Prepared by the Australian Cancer Network and Australian Prostate Cancer Collaboration based on the Guidelines for Locally Advanced and Metastatic Prostate Cancer.

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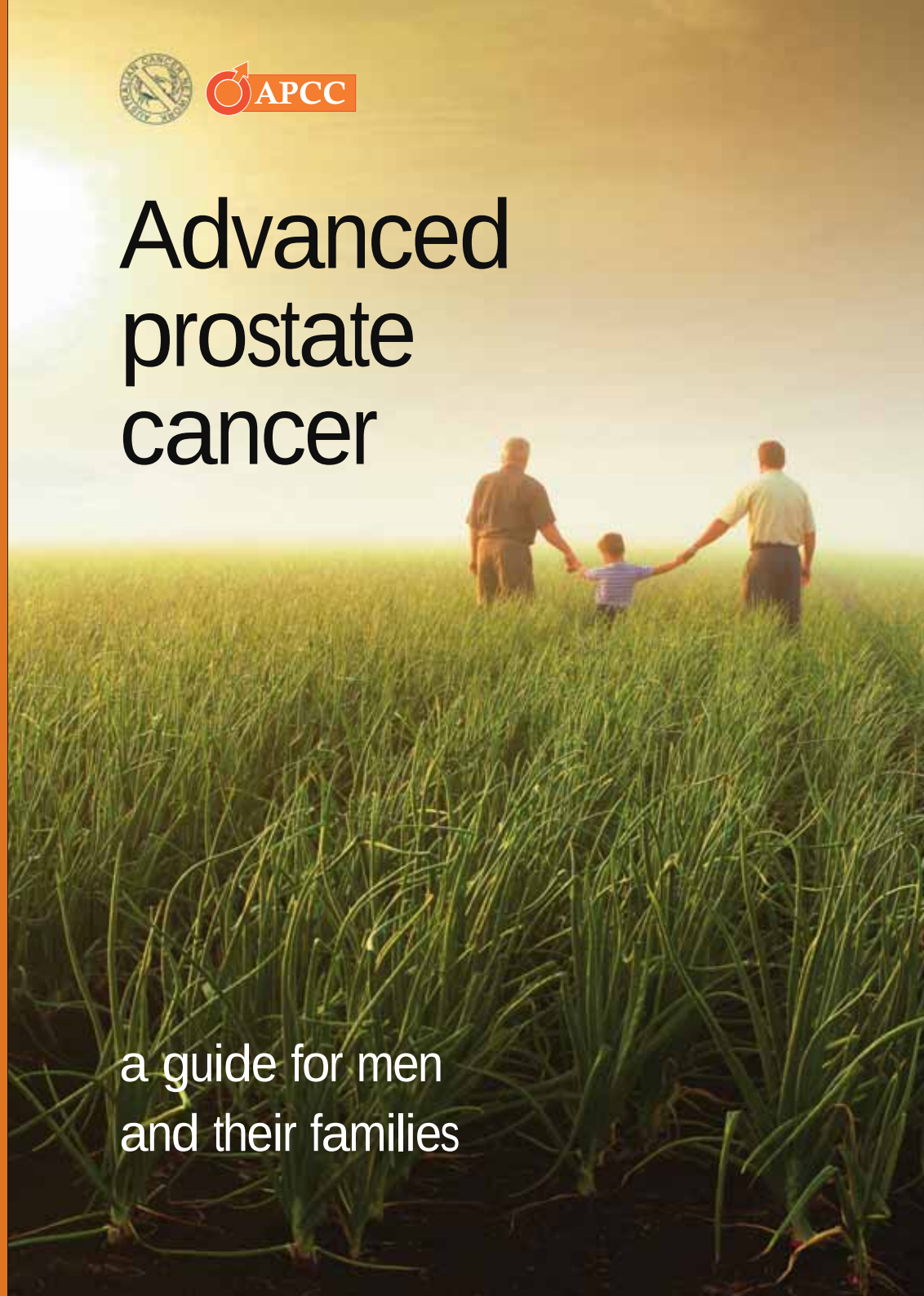
APCC

Advanced prostate cancer



a guide for men and their families

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Disclaimer

The information in this guide is not intended to take the place of medical advice. Information on prostate disease is constantly being updated. A patient's general practitioner or specialist may provide them with new or different information which is more appropriate to their needs.

Where to obtain copies

This guide can be downloaded from the Australian Cancer Network website www.cancer.org.au/clinicalguidelines, from the Lions Australian Prostate Cancer website www.prostatehealth.org.au, the Andrology Australia website www.andrologyaustralia.org, the Prostate Cancer Foundation of Australia website www.prostate.org.au or the *beyondblue* website www.beyondblue.org.au.

Copies of this guide can be ordered through:
Andrology Australia: 1300 303 878 or email info@andrologyaustralia.org
Prostate Cancer Foundation of Australia: 1800 22 00 99
Cancer Councils in each state: 13 11 20

Related Documents

The NHMRC Clinical Practice Guidelines for the Management of Locally Advanced and Metastatic Prostate Cancer can be obtained from the Australian Cancer Network, website www.cancer.org.au/clinicalguidelines.

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We are grateful to Cancer Council NSW for permission to use material from their booklet: Understanding Clinical Trials.

Lastly we would like to thank the reviewers and the hardworking members of the steering committee (listed in Appendix 10) who so generously volunteered their time and saw this project through to completion.

Preface

How we produced this book

This book was requested by men with prostate cancer as a sequel to "Localised prostate cancer: a guide for men and their families". It aims to explain the advanced stages of prostate cancer, its treatments and how men can manage their health and care while dealing with this condition.

Like its predecessor, it draws from the National Health and Medical Research Council's (NHMRC) clinical practice guidelines. The draft guidelines for Locally Advanced and Metastatic Prostate Cancer are produced by the Australian Cancer Network (ACN). A working group with strong consumer representation was convened by the ACN and the Australian Prostate Cancer Collaboration (APCC) to produce a consumer version of the Guidelines with comments and suggestions from the Urological Society of Australia and New Zealand and the Support and Advocacy Committee of the Prostate Cancer Foundation of Australia (PCFA).

The draft was reviewed by members of the national network of prostate cancer support groups that are affiliated with the PCFA and feedback was provided to the steering committee through the consumer representatives on the committee. Reviews of the whole text or particular sections were undertaken by individuals listed in Appendix 10.

How to use the book

This book is very detailed in parts, and may contain more information than you need. If this is the case, we suggest you read the key points at the beginning of each chapter to gain an overview of that topic. If you want more information, you may want to read the appendix which has more details on a number of topics. The glossary at the back can be used to look up any terms that are new to you. We provide resources for further information at the end of each chapter and questions which may be useful to take to your doctor in Appendix 9.

A message from the consumer members on the steering committee

When you are told that you have advanced Prostate Cancer, many thoughts flash through your mind. One is that I need to find out more about what is happening to my body and what can I do about it. There are 100's of books available that offer a wide variety of views, some soundly based, some offering cures without any evidence to support their theories. If you search the internet there are millions of references.

For the first time consumers now have a reliable source of information, written and reviewed by some of the nation's leading practitioners in all the modalities of treatment. Being part of the team that has produced this book has been a privilege and a learning experience. We strongly recommend this book as being the very best source of information on Advanced Prostate Cancer.

Consumer Representatives

Don Baumber
Gold Coast Prostate Cancer Support and Information Network

Bill McHugh
Brisbane Prostate Cancer Support Network

Max Shub
Prostate Heidelberg Support Group

Foreword

Many men find that the topic of their health is not high on their priority list—something to attend to when all other problems are solved. In particular, with prostate cancer, there is so much uncertainty and so many conflicting views about this disease, that it may seem there is nothing that can be done and that ignoring it is the easiest way to deal with the problem.

However this book is a timely reminder that you can do a great deal for yourself by engaging with the issues it raises. Even after a diagnosis of cancer and of advanced cancer, understanding the disease and the help available to you can help improve the situation, enable good treatment choices and importantly, help you and your partner maximise your quality of life. It can help those around you, whom you both support and whose support you need in turn—to address the disease together.

This book is drawn from the findings of a group of experts in the field, with input from men with the disease and their partners. It is written in a language which makes it accessible to most and it has plenty of resources to follow up if further information is needed.

I believe this publication will help men and their partners control their journey through this condition and avoid some of the common pitfalls. I congratulate those who have put so much time and skill into producing it—and particularly those who seek to help others with prostate cancer.

Lieutenant General Ken Gillespie, Vice Chief of the Defence Force and recently diagnosed with prostate cancer

A message from *beyondblue*

There is a lot of information to take in when you are ill, but we know that the better you understand what is happening to you, the more you will be in control of things and the better you will feel.

This booklet provides information about advanced prostate cancer and importantly, discusses some of the emotional reactions people have when they are ill or undergoing treatment. It contains advice on looking after your well-being, strategies for good mental health and information on depression and anxiety.

Prof David Clarke

beyondblue Research Adviser and Professor at the School of Psychology, Psychiatry and Psychological Medicine, Monash University

Table of Contents

Chapter 1: Introduction to Advanced Prostate Cancer

1.1 Key points

- The prostate is a small gland at the base of the bladder. It contributes to secretions in the semen.
- Prostate cancer arises in the tiny glands within the prostate.
- Prostate cancer is the second most common cancer in men after skin cancer.
- About 15% of prostate cancers are diagnosed at the advanced stage.
- When you are first diagnosed, or hear that your cancer has recurred, it may be a shock. Give yourself time to absorb the news and understand the issues before making any decisions about treatment.
- If you are diagnosed with prostate cancer at an early age (particularly if under 60 years), male family members of your immediate family (brothers and sons) may also be at higher risk of the disease.

1.2 After a diagnosis

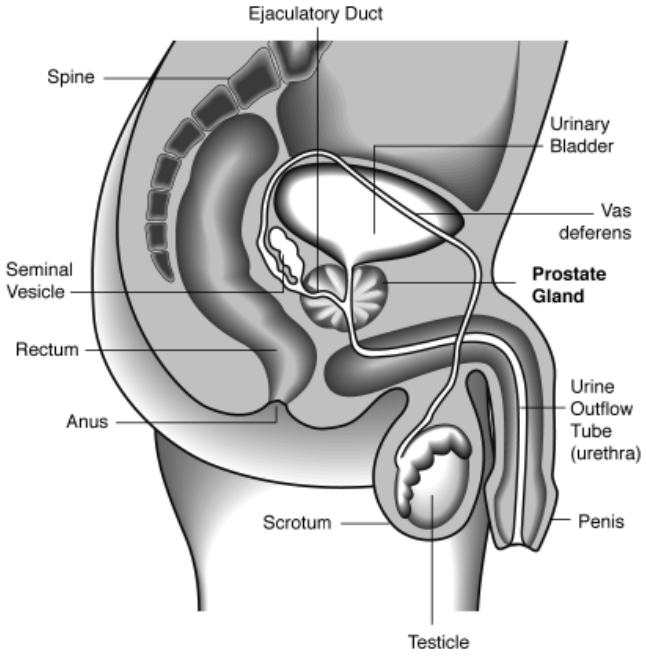
When you are first told you have prostate cancer, you may not hear much else. Hearing the word 'cancer' may be a great shock. Some men may find it hard to think of anything else for quite some time. Just as the first news of cancer may be a shock, the report that it is advanced or has returned after treatment can hit hard and revive long-buried fears.

Don't expect too much of yourself during this period. You need time to take in the information, think about it and discuss it with your family and friends. The important thing to remember is that even if you have advanced cancer, there are many treatments available that can help extend your life for years. A lot of people are available to help you and accompany you throughout the cancer journey. This guide aims to explain what is available, who can help and how you can best support yourself to lead an active and fulfilling life throughout these years.

1.3 What is the prostate?

The prostate is a small gland about the size of a walnut found only in men. It sits just below the bladder and surrounds the urethra (the tube which takes urine from the bladder through the penis). The prostate produces part of the fluid that makes up semen. The fluid is formed by many tiny cell-lined glands linked to ducts that lead ultimately into the urethra. The growth and development of the prostate depends on testosterone (the male sex hormone). Testosterone is made mainly by the testicles, which in turn are controlled by the pituitary gland (part of the brain). While the prostate itself plays an important role in reproduction, it is not essential to life and many men lead long and productive lives after its removal.

Figure 1.1: Prostate and surrounding anatomy



1.4 What is prostate cancer?

Cancer is the name for abnormal cells that divide and multiply uncontrollably, forming a mass of abnormal tissue called a tumour. Tumours can have local effects and may disrupt the function of organs lying close by, such as the bladder. They can also affect the whole system, causing a person to feel generally unwell, tired and lacking in appetite.

The prostate is made up of tiny branching glands. These are separated from each other by connective tissue and muscle called stromal tissue. With age, many men develop an enlarged prostate caused by an overgrowth in the glandular and stromal tissue. It is not cancerous. This is called benign prostatic hyperplasia (BPH).

Prostate cancer is different. It results from a cancerous overgrowth in the tiny glands in the prostate. These glands are lined with cells that secrete proteins such as prostate specific antigen (PSA). The overgrowth occurs in these secretory cells. Cancer originating in glandular tissue is sometimes called adenocarcinoma.

Cancer arises after a series of changes in the genetic material of the cell. The first noticeable pre-cancerous changes are called PIN or prostatic intraepithelial neoplasia. These cells are dividing more rapidly than normal cells but are not yet cancerous. Many men with these early pre-cancerous changes do not go on to develop prostate cancer.

However, some men do develop prostate cancer. Further genetic changes cause more cells to multiply and these eventually disrupt the internal structure of the prostate by breaking out of the little glands and invading the stromal tissue.

When the cancer progresses to an advanced stage, it breaks out of the prostate capsule and invades tissues surrounding the prostate, namely the seminal vesicles, the bladder and possibly the bowel.

The cancer spreads to lymph nodes, bone and other organs when groups of cancer cells detach from the tumour and are carried by the lymph and blood circulation to other tissues, where they start to grow and form metastases. Each of these stages is accompanied by successive genetic alterations.

A single protein is essential at every stage of disease development. Called the androgen receptor, it is located on the nucleus in the healthy prostate cell. The androgen receptor is responsible for binding the male hormone, testosterone, to the prostate. Prostate cancer cells also need an active androgen receptor. When the testosterone is bound to the receptor, it controls the working of the genes in the cell's nucleus that are necessary for cell growth and reproduction. This is essential for the survival of prostate cancer cells.

By depriving the androgen receptor of testosterone, we can stop it controlling the cancer cell genes for a while. This is achieved by blocking testosterone production in the testes.

Unfortunately this treatment often stops working after a period and the cancer progresses to its most dangerous stage, often termed 'androgen independent' or 'castrate-resistant disease'. At this late stage, the androgen receptor continues to function and support the survival of the cancer cells in the prostate, even in the absence of circulating testosterone.

Considerable energy is now being directed into understanding how this receptor continues to function, and into designing new ways to target it during late-stage disease.

1.5 How common is prostate cancer?

Prostate cancer is the second-most common cancer in Australian men after skin cancer. About one in three men over the age of 50 and nearly all men aged 80 or more have some cancer cells within their prostate[1] but are not aware of it. As most of these cancers grow extremely slowly they are not likely to cause any problems, ever, particularly in elderly men.

Each year, however, more than 18,000 Australian men are diagnosed with prostate cancer. Prostate cancer generally affects men over the age of 50, and is rarely found in younger men. Approximately half of all new prostate cancers and over 85% of prostate cancer deaths occur in men aged 70 years or more.[2] Approximately 2900 men die every year from prostate cancer.[2]

In more than 85% of Australian men diagnosed with prostate cancer, the tumour appears to be contained within the prostate (localised disease). The remaining 15% are diagnosed with prostate cancer that extends outside the prostate (advanced disease). This may remain in the pelvic area (6–9% of all prostate cancers) or may have spread to distant organs (4–6% of all prostate cancers).[3]

Some men who are initially diagnosed with localised disease will experience progression of the disease. In approximately 20–30% of patients treated for localised prostate cancer the disease will recur. Recurrence after treatment for localised prostate cancer is usually first detected by a rising PSA level. However, while many patients experience rising PSA levels (sometimes called biochemical recurrence), this is often controlled with further treatment and only some of these patients go on to die from their disease.

This guide is for men with locally advanced disease, recurrent disease (disease which recurs after treatment for localised cancer), and metastatic prostate cancer (where the cancer has spread beyond the prostate area to other regions of the body).

- More than 18,000 Australian men are diagnosed with prostate cancer each year (that equates to approximately 1 in every 170 men aged 50 years or over).
- Of these 18,000 men, about 8100 (one in every two) are aged 70 years or more.
- In more than 15,700 of these 18,000 men (17 in every 20), the disease appears to be localised at the time of diagnosis (contained within the prostate).
- In less than 3000 of these 18,000 new cases (3 in every 20), the prostate cancer extends outside the prostate at diagnosis (advanced disease).

1.6 Is prostate cancer a risk to my family?

Male first-degree relatives (a brother or son) of a man diagnosed with prostate cancer have a higher risk of prostate cancer. A recent review found that this risk is from 2.2 to 2.8 times higher than in men without such a family history.[4] If a man were diagnosed before 60 years of age, the risk for his relatives is at the higher end of the range. If a man has two relatives diagnosed with prostate cancer, his risk is 3.5 times higher than normal. Most studies suggest that the risk in brothers is higher than in father–son relationships.[4] Men with a family history of prostate cancer are at high risk of prostate cancer at an earlier age. Some recommendations suggest that if they wish to be regularly tested for prostate cancer, they should begin earlier, namely at age 40 or 45 years (www.urosoc.org.au).

The higher risk in families may be due to both environmental and lifestyle factors and genetic risks shared by the family members. Purely hereditary cancers are thought to be quite rare and account for roughly 9% of prostate cancers. Many studies have looked for prostate cancer 'susceptibility' genes, but with little success. This could be because the

onset of cancer, its progression and outcome, are controlled by many different sets of genes. A link has been found between prostate cancer and BRCA2—a gene linked to early-onset breast and ovarian cancer. A man who is a carrier for a mutation in this gene has an increased risk of developing prostate cancer (although not necessarily at an early age).

- The sons and brothers of a man diagnosed with prostate cancer are two to three times more likely to develop prostate cancer than men with no family history.
- An individual man's risk will vary by his age and by what age and how many of his relatives have been diagnosed with prostate cancer.

Example: of 100 fifty-five year old men with a family history of prostate cancer, between 17 and 52 of them can expect to be diagnosed with prostate cancer before they reach the age of 75.

1.7 Resources

Cancer Council Helpline: 13 11 20

Cancer Council Helpline to find your local familial cancer service: 13 11 20

Lions Australian Prostate Cancer Website: www.prostatehealth.org.au

Prostate Cancer Foundation of Australia: 1800 22 00 99

Prostate Cancer Foundation of Australia affiliated peer support groups: www.pcfa.org.au or phone 1800 22 00 99

Chapter 2: Following the Progress of Prostate Cancer

2.1 Key points

- Doctors use a number of measures to follow the progress of cancer. It can be helpful to know about them so you can discuss your progress with the doctor. They include:
  - cancer stage (how far it has spread) measured by the TNM system
  - cancer grade (how aggressive the cancer is likely to be) measured using the Gleason score
  - PSA level, a blood test that measures a protein produced by prostate and prostate cancer cells
- Different scans—bone scan, CT scan, MRI—are used to investigate whether cancer has spread to other regions of the body
- Cancer treatments may have different goals. The three main goals are to:
  - control the cancer
  - control symptoms caused by the cancer
  - improve quality of life
- Making decisions about treatments involves weighing up the pros and cons, but uncertainties can make this difficult. This guide includes strategies to help your understanding and to help you make treatment decisions.

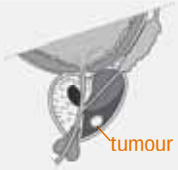
2.2 Staging: the TNM system

Stage is a measure of spread or extent of the cancer. The stage is summarised using a system called the 'Tumour–Node–Metastasis' or TNM staging system.

- T stage tells us about the local extent of the tumour
- N stage tells us if it is in the lymph nodes
- M stage tells us if the cancer has metastasised and spread to distant parts of the body

Note that in the following figure (2.1) and brief description of the TNM staging system, the T-stages described and illustrated have been simplified. Within each stage are sub-groupings a–c, which indicate the extent of spread within that stage (*see Appendix 1*).

Figure 2.1: The stages of prostate cancer

Stage	How far the cancer has spread	
T1	The tumour cannot be felt by the doctor or detected by ultrasound.	
T2	The doctor can feel the cancer but it does not appear to have spread beyond the prostate.	
T3	The cancer feels as though it has spread outside the prostate into surrounding tissues.	
T4	The cancer has grown into surrounding organs such as the bladder or rectum.	

T—local extent of the tumour

Localised disease

T1 The tumour is so small that it cannot be detected at the rectal examination or on ultrasound. Tumours of this size are usually detected by a rise in PSA.

T2 The tumour can be felt at the rectal examination but it is still confined to the prostate.

Locally advanced disease

T3 Tumour extends beyond the prostate and may have spread into fat or seminal vesicles immediately next to it, but no further.

T4 Tumour invades pelvic organs such as such as bladder, rectum, pelvic wall, which are further away than seminal vesicles.

N—indicates whether the cancer is present in lymph nodes in the pelvic region (near the prostate)

Advanced or metastatic disease

N0 Tumour has not been found in lymph nodes.

N1 Tumour is found in lymph nodes Nx. It is not known whether tumour is in lymph nodes.

M—indicates the presence of cancer in distant parts of the body such as bone or lung (referred to as metastases).

M0 No metastases have been found.

M1 Distant metastases have been found.

Mx It is not known whether tumour is in distant parts of the body.

The status of tumour spread—prostate (T), nodes (N) and metastases

(M)—may be quoted simultaneously. For example, T3 N0 M0 means that the cancer has spread outside the prostate but only adjacent to the prostate, no cancer cells have been found in lymph nodes and no distant metastases have been found.

Tests that give information about the progress of the cancer are the digital rectal examination (DRE), PSA test, serum prostatic acid phosphatise (PAP) test, bone scan, CT scan and MRI scan. The Gleason scoring system or grade gives an indication of how fast the cancer is likely to grow.

2.3 Grading: the Gleason score

Grading systems indicate how abnormal the cancer tissue looks. A higher score means the tissues look more abnormal. Normal tissue has an ordered structure but in cancer tissue the cells grow in a more chaotic fashion, so that the original tissue arrangement is not maintained. The more abnormal the tissue looks, the faster the cancer is likely to grow, so cancer grade is also a measure of cancer aggressiveness.

The most commonly used grading method is the Gleason score. The method assigns a score to the tissue, which ranges from 2 to 10. Ten is the most abnormal or most aggressive score. To estimate the Gleason score, the pathologist identifies the two most common tissue patterns in the tumour and gives them a score from 1 to 5. The score may be quoted as either the total out of 10, for example 7, or as its component scores, for example, 4+3 or 3+4. The reason for quoting the component scores is that a Gleason of 4+3 is likely to represent a greater risk than a 3+4.

