Important points

- The most important factors which can influence a man’s chance of developing prostate cancer are:
  - Getting older. More than two-thirds (70%) of all new prostate cancers are in men over the age of 65
  - Having a family history of prostate cancer, particularly having a father or a brother with prostate cancer that was diagnosed before they were 60 years of age
- A family history of these cancers can occur just by chance, because cancer is common; because family members are exposed to the same environmental factors; and because a predisposition to prostate cancer is in the family, though this is rare
- It is thought that variations in not just one but many genes may be associated with the development of prostate cancer
- While a number of ‘cancer protection’ genes in which inherited changes that make the genes faulty (mutations) have been linked to prostate cancer, no gene that contributes to a significant proportion of hereditary prostate cancer has yet been identified
- A small proportion of prostate cancers may be associated with inheriting a faulty copy of the genes predisposing to breast and ovarian cancer in women (BRCA1 or BRCA2 genes). Men who have a strong family history of female relatives with breast and/or ovarian cancer, or where a faulty BRCA1 and BRCA2 gene has been identified in a relative, have a small increased risk of developing prostate cancer
  - For these families, genetic counselling is available to clarify an individual’s risk and to discuss their options for genetic testing, the limitations of such testing, advantages and disadvantages and available prevention and early detection strategies
- Genetic testing for prostate cancer is still in the research phase
- There is considerable debate over whether all men should be screened for prostate cancer. For men with a family history of prostate cancer, however, particularly if the affected member of the family is a father or a brother with prostate cancer diagnosed before the age of 60 years, it is important to discuss the pros and cons of having prostate cancer screening with a doctor.

In a small number of families in the community, there is an increased risk for some members to develop cancer, because of an inherited predisposition to cancer. Cancers include

- Breast and ovarian cancer (see Genetics Fact Sheet 48)
- Bowel cancer (see Genetics Fact Sheet 49)
- Melanoma (see Genetics Fact Sheet 50)

This Fact Sheet discusses inherited predisposition (susceptibility) to prostate cancer.

What is prostate cancer?

The prostate, a small gland about the size of a walnut found only in men, is located at the base of the bladder. Its function is to produce part of the fluid that makes up semen.

As men grow older, especially over the age of 50, the prostate normally gets bigger. This enlargement can block the passage of urine, causing problems with urination such as difficulty in started, dribbling or slowness in passing urine. Sometimes there may be pain, blood in the urine or incomplete emptying of the bladder. While these symptoms are commonly caused by this non-cancerous enlargement, prostate cancer may also cause these symptoms.

In Australia, prostate cancer

- Affects about 1 in 11 Australian men before the age of 75
- Is rare before age 50, but is the most common cancer for men over 55 years of age

More than two-thirds (70%) of all new prostate cancers are in men over the age of 65.

What causes prostate cancer?

There is no single cause.

There are a number of factors (risk factors) which can influence a man’s chance of developing prostate cancer. The most important risk factors are:

- Getting older. More than two-thirds (70%) of all new prostate cancers are in men over the age of 65
- Having a family history of prostate cancer, particularly having a father or a brother with prostate cancer

What is meant by a family history of prostate cancer?

A family history of prostate cancer can occur

- Just by chance, because cancer is common
- Because family members are exposed to the same environmental factors
- Because a predisposition to prostate cancer is running in the family, though this is rare

A family history of prostate cancer means having one or more close male blood relatives who have, or have had, prostate cancer. These relatives could be on either the father’s or the mother’s side of the family. Close blood relatives (not relatives by marriage) are

- Parents, siblings or children (first-degree relatives – 1°)
- Aunts, uncles, nephews, nieces or grandparents (second-degree relatives – 2°)

It is not uncommon to have a few male relatives who have had a diagnosis of prostate cancer simply because prostate cancer is common in Australia. Such men may be only slightly above the average risk.

There may be a ‘stronger’ family history where a number of close male blood relatives have been affected with prostate cancer.

- Most of these men may have a moderately increased chance of developing prostate cancer
- A few will have a potentially high risk of developing prostate cancer because there is an inherited predisposition to this cancer in the family

There is an increasing risk for a man to develop prostate cancer, with a greater number of affected male relatives.
Inherited predisposition to developing prostate cancer

The majority of cases of prostate cancer cases are not due to an inherited predisposition to develop the condition.

