women in Australia, affecting about 1 in 11 before the age of 75. Men can also be affected but this is rare. About 1 in 100 women develop ovarian cancer before the age of 75. About 5% of all breast and ovarian cancers involve an inherited susceptibility.	Breast examination, mammography, prophylactic breast or ovary removal, and ovarian cancer surveillance.	Standard treatment if cancer develops.
FAP (hereditary non-polyposis coli) (GFS 49)	1:3,500	APC	Many growths called polyps develop in the bowel (usually more than 100), generally by the late teens. Without treatment, some of these polyps will certainly develop into cancer. This usually happens when the person is aged in their 20s, 30s or 40s - sometimes even earlier.	Surveillance by sigmoidoscopy from 10-15 years. Surgery to remove colon after polyps appear.	Standard treatment for bowel cancer if it develops.
Inherited susceptibility to bowel cancer and other cancers HNPCC (hereditary non-polyposis coli) (GFS 49)	Between 5-10% of all cases of bowel cancer	MLH1, MSH2, MSH6, PMS2	A small number of polyps develop in the bowel and can develop into bowel cancer. Other cancers such as endometrial cancer (cancer of the lining of the womb), ovarian, stomach, small bowel, upper renal tract, brain, skin and possibly pancreatic cancer are also more common in families where HNPCC has occurred. Onset is very variable (from 20s-80s).	Colonoscopy, surgical removal of the colon (colectomy) once cancer develops, endometrial and ovarian cancer surveillance.	Standard treatment if cancer develops.
Neurological conditions					
Huntington disease (GFS 44)	1:20,000	Huntingtin	Symptoms include jerking and twisting movements, abnormal gait, and slurred speech. Persons affected often show intellectual impairment and emotional disturbances. The typical age of onset is between 30 and 55 years	None	Supportive
Alzheimer disease - early onset (GFS 45)	1:2,500	PS1, PS2, APP	Dementia syndrome affecting memory, thought, language, personality and behaviour. This form of the condition occurs in at least 10% of cases. Onset in 40s-50s.	None	None

Condition and Genetics Fact Sheet Number (GFS) for further information	Number in population who are affected	Chromosome or Gene(s) involved	Symptoms and usual age of onset	Prevention/ surveillance for early detection	Treatment
Other conditions					
Fragile X syndrome (GFS 42)	1:4,000 boys 1:2,000 girls	FMR1	Disability that ranges from mild learning problems to severe intellectual impairment, although not all abilities are equally affected. Associated with a number of subtle physical and behavioural characteristics. Symptoms evident in the first year of life.	None	Educational and behavioural support.
Cystic fibrosis (GFS 33)	1:2,500	CFTR	Mucous build up causing lung and digestive problems. Symptoms usually present in first year of life.	Early diagnosis by newborn screening.	Physiotherapy, antibiotics, enzymes to help digest food, and dietary recommendations.
β – Thalassaemia (GFS 34)	Various depending on ethnic background.	β – globin	Severe anaemia that onsets after birth.	None	Blood transfusion, chelation therapy to remove iron build-up from transfusions.
α – Thalassaemia (GFS 34)	Various depending on ethnic background.	α – globin	Fetal death or mild to severe anaemia	None	Blood transfusion, chelation therapy to remove iron build-up from transfusions.
Hereditary haemochromatosis (GFS 36)	~1:250	HFE (for >95% of Australians)	When untreated, accumulation of iron in various body organs leads to conditions such as cirrhosis, cardiomyopathy and diabetes.	Surveillance for excess iron (iron overload).	Blood donation (venesection).
Thrombophilia - Factor 5 Leiden (GFS 39)	Various depending on ethnic background.	Factor 5	A weak blood clotting condition (6% of individuals will develop a clot in the vein [thrombus] by age 65)	Screening for individuals at high risk	Appropriate treatment of blood clots if present
Haemophilia A (GFS 40)	1:10,000 boys	Factor VIII C	A condition in which the blood clotting process is abnormal resulting in a tendency towards prolonged bleeding. Symptoms appear in the first few months of life when severe.	Not relevant	Factor VIII
Muscular dystrophy – Duchenne type (GFS 41)	1:3,500 boys	Dystrophin	The muscles do not work properly because of an abnormality in either the muscle fibres, the motor nerve cells in the spinal cord or the nerve fibres connecting them. Symptoms usually evident in first few years of life.	None	Physiotherapy, orthotics
Familial hypercholesterolaemia (GFS 53)	Various depending on ethnic background.	LDLR	Lifelong marked high cholesterol levels leads to tissue cholesterol deposition. Atherosclerosis begins in early childhood. Carotid atherosclerosis rapidly progresses during childhood. Family history.	Children of an affected parent should be screened after the age of 2-3 years.	Cholesterol-lowering diet, lifestyle modifications and drug therapy.