Cancers with a Gleason score of 6 are the least aggressive (it is rare to have a Gleason score less than 6). Those with a score of 6 are called low grade, 7 are intermediate, and tumours with scores of 8, 9 and 10 are high grade. High-grade tumours are the fastest growing and pose the greatest risk (*see Appendix 2*).

2.4 Digital rectal examination (DRE)

The DRE is used to check the prostate through the rectum (or back passage). The prostate is located just in front of the rectum, so your doctor can insert a gloved finger into your rectum and feel the size of your prostate through the rectal wall. Cancers feel harder than normal tissue. This test may feel uncomfortable, but should not be painful. A DRE can give an idea of how big the prostate cancer is and whether there is any obvious growth into surrounding tissues. The DRE findings also assist in determining the clinical stage or the local extent of the cancer. However, it is not always possible to tell how big the cancer is in this way. When the gland is removed by surgery, the actual tumour size does not always correlate well with the estimate made at the rectal examination.

2.5 PSA test

PSA or prostate-specific antigen is a protein produced by cells in the normal prostate. It is present in the ejaculate and has a role in nurturing the sperm. Normally only a little PSA leaks from the prostate into the blood stream, but when cancer is present there are many more prostate cells, therefore the PSA level usually increases. Before diagnosis, a high PSA level can be due to other conditions of the prostate, such as infection. After the prostate has been removed or largely destroyed by treatment, PSA is a good measure of how many prostate cancer cells remain in the body. The PSA test can then be used to measure the effectiveness of treatments. There is a catch, however. Not all prostate tumours release PSA. Some particularly aggressive tumours do not produce PSA and therefore do not cause a rise in PSA.

It follows that the PSA level can give a rough idea of cancer stage. A cancer with PSA greater than 20ng/ml is more likely to have grown outside the prostate. The PSA can be in the hundreds before symptoms appear. PSA levels in the thousands can occur in men with metastatic prostate cancer.

The rate at which PSA rises can indicate how much of a risk the cancer poses. PSA doubling time is the time taken for the level to double. If doubling time is longer than one year, the risk of death from the cancer is low.[5] If the doubling time is less than three months, then the risk is higher.

2.6 Bone scan

A bone scan is done to see if the prostate cancer has spread to the bones. A small amount of a radioactive material (called technetium) is injected into a vein in the arm and a scan done one to two hours later. The radioactive material is slowly absorbed into the bones in areas of new bone growth or healing activity. If the prostate cancer has spread to the bones there will often be many sites of increased activity seen on the bone scan.

A bone scan will only find fairly large numbers of cancer cells in the bones (that is, where numbers are high enough to cause bone damage). It will not find small numbers of prostate cancer cells and is rarely positive when the PSA level is less than 10. Arthritis can also appear as a positive bone scan.

2.7 CT scan

A CT (computerised tomography) scan is a technique for making detailed x-ray images. It may be done to detect any spread of prostate cancer outside the prostate. A CT scan takes about one hour. A dye is injected into a vein in the arm, then the patient drinks a fluid. The scan gives images of the pelvic organs including the prostate. Unfortunately, like bone scans, CT scans do not detect small amounts of cancer. However they can be useful in planning radiotherapy.

2.8 MRI scan

An MRI (magnetic resonance imaging) scan can tell the extent to which cancer has spread into the tissues surrounding the prostate and local lymph nodes. The test uses magnetic energy to make the images. It is completely painless, may be noisy, and takes about 45 minutes to complete. During some MRI scans of the prostate gland, the doctors may need to place a small inflatable tube into the patient's rectum (back passage) to get the most detailed information about the prostate. The MRI may be useful for planning radiotherapy as well as detecting cancer recurrence after removal of the prostate.

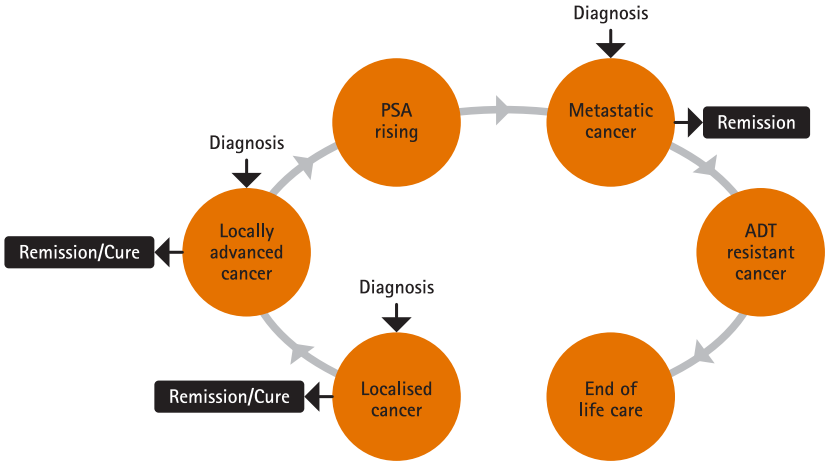
2.9 Treatment decision points for advanced prostate cancer

If prostate cancer progresses, there are four or five points at which the treatment may change or a treatment decision may need to be made (*see Figure 2.2*). They are at the finding of:

- locally advanced prostate cancer
- PSA recurrence following surgery or radiation treatment for localised prostate cancer
- metastatic prostate cancer
- metastatic prostate cancer which has failed androgen deprivation treatment
- end-of-life care

In the following chapters we will describe each of these points, what is happening with the cancer, signs, symptoms and available treatments. It should be remembered that even though these points or 'stages' loosely form a sequence, it is by no means certain that a person reaching one point will inevitably progress to the next. Treatment for locally advanced cancer, as for localised cancer, can be curative.

Figure 2.2: Treatment decision points in the progress of prostate cancer



ADT = androgen deprivation therapy

"My doctor told me that my cancer was incurable but did not tell me that it was treatable and that I could expect some years of reasonable quality of life. I am still functioning well 13 years later."

2.10 Risk and prognosis: what course is the cancer likely to take?

Because individual cancers vary so much, one of the most important questions doctors are concerned about is 'How is this particular cancer going to behave?' Even if the cancer has reached a stage where it cannot be cured, it is still possible that the cancer is slow growing and not a threat to life. Alternatively it may be many years before it becomes such a threat. The risk or threat posed by the cancer is balanced against any likely treatment side effects when choosing if or when to start a treatment.

These are important questions from the points of view of both patient and doctor. After curative treatment such as surgery or radiotherapy, at the first sign of the PSA rising again patients want to know what it means: whether the cancer has returned, whether it is a threat to life and what their prognosis might be[6]. The answers to these questions form the prognosis, or the course of the disease that might be expected for a particular patient.

While it is not possible to estimate prognosis with any degree of certainty, we do know that for most men the time taken to reach the next stage of the disease is measured in years, not months, and can be very long indeed (*Appendix 3*). One study showed that the median time between the first sign of recurrence (raise in PSA) and metastases was eight years[6]. Another found the median time between PSA recurrence and death from prostate cancer was 16 years[7], and many patients did not progress to die of prostate cancer (median means that half of the patients took a longer time, half a shorter time).

Doctors use risk factors to try to estimate how long it will take a patient to reach the next stage of disease. These risk factors usually come from test results. For example, PSA doubling time—the time taken for the PSA level to double—is a useful measure of how soon a cancer is likely to reach the next stage. In the study mentioned above, the doctors found that if the time taken for the PSA to double was greater than ten months, men usually did not develop metastases for ten years. They also found that if it took longer than two years for the PSA to rise after surgery, the chances were that metastases would not appear for ten years or more. A Gleason score below 8 also predicts a longer time to the next stage.

Risk factors for progression to the next stage can be different at different stages of the disease. However, doubling time seems to be useful across all stages. We will refer to useful risk factors in this guide as we cover each stage.

2.11 Advanced prostate cancer: goals of treatment

When discussing different treatments, doctors will often talk about the treatment goal or what they expect the treatment to achieve.

There are three broad types of treatment goals:

- cancer control (treatments which aim to cure or achieve remission from the cancer)
- symptom control (treatments aimed at removing symptoms caused by the cancer or other treatments)
- quality-of-life improvement (treatments aimed at improving general wellbeing)

2.11.1 Cancer control: cure or remission

The first purpose is to control the cancer; to reduce its rate of growth, so that it does not affect daily living. A range of treatments is available for this purpose and they are discussed in Chapters 4, 5, 7 and 8.

2.11.2 Symptom control

Treatments can cause symptoms such as fatigue and hot flushes. The cancer itself may also cause symptoms such as pain. Treatments to deal with these symptoms are aimed at improving day-to-day living. Where symptom control is complex, palliative care specialists may be consulted (note that palliative care should not be confused with end-of-life care). Palliative care is discussed more fully in Chapter 12. Treatments to control symptoms can involve medications, radiation or surgery.

2.11.3 Quality of life

Treatment to improve quality of life may not involve treating the disease. Complementary care can include approaches such as meditation to improve a sense of wellbeing, assistance with daily living needs delivered by an occupational therapist, and general support. A psychologist can help develop strategies to deal with anxiety, decision making and problem solving.

Sometimes different types of doctors provide care in each of these areas. While you are seeing one specialist, you may also see other types of doctors. The different types of care and the clinical staff that provide them are discussed in Chapter 3.

It is important to understand the goals of a treatment in making decisions about it with your doctor.

2.12 Making decisions about prostate cancer treatments

It can be difficult to make decisions about treatment for advanced prostate cancer for several reasons.

First, your doctor may suggest several different approaches to your treatment, one of which might even be to watch carefully and monitor your PSA for the moment. The idea of not actively treating the cancer as soon as possible goes against the messages we usually hear about cancer. Having to choose between difficult treatment options can seem overwhelming. Adding to this, the information about prostate cancer treatments often includes complex medical terms and statistics that can be hard to understand. When you are trying to consider a lot of complex information it becomes difficult to identify the bits that most matter for you. In other words, you can't see the wood for the trees! As well, the side effects of treatments can include things like sexual problems. For most men, these side effects are distressing to think about, making it difficult to come to a decision about them.

Second, feeling anxious is a normal reaction to finding out about advanced cancer. When people are anxious it can affect their ability to think through difficult problems. If you imagine your mind as your thinking 'work bench' or 'desk' where all your thoughts are laid out, being anxious can make it harder to organise the thoughts on your 'work bench' and the resulting 'clutter' makes it more difficult to reach a decision.

As well, most people don't like making decisions when there is uncertainty about the consequences. In the case of cancer treatments, where there is uncertainty about many things including the chances

of side effects or how well the treatment might work, it can be hard to make a decision.

There are strategies that can help. You may have tried some; others may be new to you. They include:

- **Taking time to think it through**. Usually there is no urgency to decide which treatment approach to take. Check with your doctor whether this applies to your situation.
- **Writing down your questions** before you visit your doctor (in case in the rush of the consultation you forget). Also write down your doctor's answers. This will help you get the best use out of your time with your doctor. As well, some doctors will tape the consultation for you to listen to later.
- **Taking a close friend, family member or partner** with you when you visit the doctor. Two sets of ears are better than one, and having someone with you can help you feel better supported. Your support person can also remind you later of things the doctor said that you may have forgotten or misunderstood.
- **Seeking credible information**. There is a large amount of information about prostate cancer on the Internet, in popular books, magazines and from different health organisations across the world. Some of this will be inaccurate or not relevant in Australia, or not relevant to you. Check with your doctor and call the Cancer Council Helpline (13 11 20) for credible and locally relevant information. If your doctor provides you with medical information such as booklets, ask which parts are most important for you.
- **Breaking the decision into smaller steps**. For example, the first thing to consider may be whether you and your doctor think that your cancer needs active treatment now. Once you have an idea of the answer to this question, then think about the treatment options.

- **Writing a list of the pros and cons** of each possible treatment option. This helps to get your thoughts in order (because at times it can feel as though you are going round in circles). Highlight the points on your list that matter to you most, then see which option seems the most favourable. Try talking the options through with someone close to you, like your wife or partner or a close friend, and talk to your GP or specialist doctor.
- **Talking to other men** who have advanced prostate cancer can give you an idea of what treatment might be like. There are prostate cancer support groups throughout Australia where you can meet other men who have had prostate cancer. As well, there are men available to talk one-to-one by telephone (see Resources below).
- **Involving wives and partners in the treatment decision** can be a good idea as they frequently prefer to be involved, and men themselves often find this support helpful. Probably the most important discussion is about how you would like to manage treatment decisions and how involved you each wish to be. Then tell your doctor about your decision. Communicating in an open way about how you will make treatment decisions can prevent misunderstandings and help both you and your partner feel less alone. In brief, work together as a team.

Remember that the decision you make will be the best decision for you. Be as involved as you would like to be in the process. Look for help and guidance when you need it. People you can approach for assistance include all those involved in your care: your GP, urology nurses, urologist, radiation oncologist or other specialist. You may need to get a referral to see a specialist—talk to your GP about this.

2.13 Resources

National phone helplines

Cancer Council Helpline: 13 11 20

Multicultural Cancer Information Services: 13 11 20

Prostate Cancer Foundation of Australia: 1800 22 00 99

Contacts for support groups

Prostate Cancer Foundation of Australia: 1800 22 00 99

Prostate Cancer Foundation of Australia affiliated peer support groups: www.pcfa.org.au Includes a map to locate nearest support group

Cancer Council Helpline: 13 11 20

Helpful books

Cancer Council New South Wales.
Living with advanced cancer: a guide for people with advanced cancer, their families and friends. 2007, Sydney. Available from www.cancercouncil.com.au or phone 02 9334 1900.

UsToo International Prostate Cancer Education and Support Network.
What now? Hope and options when experiencing a rising PSA, a recurrence of prostate cancer or when prostate cancer is not responding to treatment.
www.ustoo.org/pdfs/160295_PSA_Brochure.pdf.

Chapter 3: Members of the Care Team and Their Roles

3.1 Key points

- Different clinical staff may care for you at different stages in the progression of prostate cancer. These include your general practitioner, urologist, radiation oncologist, medical oncologist, palliative care specialist and urology and palliative care nurses.
- Make sure you know who is coordinating your care at any one time. Talk to your GP if you are uncertain.
- If you would like a second opinion on a particular treatment choice you can talk to your GP or arrange it with your specialist. You may need to take a summary of your medical record with you.
- If you have reached the Medicare threshold in gap payments, you may be eligible for 100% reimbursement of gap costs. Further information is available at www.medicareaustralia.gov.au.
- Keeping a record of your symptoms, treatments, test results and medications can be very helpful, both for yourself and your care team.

Several kinds of clinicians specialising in different types of care are involved in the treatment of prostate cancer. They are involved at different points in care, so you may find yourself seeing more than one specialist at a time. Alternatively, you may be referred from one specialist to the next. It is important to understand each doctor's field of expertise and how each works with your other doctors to coordinate your care overall.

3.2 Clinicians who provide care for advanced prostate cancer

The urologist is probably the first specialist you will be referred to if your blood test or rectal examination is abnormal. Urologists are usually surgeons who treat kidney, bladder, prostate and urinary

problems. They diagnose the prostate cancer through a biopsy, assess suitability for treatment and provide surgical or hormonal therapy as appropriate. Urologists may be involved with your care throughout the course of your cancer.

Radiation oncologists are specialists in the use of radiotherapy to treat cancer. For prostate cancer, the specialist may use radiation delivered externally with beams or internally with implants such as seeds and rods to treat localised or locally advanced cancer. Radiotherapy can also be used at a later stage to treat bone or other metastases.

Medical oncologists use chemotherapy to treat cancer. They have a great understanding of the problems experienced by the person with advanced cancer. Your urologist may refer you to a medical oncologist to take advantage of new types of chemotherapy that have recently become available for the treatment of advanced prostate cancer.

The pathologist is one of the medical specialists you may never meet. Pathologists examine body tissues and fluids to assess the stage and aggressiveness of your cancer.

Urology or prostate care nurses can help you throughout your prostate cancer journey. They can answer your questions about treatment and its side effects and help you to manage incontinence, sexual dysfunction and related problems. They can be helpful to both you and your partner.

Palliative care specialists are expert in pain and symptom control, particularly for people with advanced cancer. They work closely with your other doctors. You may be referred to a palliative care specialist or team if you have symptoms that affect your quality of life, particularly if they are complex and involve several organ systems in the body. The palliative care team can help you and your family with physical symptoms, psychological and spiritual needs.

Psychologists can help you develop the decision making, problem solving and other skills to cope with emotional, social and spiritual challenges. They also help people experiencing anxiety and depression. A psycho-oncologist is a psychologist who specialises in helping people deal with cancer.

Social workers help people manage their personal and social problems. They help people to access useful support services and sometimes provide counsel through a crisis.

Occupational therapists and physiotherapists can help you with the physical side of your daily life that is affected by treatments, and provide rehabilitation exercises to overcome treatment complications such as incontinence.

Your general practitioner (GP) is your family doctor who knows you and your circumstances personally and who will continue to provide you with routine medical care and monitor your health and wellbeing. This doctor can play a key role throughout the course of your prostate cancer, explaining treatment options to you and your partner, providing referrals, and following your care when multiple specialists are involved. Your GP can also deliver hormone therapy and monitor your progress with blood testing in collaboration with your specialists. It is important to ask your specialist doctors to keep your GP informed of your care.

Your pharmacist is easy to access and can help you understand and manage your medications. If you have more than one health problem for which you are taking medicines, your pharmacist can review your medicines for any harmful drug interactions and contact your doctor if necessary. This can be particularly useful if you are receiving care from more than one doctor. If you are taking a number of medications at different times, your pharmacist can pre-package them to make it easier for you to remember which to take, how many and when.

If you need to see a different doctor or are travelling, your pharmacist can print out a list of the medicines you have been taking for your records.

Your pharmacist can help you with the Pharmaceutical Benefit Scheme (PBS) Safety Net. Once the cost of you or your family's medications reaches a certain threshold (usually over $1000) you qualify to receive them at a lower rate. Your pharmacist will issue you with a card when this happens and can answer your questions about the scheme.

Figure 3.1: Specialist clinicians who may provide care at different stages of advanced prostate cancer

3.3 Coordinating your care

Normally when your GP refers you to a specialist, the specialist will write back to your GP reporting your progress. If your specialist (say urologist) refers you to another specialist (say medical oncologist) he or she will report back to the referring doctor (in this case the urologist) but not necessarily to your GP. It is very important to keep your GP up-to-date with your progress, and you can ask any specialist to do so.

Your specialist will normally coordinate the care for your prostate cancer. However your GP is still responsible for your overall care and is the person to return to if you are not sure who is responsible for your care, or if you develop medical problems other than prostate cancer. Your GP may be more accessible than your specialist if you develop acute symptoms or need immediate care. In this case, your GP would normally contact your specialist, so it is important that he or she has up-to-date details of the specialists you are seeing. In rural areas, the GP is sometimes the lead doctor coordinating patient care. You can ask your specialist doctors to keep your GP informed as your care changes.

3.4 Multi-disciplinary care

Multi-disciplinary care (MDC) is a new approach to care that provides many benefits for patients. MDC involves a team of clinicians from different specialties that meets regularly to plan treatment for a group of patients. The team includes many of the specialists listed above, thus ensuring that the patient has access to the full range of therapies. Sometimes a patient's own general practitioner is included. Patients are told about the team's discussion of their case and its recommendations.

MDC is primarily hospital-based and depends on a specialist leading the team. Its availability and funding varies between states. Currently it is available through only a limited number of treatment centres.

You and your partner have a primary role with your doctors in making decisions about your care. You can do this better if you understand the types of treatments available, how health care is organised and what resources (human and otherwise) are available to you. That is the aim of this guide. At the end of the chapter we list other resources you may find helpful in managing your care.

3.5 Obtaining a second opinion

It is important that you feel your specialist can give you the help and answers you need. Obtaining an opinion from another doctor about your cancer and treatment can help you be confident that you are doing the right thing. If you would like another specialist to assess your case you can seek a second opinion. This is your right. Most doctors are used to patients seeking a second opinion. There are two ways to do this. You can ask the specialist or your general practitioner to organise a referral. The second doctor will need to access your medical record or be provided with relevant information by the referring doctor. Being confident in your specialist is an important part of your treatment.

3.6 Changing doctors

Sometimes a different doctor will take over your care. This can happen for many reasons including retirement, unavailability, or a change in treatment approach that requires a specialist in a different discipline. In addition, *you* may want a change. Some people find this a difficult time, particularly if they have been in the care of the first doctor for several years. Remember that prostate cancer involves a team of people who can offer you different types of care that is appropriate at different stages. Your specialist may refer you to the new specialist or your GP can help if you are not sure who is looking after you or coordinating your care.

3.7 Medicare safety net

Frequent visits to the doctor or out-of-hospital treatments can cost a great deal in 'gap' payments (the difference between the scheduled fee and the amount Medicare refunds). Once you have paid over a certain threshold in gap payments, Medicare will increase the amount it reimburses to 100% of the scheduled fee. Information on this and other safety net features can be found at www.medicareaustralia.gov.au or call 13 20 11.

3.8 Keeping a treatment record

You may find it useful to record key information about your diagnosis and treatment. This can help a doctor track your progress if all your medical records are not available and it may also help you keep track of changes in your care. In its simplest form, your treatment record is just a diary comprising a date, what happened, symptoms, test results and reminders to yourself about what you need to do.

If you enter the date of a future doctor's visit—use the treatment record to list your questions before you go.

It is always good to keep a medication list. This records the medication name (brand name, generic drug name), dose and how often you take it. Ideally you would also have the start and stop date.

One approach developed by US physician Dr Steven Strum is called the prostate cancer digest. The link is included under *Resources*.

The Prostate Cancer Foundation of Australia has produced a Prostate Cancer Personal Organiser for keeping a record of treatments, investigations, medical appointments and medications. It will be available from the PCFA in 2010.

3.9 Resources

Cancer Council Helpline: 13 11 20

Locating a specialist: Lions Australian Prostate Cancer Website www.prostatehealth.org.au/treatment.html

Medicare Safety Net: www.medicareaustralia.gov.au

Prostate Cancer Personal Organiser: Prostate Cancer Foundation of Australia: www.prostate.org.au or phone 1800 22 00 99

Keeping a record of your treatment: The 'prostate cancer digest' and other records. www.hrpca.org/bookletch6.htm

Prostate Cancer Foundation of Australia affiliated peer support groups: www.pcfa.org.au or phone 1800 22 00 99

Chapter 4: Locally Advanced Prostate Cancer

4.1 Key points

- Locally advanced cancer has spread beyond the prostate, but is still within the prostate region.
- It is suspected if any of the following has occurred:
  - cancer can be felt outside the prostate on DRE
  - cancer can be seen outside the prostate on scans
  - there are cancer cells remaining in the fat outside the prostate, or in the seminal vesicles after the prostate has been removed at operation
  - the PSA blood test does not go to less than 0.1ng/ml after surgery
  - the PSA went to less than 0.1ng/ml after surgery, but starts to rise again
- It carries a high risk of recurrence around the region of the prostate, so more than one type of treatment is often used.
- The most common treatments are radiotherapy, androgen deprivation therapy or a combination of these. A combination is the most effective treatment.
- Usually there are no symptoms. However if the cancer is causing urinary symptoms, these can be relieved with a TURP (trans-urethral resection of the prostate), radiotherapy, hormone therapy and occasionally insertion of a stent.