A very small number (estimated around 5%-10%) of the cases of prostate cancer in Australia involve an inherited predisposition to develop the cancer. In these cases, the men have inherited a copy of a faulty ‘prostate cancer protection’ gene (see Genetics Fact Sheet 47 for further information about ‘cancer protection’ genes and inherited predisposition to cancer).

Cancer is a result of uncontrolled cell growth and division in a particular part of the body, eg. in the prostate, if the cells divide and grow out of control, they accumulate into a cancer.

We all have two copies of a number of different genes that normally ensure ordered growth and division of our cells throughout life. These genes can therefore be thought of normally acting as ‘cancer protection’ genes. All cancers can be considered genetic in origin though not necessarily inherited because they arise from changes in the normal ‘cancer protection’ genes that we all have.

A variation in the information in a ‘cancer protection’ gene that makes the gene faulty (a mutation) stops the gene working properly. The cause of the variations that make the ‘prostate cancer protection’ genes faulty is unknown, but it may be due to a combination of genetic factors, environmental factors and the process of ageing. Further research is being undertaken to better understand the cause of specific genetic mutations in the cancer cells.

The development of prostate cancer is not a quick or simple process. It is a process involving a build-up of variations in a number of different ‘cancer protection’ genes in the cells of the prostate over a man’s lifetime (see Genetics Fact Sheet 47). This is why the development of prostate cancer can take many, many years, and is usually seen in older men.

Most men are born having two working copies of each of the different ‘cancer protection’ genes in their cells. This means that most men have not inherited a genetic predisposition to developing cancer and have an average chance of developing these cancers.

Between 5% and 10% of all prostate cancers are believed to be due to having inherited a faulty copy of one of the ‘cancer protection’ genes that usually control cell division and growth in prostate tissue (see Figure 51.1)

- From birth, the division and growth of cells in these men’s prostate tissue is not as tightly controlled as it is in other men in the population
- Although these cells would be on the first step on the ‘staircase’ towards becoming cancerous, the other copy of that ‘cancer protection’ gene and additional ‘cancer protection’ genes in the cells, are still working correctly so the process of cell division and growth in the prostate tissue is still largely normal
- The chance of developing these cancers is higher than average but unless further mutations occur over time in a number of other ‘cancer protection’ genes in prostate cells, those cells will never become cancerous
- It is thought that not just one but many gene changes are needed for prostate cancer to develop

It is important to remember that prostate cancer itself is not inherited, although cancer that arises from an inherited faulty ‘cancer protection’ gene is sometimes called hereditary cancer.

What are the inherited faulty ‘cancer protection’ genes involved in predisposition to prostate cancer?

The inheritance of a predisposition to prostate cancer is not well understood and research is continuing.

- No single gene contributing to a significant proportion of prostate cancers occurring in families with a strong family history (familial prostate cancer) has yet been identified
- It is thought that familial prostate cancer is associated with variations (mutations) in a number of different prostate ‘cancer protection’ genes that makes those genes faulty. These faulty genes may in combination cause an inherited predisposition

It is known that inheriting a copy of one of the faulty ‘cancer protection’ genes involved in a predisposition to breast and ovarian cancer in women, can also mean a small increase in risk for prostate cancer in the male members of the family. These genes are known as:

- The Breast Cancer 1 gene (BRCA1)
- The Breast Cancer 2 gene (BRCA2)

All people have the BRCA1 and BRCA2 genes in their cells and the role of these genes is in ‘cancer protection’.

If a man is born with either a faulty BRCA1 or BRCA2 gene copy, their lifetime risk for developing prostate cancer may be up to 10%. Research is still continuing to better define this increase in risk associated with these faulty genes (see Genetics Fact Sheet 47).

- It is important to remember that only about 5%-10% of all prostate cancers are due to inheriting a faulty ‘cancer protection’ gene and probably less than 2% are due to inheriting a faulty copy of the BRCA1 or BRCA2 gene(s) (Figure 51.1).
**What is the pattern of inheritance in families with a faulty BRCA1 or BRCA2 gene?**

Two factors influence the pattern of inheritance of a faulty BRCA1 or BRCA2 gene in families.