- When this normal process is impaired a condition affecting growth, development or health may be triggered. Examples of epigenetics and its impact are discussed in Genetics Fact Sheets 14 & 15.

Complex patterns of inheritance and penetrance

Understanding the patterns of inheritance of genetic conditions in families is becoming increasingly complex.

The result of the interaction between information in the genes and other factors is that, despite the presence of the faulty gene, the condition does not always develop. This is described as ‘incomplete penetrance’ of the faulty gene. For example, not all women who inherit a faulty breast cancer susceptibility gene copy will develop breast cancer. Other factors must be present for a breast cancer to develop.

With many common conditions that run in the family, providing individuals with their chance for developing the condition, or having a child with the condition, is very complex and inexact.

Genetic counselling is therefore essential to ensure that all factors are taken into account in risk estimation (see Genetics Fact Sheet 3).

What can be done about genetic conditions?

(a) Prevention and early detection

As shown in *Table 2.2*, for some conditions prevention and early detection strategies are available. This is usually relevant for people with family histories of those conditions caused by the interaction of environmental factors with their inherited genetic information. Family members may be ‘genetically predisposed’ to develop these conditions. The presence however, of an environmental ‘trigger’ is necessary for the person to be affected with the condition.

In some cases, prevention of the condition can be achieved by understanding the particular environmental factor that will trigger the condition. For example, it is possible to prevent about 70% of the cases of spina bifida in babies (a neural tube defect, see Genetics Fact Sheet 59) if their mothers take the vitamin folic acid before, and during early pregnancy (see Genetics Fact Sheet 19).

In some genetic conditions, early diagnosis, sometimes even before the symptoms appear, can lead to specific treatment. For example, all newborn babies in Australasia are screened for a condition called phenylketonuria (PKU) by a simple blood test. Diagnosis and treatment within the first month of life are crucial to avoid intellectual disability (see Genetics Fact Sheet 20). For some cases of breast cancer, bowel cancer, melanoma and prostate cancer, strategies are also available to detect them early enough to enable treatment to take place (see Genetics Fact Sheets 48, 49, 50 & 51).

Checking the family health history may determine if a person or another blood relative are at risk for developing a genetic condition or for passing it on to their children (see *The Importance of Your Family Health Information*).

(b) Genetic Counselling

Genetic counselling is available to families and individuals that have concerns about a condition in their family that may have a genetic basis. A team of health professionals which may include clinical geneticists, genetic counsellors and social workers, work together to provide information and supportive counselling so that families may be better able to understand, and adjust to, the diagnosis of a genetic condition (see Genetics Fact Sheet 3).

Genetic testing, if it is available and appropriate, can also be organised on the basis of informed consent (see Genetics Fact Sheet 21). Genetics Services are available throughout Australasia and provide genetic counselling to assist in informed decision making regarding genetic testing (see Genetic Facts Sheet 3).

(c) Support Groups

Support groups provide affected individuals and families with information about the condition and community resources, as well as an understanding and empathic ear. There are over 200 genetic conditions for which there are over 850 support groups/branches in Australasia (see Section 1).

There are also a number of ‘umbrella’ organisations for genetic support groups that provide support and information for those families and individuals affected by a condition so rare that there is no specific support group. These groups can also provide information about individual support groups in Australasia.

Other Genetics Fact Sheets referred to in this Fact Sheet: 1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 15, 19, 20, 21, 28, 31, 32, 33, 34, 35, 36, 39, 40, 41, 42, 44, 47, 48, 49, 50, 51, 53, 59

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