Prostate cancer that has extended beyond the prostate into the surrounding tissue, into other organs or into distant parts of the body, is called advanced prostate cancer. 'Locally advanced' refers to prostate cancer that extends outside the prostate gland itself but is still confined to nearby tissue or organs. Locally advanced cancer can still be cured. Cancer which has spread to more distant parts of the body (such as the bones) cannot be cured, but can be treated to slow the growth of the cancer, often for many years. In some men who have surgery to remove their prostate, prostate cancer cells are found in lymph nodes close by. Because lymph nodes are the 'policemen' for escaping prostate cancer cells, this finding suggests that cancer cells may have spread beyond the prostate and possibly to distant parts of the body.

4.2 What it is, what it means

Locally advanced prostate cancer has spread outside (beyond the capsule of) the gland itself, but is still confined within the prostate region. It may be in the fat immediately adjacent to the prostate or may have spread into the seminal vesicles (*tumour stage 'T3', see Appendix 1*) or other surrounding organs such as the bladder or rectum (*tumour stage 'T4', see Appendix 1*).

Locally advanced prostate cancer carries a high risk of recurrence after treatment by surgery or radiotherapy. This means that more than one type of treatment may be needed to control that risk, and there is a higher chance of complications.

4.3 Signs and symptoms: how we know the cancer is locally advanced

There are unlikely to be symptoms at this stage of disease. However, the following signs and symptoms can be relevant:

- As the tumour grows it sometimes squeezes the urethra, causing problems with urination. These urinary symptoms can be similar to those caused by benign enlargement of the prostate. They include frequent urination (frequency), poor stream, difficulty starting (hesitancy), and waking frequently at night to urinate (nocturia).

- The cancer can at times cause bleeding in the urine (haematuria), which may or may not be visible to the naked eye.
- Locally advanced prostate cancer can cause pelvic pain or bowel symptoms such as constipation and narrow bowel motions.
- A rectal examination (*DRE, see Chapter 2*) that indicates some extension beyond the prostate may be the first sign that the cancer is locally advanced.
- A PSA over 20ng/ml means there is a high likelihood that the tumour extends beyond the prostate.
- A positive surgical margin after surgery indicates locally advanced prostate cancer. Often locally advanced prostate cancer is diagnosed after a radical prostatectomy when the tumour is found to extend to the cut edge of the removed tissue (a positive surgical margin). This means that some cancer tissue remains in the body.
- Positive pelvic lymph nodes indicate advanced prostate cancer. These may be identified by a CT scan or during a radical prostatectomy. The surgeon may remove lymph nodes to check whether the cancer has reached them. A pathologist will report the nodes are positive if cancer cells have been found.
- Also after a prostatectomy, the pathologist will report whether the tumour extends to the seminal vesicles (seminal vesicle invasion) or into the fat around the prostate (extracapsular extension). This is called T3 disease and indicates the cancer is locally advanced.
- If the PSA has not fallen below 0.1ng/ml and stayed there after radical prostatectomy, it is considered locally advanced.
- If after radiotherapy the PSA stays steady, or continues to rise after reaching a low point (nadir), it is considered advanced.

4.4 Cancer control treatments for locally advanced prostate cancer and side effects

4.4.1 External beam radiotherapy with a period of androgen deprivation therapy

This is the most proven treatment for locally advanced prostate cancer. External beam radiotherapy (EBRT) is like having a 15-minute x-ray, five days a week, for up to eight weeks. It is a fairly simple, non-invasive process. Patients are never 'radioactive'—you can still hug your partner and grandchildren.

EBRT has advanced considerably in the past few years, resulting in cure rates even higher than previously, and having fewer side effects. New advances such as intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT) are being used increasingly. They increase the accuracy of radiotherapy and decrease the dose of radiotherapy to normal tissues. These types of radiotherapy accurately target and kill prostate cancer cells both within the prostate and in the fat and glands around the prostate. EBRT is able to destroy locally advanced cancer without patients requiring surgery.

By the time it has been diagnosed, locally advanced prostate cancer has often already sent tiny cancer cells to other parts of the body, such as the bones. These micro-metastases are usually not picked up by scans or tests. To give the best chance of curing the cancer so that it never returns, successful treatment usually requires a combination of both EBRT and androgen deprivation therapy (ADT). ADT (*see Chapter 7*) removes male hormones which are necessary for prostate tissue to grow and seems to be more effective when combined with radiotherapy. ADT may be administered before radiotherapy (neo-adjuvant), at the same time as radiotherapy (concomitant) and/or immediately after radiotherapy (adjuvant). This therapy may last as long as two to three years in total. ADT and EBRT combine to cause the death of cancer cells both within and outside the prostate. Combined therapy using EBRT and

hormone therapy gives the highest chance of curing locally advanced prostate cancer.

Most patients treated with EBRT and hormone therapy are happy with their results. Mild side effects are common, but usually do not significantly affect the patient's quality of life. Almost all patients are able to continue normal activities such as working, driving and exercising during and after radiotherapy. Side effects during EBRT can include tiredness, the need to pass urine or bowel motions more frequently, and the feeling of 'when you've got to go, you've got to go'. These symptoms usually appear towards the end of EBRT and are generally mild and easily treated. They usually resolve within a month or so of completing EBRT. Longer-term effects can occur, but again are generally mild. They include erectile dysfunction, and changes in bowel or bladder function. These can usually be treated, so it is important to report them to your doctor. Leakage of urine is another but very uncommon side effect.

Long-term ADT may have continuing side effects (*see Chapter 7*). It is important that your general practitioner (GP) monitor you for possible side effects.. These can include erectile dysfunction, a drop in sex drive, shrinking of sex organs (testes and penis), enlarged breasts (gynaecomastia), tiredness, hot flushes, thinning of the bones which can lead to fractures, weight gain, diabetes, high blood pressure and cholesterol, and a reduction in muscle mass and strength. Some men experience mood swings and notice changes in mental function. Over the short periods when ADT is used in combination with EBRT for locally advanced disease, the effects are not as noticeable as when ADT and EBRT are used continuously as for metastatic prostate cancer. However some effects may be noticed in the short term. Dietary changes, vitamin D and calcium supplements can reduce the risk of bone fractures. A regular exercise program, particularly strength exercises, can reduce muscle loss and tiredness and may help with mood effects as well. We cover these and other measures you and your GP can take to reduce these side effects in Chapter 6.

4.4.2 External beam radiotherapy plus brachytherapy

There are two main types of brachytherapy:

- *Low dose rate*: small radioactive seeds are implanted directly into the prostate. This involves a single procedure as the seeds remain permanently in the prostate. Low-dose brachytherapy can be done as a 'boost' to the dose of radiation given to the prostate after EBRT. However it is usually not recommended for locally advanced prostate cancer.
- *High dose rate*: A highly radioactive source is guided into different positions in the prostate with multiple catheters. This is repeated a number of times over a period of days, so that the prostate receives a high dose. This type of brachytherapy is usually used in combination with five to six weeks of EBRT as well as two to three years of ADT for high-risk cancers. High dose rate brachytherapy appears to give the same results as EBRT, although there is less evidence to support its use in prostate cancer.

Brachytherapy has similar side effects to EBRT, with urinary symptoms more common.

4.4.3 External beam radiotherapy immediately after surgery ('adjuvant radiotherapy')

There are several important things that a pathologist will look for in tissue removed at surgery for prostate cancer. These important high-risk features indicate whether the cancer may come back in the area around the 'surgical bed' where the prostate used to be. The pathologist will answer questions including:

- *Has all of the cancer been taken out?*
  If the cancer goes up to the cut edges of the tissue removed by the surgeon, there are cancer cells left in the body and the cancer can return.

- *Has the cancer gone out of the prostate into the fat?*
  If it extends into the fat (known as extracapsular spread) it can come back, even if it looks as though the surgeon removed all of the cancer.
- *Has the cancer gone into the seminal vesicles?*
  The seminal vesicles are glands that sit on top of the prostate. Again, if the cancer is in the seminal vesicles then it can come back in the surgical bed, even if it looks as though the surgeon removed all of the cancer.

If the cancer goes right up to the cut edge of the tissue (first question), is into the fat (second question) or has gone into the seminal vesicles (third question), then adjuvant radiotherapy is recommended within four months of surgery. Radiotherapy should be given in any of these situations even if the PSA is undetectable after surgery (i.e. the PSA is less than 0.1).

Adjuvant radiotherapy is also given immediately after surgery if the PSA does not fall to less than 0.1, and even if there are no other high-risk features.

Radiotherapy immediately after surgery (adjuvant radiotherapy) has been shown to improve the cure rate, stop the prostate cancer spreading to other parts of the body (such as bones), and give the best chance of long-term survival.

Radiotherapy can also be used many years after surgery if the PSA starts to rise again. This is called salvage radiotherapy (*see Chapter 5*).

Side effects of radiotherapy after surgery are similar to those described for EBRT.

4.4.4 Androgen deprivation (hormone) therapy alone

Androgen deprivation therapy (ADT) aims to reduce levels of testosterone in the body, thus preventing prostate cells from growing and multiplying as well as killing cancer cells. ADT is recommended when cancer cells are likely to have spread beyond the prostate region. Specialists agree that two to three years of ADT should be used when combined with radiotherapy in locally advanced prostate cancer (neo-adjuvant or adjuvant therapy). However, not all specialists agree on the best time to start long-term ADT for patients with locally advanced prostate cancer who are not being treated for cure, or for patients with metastatic prostate cancer.

It is not known whether there is a benefit in starting ADT before there is evidence of metastases, that is, if the cancer has not spread beyond the prostate region to other parts of the body. At least one study suggests that ADT in men with positive pelvic lymph nodes improves cancer control and survival after surgery in men with locally advanced disease.[8] However ADT alone is not as effective in prolonging survival as ADT combined with EBRT.

As we explain above, long-term ADT has considerable side effects that may affect your quality of life. These are an important consideration in deciding if or when to go on ADT.

4.4.5 Surgery with or without androgen deprivation therapy

The standard approach when trying to cure patients with locally advanced prostate cancer is a combination of EBRT and hormone therapy. There is not a lot of research supporting the use of surgery when attempting to cure locally advanced prostate cancer. Surgery is usually used only to help with symptoms of cancer, particularly if radiotherapy is not possible.

Sometimes surgery (a radical prostatectomy or trans-urethral resection of the prostate) is done if the patient is experiencing symptoms of urinary obstruction, or if this is likely to be a problem. The surgery improves 'local control' in the area of the prostate, so that the cancer does not cause problems by obstructing the flow of urine and spreading to the bladder and other organs. However, the purpose of

the surgery is to treat or prevent symptoms, not to cure the cancer or improve overall cancer survival.

Side effects of these types of surgery include high rates of erectile dysfunction (over 50%) and a risk of urine leakage or blockage of urine due to scar tissue (strictures).

4.5 Treatments for cancer-related symptoms

Locally advanced prostate cancer that has not metastasised may not cause symptoms. However, if the tumour obstructs the outflow of urine it may cause urinary symptoms. If the blockage is in the tube carrying urine from the bladder (urethra), symptoms can include frequent urination, poor stream, hesitancy, waking at night to urinate and blood in the urine. More rarely, the tube from the kidney to the bladder (ureters) can be blocked, and may cause loin pain.

Treatments may include:

- *Surgery*. A trans-urethral resection of the prostate (TURP) in which a cutting instrument is inserted into the urethra and any tissue blocking the flow of urine is cut away.
- *Insertion of a stent*. Occasionally a small tube is inserted into the ureter to support the walls of the urethra and maintain urine flow from the kidney to the bladder.
- *External beam radiotherapy*. EBRT directed at the prostate destroys the cancer cells, which may be blocking the urine outflow tubes.
- *Androgen deprivation therapy* (ADT) may also help relieve symptoms.

4.6 Resources

Cancer Council Helpline: 13 11 20

Lions Australian Prostate Cancer Website: www.prostatehealth.org.au

Prostate Cancer Foundation of Australia: 1800 22 00 99

Prostate Cancer Foundation of Australia affiliated peer support groups: www.pcfa.org.au or phone 1800 22 00 99

UpToDate for Patients: *Patient Information: Advanced Prostate Cancer* www.uptodate.com/patients/index.html

Chapter 5: PSA Rising After Treatment for Localised Prostate Cancer

5.1 Key points

- A continuous rise in PSA after surgery, radiotherapy or other potentially curative treatment for prostate cancer usually means that cancer remains in the body.
- A temporary rise in PSA after radiotherapy may be due to PSA 'bounce' rather than recurrence.
- The first step is to find out whether the recurrence is local (near the prostate, in the pelvic region) or distant (occurring as metastases in other parts of the body).
- If the cancer is local, 'salvage' treatment (usually radiotherapy) may destroy the cancer.
- If the cancer is metastatic, the usual options are hormone therapy, chemotherapy, or sometimes just observation.

5.2 What it is, what it means

After surgery or radiotherapy for localised prostate cancer, or when a patient is on a program of active surveillance, regular testing of PSA levels is the main way of monitoring the cancer. This can be over months, or often over many years. If the PSA levels start to rise again, it can be a very anxious time. It raises many questions: What does it mean? Is the cancer back? What is the best treatment? When should the treatment be given?

After primary treatment, a doctor will first work out whether the rise is likely to be due to cancer remaining in the body after treatment and if so, whether it is still in the local prostate region. This will help decide the best treatment and the timing of the treatment.

5.3 Signs and symptoms of a rising PSA

Normally there are no symptoms when the PSA is rising because the cancer can still be at an early stage. Doctors base a decision on whether the cancer has returned on a precise definition of PSA behaviour. This definition is different after surgery and radiotherapy.

After surgery, the decline is rapid and the PSA should become undetectable (less than 0.1ng/ml) within two to three months. If the PSA does not fall below 0.1ng/ml, or if it rises on two consecutive occasions above 0.03ng/ml, this is an indication that prostate cancer cells remain in the body.

After external beam radiotherapy and brachytherapy, the cancer cells die more slowly and consequently the PSA decline is slower. Counter-intuitively, the slower the decline the more promising the result. It can take up to four years following treatment for the PSA level to reach its lowest point (the nadir) as some of the normal prostate cell population recovers. These slow-growing tumours have a good prognosis.

Ideally the lowest point should be less than 0.5ng/ml.[9] The PSA decline may slow, stop, then start to rise again. If the PSA rises by 2ng/ml above the nadir, there is a high chance that prostate cancer cells remain in the body.

Many PSA rises after radiotherapy are not due to cancer. Sometimes the rise occurs after stopping hormone therapy as the body's testosterone recovers. Very rarely, a second cause of a rise in PSA is a small, slow rise due to some residual benign prostate tissue that remains after treatment. A third cause is a temporary rise in PSA called 'PSA bounce'.

5.3.1 PSA 'bounce'

Even in the case of successful radiotherapy, the fall in the level of PSA is not always smooth. It may rise again for a period of a few months before falling towards its final minimum value.[10] This 'bounce' in PSA has been studied mainly in men following treatment with brachytherapy or EBRT.[11,12]

The reason for PSA bounce is not well understood, but may be due to its release from dying prostate tissue. Between one third and half of patients experience bounce, which can occur anywhere between four months to four years after treatment. The magnitude of the bounce lies in the range of about 0.5–3ng/ml. It may last from a few months to a year or more. Sometimes a second bounce may occur. The other common cause of a bounce is recovery of testosterone after ceasing ADT used in combination with radiotherapy.

The amount of PSA variation after treatment is different from patient to patient. It is important not to jump too rapidly to the conclusion that treatment has failed because of small increases in PSA values. A doctor may monitor the PSA at three to six monthly intervals to establish that the PSA is rising in a sustained and significant way before deciding that the cancer has recurred.

5.3.2 Investigations to find the site of the recurrence

If the PSA rise seems to be due to remaining cancer cells, the next step is to investigate whether these are located in the prostate region or elsewhere in the body. Investigations can include:

- a biopsy or digital rectal examination to detect cancer in the prostate region
- a bone scan to look for cancer deposits (metastases) in the bone (however a bone scan will not detect very small deposits [micro-metastases] and is usually normal at the time of a PSA rise)
- a CT or MRI scan to look for spread to the lymph nodes or other organs such as the liver

After radical prostatectomy, indications that the recurrence may be local (in the prostate region only) are as follows:

- the pathology report showed cancer extending to the cut edge of the tissue removed (positive surgical margin), or cancer extending into the fat surrounding the prostate (extra prostatic extension) or invading the seminal vesicles
- the PSA rise happens a relatively long time after the surgery (1–2 years or more[13])
- bone scans, CT and MRI are all negative
- having low-risk disease (Gleason score 7 or less, PSA less than 1.5ng/ml at recurrence and a long PSA doubling time), which is also thought to increase the chance that if a recurrence happens it is local only[13]

After radiotherapy, indications that cancer is in the local region include a positive DRE and a PSA less than 2ng/ml.

It is important to point out that these indicators are not 100% accurate, and that recurrence may be local even in other circumstances.

5.3.3 Prognosis

'Recurrence' or 'treatment failure' defined by a rise in PSA does not necessarily mean that a patient is destined to die of prostate cancer. A local recurrence of the cancer after surgery can sometimes be successfully cured with radiotherapy. A distant recurrence can be treated to slow the progression. The threat posed by the tumour is based on a number of risk factors:

- the PSA before treatment
- the Gleason score of the biopsy or pathology specimen (for surgery patients)

- the rate of increase of PSA after treatment (often measured as doubling time) indicates risk (one study reported that a doubling time of less than nine months following prostatectomy predicted a higher long-term risk of dying from prostate cancer[14]
- the length of time after treatment before the PSA starts to rise again (time to PSA failure) also indicates the threat posed by the recurring tumour—a longer time (years) means a better prognosis

Sometimes risk factors are combined into tables or nomograms (mathematical expressions). These give an estimate of the likely course of the disease, based on the past experience of other patients with similar clinical measures. One study of patients after surgery gives the likelihood of surviving for 10 and 15 years after the recurrence. They make these predictions based on Gleason score, PSA doubling time and the time it took for the PSA to recur after treatment.[15]

Your doctor may discuss these factors with you, when talking about prognosis. One US hospital (Memorial Sloane-Kettering Institute) has published these prediction tools online for interested patients (see Resources). You may need to see your doctor to obtain the details of your cancer if you want to use these tools.

5.4 Cancer control treatment

5.4.1 Local recurrence

After surgery

If the PSA rise is thought to be due to a local recurrence after prostatectomy, meaning the remaining cancer is still in the prostate region, 'salvage' radiotherapy may be the best option. This treatment can sometimes be curative. The chances of successful treatment are higher if the PSA is low, ideally less than 1ng/ml when the treatment is started.[16] A European expert body has suggested secondary treatment after local failure of surgery should begin before PSA levels reach 1.0–1.5ng/ml. However many doctors will offer salvage radiotherapy when the PSA is lower (eg even when the PSA is less than 0.1). If the PSA is consistently rising even at very low levels, it may indicate that cancer cells are growing.

Salvage radiation therapy is potentially curative. According to one study, 56% of patients were relapse-free after eight years.[17] PSA doubling time (rate of increase) is a good predictor of response to salvage radiotherapy. In one study, patients with a doubling time of five months or more all responded to therapy.[18]

Salvage radiation therapy can increase the likelihood of urinary incontinence and erectile dysfunction.[19] These problems can occur some years after treatment. A small proportion of patients will also experience rectal problems. However it appears that radiotherapy after surgery improves long-term quality of life, presumably due to the benefit of decreasing the recurrence and spread of cancer.

After radiotherapy

If the PSA rises because there is local recurrence after radiotherapy, surgery is still possible but is less frequently offered as a salvage treatment. This is because radiotherapy causes scarring in the pelvic region, which makes surgery more difficult. Complications after surgery, such as urinary symptoms, incontinence and erectile dysfunction, are more common. However both surgical and radiotherapy techniques have improved in more recent times, and these side effects are not nearly as common as they were. Salvage radical prostatectomy can be suggested as an option in patients with few other illnesses, low-risk prostate cancer and a longer life expectancy, according to recent guidelines.[20]

Salvage treatment after radiotherapy can include ADT alone, or local treatments such as high intensity focused ultrasound (HIFU) or cryotherapy (freezing of the tissue). Cryotherapy is most successful in

patients with a PSA less than 10ng/ml. It can have side effects such as impotence, urinary incontinence and perineal pain.[20]

5.4.2 Distant recurrence

In many men, rising PSA indicates that they have distant recurrence. Even so, this recurrence may not lead to the development of symptoms of metastatic disease in all patients. For example, in men with a Gleason score of 5–7, the probability of remaining free of metastases for seven years is 62%.[6] Consequently one option for treatment is observation only.

Androgen deprivation therapy (ADT) is the main treatment for men who have developed metastases. Also called hormone therapy, it involves removing male hormones from the body, or blocking their action. We cover this treatment and its side effects in Chapter 7.

ADT given before metastases are proven or highly likely (eg PSA is over 10–20ng/ml) is called early hormonal therapy. The therapy is controversial and ADT has considerable side effects. A number of clinical trials are underway to see whether early hormone therapy improves survival[21]'

Chemotherapy with agents known to be effective at later stages might be considered by some doctors (*Chapter 8*). As is the case for ADT, we do not know whether chemotherapy given at this early stage is effective and it does have side effects.

Observation only. The idea of not taking action if the PSA starts to rise can be stressful. However, this may be the best course if:

- there are no symptoms such as bone pain
- metastases cannot be shown on scans
- the risk of metastases being present is not very high

You can discuss this approach with your doctor.

5.5 Symptom control: treatments

As for locally advanced prostate cancer, patients with a PSA rising after a first primary treatment such as surgery or radiotherapy may still be at an early phase of their disease. The disease itself is therefore unlikely to be causing any symptoms.

The symptoms that are experienced may be due to the treatments offered such as surgery, radiotherapy and androgen deprivation therapy (*see Chapter 7*).

5.6 Preventive and supportive care

This period, when there is a signal that the cancer is present but it is still at an early stage, is an important time for building your body's natural resources and resistance. In Chapter 6 we describe diet, exercise and complementary therapy approaches that can be helpful in a number of different ways.