1. The BRCA1 and BRCA2 genes are located on chromosomes 17 and 13 respectively. Both of these chromosomes are autosomes (one of the numbered chromosomes)
2. The effects of changes in the BRCA1 and BRCA2 genes are ‘dominant’ over the information in the working copy of the genes on the partner chromosomes 17 and 13 (see Genetics Fact Sheets 1, 4 & 5)

The pattern of inheritance in families of the faulty genes causing predisposition to prostate cancer is therefore described as **autosomal dominant inheritance** (see Genetics Fact Sheet 9).

In Figure 51.2 the autosomal dominant faulty gene causing predisposition to prostate cancer is represented by ‘D’; the working copy by ‘d’.

Where one of the parents has or has had cancer caused by a faulty BRCA1 or BRCA2 gene, or is a carrier of a faulty BRCA1 or BRCA2 gene, **in every pregnancy**, each of their children has

- A 1 chance in 2 (50% chance) of inheriting the faulty gene from the affected parent
- A 1 chance in 2 (50% chance) of not inheriting the faulty gene and only inheriting a working copy of the gene from both parents

Some important things to note:

- Cancer will not develop in a man who is a carrier of a faulty BRCA1 or BRCA2 gene unless further mutations occur in other ‘cancer protection’ genes in the cells during life
- Men who have not inherited the faulty gene are not at increased risk of developing prostate cancer over their lifetime and cannot pass the faulty gene on to their own children. However, they still have the same risk for developing prostate cancer as the average man in the Australian population
- While Figure 51.2 shows the father as the parent carrying the faulty BRCA1 or BRCA2 gene, the same situation would arise if it was the mother
  - A faulty BRCA1 or BRCA2 gene can be inherited from either the mother or the father
- The environmental factors that cause the mutations in the BRCA1 or BRCA2 gene(s) are still largely unknown. The identification of these factors and preventing their action paves the way for the prevention of many cancers. This is the subject of intense research
- The identification of the environmental factors causing the mutations in other additional ‘cancer protection’ genes over the man’s lifetime that eventually lead to prostate cancer are also unknown

**What is the pattern of inheritance of faulty prostate ‘cancer protection’ genes in families where the genetic cause is unknown?**

As other faulty ‘cancer protection’ genes involved in prostate cancer are still unknown, the pattern of inheritance is also unknown.

**What are the clues in a family history of prostate cancer that suggest that family members are at potentially high risk due to an inherited predisposition?**

While the genetic basis is still not well understood, it is clear that men who have a father or brother with prostate cancer are at increased risk.

- Children or brothers of men who developed prostate cancer when they were less than 60 years old have at least a 2 fold increase in risk of prostate cancer in their lifetime
- The incidence is further increased in families where two or more members on the same side of the family are affected

Documenting the health history of family members over several generations is important in determining if a condition is running in the family. It is important to note

- How the individual is related to you
- The type of cancer they have or had
- The age of the individual when it was first diagnosed

A guide to documenting a family health history is available from the Centre for Genetics Education. Anyone with concerns about a family history of cancer can seek advice from their doctor. It is important to keep the family health history up-to-date as family members are born, die or develop new health problems.
Can a person determine if they have inherited a faulty gene predisposing to prostate cancer?

Currently, genetic testing for prostate cancer is still in the research phase. It is likely that variations in a number of different genes will be involved in predisposing to prostate cancer and so the testing and interpretation of the results will be complex.

Men with a strong family history of prostate cancer in their male relatives, breast and/or ovarian cancer in their female relatives or, where a faulty BRCA1 or BRCA2 faulty gene has been identified in their family can seek advice from a specialist family cancer service (if available) or their local genetic counselling service. The risk of developing prostate cancer, is determined based on their family history and can be estimated and discussed in more detail (see Genetics Fact Sheet 3).

What can be done for men with a father or brother with prostate cancer?

Screening men who are well with no symptoms of prostate cancer is a controversial issue as there is no test reliable enough to support screening all men for prostate cancer.

For men with a family history of prostate cancer, however, such as having a father or brother with prostate cancer, diagnosed before 60, it is important to discuss the pros and cons of having prostate cancer screening with a doctor.

In addition, the progression to prostate cancer requires mutations to build up in a number of the ‘cancer protection’ genes in the prostate cells over time. If it was possible to identify the environmental factors that cause these mutations, preventive strategies could be implemented. Currently, there is limited understanding of these factors. A ‘best bet’ should include a healthy diet and a healthy lifestyle.

Other Genetics Fact Sheets referred to in this Fact Sheet: 1, 3, 4, 5, 9, 47, 48, 49, 50

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