5.7 Resources

Cancer Council Helpline: 13 11 20

Lions Australian Prostate Cancer Website: www.prostatehealth.org.au

Memorial Sloan Kettering Prostate cancer nomograms: www.mskcc.org/mskcc/html/10088.cfm

Prostate Cancer Foundation of Australia: 1800 22 00 99

Prostate Cancer Support Groups: www.pcfa.org.au or phone 1800 22 00 99

UpToDate for Patients: *Patient Information: Advanced Prostate Cancer*: www.uptodate.com/patients/index.html

Chapter 6: Complementary Care and Lifestyle

6.1 Key messages

There are things you can do which could (we are not sure) slow the progress of the cancer and will reduce the impact of the cancer and its treatments. These include:

- taking up exercise—particularly resistance exercise
- maintaining a healthy bodyweight
- choosing a healthy diet high in vegetables, fruit and whole grain cereals and low in saturated fat. Legumes, soy products, tomatoes and fish all contain nutrients that may be beneficial for men with prostate cancer
- ensuring your diet includes sufficient vitamin D and calcium, which are important for healthy bones, particularly if on androgen deprivation therapy (vitamin D comes from sun exposure as well as diet and can be low in older persons)
- note: vitamin supplements have not been shown to be helpful. Excess amounts of some nutrients, including vitamin D, can be harmful
- considering complementary therapies such as meditation, massage and touch therapies which can help to relieve stress, tension and pain
- note: always check with your doctor before starting a new therapy. It is possible to do harm, even with supportive therapies

While you are receiving medical care there are additional ways in which you can improve your body's resistance to cancer and its treatments. We are not certain whether these can change the course of the disease, but they can strengthen the body in a number of ways and reduce the impact of the illness. In this chapter we discuss complementary care and lifestyle changes which may improve aspects of life with prostate cancer.

6.2 Physical activity

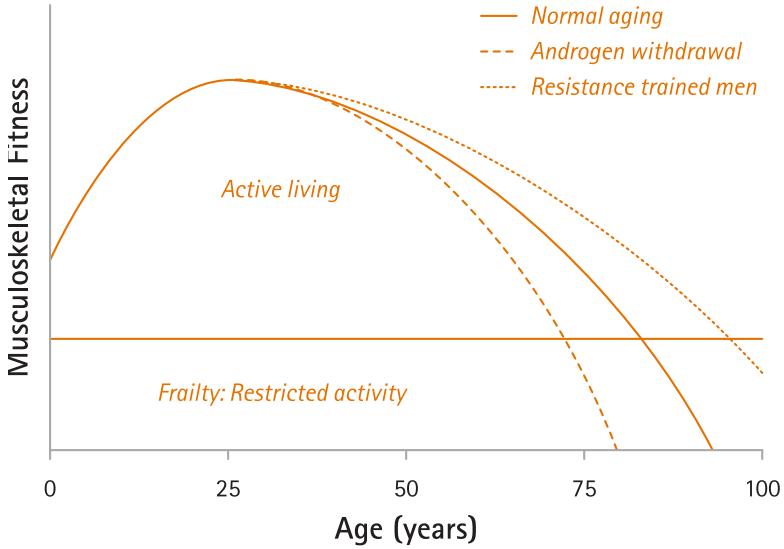
Any activity that uses muscle to move burns energy (kilojoules/calories) and is called physical activity or exercise. This includes domestic activities such as gardening as well as housework, walking, and swimming. Recent research has found that certain types of physical activity can reduce the impact of some side effects caused by prostate cancer treatments. Exercise can also help prevent other common chronic diseases such as cardiovascular disease. Physical activity does not have to be strenuous to have a benefit.

6.2.1 Resistance exercise for muscle mass and strength

Moderate to strenuous physical activity in the form of resistance exercise, with expert supervision, can improve your muscular fitness and quality of life. Such exercise can reverse some of the effects of androgen withdrawal (*see Chapter 7*). It strengthens your bones, increases your muscle mass and although it sounds odd, resistance exercise can actually reduce fatigue and its effect on your daily life. Over time it can also give you a sense of wellbeing, positively affecting your mood.

Resistance exercises can help maintain musculoskeletal fitness and an active lifestyle by working the muscles of the arms, legs and torso against a resistance. The resistance can be provided by gravity, devices such as exercise elastic bands, or a machine at the gym. These exercises can be done with little or no expensive equipment and do not require a large amount of space. (*See Appendix 4 for more details on this very helpful approach*).

Figure 6.1: Reduction in fitness during aging, when on androgen withdrawal therapy and in resistance-trained men



Adapted by permission from Macmillan Publishers Ltd: Prostate Cancer and Prostatic Diseases, copyright[22]

Muscle mass and fitness normally decline with aging. Treatments such as androgen withdrawal (hormone therapy) can speed up this loss, leading to frailty at an earlier age. Figure 6.1 shows how resistance exercises can improve the normal decline in musculoskeletal fitness with age, and the even greater decline with androgen withdrawal therapy.

An example of a resistance exercise program is given in Appendix 4.

6.2.2 Aerobic exercise for cardio-vascular fitness

Maintaining cardio-vascular (aerobic) fitness is also helpful. Aerobic exercise makes you 'huff and puff' and increases your heart rate. It can help to increase bone strength, reduce body fat, and increase endurance—all helpful effects for men on androgen withdrawal therapy. It improves heart health by increasing the amount of blood pumped around the body and reducing the normal heart rate.[23] In addition to the benefits for heart health, exercise can improve erectile function.[24] Men with healthy blood vessels are more likely to have good erectile function and maintain it after treatment for prostate cancer.

It goes without saying that smoking or too much alcohol is likely to have the opposite effect.

Note that if you have unstable bone lesions (areas of bone weakness) or other medical problems such as cardiovascular disease, you may not be able to do every kind of exercise. Ask your doctor for guidance in choosing the right type and amount of exercise for you.

6.3 A diet high in vegetables and fruits and low in animal fats

A healthy diet helps in many different ways. During cancer treatment, it can help you cope better with any side effects and aid the healing of any wounds or damaged tissues. A healthy diet also improves the immune system, which helps to fight off infections, and can promote a healthy heart and blood vessels. It also helps men who are overweight—an unfavourable factor in prostate cancer.

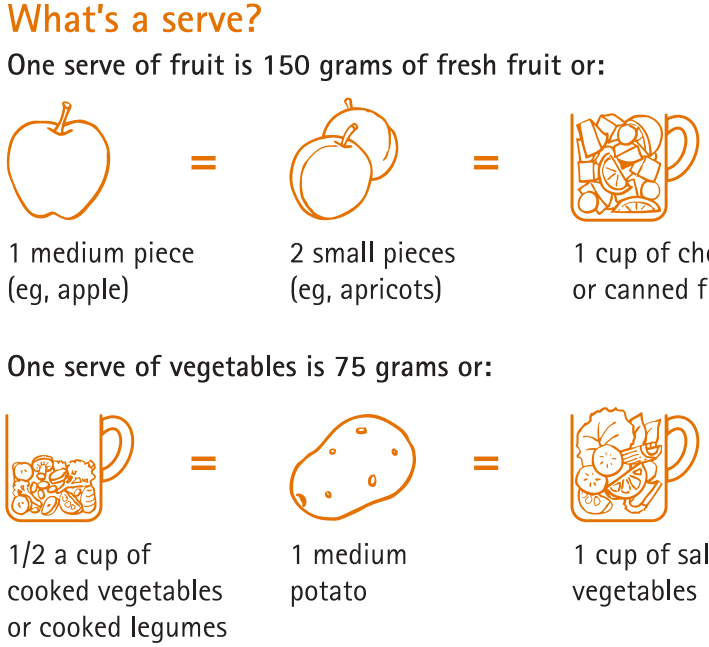
The NHMRC Australian Dietary Guidelines (2003) recommend that we eat a variety of fruit, vegetables, wholegrain cereals and reduce the amount of saturated fat, sugar and salt .

The Mediterranean style of diet is also a good guide for healthy eating. Followed in countries bordering the Mediterranean, it is rich in fruits, vegetables, legumes (such as peas, beans and lentils) and cereals. It is high in fish, includes a little red meat, and olive oil is the main source of fat.

These types of diets not only increase your intake of anti-oxidants, fibre, phyto-oestrogens and omega-3 fatty acids, they also reduce intake of saturated fatty acids. These changes may be directly beneficial for prostate

cancer. Fruits and vegetables in particular contain plenty of anti-oxidants and phyto-oestrogens. Aiming to eat five serves of vegetables and two serves of fruit every day is good advice and promoted in the Go for 2&5® healthy diet program. The diagram below explains how to estimate a serve.

Figure 6.2: Serving sizes



From: Go for 2&5® campaign: an Australian Government, State and Territory health initiative www.gofor2and5.com.au

6.4 Maintaining a healthy bodyweight

Eating a balanced diet and being physically active help in maintaining a good bodyweight. Recent research suggests an association between obesity and aggressive prostate cancer.[25] Obese men have been reported to have higher chance of recurrence and death after treatment for prostate cancer[26, 27]. It is not clear why this is so, but it is possible that prostate cancer is diagnosed later in obese men because their PSA appears lower due to a dilution effect.[28] However, a measure of obesity called the Body Mass Index (BMI) predicted prostate cancer death irrespective of clinical stage in one study, suggesting that later diagnosis is not the whole story.[27]

You can calculate your BMI by taking your weight in kilograms and dividing by your height in metres squared. For example, if your weight was 70kg and height 1.8m, your BMI would be 70 ÷ (1.8 x 1.8) = 21.6. Appendix 5 includes a BMI chart that makes it easy to calculate your BMI. You have a healthy body weight for your height if your BMI is between 18.5 and 25.

Waist circumference can also be used to see if you have a healthy body weight. To work out your waist measurement simply put a tape measure around your body at the level of your navel. For men, the risk of disease increases if your waist is 94cm or more. This risk is substantially increased if your waist becomes 102cm or more.

It is prudent to set a goal to lose weight if your BMI is more than 25 or waistline greater than 94cm.

Aim for BMI less than 25 and waist less than 94 cm

And remember, don't give up too many things you enjoy—just get the balance right!

6.5 Dietary supplements

6.5.1 Vitamin D

Vitamin D is found in food or supplements and can also be produced in the body after exposure to ultraviolet rays. It is important to have adequate vitamin D to maintain strong bones and it may also help maintain a healthy immune system, cell growth and tissue development. Early findings from a number of studies linked low blood levels of

vitamin D to increased risk of prostate cancer, although this has not been confirmed in recent studies.[29]

Most vitamin D is made in our skin after exposure to ultraviolet rays from the sun. However production of vitamin D decreases with age. The ability of the skin to produce vitamin D in men 75 years and older has been shown to be about 40% less than in men 60 years and younger.[30]

The best naturally occurring sources of this vitamin include oily fish, such as salmon, tuna, mackerel and fish liver oils. Small amounts are also found in beef liver, cheese and egg yolk. Much of our vitamin D comes from fortified foods like milk and cereal.

Most of us have enough sun exposure to get all the vitamin D we need. However it is important to balance the need for a sufficient dose of sunlight with increasing the risk of skin cancer. It has been estimated that fair-skinned people can achieve adequate vitamin D levels in summer by exposing the face, arms and hands or the equivalent area of skin to a few minutes (5–9 minutes) of sunlight on either side of the peak UV periods on most days of the week.[31] In winter, in the southern regions of Australia where UV radiation levels are less intense, maintaining vitamin D levels may require 30–50 minutes of sunlight exposure to the face, arms and hands or equivalent area of skin over a week.[31, 32]

At least 200 International Units (IU) (5 µg) per day for those less than 50 years, and 600 IU (15 µg) per day for those over 70 years are needed for adequate intake. People who do not have much sun exposure may need supplementary vitamin D.[32]

If you do not consume foods rich in vitamin D or fortified foods and do not have regular sun exposure, you may need to consult your doctor about a supplement. Older adults particularly may need to boost their vitamin D intake. Some guidelines recommend that patients on androgen withdrawal take both a calcium and vitamin D supplement.[33]

While adequate vitamin D intake is necessary, if taken in large amounts vitamin D can upset calcium metabolism and be toxic. Symptoms include muscle weakness, nausea, vomiting, headache and bone pain. It is advisable to talk to your doctor about checking your vitamin D level before taking a supplement.

6.5.2 Tomatoes and lycopene

Several studies have examined whether tomatoes or tomato-rich foods can protect against prostate cancer. There is some evidence to support an anti-cancer effect of lycopene (the anti-oxidant compound that gives tomatoes their colour). One study found that lycopene combined with orchidectomy (surgical androgen withdrawal) was more effective in slowing progression of bone metastases than orchidectomy alone.[34] Two studies suggest that consuming two to five servings of tomato per week may also be protective against prostate cancer.[35]

Lycopene belongs to a family of pigments called carotenoids, which are strong anti-oxidants. While tomatoes are the best source of lycopene, significant amounts are also present in apricots, guavas, watermelon, papaya and pink grapefruit. Cooked tomatoes and foods like tomato sauce and paste are a richer source of lycopenes than fresh tomatoes.

Anti-oxidants can protect body cells against damage from free radicals (unstable molecules). Vitamin C and vitamin E also act as anti-oxidants. While there has been concern that anti-oxidant supplements may interfere with the work being done by chemotherapy or radiation, eating fruits and vegetables high in anti-oxidants is considered safe during cancer treatment. If you plan to take lycopene capsules, talk to your doctor first.

6.5.3 Phyto-oestrogens

Foods containing phyto-oestrogens (plant hormones) may also be beneficial. These are compounds in plants that can block or mimic the effects of steroidal hormones in the body.

Foods that are particularly high in phyto-estrogens include soy products such as soy milk and yoghurt, tofu and tempeh (a fermented soy product).

In countries where consumption of these compounds is high, such as in China and Japan, there is traditionally a low level of breast and prostate cancers. This has raised interest in whether adding these compounds into the Western diet may reduce the risk of prostate cancer or improve treatment outcomes.

Phyto-oestrogens may decrease production of the most active form of testosterone. So far, however, studies have been unable to show a convincing association between eating soy foods and a lower risk of prostate cancer. Two randomised controlled trials assessing the effects of a soy-containing multivitamin supplement found that it slowed the rate of rise of PSA.[21] However the trials did not find an effect on survival, tumour response, or pain, or report on the potential harms of these treatments.

It is a good idea to eat some soy foods as part of a generally healthy diet rich in plant foods. Always check with your doctor before taking any dietary supplements, including soy supplements.

6.5.4 Selenium

Selenium is a trace mineral that is essential for good health. We need only small amounts. Selenium is incorporated into proteins in the body to make important anti-oxidant enzymes. The anti-oxidant properties of seleno-proteins, as they are called, help prevent cell damage from free radicals.

The selenium content of foods (mainly derived from plant foods such as bread) depends on the selenium content of the soil where plants are grown. Some soils in Australia are thought to be deficient in selenium.[36] Seafoods such as tuna and some nuts are also a good source.

A study called the Selenium and Vitamin E Cancer Prevention Trial, or SELECT, investigated whether vitamin E and selenium could prevent prostate cancer. This study involved more than 35,000 men in their 50s and showed that selenium did not lower the risk of prostate cancer.[37] It is thought that selenium may be of benefit, but only in men who start with low levels of selenium.[38] Selenium is toxic in high doses (*see below*).

A 75-year-old man with prostate cancer read on the Internet that selenium might be helpful. He ingested 10g of sodium selenite (a selenium salt) and developed acute selenium poisoning. Despite intensive care treatment he suffered a cardiac arrest and died six hours after ingestion.[39]

6.5.5 Multivitamin supplements

Theoretically, supplements containing anti-oxidants such as multivitamin preparations should be beneficial if these are the components of vegetables and fruits which are protective. However, studies to date have failed to show a benefit.

A major observational study of 295,000 men followed for five years showed that multivitamin use was not associated with reduced risk of prostate cancer.[40] To the contrary, men reporting excessive multivitamin use (more than seven times per week) had more advanced or fatal prostate cancers.

Recent studies of supplements containing vitamins C and E have also had disappointing results.[41]

As always, you should talk to your doctor before taking any dietary supplements.

Having vitamins in food seems to be better than getting them from supplements. This may be because dietary supplements are unable to replace all the beneficial properties in food such as fibre and minerals. In addition, it could be a combination of nutrients in food that work together against cancer, rather than a single nutrient.

6.6 Supportive care for men with prostate cancer: activities and therapies that can reduce the impact of illness

It can be difficult not to focus on your illness; however sometimes dwelling on your cancer makes it feel overwhelming. At times like this, it can be helpful to try and shift your thoughts away from what you are going through. The techniques for doing this may also help change the way in which you perceive and approach the cancer and its effects. Chapter 10 discusses worries, what causes them and how to deal with them.

Everyone is in a different situation so not everything mentioned here will be relevant to you.

6.6.1 Meditation

Meditation is an ancient practice that focuses on breathing techniques and quietening the mind. It can help to relieve stress, tension and pain and to clarify thoughts and feelings. Typically, it encourages you to stay in the moment while maintaining a non-judgmental attitude to whatever thoughts or feelings cross your mind. There are many schools of meditation.

Yoga, hypnotherapy and guided imagery offer similar benefits. The last is a type of meditation where a person imagines a series of scenes that promote healing thoughts in order to achieve peace, pain relief and relaxation.[42]

Stillness can also come from Tai Chi, which is sometimes called 'moving meditation'. Tai Chi uses slow, light and gentle movements that incorporate movement, breathing techniques and meditation to create stability in the body.

6.6.2 Massage and touch therapies

Many scientific studies have been conducted on massage and touch techniques for people undergoing cancer treatment. Research shows that they can reduce pain, fatigue, anxiety, depression and nausea.[42]

Like food and water, touch is essential. It benefits people at all stages of life and on every level—physical, emotional and mental. It can be calming, improve sleep and wellbeing, reduce muscular tension and make you feel better about yourself.

During illness, touch can be a powerful expression of care, acceptance and emotional nourishment. In the midst of discomfort or anxiety, it can be reassuring and calming.

Some people find massage helps to reduce their pain and improve their mood. While the effects may not be long-lasting, a massage has the potential to interrupt a cycle of distress by inducing relaxation, increasing blood and lymphatic circulation and manually releasing muscle spasms.

If you are on active treatment or have a high risk of bleeding or fractures, you should check with your doctor before having a massage. Also, be sure to visit a qualified massage therapist.

There are several other touch therapies that you can explore, such as reflexology, which uses pressure points in the hands or feet to positively affect function in other parts of the body.

6.6.3 Other therapies

Cancer Council NSW has produced a booklet on complementary therapies that includes a summary of therapies shown to be helpful (*see Resources*).

In clinical trials, some therapies have been shown to be beneficial for the various effects of cancer and its treatment:

- counselling, meditation, relaxation, support groups help reduce stress and improve self esteem
- art and music therapy provide focused attention that aids relaxation, pain reduction, and the expression of feelings

- spiritual practices help reduce stress, instil peace and improve one's ability to manage challenges
- massage can help reduce pain, fatigue, insomnia, anxiety, depression and nausea
- aromatherapy improves sleep and aids relaxation
- reflexology reduces anxiety
- acupuncture reduces nausea, vomiting, fatigue and pain
- yoga and physical activity improve sleep, reduce stress, anxiety, depression, fatigue and muscle wasting
- tai chi relieves pain, improves flexibility and strength, and reduces stress
- qi gong improves quality of life, reduces fatigue, pain and side effects of treatment, and improves mood
- nutrition helps wounds and damaged tissue to heal better, and improves the body's immune system
- herbal medicine relieves digestive disturbances, improves appetite and increases resistance to infections

From: Understanding Complementary Therapies: A guide for people with cancer, their families and friends. Cancer Council NSW October 2008

6.7 Can I do myself any harm?

You are unlikely to come to any harm in trying different complementary therapies so long as you discuss your use of them with your health team, and you use your common sense when finding a therapist, participating in a class, or taking dietary or herbal supplements.

It is best to do all things in moderation and to talk to your doctor before starting a new regime. Complementary therapies should be treated in the same way as conventional therapies: it is important to choose the most appropriate therapy or the correct remedy and to respect the recommended dose.

For guidance, seek professional advice from a qualified complementary therapist and/or your doctor.

- If you are starting an exercise regime, make sure it won't affect any of your other conditions and injuries.
- Some special diets may be nutritionally inadequate and not support your body when it is already under stress—be careful not to lose too much weight.
- You should be suspicious if a remedy is very costly and claims to cure your disease—no complementary therapies are known to cure prostate cancer.

Useful questions to ask when considering alternative or new treatments include:

- Is this therapy specifically used for cancer patients?
- What will the therapy aim to achieve?
- Has it been tested in a clinical trial?
- Are there any side effects?
- Will it interact with any of my existing treatments?
- Who will be involved in delivering the therapy?
- Are they qualified and registered with a professional organisation?
- What are the costs of the therapy and does my health insurance provider or Medicare cover them?
- How long can I use this therapy?
- Should I check with my doctor before taking it?

6.8 Confused about terms?

Complementary therapies are therapies that can be used in conjunction with conventional medicine, are fairly safe if used with care, offer improved wellbeing and reduce side effects for many people.

Integrative medicine incorporates aspects of complementary medicine into comprehensive treatment plans alongside orthodox methods of diagnosis and treatment. Alternative therapies are therapies used instead of conventional medicine and are often not supported by scientific evidence. Patients using them may forgo the benefits of conventional medicine. They may be unsafe.

6.9 Resources

BMI calculator: en.wikipedia.org/wiki/Body_mass_index. Also see Appendix 5

Food and cancer: a guide to nutrition for people with cancer. Cancer Council NSW, 2009. www.cancercouncil.com.au

Go for 2&5® campaign: www.gofor2and5.com.au

Massage and cancer: an introduction to the benefits of touch. Cancer Council NSW. www.cancercouncil.com.au

National Centre for Complementary and Alternative Medicine: nccam.nih.gov

Medicines Line of the National Prescribing Service provides evidence-based information on dietary supplements. 1300 888 763

Promoting Wellness for Prostate Cancer Patients. Mark Moyad MD, MPH 2006.JW Edwards, Ann Arbor MI.

Understanding complementary therapies: a guide for people with cancer, their families and friends. Cancer Council NSW 2008. Available at www.cancercouncil.com.au

Chapter 7: Metastatic Prostate Cancer

7.1 Key points

- Prostate cancer is called metastatic when groups of cancer cells have left the prostate region and started to grow in other parts of the body. These deposits are called metastases.
- The most common site of metastases is bone.
- Bone scans, x-rays, CT and MRI scans are used to look for signs of metastases.
- Bone pain is a common sign of metastases. This can be effectively treated with radiotherapy.
- The best treatment to slow the growth of the cancer outside the prostate region is called androgen deprivation therapy (ADT) or hormone therapy.
- ADT deprives the cancer cells of the male hormones they need to grow—wherever they are in the body.
- ADT can be delivered as drugs (which is reversible) or achieved by surgical removal of the testes (not reversible). Both forms of treatment are equally effective.
- Both forms of ADT have side effects, which can include hot flushes, lack of sexual desire, mood changes, bone thinning, increased risk of cardiovascular disease and muscle wastage.
- Exercises—particularly the type that build strength—medications, and a type of ADT called intermittent therapy (starts and stops the medications) can minimise these effects.
- This chapter includes other approaches to managing the side effects of ADT.
- Life can be active and rewarding despite a diagnosis of metastatic prostate cancer

7.2 What is metastatic prostate cancer?

Prostate cancer is called metastatic when small groups of cells have left the primary tumour site and started to grow in other parts of the body. These small deposits of tumour cells are called metastases (secondary tumours). In prostate cancer, cells are most likely to travel to bone. The next most common location is the lymph nodes in the same area as the prostate (pelvic lymph nodes) or the back of the abdominal cavity called the retro-peritoneum. The cells can also go elsewhere in the body such as the lungs and liver, but this is far less common.

7.2.1 Signs and Symptoms of metastatic prostate cancer

In its early stages, metastatic or secondary prostate cancer may not cause symptoms. Doctors rely on investigations such as blood tests and scans to indicate whether cancer cells have spread to the lymph nodes, bones or other parts of the body. Back pain and pain in other bones are symptoms which usually occur at a more advanced stage. Other symptoms at this stage can be unexplained fatigue and loss of weight.

PSA

A rising PSA indicates disease is growing either in the prostate, immediately adjacent, or elsewhere in the body. The presence of metastases is usually suspected if the PSA is above 20ng/ml[43], although metastatic cancer can occur with lower PSA readings. A rapidly rising PSA indicates a more aggressive cancer and one that has already or is more likely to metastasise. This is especially true for men with a PSA doubling time (the time it takes PSA levels to double) of less than three months.[44]

Bone scan

A bone scan is usually suggested if bone pain is present, the PSA is above 20ng/ml, or the Gleason Score is 7 or greater.[45] A bone scan only identifies areas of increased bone turnover, so healing fractures and arthritis as well as cancer deposits will show as 'hot spots'. A radioactive 'tracer' substance is injected into a vein in the arm. The tracer then travels through the bloodstream and into the bones, where it can be detected and displayed. The image is recorded by a special camera. A 'tracer' is an unstable chemical that emits low levels of radiation.

Metastases may still be present even if a bone scan is negative. Metastases may either be too small to show on bone scans (called micro-metastases), or may be in another tissue that the bone scan does not image (such as lymph nodes).[43]

X-rays

Sometimes x-rays may be used to examine a painful bone area.

MRI and CT scans

Magnetic resonance imaging (MRI) is useful to look at the soft tissues of the pelvis and lymph nodes as well as bones. MRI uses a powerful magnet and radio waves to produce high-quality cross-sectional pictures in sequence along the body. Each picture represents a virtual slice through the body. The patient lies on a moving table passing through the magnetic field. As each picture is taken, you hear a banging noise.

A computerised tomography (CT) scan is also used to produce images of the soft tissues of the body. A CT scan uses x-ray energy in beams at different angles to image the area of interest.

CT and MRI scans enable specialists to examine abnormal tissue close to the prostate such as enlarged pelvic lymph nodes. They can also evaluate more distant tissue such as liver and show any effects on the kidneys. For example, if the cancer has grown sufficiently to block the ureters (the tubes carrying urine from the kidney to the bladder), scans can show enlargement and distension of the kidney due to 'back pressure' in the kidney's draining systems.[45]

7.2.2 Symptoms of metastatic prostate cancer

The symptoms of metastatic prostate cancer can vary depending on the extent of spread. If the spread is minimal there may be no symptoms at all. The most common symptoms result from metastases to the bones.

Metastases in bones can cause a deep pain or stiffness in the lower back, upper thighs, or hips, or an ache in any bone. The cancer may thin the bones in the limbs making fractures more likely. Swelling in the legs and feet from obstruction of the blood vessels of lymphatic system as well as weight loss and anaemia can also occur, but these are less common as presenting features of metastases.

Any numbness, pins and needles or weakness in the legs, trunk or arms are symptoms that need urgent attention as they can be related to instability in the spine. Unexplained constipation or urine or bowel incontinence should be investigated, particularly if associated with back pain. If the cancer spreads in the pelvic region, there can be urinary symptoms.

Symptoms can usually be controlled with androgen deprivation therapy. Some bone deposits may require radiotherapy. Sometimes surgery (a trans-urethral resection of the prostate) is used to remove urinary obstruction in the pelvic region.

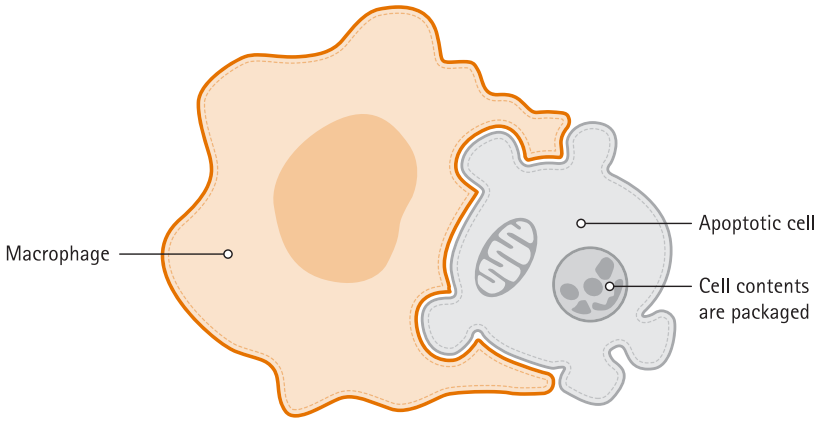
We discuss androgen deprivation to control growth of metastases below. Radiotherapy to treat painful metastases in bone and drug therapy to prevent bone loss and fractures are covered in *Chapter 8*.

7.3 Treatment to control cancer: androgen deprivation (hormonal) therapy

Once prostate cancer has spread beyond the prostate to distant organs, a treatment is needed that will attack the cancer wherever it is in the body. Doctors call this systemic therapy. The most effective systemic therapy for prostate cancer is called androgen deprivation, or the removal or blocking of the male hormone. Other terms used to describe this treatment are also hormone therapy, androgen ablation or androgen deprivation therapy (ADT). Throughout this chapter, androgen deprivation and hormone therapy will be used interchangeably.

All prostate cells and most prostate cancer cells need androgens, in particular the male hormone testosterone, to survive and grow. Without it, they die in a process called 'apoptosis'—a type of cell suicide (*see Figure 7.1*). The sick cell separates from healthy cells and starts to alter itself. It packages up its internal structures and awaits engulfment by a clean-up cell known as a macrophage. Apoptosis is used by the body to remove cells damaged by chemicals, UV radiation or other means. Many cancer treatments act by triggering apoptosis. Androgen deprivation causes apoptosis of cells. It also affects the new blood vessels that tumour masses develop to support their growth.

Figure 7.1: Apoptosis—the self-destruct program for getting rid of damaged cells

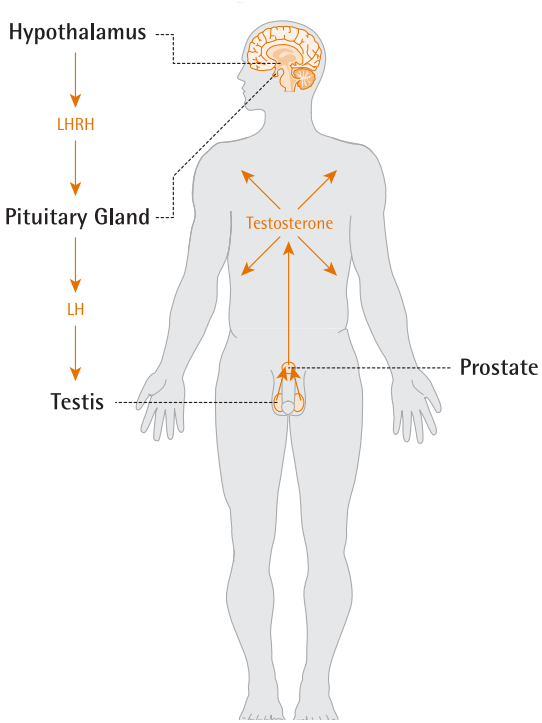


Cancer cells die in a process called Apoptosis. They are then swallowed by Macrophages.

Testosterone is produced mainly by the testicles. Its production is stimulated by a hormone called leuteinising hormone (LH), which is produced by the pituitary in the brain. Production of LH is in turn controlled by another hormone, leuteinising hormone releasing hormone (LHRH), produced by another part of the brain, the hypothalamus. This whole sequence of events is called the hypothalamic–pituitary–gonadal axis (*see Figure 7.2*). Each stage of this sequence of events can be targeted by drugs or treatments to stop production of testosterone. These treatments decrease testosterone levels in the body and block the fuel needed by prostate cancer cells to survive. They can prevent the growth of prostate cancer cells wherever they are in the body.

Hormonal or androgen deprivation therapy aims either to prevent the production of testosterone or to block its action in the tissues.

Figure 7.2: Production of testosterone



Testosterone is produced by the testes when they are stimulated by leuteinising hormone (LH) from the pituitary in the brain. The pituitary is in turn stimulated by leuteinising hormone releasing hormone (LHRH) from the hypothalamus, also in the brain. The types of ADT and their actions are shown in Table 7.1.

Table 7.1 Types of androgen deprivation therapy

Drug or treatment type	Name (generic for drugs)	Brand names	Where it acts	Action	How administered
Surgery	Orchidectomy/ orchiectomy	-	Scrotum	Testes removed from scrotal sac	Operation under general anaesthetic
LHRH agonists*	goserelin, leuprorelin	Zoladex® Lucrin® Eligard®	Pituitary gland	Suppresses production of LH and FSH	Injection monthly, 3-, 4- or 6-monthly
Anti-androgens (non-steroidal)	bicalutamide flutamide, nilutamide	Cosudex® Eulexin® Anandron®	Prostate and prostate cancer cells	Blocks androgen receptors on cells	tablet
Anti-androgen (steroidal)	cyproterone	Androcur®	Prostate and prostate cancer cells	Suppresses adrenal activity	tablet

**also called gonadotropin releasing hormone (GnRH) agonists*

There are three main categories of ADT: surgery to remove the testicles (orchidectomy), LHRH agonists (drugs which prevent the production of testosterone from the testes) and anti-androgens (drugs which prevent the action of testosterone in the tissues). There are also drugs that suppress the small amount of androgen production by the adrenal glands.

Another drug, finasteride (Proscar®), is used for benign prostate disease rather than cancer. It blocks conversion of testosterone to its more active form, 5-alpha-dihydrotestosterone (DHT). Finasteride may help prevent prostate cancer.[46] Combined with an LHRH and anti-androgen, use of finasteride or a second drug called dutasteride is sometimes referred to as 'triple androgen blockade'.

7.3.1 Timing of androgen deprivation therapy

Typically, the first indication that cancer may remain in the body after a radical prostatectomy or radiotherapy for localised disease, is a rising PSA. One of the uncertain areas is whether to begin androgen deprivation when the PSA first starts to rise, but before signs and symptoms of metastases appear. At the time of writing the guidelines, there is no definitive evidence to show a benefit from starting hormone therapy early, that is, when PSA first starts to rise. It is probable that such an early introduction will delay the time to cancer deposits being seen, but at the cost of longer exposure to hormone therapy and its side effects. We do not know whether early introduction of androgen deprivation prolongs life.[47]

The speed at which PSA is rising can be a guide as to when to start ADT treatment. Patients who have only a slowly rising PSA may prefer to wait until metastases are seen on a bone or CT scan. Patients who have severe osteoporosis, cardiovascular disease or other illnesses that may put them at risk from ADT may also prefer to wait. ADT can also be delayed for quality of life reasons. Some guidelines recommend that only men with high-risk cancer, for example PSA over 50ng/ml and/or rapid rate of PSA increase, would benefit from the early introduction of androgen deprivation.[33] However once evidence of metastatic cancer and its symptoms appear, all men should be offered ADT as it does control such symptoms effectively. Some doctors recommend the introduction of ADT when the PSA reaches a certain level, such as between 10 and 20ng/ml.

7.3.2 LHRH agonists and orchidectomy

The most effective forms of systemic therapy are orchidectomy and LHRH agonists (an agonist is a drug which binds to the same receptors as the natural hormone).

LHRH agonists are drugs that block production of testosterone. They do this by initially stimulating release of the pituitary hormone called leuteinising hormone (LH) that triggers release of testosterone by the testicles causing 'flare' (see below). Testosterone production then drops. The drug is delivered by injection into the fat or muscle and can be given monthly or every three, four or six months. The effect is reversible in most patients in that if the medication is stopped, testosterone levels return to normal after some months.

For this reason, many men opt for androgen deprivation using this method rather than orchidectomy. Examples of LHRH agonists are goserelin and leuprorelin (Zoladex®, Lucrin® respectively). These costly medicines are covered by the Pharmaceutical Benefit Scheme.

Because these drugs may not be fully effective in reducing testosterone levels in all men, it is normal to check blood testosterone levels some months after starting the hormone or when they are no longer working. Unless you choose a form of androgen deprivation called intermittent androgen ablation (described below), it is normal to continue this form of androgen deprivation indefinitely.

Orchidectomy (also called orchiectomy) is an operation to remove the testicles (orchid is the ancient Greek medical term for the testis or

testicle). Surgery to remove the testes is performed under anaesthetic. The procedure requires two small incisions so that the testes can be removed while leaving the scrotal sac intact. It involves either an outpatient procedure or a one- or two-day stay in hospital. It can be considered a convenient option because it is a once-only treatment. On the other hand, it is irreversible, and does not offer the option of intermittent androgen deprivation (*see below*). As with any operation, there is a risk of infection, although this is very low. Implants can be used to retain the normal appearance of the scrotal sack if needed. Orchidectomy can be used to treat those who do not respond to LHRH agonist drugs, that is, they do not have a lowered testosterone.

The patient and the doctor generally discuss which form of ADT is preferred. Both treatments are equally effective in controlling cancer growth and the side effects are also similar. Patient preference is an important factor in this decision. If fertility is an issue, then sperm banking is an option.

The benefit of using drugs over surgery is that they can be discontinued or stopped for a period and started again only when the PSA starts to rise. This is called intermittent androgen deprivation and is discussed in detail below.

One temporary effect of using one of the LHRH agonist is called 'flare'. Specifically, when an LHRH agonist (an agent which causes stimulation) is first started, it can cause a rise in the pituitary hormone LH during the first 5–12 days. The LH rise in turn stimulates the testicles to make testosterone. After prolonged binding of the LHRH agonist to its receptor, it turns off production of the LH and testosterone levels then decrease. The initial surge in testosterone can be seen in a blood test. Occasionally it briefly stimulates tumour growth (ie in the first month only, before the testosterone levels decline). If there are metastases (tumour deposits) close to important structures such as the spinal cord, this can trigger symptoms such as paralysis, nerve pain, obstruction

of urinary flow or increase in bone pain. Flare can be prevented by using anti-androgens which block the testosterone from getting to tumour DNA and stimulating the cell proliferation. This class of drug (eg bicalutamide, flutamide, nilutamide, also known respectively as Cosudex®, Eulexin® and Anandron®) is given just before or at the same time as commencing LHRH therapy.

Oestrogens were used to treat prostate cancer many years ago, as they also cause a decrease in testosterone production. Use of oral oestrogens, however, has been largely discontinued as a first-line treatment because of their tendency to cause blood clotting, heart attacks and strokes.

7.3.3 Anti-androgens on their own

Anti-androgens (AA) are taken in tablet form and act by blocking the action of testosterone at the cellular level. Because small amounts of circulating male sex hormones are produced by the adrenal glands in addition to the testicles, anti-androgens are often combined with LHRH agonist therapy or orchidectomy to ensure a complete blockade of testosterone action (see below).

Anti-androgens (bicalutamide, nilutamide and flutamide, also known as Cosudex®, Eulexin® and Anandron®, respectively) when given alone do not have the full spectrum of effects that LHRH agonists and orchidectomy do and it is possible to retain some sexual function when taking these alone. On their own they are considered as a form of ADT (anti-androgen monotherapy). However, they are not as effective in controlling the cancer, and so are not recommended as a stand-alone treatment for metastatic prostate cancer.[48] They are more likely to cause breast growth (called gynaecomastia) and breast pain than LHRH, as well as hot flushes.[49] They are not approved as sole agents for androgen deprivation on the Australian Pharmaceutical Benefits Scheme.

7.3.4 Combined androgen blockade

Androgen deprivation removes 95% of circulating male sex hormones. However it does not remove the small amount produced by the adrenal glands. Addition of an anti-androgen (non-steroidal) can block the effect of the remaining testosterone by blocking access to the prostate cancer cell genes. A combination of LHRH agonists and anti-androgens is called combined androgen blockade (CAB) or maximal androgen blockade. Because there is a small benefit of combined treatment compared with LHRH only (about a 3% increased survival after five years of follow-up)[49] this additional treatment is recommended as a standard by some guidelines.[33, 49] However the survival benefit is small and is at a cost of increased side effects (see above). Consequently, many doctors do not start treatment with maximal (combined) androgen blockade.

7.3.5 Intermittent androgen deprivation

Intermittent androgen deprivation is an approach to androgen deprivation which, it is hoped, will reduce the impact of side effects on quality of life. There is also speculation that it may extend the useful life of this treatment, by delaying failure of ADT (see Chapter 8). Definitive clinical trials addressing these issues have been done, however the results are not yet known. Typically, the deprivation drug is taken only until the PSA drops to a low level (less than 4ng/ml) then restarted when the PSA reaches a threshold of say 10–20 ng/ml unless symptoms of recurrence have occurred at a lower PSA level.

The time off the drug can be considerable—many months to more than a year in some cases. It is hoped that intermittent androgen deprivation extends the time before a resistant group of cancer cells starts to appear, and the androgen deprivation drugs are no longer effective (*called 'castrate resistance'—see Chapter 8*). We do not know yet whether this treatment prolongs survival or if it has a big effect on quality of life. Some results suggest that it is comparable to continuous therapy in cancer control and has a smaller long-term impact on quality of life.[49] Although it is considered only experimental by some[47], many doctors use intermittent androgen withdrawal as a treatment option.

Table 7.2 summarises factors to consider in choosing an ADT.

Table 7.2 Choosing androgen deprivation therapy

Drug or treatment type	Benefits	Disadvantages and side effects	Person most likely to benefit
Orchidectomy	Effective, inexpensive, convenient once-off administration Does not cause 'flare' (temporary worsening of cancer symptoms)	Irreversible, cosmetic change, permanent impact on sexual function. Intermittent treatment is not possible	Person with painful metastases, extensive cancer that could cause urinary obstruction or spinal cord compression Person living in rural or remote area or who is not able to attend for monthly or 6-monthly visits to doctor
LHRH agonists	Effective, reversible, albeit after a delay while testosterone levels return to normal, so can use intermittently to limit impact on sexual function, other untoward effects	Requires repeated trips to doctor for injections	Person with metastases who prefers a reversible form of therapy or when used for a time in conjunction with radiation therapy for high-risk localised disease
Anti-androgens (non-steroidal)	Tablet only, fewer side effects including less impact on potency, libido and bone density when used alone Most often used with LHRH agonists to prevent flare or as combined androgen blockade	Not as effective when used on their own Can irritate the liver, cause breast growth, and breast pain, hot flushes	Person with metastases, or who is on LHRH agonists and needs short-term protection against flare or prefers complete androgen blockade
Anti-androgens (steroidal)	Not as effective when used on their own Loss of libido, erectile dysfunction, rarely breast growth, liver problems, and may cause depression	Not as effective when used on their own Loss of libido, erectile dysfunction, rarely breast growth, liver problems, and may cause depression	Person with metastases, or who is on LHRH agonists and needs short-term protection against flare
Combined androgen blockade	Slightly more effective than LHRH alone (~3% increased survival in one study)	Combined side effects of both types of drugs	Person with metastases taking LHRH agonists who wants maximum androgen deprivation after considering the additional side effects
Intermittent androgen deprivation	Gives periods of time without side effects of LHRH. May extend the effectiveness of androgen deprivation	Need for close monitoring (repeated PSA tests). Still considered experimental by some	Person with metastases who wants to limit side effects of androgen deprivation and has considered the uncertainties of intermittent therapy

7.4 Dealing with side effects of androgen deprivation therapy

The side effects of androgen deprivation vary from person to person and are summarised in Table 7.3. While some men tolerate it quite well, others can be deeply affected. There are ways of minimising the effects and we discuss these in this section. We also recommend that you read Chapter 6 with a view to improving quality of life while on ADT.

Because testosterone has many functions in the body, removing it has a number of different side effects. Broadly, these include reduced energy levels, reduced sexual interest and changed fat metabolism, affecting quality of life and risk of heart disease. Other effects can include hot flushes, impotence, mood swings, depression, loss of muscle strength and osteoporosis. However, because such treatment can control cancer growth and relieve some of the symptoms, it may be the best treatment choice. The balance between the benefits of cancer control and symptom control weighed against the impact it may have on quality of life is an important consideration and one your doctor will discuss with you.

One approach to reduce the side effects of ADT would be to use only anti-androgen drugs (anti-androgen monotherapy). Because these drugs do not reduce circulating levels of testosterone but rather, block its effects in the prostate tissues, they have less of an impact on diminishing quality of life. On the other hand they have been shown not to be as effective in controlling the cancer as treatment with LHRH agonists, and so it is not recommended to use this class of agents alone.[33] Intermittent androgen deprivation is another approach that has quality of life benefits (*see above*) and may be as effective as continuous LHRH therapy, although it is too early to say definitely.

The other way of managing side effects is to treat each one individually and these approaches are described below. Your doctor will discuss the best approach with you.

7.4.1 Hot flushes

One of the most common and sometimes bothersome symptoms is hot flushes, sudden intense sensations of heat in the face, neck, upper chest and back. It may be accompanied by sweating or nausea and may be intense enough to wake you up. Hot flushes may be triggered by heat, hot liquids, stress, sudden changes of body position[50] or just come 'out of the blue' at any time and last for seconds or up to an hour.

A number of drugs can be used to treat hot flushes, including low-dose Androcur®, progestins, some anti-depressants drugs called SSRIs (selective serotonin reuptake inhibitors), and small doses of oestrogens. Some alternative treatments reported to be helpful include acupuncture, soy products (probably for their phyto-oestrogen content) and vitamin E, or even drinking an ice cold drink when you feel a hot flush coming on.[50]

Most drugs have their own set of side effects and so the benefit of these treatments needs to be balanced against any new side effect they may cause.

7.4.2 Reduced sexual function

Because testosterone plays an important role in normal male sexual function, loss of sexual interest and poor erections are common side effects of treatment with androgen deprivation. These side effects can have a significant impact on relationships, which is something to discuss and plan for with your partner. In Chapter 10 we list some of the ways of maintaining closeness and intimacy in a relationship while receiving this treatment.

The effects of androgen deprivation on sexual function are not as marked with anti-androgens, although the latter drugs are not as effective in cancer control (*see Table 7.2*). Intermittent therapy, described above, also appears to reduce these effects. Some normal sexual function may return during the 'off phase' of the treatment cycle, and this may be quite long (many months).

There are some treatments for erectile dysfunction that may help some men. They include medications similar to viagra® (also called PDE-5 inhibitors), penile injections and vacuum erection devices. As with treatment for erectile dysfunction after surgery, there can be benefits to 'exercising' the penis using these means to maintain healthy blood flow and erectile tissues. This is something you can discuss with your urologist at the time of starting androgen deprivation. Urologists are specialists in the area of erectile function.

7.4.3 Bone pain and fractures

Androgen deprivation increases osteoporosis or thinning of the bones. This can particularly affect the hip, spine and forearm bones. Older men treated with androgen deprivation have been reported to have 2.5 times the rate of fractures compared with those not treated.[51]

This side effect is particularly of concern for patients who may be on hormonal therapy for a long time before the cancer grows and also causes bone problems. For example, a person who starts androgen deprivation after prostate gland removal on a rising PSA and no evidence of metastases, may be on the treatment for many years. He may be more troubled by a fracture caused by bone thinning due to androgen deprivation than by bone metastases due to progressive cancer.

In contrast, a person with cancer seen on a bone scan is more likely to have pain from progressive and untreated cancer, and the risk of a fracture from bone thinning due to osteoporosis is far less relevant.

It is important to assess bone health and vitamin D levels before beginning ADT, particularly if other factors such as age and history of fall may mean you are at risk of bone-related side effects.

A number of lifestyle changes can help prevent bone loss with androgen deprivation:

- taking regular weight-bearing (resistance) exercise
- ceasing smoking
- moderating coffee and alcohol intake.

These can also benefit other side effects such as metabolic changes, mood changes and fatigue (*see Chapter 6*).

Resistance exercises are particularly effective. They work the muscles of the arms, leg and torso against a resistance and have been shown to improve quality of life and reduce fatigue on men with ADT.[52, 53] We give examples of these exercises in Appendix 4.

Increasing vitamin D and calcium intake can also be beneficial, particularly if your intake of these nutrients and your blood levels are low. Your doctor may recommend these supplements when you start ADT.

A class of drugs called bisphosphonates can increase the bone mineral density when given with calcium and vitamin D. Work is continuing to determine when it is best to commence these agents. We discuss bisphosphonates and their side effects in Chapter 8.

7.4.4 Mood and cognitive changes

Studies have shown that men receiving hormone therapy have higher levels of anxiety and depression than men receiving other treatments. However we do not know whether that is related to the stage of cancer rather than the treatment.[54]

Experience of anxiety and depression prior to treatment does increase the risk of psychological problems down the track, however[55], so it can help to be aware of this possibility and be willing to take action at an early stage. Lifestyle factors such as general engagement in activities with friends and family, exercise and the willingness to seek

help are all important approaches to minimising the impact of these challenges on mood and wellbeing.

Take action early if low mood persists and discuss it with your doctor. It may be related to your treatment, which can be changed. Help is available for this problem.

Every treatment for cancer involves some losses, and grief for them can go unrecognised. You and your partner will experience some shared losses and some that are different for each of you. Talking through grief can be an important part of coming to terms with these issues. We discuss approaches to maintaining wellbeing for men in Chapter 10, and their partners and family in Chapter 11.

Men on this therapy may notice small changes in memory function. They may have a reduced ability to multi-task and also may notice changes in spatial ability. However according to one investigator[56], these are subtle changes and not across all areas of functioning. Some reports also suggest that depression may be more common in men receiving this treatment for prostate cancer[57] and that depression, as well as the low testosterone level, may be contributing to any memory difficulties.

In Chapter 10 we discuss the importance of keeping alert for these signs and what to do if you feel they are affecting you. It is possible that a treatment can lead to a sequence of side effects. It may be difficult to separate the side effects from those of the cancer, its treatment and other sources of normal health problems. Having someone with whom to discuss these changes (a family member, GP, nurse or counsellor) can provide a helpful external reference point if this happens.

7.4.5 Changes in body composition, metabolism and risk of heart disease

Androgen deprivation tends to decrease the muscle mass in the body and increase fat mass. The reduction in muscle can reduce capacity for strenuous activities such as gardening and increase frailty and consequently the risk of falls. It can also contribute to fatigue. These effects can be minimised with resistance exercises (*see Chapter 6 and Appendix 4*).

Androgen deprivation also has effects on the body's fat and sugar metabolism[58], increasing total cholesterol, particularly the 'bad' fats (low density lipoprotein cholesterol) and reducing the 'good' ones (high density lipoprotein cholesterol). It also increases fasting insulin levels, a marker of insulin resistance. These changes are associated with an increased risk of diabetes and heart disease. One study of 22,816 men diagnosed with prostate cancer found that those on ADT had a 20% greater risk of a new cardiovascular event than those not on the therapy.[59]

On balance, we know hormonal therapy has definite benefits in terms of increasing overall survival in some situations (eg hormone therapy can improve survival when added to radiation therapy in patients with high-risk localised cancer). However, the side effects of hormone therapy mean that the benefits need to be carefully weighed up against the risks.

Because the risk factors for heart disease can be reduced with diet and exercise, these lifestyle changes are particularly helpful for men on ADT. Diet changes that decrease saturated fats and increase plant-derived oils (from fish, nuts and cooking oils) as well as dietary fibre also help. Avoiding smoking and taking moderate aerobic and resistance exercise as discussed in Chapter 6 are recommended. A heart-healthy lifestyle is also a prostate-healthy lifestyle.[60]

Improving the diet and taking up exercise can have many benefits for men on ADT

7.4.6 Lethargy and fatigue

Fatigue is a very common problem in man receiving ADT. It may be enhanced by anaemia, with muscle loss and cognitive changes, and may contribute to or be caused by depression. Fatigue can limit your engagement in normal activities. It is an important factor in your quality of life. Exercise can counter some of these effects by building muscle mass and fitness, which have been shown to reduce fatigue.[61]

If anaemia is present this can also be treated. We discuss lifestyle changes, including exercise that may be helpful, in Chapter 6. Keeping up active interests, including exercise (both aerobic and resistance) for at least 30 minutes a day, is recommended by experts in this area.[60]

Table 7.3 Side effects of treatments for metastatic prostate cancer and their treatment

Drug or treatment type	Side effect	Treatment or side effect
Orchidectomy or LHRH agonists	Hot flushes	Drugs such as progestins, antidepressants Alternative: phyto-estrogens such as soy, vitamin E, acupuncture
	Loss of libido	Intermittent androgen deprivation if on LHRH agonists
	Erectile dysfunction	Sildenafil and similar drugs, penile injection, vacuum devices
	Increase in body weight and fat tissue	Aerobic and resistance exercise
	Muscle wasting	Resistance exercise
	Anaemia	If present is mild and may not require therapy
	Thinning of the bones	Exercise, calcium and vitamin D, (bisphosphonates if severe loss present)
Anti-androgens non-steroidal	Breast growth, breast pain, hot flushes	Radiotherapy to affected area prior to starting anti-androgen, mammectomy, discontinuing anti-androgen
Oral oestrogens	Cardio-vascular effects, stroke, thrombosis	Anticoagulants, avoid usage in oral form

7.4.7 Breast growth (gynaecomastia)

Enlargement of the breast is most common in patients receiving non-steroidal anti-androgens such as bicalutamide (Cosudex®), particularly at high doses. It can also be accompanied by breast pain.

Radiation prior to starting on the medication or tamoxifen (a drug which opposes the effects of oestrogen) taken at the same time as the anti-androgen can prevent this symptom in most cases.[62]

This list of side effects is not exhaustive, for example, LHRH agonists can produce joint and muscle pains among other unwanted effects in some patients. As with oral oestrogens, steroidal anti-androgens are not recommended as first-line drugs for prostate cancer.[49]

Although the list of side effects is extensive, many men tolerate the therapy well and lead successful and active lives. Table 7.4 will help you and your doctor prepare when you are starting on androgen deprivation treatment.

Table 7.4: Checklist for starting on androgen deprivation treatment

Tests your doctor can do to monitor your health	To check for	How you can reduce risk from the condition and maintain your health
Bone mineral density (DEXA scan)	Osteoporosis risk	Healthy diet with calcium, foods rich in vitamin-D, resistance exercise
Blood calcium and vitamin D	Bone health	Calcium, vitamin-D rich foods
Full blood count	Anaemia	Iron-rich food
Cardiac assessment	Risk of heart attack	Healthy diet, aerobic exercise
Body mass index, weight	Overweight	Healthy diet, aerobic exercise
Blood pressure	Risk of cardiovascular disease	Healthy low-salt diet, exercise
Muscle mass, balance	Risk of falls	Healthy diet, resistance exercise
Screen for distress (anxiety and depression) and psychosocial problems	Depression and any concerns or causes of distress	Accept help, support and encouragement from family and friends. Seek information from health professionals. Keep active interests, exercise regularly, healthy diet If low feelings persist, speak to your doctor
Cognitive screen	Memory loss or thinking difficulties	Maintain an active body and active mind
PSA	Cancer control	See Table 7.2
Liver function tests	Liver working well	Healthy diet, low alcohol intake
Blood sugar levels	Diabetes risk	Healthy diet, exercise

A healthy diet for men starting ADT[60] means foods low in saturated fat, a diversity of fruits and vegetables, high dietary fibre, moderate amounts of soy and 'plant oestrogen' products such as ground flax seed, fish and other sources of omega-3 fatty acids, dietary vitamin D, vitamin E and selenium (supplements not recommended).

Exercise in this context means physical activity for at least 30 minutes a day and resistance exercise several times a week.[60, 61] See Chapter 6 and Appendix 4 for more details.

Working with your GP on these changes can motivate you as well as ensuring you exercise and modify your diet safely. A dietitian can help you create a diet plan to meet your specific needs.

7.5 Life with metastatic prostate cancer

ADT can be effective in controlling the cancer and its symptoms for many years. There are ways to minimise its effects on your quality of life. In Chapters 6, 10 and 11 we talk about approaches that may help.

Life can be active and enjoyable despite a diagnosis of advanced prostate cancer. The activities that men have described while on ADT show that active life can continue. These included chairing meetings, organising fund-raising events, public speaking, ball games, practising soccer skills with grandchildren, walking in hilly country, taking interstate and international trips, writing an autobiography, composing music, performing as a singer-songwriter and forming a new relationship. If you join a prostate cancer support group in your local area you will meet others who are enjoying life, even with advanced prostate cancer. This can give you a sense of what is possible and awareness that you are not alone.

Barry Oakley, a long-term prostate cancer survivor, writes about how to maintain a quality of life in his book: Life's in the Pink.[63] He writes about the importance of a positive story, of maintaining a sense of control, of support, and of setting long- and short-term goals:

"Goals pull you forward. It is like throwing an anchor out into the distance then pulling yourself in on a rope. While you are doing that you are more concerned about the achievement of getting there than what might or might not be happening and you experience a much richer and satisfying quality of life."

It may be useful to re-read Chapters 6, 10 and 11 at different stages in your prostate cancer journey as some of the approaches may be helpful at different times. The chapters also include lists of useful resources.

7.6 Resources

Advanced prostate cancer

UpToDate for Patients: Advanced prostate cancer
www.uptodate.com/patients/content/topic.do?topicKey=cancer/4898>

Cancer Research UK: www.cancerhelp.org.uk/help/default.asp?page=2849

Andrology Australia: Advanced Prostate Cancer
www.andrologyaustralia.org/pageContent.asp?pageCode=ADVANCEDPROS

Information on bisphosphonates

Medline Plus:
www.nlm.nih.gov/medlineplus/druginfo/meds/a605023.html

Peer support

Advanced Cancer Telephone Support Group:
www.cancercouncil.com.au/editorial.asp?pageid=238

Cancer Council in your state: 13 11 20

Prostate Cancer Foundation of Australia affiliated peer support groups:
www.pcfa.org.au or phone 1800 22 00 99

Chapter 8: Metastatic Prostate Cancer Unresponsive to Hormone Therapy

8.1 Key points

- After several years on androgen deprivation therapy (ADT), prostate cancer may start to progress, despite low testosterone levels in the body. The cancer is said to have failed ADT and is sometimes called castrate-resistant prostate cancer.
- Symptoms at this stage can include bone pain, urinary symptoms, anaemia and fatigue.
- Treatment for this stage of prostate cancer may include a form of ADT that is different from the first-line treatment, chemotherapy and new types of treatments offered in clinical trials.
- Treatments for bone metastases include radiotherapy to the affected bone, radioisotopes and bone-targeting drugs called bisphosphonates.
- All of these treatments have side effects and it is important to draw on your support team and look after yourself during this phase of therapy. Refer to the complementary therapies in Chapter 6 and some of the hints in Chapter 11 to stay as healthy as possible.

After several years, prostate cancer may progress despite hormone therapy. If testosterone levels have remained low, this suggests that the disease is able to progress without normal circulating levels of testosterone. In the past this condition has been known as 'hormone refractory' cancer and 'androgen independence'. More recently, doctors prefer the term 'castrate resistance' because it emphasises progression despite very low (castrate) levels of circulating testosterone. Within the cancer cell, androgen activity may still play a role in cancer progression.

8.2 What causes androgen deprivation therapy to fail?

Most prostate cancer cells need the male hormone testosterone to grow and multiply. For this reason withdrawing the male hormone through chemical means (drugs) or surgery (removing the testes) is the best way to stop it growing once it has spread to different areas of the body. This treatment is called androgen withdrawal or blockade. Without testosterone, the vast majority of prostate cells that have spread throughout the body die through a process called apoptosis (*see Figure 7.1*).

After a number of years, however, prostate cancer cells that escaped during this treatment can start to grow again, even when testosterone levels are very low. It is believed that the cells that regrow had already developed changes during treatment that allow them to grow without external testosterone. These cancer cells were called 'androgen independent', 'hormone refractory' or, more recently, 'castrate-resistant'. The doctor knows this process has begun if, when a man is receiving androgen withdrawal therapy, his PSA levels start to rise. The situation in some patients is a little more complex as the cancer may actually be growing due to super-sensitivity to persisting but very low levels of male hormones in the blood. This is probably why some patients respond to further hormone manipulations such as blocking adrenal gland production of these hormones using other types of drugs.

The reasons ADT fails are not fully known. However they are the subject of intense research and investigation as they hold the key to blocking progression of the cancer. Understanding these mechanisms would make it possible to target treatments to prostate cancer cells only, thus reducing the side effects of treatments. We know that a protein in the cell called the androgen receptor is responsible for binding the male hormone and activating genes in the nucleus which control cell growth and development. These receptors may hold the key to the development of androgen independence. We discuss some of the models by which this may happen in Appendix 6.

8.3 Symptoms and indications

The most common indicator of resistance to androgen deprivation therapy is a rising PSA despite very low levels of circulating testosterone (20–50ng/dl).[49] The levels of PSA vary, but they may develop into the hundreds or even thousands in some cases. The rate of PSA increase is an indicator of the time taken to develop new cancer deposits on scans, and their symptoms. For example, a PSA doubling time of greater than six to ten months has a better prognosis than a shorter PSA doubling time.[14] A raised PSA does not in itself cause symptoms. However, while it is uncommon, some patients' cancers do progress with only a small change in PSA levels. Sometimes cells can be so cancerous that they no longer resemble or behave like prostate cells. Such cells may no longer produce PSA, although their Gleason score may be as high as 10.

While symptoms are common at this stage, they do not all necessarily occur and some men continue to have a good quality of life:

"I have…plenty of energy left…I chop wood…and I go to choir practice in the evenings and…play guitar…so I have plenty to do".[64]

After a cancer diagnosis it is easy to assume every pain is related to the cancer and this can cause anxiety. It is a normal part of growing old to have occasional general discomfort, headaches, pains, and muscle strains in daily life, and this will continue even after a cancer diagnosis. Not every pain is related to or caused by cancer! The type of symptoms that often eventually occur depends on where the metastases or cancer deposit(s) might be. However one of the most common symptoms is bone pain.

8.3.1 Bone pain

The most common site of prostate cancer metastases is bone. Prostate cancer cells interact with osteoblasts, the bone-forming cells, stimulating rapid multiplication and promoting bone deposition. This follows previous bone loss, and the new bone formed is different from normal bone. This disruption of the normal bone physiology and structure can lead to bone pain, fractures and very rarely, high blood calcium levels. ADT can also contribute to the loss of bone. If the cancer cells invade the bone marrow they can disrupt blood cell formation causing anaemia and consequently fatigue and shortness of breath.

Bone pain may correspond to the location of the metastasis, such as a new and progressive back pain if the metastasis is in the back. Some men have more diffuse and migratory pains, however. If metastases occur in the bones around the spine (vertebra) and the cancer is left unchecked, it can cause a condition called 'spinal cord compression'. This is when pressure on the cord causes narrowing or distortion of nerve tissue. Symptoms can be pain, 'pins and needles' in the hands or feet, limb weakness, and decreased movement. If you experience these symptoms, report them to your doctor immediately. Early detection of this condition is important in order to prevent permanent injury such as paralysis of the lower limbs. When suspected, spinal cord status may be monitored by MRI.

Bone loss or thinning of the bones can also be caused by long-term ADT. Controlling bone metastases and preventing bone thinning is an important part of care at this stage. There are a number of effective treatments. These include radiotherapy, radionuclides and drugs called bisphosphonates. Bisphosphonates have two roles: preventing bone thinning caused by ADT, and controlling bone metastases caused by the cancer. We discuss these later in this chapter. Use of low-dose radiotherapy ('spot-welding'), radioisotopes and bisphosphonates are very effective in controlling bone pain and limiting the progression of bone metastases.

8.3.2 Urinary symptoms and retention

Local cancer can recur after prostate removal. If the prostate growth blocks the outflow of urine from the bladder, you may experience slowing of the stream, increased frequency and other symptoms. If the flow of urine stops

altogether (called urinary retention), this is considered an emergency and you should seek medical help. It can be temporarily relieved by insertion of a catheter (a very thin, flexible tube passed along the urethra to the bladder). Then investigations can be undertaken to find the cause of the blockage and the best treatment.

Surgery (trans-urethral resection of the prostate or TURP) can effectively treat such blockages in the prostate region. If the blockage is closer to the kidney, other measures are possible. Radiotherapy can also be helpful in some cases.

8.3.3 Fatigue and other symptoms

In Chapter 7 we talked about fatigue caused by ADT. If cancer is in the bone marrow, it can reduce the number of blood-forming cells causing anaemia. This can be another source of tiredness. Your doctor can monitor this with a blood test. Fatigue may be experienced as physical fatigue and weakness, tiredness, or a lack of mental energy and initiative.

"You don't have the same speed, you don't take as much initiative now as before, you feel...well, it's a bit of a problem and you tend to just sit rather than doing something...something that you usually do".[3,64]

Tiredness may interfere with doing physically demanding activities, such as taking exercise or gardening. However it is by no means a universal experience.

Swelling in lower limbs can also occur if cancer is in the pelvic lymph nodes and causing fluid retention by either blocking lymphatic drainage or blood vessel flow. Mild exercise of the legs, massage and compression stockings can help the return circulation from the lower limbs.[65]

If metastases are in the liver they may cause a loss of appetite and weight loss or nausea, although nausea is not a common symptom at this stage.

Other symptoms can be due to treatments or medications themselves. For example, constipation can be caused by some pain medications, while others, such as steroids, have the potential to affect mood.

Every patient responds differently so these are all things to discuss with your urologist or medical oncologist. There are good medications that can deal effectively with symptoms such as nausea and constipation and also improve mood. Talk to your pharmacist and doctor if you need information on these drugs.

Remember to talk to your doctor if you are having symptoms such as nausea, pain, dizziness or limb weakness. These symptoms can be treated with drugs or by changing your treatment regimen.

8.4 Treatments for prostate cancer which is no longer responding to androgen deprivation therapy

Treatment for ADT-resistant prostate cancer is tailored to the individual. It depends on the treatments you have had previously, which ones are effective for you, your symptoms and how the disease is progressing. The doctor has a number of treatments to choose from. Some are best at controlling the cancer, some the symptoms, some both. The first approach generally taken is further androgen deprivation therapy (also called 'secondary hormone manipulation').

8.4.1 Further androgen deprivation therapy

Even when cancer becomes refractory to one form of androgen withdrawal, the androgen receptor in the cancer cells may remain active. For this reason androgen deprivation using LHRH analogue drugs is usually continued. In the initial approach to rising PSA levels, different types and combinations of ADT, called secondary hormone manipulation, can provide some benefit, reducing PSA levels in a proportion of patients for some months. The particular combination used depends on the previous ADT (*see Table 8.1*).

In a healthy man, a small amount of testosterone is produced by the adrenal glands. Use of drugs, which block this production, can have some benefit. Combining anti-androgens with drugs such as ketoconazole, (an antifungal drug which also blocks the production of male hormones by the adrenal glands), can extend the time to progression by several months.[49] More specific and potent drugs targeting this hormone production pathway are undergoing clinical trials to determine their effectiveness.

Patients who have not yet been taking an anti-androgen such as nilutamide, bicalutamide or flutamide (Anandron®, Cosudex®, Eulexin® respectively) in conjunction with an orchidectomy or LHRH agonist can be treated by adding this class of drug. This strategy blocks the remaining testosterone and testosterone-like hormones from driving cancer cells which are supersensitive to low levels of hormones.

Another treatment manipulation, which may lead to prostate cancer regression, is to stop the anti-androgen.

This is because these drugs can change from being an 'off switch' to an 'on switch' due to changes in the androgen receptor. Stopping this class of drug results in prostate cancer regression in about 10–15% of patients. A favourable response is more common in patients who have been receiving the agent for a protracted period. This is called 'anti-androgen withdrawal phenomenon'.

Some prostate cancer cells express oestrogen receptors, and oestrogens such as diethyl stilbestrol (DES) have been investigated as treatments. While they achieve a PSA response in patients, they also have side effects such as deep vein thrombosis and heart attack in a significant number of patients. Therefore oestrogens in an oral form are not normally used. An alternative delivery method is through the skin, as skin patches may avoid some side effects.

Oestrogens may be beneficial in preventing bone thinning, a common problem with long-term ADT. They may also have a role in replacing LHRH agonist therapy when the latter causes agitation and distress in some patients.

Table 8.1 After ADT fails, initial treatment depends on previous treatments

Previous Treatment	Treatment type	Drug	Where it acts	Action
Orchidectomy	Secondary hormonal manipulation	Anti-androgens	Androgen receptor in cancer cells	Competitively inhibits residual testosterone binding to androgen receptor
LHRH agonists	Secondary hormonal manipulation	Add or change anti-androgens	Androgen receptor in cancer cells	Competitively inhibits residual testosterone binding to androgen receptor
Complete androgen blockade	Secondary hormonal manipulation	Anti-androgen withdrawal: 4–6 weeks after discontinuing bicalutamide or flutamide[49]	Androgen receptor in cancer cells	Androgen receptor complex goes from being an 'off switch' to an 'on switch' due to changes in the receptor or the complex of proteins in the cell which regulate its function
Initial or secondary hormonal manipulation	Second-line treatments Steroids	ketoconazole, corticosteroids, prednisolone dexamethasone cyproterone	Adrenal glands	Inhibit adrenal synthesis of steroids by suppressing ACTH secretion from the pituitary Corticosteroids may reduce pain, fatigue
Initial or secondary hormonal manipulation	Second- line treatments Oestrogens	Diethyl-stilbestrol (DES)	Oestrogen receptor on cancer cell	Can cause clotting and heart attack. Trans-dermal delivery (skin patches) may reduce some of these effects

8.4.2 Tips for taking medications safely

The following tips could help you get the best out of your medication:

- Every prescription drug comes with a consumer information leaflet. These leaflets provide very useful information on risks, interactions and side effects. Ask your pharmacist for this leaflet whenever you are prescribed a new medication.
- If you are taking a number of medications at different times, your pharmacist can help you prepare a medication schedule to make it easier to remember which to take, how many and when. Alternatively they can pre-package your medications to make things simpler.

8.4.3 Chemotherapy

Chemotherapy is the use of certain drugs that act throughout the body to cause rapidly dividing cells to die. Because cancer cells are nearly always divide more rapidly than normal cells, chemotherapy kills cancer cells at a higher rate than normal cells. The therapy affects normal rapidly dividing cells such as those at the base of hair follicles, in the mouth and throughout the digestive system. Because of this, chemotherapy has significant side effects. The most effective chemotherapy drug for prostate cancer is docetaxel, trade named Taxotere®. This drug comes from the needles of the English yew plant, and is also used to treat other cancers, including breast cancer. It kills cancer cells by disrupting formation of the internal skeleton that allows cells to divide and multiply.

Like other agents, docetaxel is administered by injection or infusion. The infusion may take some time, often about an hour, and is therefore nearly always administered in hospital or a clinic. Side effects may include low blood counts, lethargy, hair loss, taste and nail changes, mouth sores, nausea and diarrhoea. Many of these can be managed or prevented with use of drugs and simple interventions. There are medications to prevent nausea and drugs to increase white blood cell counts. Currently there are no treatments for fatigue or hair loss. Sucking on ice while receiving treatment can prevent mouth problems.

Compared with other agents, docetaxel is the first chemotherapy agent that has been shown to increase a patient's chance of being alive at 12, 18 and 24 months after starting chemotherapy. In addition, despite its side effects, docetaxel helps maintain function and a satisfactory quality of life. One third of patients experience a decrease in pain.[49] Other agents such as mitoxantrone do not have an effect on the overall survival, but can improve quality of life by reducing pain.[66]

8.4.4 New treatments

New agents and approaches to treat prostate cancer are constantly being trialled. New chemotherapy agents to use after docetaxel are called second-line chemotherapy agents. Drugs that interrupt stages in the pathway to ADT independence are being developed. A new class of treatments being investigated, called targeted therapies, is designed to target pathways that are overactive in cancer cells and hopefully minimise damage to normal cells.

Your best access to new treatments is through a clinical trial, many of which are designed for men whose prostate cancer is not responding to ADT treatment. You can ask your doctor about the availability of trials that may be appropriate for you. Many have strict criteria for entry, which your doctor can explain. We discuss clinical trials and new treatments in Chapter 9.

8.5 Bone metastases and their treatments

8.5.1 Radiotherapy

Radiotherapy that targets metastases in bone is very effective and may control pain for many months. When used locally it has very few side effects, although it can cause side effects if it is close to vital organs.

This is why the radiation oncologist undertakes careful planning to line up the area to be irradiated. Be sure to ask your radiation oncologist about side effects when he recommends your treatment. Some areas in the body tolerate more radiation than others and can be treated more than once, whereas others can be treated only once.

Radiotherapy is also very important for decreasing the size of cancer deposits in very intricate areas such as the vertebrae. Untreated, these would grow and compress the spinal cord.

Radiotherapy for this purpose can be delivered as a single dose or 'fractionated'—the dose is smaller and given as fractions of the total dose over a series of repeat treatments. A single dose appears to be as effective as highly fractionated doses[21] and this may be more convenient, requiring fewer visits to the treatment centre. However, it may not be feasible if the area to be treated is near an important radiation-sensitive organ. It also increases the chance the area will require repeat treatment.

8.5.2 Radioisotopes

Bone-seeking radioisotopes are radioactive particles that emit low-dose energy radiation. When injected into a vein, they concentrate in the areas of bone that contain cancer and destroy the cancer cells by emitting radiation over a very short distance.

The most common types of radioisotopes are strontium-89 and samarium-153. Both of these agents are particles similar to calcium, and can provide pain relief in about 70% of patients. The maximum effect is usually within two to four weeks and it can last for periods exceeding three months.[66]

The most common side effect is mild suppression of bone marrow so that it produces fewer white cells or platelets (called thrombocytopenia) or fewer red cells (anaemia). Because marrow suppression can persist so that chemotherapy cannot be given,

radioisotopes are not used as frequently now as they used to be. They may take one to three weeks to have their maximum effect so they are not used when a more rapid effect is needed.

8.5.3 Bisphosphonates

Bisphosphonates are drugs that are active in bone metabolism. They prevent bone loss and have been used for many years to treat patients with osteoporosis or bone thinning. Recently some forms such as zoledronic acid (also known as zoledronate, brand name Zometa®) have also been used to minimise complications from bone metastases. They are thought to reduce cancer cell proliferation.

For men with bone metastases that are not causing significant symptoms, zoledronate has been found to reduce complications such as fractures and the development of bone pain caused by the cancer cells. It is the only bisphosphonate to have been shown to be of benefit in patients with prostate cancer.[21]

Zoledronate is more effective when used at in the early stages in the development of cancer that is unresponsive to ADT. It is approved on the Pharmaceutical Benefit Scheme for men who have bone metastases, disease growing and a castrate level of testosterone.

The drug is delivered every four weeks by injection. There appear to be few side effects of zoledronate treatment. Some fatigue, fevers and muscle pain may occur with the first few doses and can be prevented with paracetamol. High doses may affect kidney function. Changes in heart rhythm may also be a concern in some people. Recently there have been reports[67] of a complication called 'osteonecrosis of the jaw' (ONJ) in patients undergoing bisphosphonate therapy. This refers to areas of dead bone, not covered by gum in the jaw.

With prolonged use of zoledronic acid there is a 5% risk of this painful complication, even without any injury to the jaw. There is no treatment

to heal the problem, once started. Prolonged length of time on the drug is an important risk factor. Dental visits and good dental hygiene are recommended to prevent this from happening (*see below*).

Patients should be dentally fit before starting the medication. Symptoms may persist even when the drug is withdrawn.

Good dental health while on bisphosphonate therapy

The following are tips for maintaining good dental health while taking bisphosphonates.

- Have a dental check-up before beginning treatment.
- Be sure to tell your dentist you are being treated for cancer and with a bisphosphonate drug.
- Be sure to tell your doctor what medications, herbs and supplements you are taking—there can be interactions.
- Gum disease, poor dental health, poor blood circulation, smoking and alcohol abuse can increase your risk of osteonecrosis of the jaw.
- Once treatment has started, if you experience any pain in your mouth, teeth or jaw, or any other dental problems, tell both your dentist and oncologist immediately.
- Take care of your teeth by gentle brushing after every meal, flossing once a day, keeping your mouth moist by rinsing with water often, and avoiding use of mouthwash that contains alcohol.

Sources: www.us.zometa.com/info/cancer_bones/dental_health.jsp?site=zometa_us, www.nlm.nih.gov/medlineplus/druginfo/meds/a605023.html (accessed 20.4.09)

8.6 Looking after yourself

If you feel that the experience of illness is becoming too tiring and stressful, it may be time to revisit the strategies we discuss in Chapters 6, 10 and 11. Some of them, such as relaxation, guided imagery, taking things one day at a time, can get you through a low point. Friends, support organisations and help lines can also be useful if you need extra support. *See Resources sections*.

8.7 Resources

Clinical trials

Australia and New Zealand Clinical Trials Registry: www.actr.org.au

Cancer Council New South Wales Cancer Clinical Trials website: www.cancercouncil.com.au/editorial.asp?pageid=243

Cancer Research UK: www.cancerhelp.org.uk/help/default.asp?page=2849

UpToDate for Patients: Advanced Prostate cancer: www.uptodate.com/patients/content/topic.do?topicKey=cancer/4898

Information on bisphosphonates

Advanced Cancer Telephone Support Group: www.cancercouncil.com.au/editorial.asp?pageid=238

Cancer Council in your state: 13 11 20

Hormone Refractory Prostate Cancer website: www.hrpca.org

Medline Plus: www.nlm.nih.gov/medlineplus/druginfo/meds/a605023.html

Prostate Cancer Foundation of Australia affiliated peer support groups: www.pcfa.org.au or phone 1800 22 00 99

Chapter 9: Clinical Trials and Emerging Treatments

9.1 Key points

- New treatments must go through a series of trials before they become widely available. Joining a trial can be your best way of accessing a new treatment.
- There can be advantages and disadvantages to joining a clinical trial. We provide questions that can help you decide whether to join a trial.
- New treatments for each stage in the progression of advanced prostate cancer are being investigated.
- New treatments include new types of radiotherapy, new forms of androgen deprivation (hormone therapy), new chemotherapy agents, and a new class of treatment called immunotherapies or cancer vaccines. These have shown encouraging results.
- New approaches to psychosocial support and complementary therapies such as pomegranate juice and green tea are also the subjects of trials.
- Trials are being conducted on combinations of therapies that show a better result than either therapy on its own.
- Advances in prostate cancer treatment are likely to be made in small steps rather than large breakthroughs, but over time they can have a big impact on prostate cancer control.

New treatments for prostate cancer are continually being developed. These include new drugs, drug combinations, new types of radiotherapy, chemotherapy agents, vaccines and other approaches. There is a particular focus on new treatments for cancer that is no longer responding to androgen deprivation therapy.

9.2 Clinical trials

Before they can be widely used, new treatments go through a series of trials called phase 1, 2 and 3 trials. For new drugs, these trials establish the best way of administering the treatment: the best dose, its safety, and its side effects (particularly for new drugs). The effectiveness of the new treatment is also compared with standard treatment. Only when one phase has been successfully completed, can the new treatment proceed to the next. The different phases of trials are as follows:

9.2.1 Phase 1 trials

- are the first trials that involve people, rather than animals or laboratory experiments
- look at ways of delivering the treatment, how often and, if it involves medication, what dose is safe
- usually involve only a small number of people

9.2.2 Phase 2 trials

- continue to test the safety of the treatment using a defined dose and group of patients
- assess how well the new treatment seems to work
- involve a larger number of people (approximately 30 to 50)

9.2.3 Phase 3 trials

- compare the effectiveness of the new treatment to the best standard ('control') treatment
- assign people at random to receive the new treatment or the control treatment (meaning that neither you nor your doctor can choose which you receive)
- sometimes involve blinded treatment (meaning that neither the doctor nor you know whether you are receiving the new or the control treatment)

- usually involve a larger number of patients, often hundreds and occasionally thousands of people

By participating in a clinical trial you can gain access to new treatments before they are widely introduced. Because of their size, phase 3 trials are usually offered at many different treatment centres or hospitals around the country. They are the type of trial most accessible to patients.

9.2.4 How new drugs become available to Australian patients

These clinical trials are needed to prove a new drug is both safe and effective. Once this is shown, they may be eligible to be listed under the Pharmaceutical Benefits Scheme (PBS). Through the PBS the Australian Government subsidises the cost of many prescription medicines, making them more affordable. Around 80% of prescription medicines dispensed in Australia are subsidised under the PBS.

For a medicine to be subsidised by the PBS:

- the manufacturer must supply evidence of the benefit of the medicine to support a recommendation that it be listed
- the manufacturer must register the medicine with the Therapeutic Goods Administration (TGA) for the treatment of a specific condition (the TGA through assessment and testing ensures that medicines are safe and effective)
- the government's independent expert committee—the Pharmaceutical Benefits Advisory Committee (PBAC)—must evaluate the medicine, determine whether its benefits are worth the cost and if so, recommend it be listed on the PBS

As an example, Taxotere® (docetaxel) obtained listing on the PBS in 2007 for the treatment of men with prostate cancer that no longer responds to ADT. According to the trial data supplied by the manufacturer, the drug improved the chance a patient would be alive two years after starting the therapy by about 20% compared with another form

of chemotherapy. Before it was listed on the PBS, Taxotere® cost approximately $18,286 for the average course of treatment per patient. After listing on the PBS, patients pay no more than about $320 for a full course of treatment.

Non-prescription medicines such as herbal, vitamin, mineral and other alternative or complementary medicines and preparations are available without prescription at chemists, supermarkets and health product shops. These products can be considered for PBS listing but are subject to the same evidence-based requirements as other medicines. It is unusual for these types of clinical trials detailing the risks and benefits of a given herbal medication to have been conducted.

9.2.5 Finding a clinical trial

Clinical trials often have quite strict entry conditions that can restrict the acceptance of a willing potential volunteer. These may include the volunteer's age and require that he is generally healthy and available for visits to the trial centre. The trial may include only patients who are at a particular stage, have had a certain sequence of treatments, have a PSA within a certain range, and so on. For this reason, if you are interested in participating in a clinical trial, the first step is to discuss with your doctor whether there are any trials available that are suitable for you.

You can search for prostate cancer clinical trials yourself through trial registry websites. One of the most comprehensive is the Australian and New Zealand Clinical Trials Registry at www.anzctr.org.au. You can search for prostate cancer trials (use the advanced search function) and the listing will show the conditions for entry and whether the trial is still open (currently recruiting patients). The location of the trial and sometimes a contact person for public enquiries will be given.

9.2.6 Deciding whether to join a clinical trial

All trials require ethical approval from an ethics committee accredited by the National Health and Medical Research Council (NHMRC). Consequently investigators are required to disclose any risks for the patient and to describe what the patient will be asked to do. Your doctor should discuss with you:

- the expected course of your cancer and its outcome, with and without treatment
- possible benefits from both the standard treatment and the new one in the study
- any risks and side effects from the new treatment that might influence your decision
- where and how the treatment will be done
- where and how the follow-up will be done
- time and costs involved

You should be given a written information sheet, the opportunity to ask questions and time to consider your decision before completing the consent form. During the trial you have a right to withdraw at any time.

The decision about joining a trial depends on balancing the advantages and disadvantages. You should be confident that you understand these before going ahead.

In general terms, the pros and cons of participating in a clinical trial are given below. However, it may be helpful to make your own list for the specific trial you are considering.

Pros

- you might have access to a new, effective treatment
- you will receive the current best standard of care, even if you don't receive the new treatment
- you will receive closer medical attention and personalised care from doctors and nurses than is usual, although this is often the result of having to go through extra tests and answer more questions
- you are contributing to the growth of knowledge about new treatments—essential for the development of better treatment.

Cons

- the new treatment may not be effective or may be less effective than standard care
- you may not be in the group that receives the new treatment (in randomised studies)
- the new treatment may have side effects, including some in addition to those listed (which are as yet unknown)
- the side effects may be worse than those of standard treatments
- you may be required to attend a hospital or clinic more frequently, or the trial may involve you in extra tests and additional time-consuming tasks

9.2.7 Questions to ask when considering a clinical trial

The following checklist of questions may help you when discussing a clinical trial.

- Which treatments are being tested and why?
- What are the possible benefits to me or to others?
- What extra tests apart from my normal treatment will I be involved in?
- What are the possible risks or side effects?
- How long will the trial last?
- Will I need to go to hospital for treatment?
- What will I do if any problem occurs while I am in the trial?
- Can the trial affect my options for future treatment?

- Can I withdraw from the trial if I change my mind?
- Can I be on more than one trial at a time?

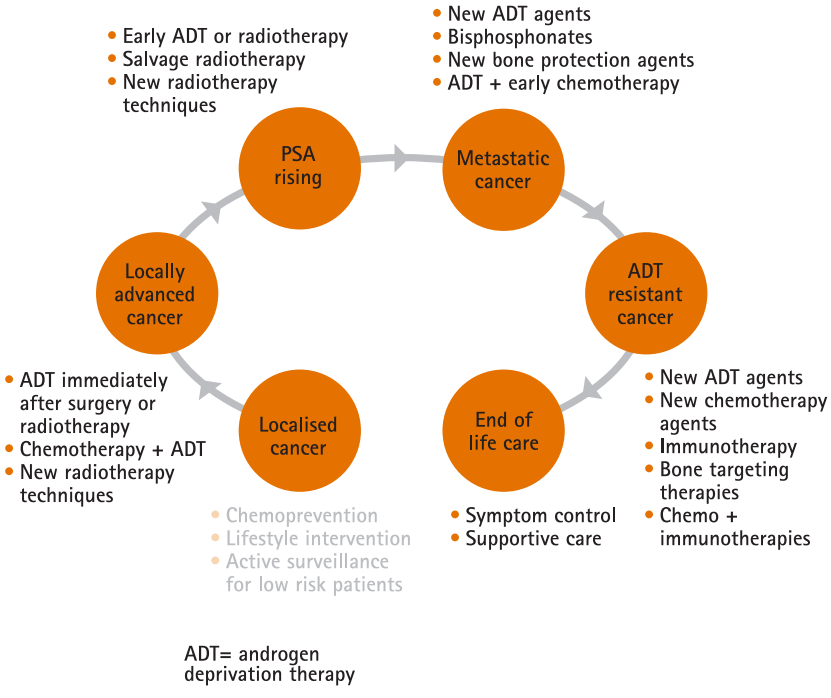
"The best thing about the trial was all the attention I was getting".

9.3 Emerging treatments

In this section we discuss treatments that are currently being investigated. Because these are still experimental, no recommendations can be made as yet.

Research into new prostate cancer control therapies has been occurring at all the stages of prostate cancer discussed in this guide. The different types of treatments at each stage are shown in the diagram. Some of the new agents (drugs) are listed in Figure 9.1

Figure 9.1: Emerging treatments currently in phase 3 trials



9.3.1 High-risk or locally advanced cancer

Radiotherapy is a common treatment recommendation for locally advanced prostate cancer. New methods of delivering radiotherapy, such as intensity-modulated radiotherapy (IMRT), are under investigation. Dose escalation (higher doses of radiation) increases cure rates and IMRT decreases the side effects of radiation. Further phase 3 trials are under way.

Adjuvant therapies are additional treatments offered with or immediately after the first one. Adjuvant therapies after surgery or radiotherapy are being investigated particularly for 'high risk' or locally advanced prostate cancer.

One recently launched phase 3 trial (radiotherapy adjuvant versus early salvage, or RAVES trial) for patients at high risk of recurrence following surgery (they have positive surgical margins or disease extending beyond the prostate) will compare whether 'salvage' radiotherapy given at PSA recurrence is as effective as earlier 'adjuvant' radiotherapy given within four months of radical prostatectomy.

Adjuvant androgen deprivation (hormone therapy) may be particularly helpful after radiotherapy or surgery.[68, 69] Adjuvant chemotherapy is also being investigated and combined with hormonal therapy. In some cases it is being used alone. Other studies combine chemotherapy with radiotherapy to try to improve cure rates of locally advanced prostate cancer.

This is a promising area of research. Its focus is on treatments used early in the progression of advanced prostate cancer, when the cancer cells are possibly less resistant to therapy.

9.3.2 PSA rising after surgery or radiotherapy

Sometimes there is a long period between the time the PSA first rises and the appearance of metastases. A number of studies are examining the possible benefits of treatment during this period. Starting hormone therapy early during this time appears to delay metastases in men with high-risk cancer, but not in all patients. It is also not known whether

the longer exposure to the harmful as well as beneficial effects of the hormone therapy means there is no improved overall survival.[70] The timing of androgen deprivation (TOAD) trial investigates whether starting androgen deprivation treatment immediately is better than starting the same treatment after two years or if the patient has symptoms or a rapidly rising PSA.

Salvage radiation therapy is another option for local recurrence after radical prostatectomy. Recent studies show that radiotherapy after surgery increases cure rates and survival if the cancer extends beyond the prostate into the tissue surrounding it (extraprostatic extension) or into the seminal vesicles, or if there are positive surgical margins (not all the cancer removed at surgery). A recent study suggests that the results are best if radiotherapy is started early—before PSA reaches 0.5ng/ml.[71]

A phase 2 trial described at the recent American Urological Society meeting reported that pomegranate juice taken daily by men with a low-to-moderate Gleason score but a rising PSA slowed the rate of this rise.[72] A phase 3 trial is now under way. There are no current recommendations regarding its use.

In the US, a trial is testing the effects on PSA levels of an intensive nutritional intervention comprising a low-fat diet high in fibre, fruits and vegetables, green tea and vitamin E. Another dietary trial for men with rising PSA tests the effects of lycopene plus vitamin E on the rate of change of PSA.[21]

9.3.3 Metastatic, androgen therapy responsive cancer

Androgen deprivation therapy (ADT) (*see Chapter 7*) is the standard care for men with metastases. New hormone therapy agents as well as different combinations and methods of delivery are being investigated. Continuing studies are evaluating whether ADT can be given intermittently to improve side effects without compromising

outcomes. Other trials are investigating whether bisphosphonates (drugs which interfere with the development of bone metastasis[73]) and the chemotherapy agent, docetaxel slow down progression if they are given when ADT is first started. In essence, these studies are asking whether chemotherapy (docetaxel) or Zometa® given when starting ADT is more effective than chemotherapy given only when the cancer is no longer responding to ADT.

For men on ADT, a number of trials are testing the effect of resistance training on body composition, bone density, fatigue and physical performance.[21]

9.3.4 How new drugs are licensed

Recommendations can be made on experimental drugs once they have finished their phase 3 trials. New drugs need to be approved by licensing bodies before being made available to patients outside clinical trials. In Australia, this body is the Therapeutic Goods Administration.

9.3.5 Metastatic prostate cancer no longer responding to ADT

Chemotherapy is the standard treatment normally offered when the cancer is no longer responding to hormone therapy. A number of studies are investigating whether adding another treatment to docetaxel, the main chemotherapy agent, can prolong its effectiveness (*see Table 9.1*).

Bisphosphonates are also used for patients with this type of cancer. They are known to prevent complications of bone metastases from prostate cancer when given before chemotherapy.[77]

Abiraterone is a new drug that targets the synthesis of testosterone wherever it occurs in the body, including within the cancer cells themselves. In earlier trials[74] this drug reduced PSA levels by half in 44% of patients who had prostate cancer that no longer responded to ADT. More recently, nearly three-quarters of patients were reported to have PSA reductions of 50% or more after 12 weeks of therapy.[75] A

large multicentre phase 3 trial is now underway in patients with disease growing despite a low circulating level of testosterone—both before and after chemotherapy. Abiraterone is taken orally and is often combined with prednisone to reduce side effects. It is hoped that better methods of androgen deprivation will lead to longer hormonal therapy control.

MDV3100 is a new synthetic anti-androgen drug. Unlike other anti-androgens, MDV3100 binds very tightly to the androgen receptor (AR) and stops its 'translocation' into the nucleus of the cell.

This prevents the AR from binding with DNA and stimulating prostate cancer growth. Taken orally, the drug has shown very high rates of PSA reduction (13/14 patients) in early studies. It will proceed to a phase 3 trial later this year.[76]

Satraplatin is an example of a chemotherapy drug that was evaluated recently as a second-line chemotherapeutic agent. It showed promise by increasing time to progression by 30%, however it did not show improvement in overall survival and was not able to be approved.

Immunotherapy is a particularly promising treatment approach. Usually the 'normal' immune system does not find it easy to eliminate cancers for a number of reasons: tumours are not good 'presenters' of antigens so that immune cells cannot recognise them as foreign cells and mount an attack. Antigens expressed by a tumour can vary over time and between patients, making it difficult to develop a vaccine in the way we do for infectious diseases. Unlike infectious diseases, the immune response to cancer cells is not perpetuated by 'memory' of an earlier exposure. This means that the body's immune response has to be helped or enhanced to become effective against the cancer.

Dendritic cells are immune cells that present antigens to other immune cells (T-cells), which then become 'armed' to seek and destroy cancer cells. In this type of therapy, blood is taken from the patient and his

immune cells are sensitised to antigens expressed by his prostate cancer and their numbers amplified. The large population of sensitised immune cells is then returned to the patient. In trials so far, there have been some very favourable responses to this approach, and some not so.

Sipuleucel-T immunotherapy (Provenge) is one of the earliest and most successful of this type of treatment and is well advanced in trials. A patient's blood is taken and the dendritic (immune) cells exposed to PAP (a protein secreted from the surface of 90–95% of prostate cancer cells) and GM-CSF (granulocyte macrophage colony stimulating factor) to enhance the response. The 'immune enhanced' blood is then returned to the patient. This is repeated in several cycles.

The results of a small phase 3 trial showed improvements in survival with 34% in the treatment group alive at three years compared with 11% in the placebo.[78] Results from a second and larger phase 3 trial were released at the American Urological Association's 2009 meeting. The results are similar.[79] Provenge improved three-year survival by 38%, with about 31% of patients who underwent immunotherapy surviving this long, compared to 23% of the placebo-treated patients according to investigator, Dr David Penson.

Bone targeting treatments. Tumours produce substances that attract cells (called osteoclasts) which break down bone. This process releases chemicals that in turn help the tumour cells grow. A number of treatments are being developed to block this process. One such drug is denosumab, which targets osteoclasts.

Endothelins are chemicals in bone which are known to stimulate metastases. New drugs are being developed which block endothelins from binding to their receptors. One of these is atrasentan. This drug showed promise in early trials. A phase 3 trial for men without metastases did not show an overall improvement in survival in treated patients but did show a trend towards a delay in the development of bone metastases.[80] Atrasentan has shown some synergy with the

chemotherapy drug docetaxel. Trials are continuing.

Another approach is to target an enzyme called cathepsin-k, which occurs entirely within osteoclasts. Suppressing this enzyme may prevent bone resorption and this is another area of promising research.

New chemotherapeutic combinations. There was much excitement when the first chemotherapeutic agent (docetaxel) was found to extend survival in men with castrate-resistant prostate cancer in 2004.[81] Since then, combinations with other drugs and treatments have been investigated and shown some promise. Studies include agents that target bone, tumour blood supply and the vitamin D receptor, as well as other chemotherapy agents such as Satraplatin (described above). Combining docetaxel with the immunotherapy has shown promise.[82] Some of these combinations, such as with immunotherapy, resulted in impressive improvements in survival and in quality of life. Further trials are being planned.

Table 9.1 Types of emerging therapies with examples

Type	Agent	Potential effect	Trial phase
New forms of androgen deprivation	Abiraterone MDV3100	May cause reductions in testosterone and PSA levels	3
Chemotherapeutic agents as single agents after docetaxel	Satraplatin Epothilones Pemetrexed	Chemotherapeutics which stop the ability of cancer cells to replicate by blocking processes such as new DNA production	2–3
Immunotherapies	Sipuleucel-T (Provenge®)	Enhance body's immune system to fight cancers	3
Selective Endothelin A Receptor Antagonist (SERA™)	Atrasentan Zibotentan	May block prostate cancer growing in bones	3
Anti-angiogenic drugs	Sunitinib Bevacizumab	Block new blood vessel formation (angiogenesis). Bevacizumab is a monoclonal antibody which targets vasculo-endothelial growth factor	Up to 3
Complementary therapies	pomegranate juice	May slow a rising PSA after treatment for localised prostate cancer[72]	3
Combination therapies with docetaxel	Docetaxel plus another anti-cancer agent: Calcitriol, Capecitabine, Thalidomide, Bevacizumab, Atrasentan	Attack cancer cells in different ways and hopefully more effective in overcoming cancer cell defences	Up to 3
Radiotherapy	Dose escalation IMRT Chemotherapy + radiotherapy	Kills more cancer cells and may increase cure rate Decreases side effects Kills more cancer cells and may increase cure rate	3 2–3 2–3

9.3.6 Other agents

Statins

Statins are drugs used to lower cholesterol levels in people at risk of cardiovascular disease. A number of observational studies have shown that statin use is correlated with lower risk of advanced prostate cancer.[83] It was also associated with lower rate of recurrence after prostate surgery in one recent study.[84] However these agents have not yet been tested in randomised trials and so it is possible these associations are due to factors other than statin use. This is a developing research area.

Green tea

A phase 2 clinical trial in 2003 found that green tea lowered PSA levels in 2% of men with prostate cancer that no longer responds to ADT.[85] Since then phase 1 and 2 trials have investigated its role in treating patients undergoing surgery for prostate cancer and in one continuing trial, its role in preventing prostate cancer. Green tea as a component of dietary supplements is also being investigated, including one phase 3 trial to see whether two dietary supplements can reduce PSA levels in patients with prostate cancer.[86] The trial is continuing.

Auron misheil therapy (AMT)

AMT, a blend of camomile extract, calcium, vitamins, antihistamine and insulin, is being trialed in patients with cancer that is no longer responsive to ADT to investigate its effects on symptoms, quality of life and overall survival.

It should be remembered that although some of these agents show promise, the full regimen of phase 1–3 trials must be completed before recommendations based on effectiveness and safety can be made.

9.3.7 New approaches to psychosocial support

The major funding bodies in Australia (Cancer Australia, *beyondblue*, Prostate Cancer Foundation of Australia—PCFA) are supporting research into new ways of providing support to men with prostate cancer and their families. Continuing studies investigate new ways of reducing psychological distress, supporting couples, and providing telephone support. This new focus on reducing the impact of the disease on the psychological wellbeing of men and their families adds to previous Queensland and NSW research on the support needs of men with prostate cancer and the beneficial effects of peer support groups.

Today all men diagnosed with prostate cancer and their families should have access to some form of support. This includes the peer support groups affiliated with the PCFA (*see below*), a specialised advanced prostate cancer telephone support pilot program run by Cancer Council Victoria, and the Cancer Council Helpline (*see Resources*). We cover this topic in Chapter 10.

9.3.8 Future developments

As with other cancer sites, prostate cancer research progresses in small steps rather than large breakthroughs. Nevertheless improvements at each stage can have a big impact on the overall course of the disease. Research suggests that combining treatments with different mechanisms may have synergistic effects—the results are better than with each treatment alone. Support for fundamental research—studies into the molecular processes involved in prostate carcinogenesis, clinical trials at all phases, patient participation and licensing of promising new treatments—are all essential to this process. This support will ensure that these incremental improvements continue into the future, giving ample reason to be optimistic about our ultimate capacity to control this disease.

9.4 Resources

Clinical trials

Australia and New Zealand Clinical Trials Registry: www.anzctr.org.au

Cancer Council New South Wales Cancer Clinical Trials website: www.cancercouncil.com.au/editorial.asp?pageid=243

National Prescribing Service Medicines Line: 1300 888 763
Australian service providing independent advice on prescription and over-the-counter medicines

NHMRC Clinical Trials Centre: www.ctc.usyd.edu.au

Pharmaceutical Benefits Scheme (PBS), Pharmaceutical Benefits Advisory Committee (PBAC) Pharmaceutical Benefits Scheme (PBS) and Therapeutic Goods Administration (TGA): www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-general-faq.htm-copy2

Therapeutic Goods Administration (TGA): www.tga.gov.au.
This website has a consumer section

US National Institute of Health Trials Registry: clinicaltrials.gov

WHO international Clinical Trials Search Platform: www.who.int/ictrp/en

Support

Cancer Council Helpline: 13 11 20 in each state

Prostate Cancer Foundation of Australia affiliated peer support groups: www.pcfa.org.au or phone 1800 22 00 99

9.5 Acknowledgement

We are grateful to Cancer Council NSW for permission to use material from their booklet: Understanding Clinical Trials: ww.cancercouncil.com.au/html/research/cancertrials/downloads/understanding_clinicaltrials.pdf

Chapter 10: Maintaining Your Wellbeing

10.1 Key points

- The return of cancer can be difficult to deal with. It can trigger many questions; grief, anger, fear and anxiety.
- Through peer support programs it can be reassuring to talk to others who have had this experience (see Resource section).
- Maintain open communication with your partner on all the important issues. Couples who face problems together do better.
- Use many different ways to maintain intimacy with your partner. Recognise and solve barriers to intimacy such as not wanting to upset or involve your partner.
- Men and women approach worry and problems in different ways. Recognise and accept each other's differences.
- Grief, anger and despair can be a potent mix. If you are feeling overwhelmed or you are losing interest in life, seek help from your doctor or the helplines listed under Resources. No man need travel this path alone. Your local support group or telephone helpline has people experienced in dealing with these issues.
- Maintain an active lifestyle that includes physical exercise and the normal activities you enjoy. Many men with advanced prostate cancer lead active lives as valued members of the community.

10.2 Worries and how to deal with them

Being told that you have cancer or that it has spread or returned can be devastating. Many men find it more difficult to deal with the recurrence of prostate cancer than it was to deal with the initial diagnosis. They experience a range of different emotions and may feel

shocked and overwhelmed. Some say they feel numb and unable to take in all that is being said.

"I had been worried because I knew my PSA was rising; but when my doctor finally told us the news, I was numb. I found myself in a daze for the first few weeks. I couldn't think straight. I just kept thinking that it couldn't be back ... there had to be a mistake. What did I do wrong for this to happen again?"

The news triggers many thoughts and questions. What does this mean? Can I have any further treatment? Am I going to die? Learning that your cancer is no longer curable threatens your sense of self, your way of life and your future. You may wonder: What can I expect? Can I keep doing the things I usually do? How much time do I have?

You may have a deep sense of loss and sadness. If you were previously treated, you may have thought you had been cured and now wonder if everything possible was done then. You may feel guilty or somehow responsible because your treatment has not worked. Other common reactions include feeling anxious or afraid about what the future may bring. Some men are confused or feel it is unfair (Why me?). Others feel angry.

"I felt really angry. How could this have happened? I had just retired when I was first diagnosed and we had to put off plans for our trip overseas. Joan and I have just begun to feel settled after my radiation treatment and now this! I feel as if my life has been taken away from me."

If you have these feelings, it is important to understand that you are not 'going crazy' and you are not 'weak'. You are having a normal reaction to a very difficult situation. Understanding your reaction can help you to manage these feelings better and regain a sense of normality.

Most of us have a particular way of responding to difficult situations, usually without giving it much thought. We learn and practise this approach to problems as we deal with the challenges of daily life. Some people get advice or seek information; some distract themselves by keeping busy; others talk about the problem. Religious faith or a sense of spirituality can also be a source of strength and comfort. There is no single best or right way of coping.

10.2.1 Things that may help

You may find the following helpful:

- Write down your worries and concerns and then identify practical steps you can take to address them.
- Talk to others about what is happening, especially your partner or a trusted friend. If you are uncomfortable talking to those close to you, a prostate cancer support group may be helpful.
- Peer support groups, provide patients, carers and family members with an opportunity to share experiences with others in a similar situation. It can be reassuring and helpful to meet with others who have dealt with these problems. The Prostate Cancer Foundation of Australia has a national network of affiliated support groups. The Cancer Council Helpline can also put you in touch with a trained support volunteer or counsellor (see Resources section for details).
- Allow yourself to feel sad or fearful from time to time. Remind yourself that this is to be expected given all that you are facing.
- Find ways to help manage stress. The aim of relaxation and stress management is not to make stress 'disappear', but to 'manage' it in a helpful way. See *beyondblue* Fact Sheet 6—Reducing stress.
- Structured education and support programs can relieve worries, improve wellbeing, and help maintain a positive outlook. Call the Cancer Council Helpline for programs in your area.

- Resistance exercise (i.e. weight bearing exercises) and moderate to strenuous physical activity can improve quality of life and muscular fitness and reduce fatigue. Talk to your GP for a referral to an exercise specialist. See Appendix 4 and *beyondblue* Fact Sheet 8—Keeping active.
- Draw on your strengths. Remind yourself of things that have helped you manage difficult times in the past and use these same strategies now.
- Don't expect to have all the answers. It is OK to feel unsure about the future.
- Keeping hope alive by allowing yourself plans and dreams.
- Spiritual guidance or counsel, as you adjust to the uncertainty of living with advanced cancer.
- Asking your doctor for help or talk with a mental health professional if you find that sadness or worry is affecting your relationships or interfering with your daily life. Also see the section below 'When things feel beyond repair: depression/anxiety'.

All *beyondblue* fact sheets are available from the *beyondblue* info line 1300 22 4636 or www.beyondblue.org.au.

10.2.2 The PSA test can be a worry trap

"It was hard for me to accept my doctor's advice to monitor my PSA levels only every six months. I wanted the test done monthly. Surely the sooner we noticed a change, the sooner we could do something different? He explained how my cancer could change in time and what the next steps might be. I still get jittery every time I go to see him for the latest results!" Ron 67 years

Managing your cancer over time usually means regular monitoring of PSA levels. This can be a source of worry as the time for the test approaches. It is important to learn how to manage the thoughts that cause anxiety. Our minds like to run away with thoughts of what might happen in the future, and usually it is the worst-case scenario! Taking control of your thinking can be as simple as staying focused on the facts you have in hand and what you know today.

It can also help to acknowledge you are worried and try to distance yourself from these thoughts. For example, try thinking about putting your worries in a box and closing the lid. Remind yourself that it is normal to be anxious about your results and give yourself permission to worry when you need to.

If you find worries are taking over your life and preventing you from enjoying normal activities, the section 'When things feel beyond repair: depression/anxiety' might prove helpful.

10.3 Maintaining intimacy and satisfying relationships

A loving and supportive partner can be a source of comfort and strength as you face the challenges of advanced prostate cancer as a couple. However, this experience can also put increased stress on your close relationships. Your world may feel as though it has turned upside down and making time to talk, share and stay connected can easily become a low priority.

Treatment for advanced prostate cancer often means lowering testosterone levels in the body. These changes commonly lead to lowering of sexual desire and arousal. This loss of sexual feeling may cause some men to see themselves as less masculine, particularly if they are dealing with other body changes from hormone therapy. The effect of this on their partner may also be a concern.

Some side effects of hormone therapy, such as lowering of sexual desire, hot flushes and weight gain, are talked about quite openly among men with prostate cancer. Other effects, such as breast enlargement and changes in the penis, may be kept more private. Some men are

frustrated to find that since they started hormone therapy, they are no longer as sharp mentally. They may be forgetful and feel 'foggy'. Others talk of being irritable and emotionally sensitive, crying easily and for no apparent reason. Fatigue and muscle weakness can interfere with usual routines and undermine a man's sense of usefulness.

The combined effects of diagnosis, treatment and side effects can induce a deep sense of loss. Some feel they are no longer the man they used to be and withdraw from their partner and friends. This can be an emotionally challenging time. Sex and desire may seem even more important now that they are gone and men may find their thoughts turning to the past and the memory of all that has been lost. Feelings of depression are common during this time of adjustment and some men feel there is nothing out there that could help.

Research has shown that couples who face problems together adjust better to the uncertainties of advanced cancer, as do men who have strong support networks, including family members and friends.

10.3.1 Things that can make it more difficult to stay connected

Keeping your feelings from your partner can make them feel 'shut out' and they may start to believe that you have stopped trusting or caring for them. Withdrawing also makes it very difficult for your partner to know how best to support you.

Some of the things that made it harder to stay connected are:

- being too busy with the increased demands on your time, for example, getting things done at work or around the house, attending doctor's appointments, and so on
- not knowing what you think or feel or not knowing how to put it into words
- a belief that there is no point talking or involving your partner as they won't understand
- a belief that there is no point involving your partner or that talking to them could make things worse
- not wanting to upset yourself by talking about difficult issues
- not wanting to upset others by bringing things up

"From a wife-carer point of view of wives and carers, it is very important to keep communicating".

10.3.2 Things you can do to build closeness and trust

- Share what is happening for you with your partner and accept each other's differences. It is common for partners to have different ways of coping when they are feeling down. One partner may want to talk while the other needs time alone to work out their feelings. Accepting these differences can help to prevent misunderstandings. We so easily assume that our view of the world is the only right one and that others see things just as we do.
- Invest in the relationship. It is especially important to do things together that build closeness, such as fun activities just for the two of you, and to find different ways to say 'I love you'. Happy couples tend to keep showing they care about each other. Some couples may find it helpful to actually sit down and talk about the small things they can do for each other to show caring and support during this time. This may be as simple as a cup of tea in bed in the morning or a back rub in the shower.
- Make time regularly to catch up and talk about how you are both managing. This can be as informal as having a coffee together or going out for a walk. Staying open and honest about your concerns helps you both feel connected.

- **Focus on the strengths in your relationships.** Hormone therapy causes many changes in your body and your sex life. This may lead you to think of yourself as less masculine and cause you to question your self worth. Reflecting on the strengths in your relationship, on your personal achievements and on what others value in you as a friend, a father, a brother can help you realise you are loved and valued for so much more than your physical abilities. Make some time to reflect on your life. Review the ways you have contributed through family, friends, work and community activities. This can help remind you of your achievements and strengths.
- **Work on intimacy every day.** Explore other ways to be physically close and experience sensual pleasure apart from sexual intercourse. Intimacy is about more than sexual closeness. Be flexible and open to different ways of expressing love and sharing pleasure. Physical touch can send powerful messages of love and care. How often do you look into your partner's eyes when you are talking; hold hands when you are walking or just hug each other?
- **Set goals and plan together.** Learning to talk together about your needs can help you find ways to move forward and strengthen your relationship. Remember to plan for things outside of 'cancer'; and to balance time together with time for your own individual activities as well as time spent with family and friends.
- **Use the supports around you.** Sometimes, it is easier to talk with a trusted friend or your doctor about your concerns. Your local Prostate Cancer Support Group can be a useful source of information and support.

10.3.3 Finding support: peer support groups

For men who live alone, are widowers or away from their family, the experience of a serious illness can be a very isolating. They miss not having a partner, family or friend to accompany them to appointments, discuss treatment issues and help them find additional information. If you are alone, it may help if you build up your support network in other ways. A number of approaches may be helpful.

For men with a partner, support groups can also help by providing the partner with additional contacts and opportunities to share information. They can provide man and partner with a support network, so that if one of you goes through a difficult period, the other has support.

Peer support groups have meetings with invited speakers who are often experts on prostate cancer. They have good libraries of resource material and provide a forum to discuss many issues. These groups are located around the country (*see Resources section*).

Cancer Councils also have information programs and peer support services that allow men to talk with others who have had a similar experience, and a help line which can provide contact details and answer questions. The Prostate Cancer Foundation of Australia gives information about where to find support groups.

A number of reputable 'chat rooms' and bulletin boards are now available on the Internet and may help connect men and provide updates (*see Resources section*).

Prostate cancer is a very common condition. Resources and supports have multiplied in recent years. These days, there is no reason for anyone to travel this path alone.

10.3.4 Dealing with grief and anger

Two particularly difficult emotions that may seem very much bound together are grief and anger. Grief experienced by men with advanced prostate cancer can be caused by a chain of losses—loss of health, loss of time with loved ones, loss of cherished plans such as being present at birthdays, anniversaries and other special times. Anger grows out of feeling powerless or being 'forced into a corner', of feeling that all of this

may have been preventable, of having a sense that an injustice was done, or out of being fearful.[87]

Men tend to respond to grief in different ways to women. They may not be as verbal, 'self-caring' or 'help-seeking'. In his book 'Taking care of yourself and your family', John Ashfield explains this:

"Men pay less attention to emotional pain than women, until those around them appear 'safe' and things appear in order. This is because men often distance themselves from the emotional content of difficult or 'threatening situations' in order to remain vigilant and caring to others."

Ashfield suggests that, on the other hand, men get benefit from 'activities, action, and mulling things over'. They benefit from 'the company of other men (or working alongside other men); not necessarily from any verbal exchange, but just by another man being "present" who cares, but doesn't intrude. Having time alone, writing down thoughts, spending time with supportive people is also helpful.

Anger is a normal and potentially powerful emotion. If used thoughtfully, it can energise and motivate us to face things previously ignored, solve problems constructively, even find a solution to injustice.[87] However, when used destructively, it can cause us to be thoughtless, impulsive, frequently blame others, accuse or be violent. Frequent or prolonged anger can affect our health and lead to relationship problems.

There are many approaches to dealing with anger. Active problem solving involves identifying the problem, understanding it, and working towards a solution. This can restore a sense of control and meaning.

Removing sources of physical stress, and relieving tension through exercise, relaxation, getting plenty of sleep and spending time with reliable friends can support this. However, if anger feels overwhelming,

seek professional help from your GP or nearest community health service. Ashfield suggests asking for someone with 'knowledge and experience appropriate to working with men'. Finding the right person is the key to effective assistance and you may need to travel to do this.

Debate and confusion continue to surround many aspects of prostate cancer—in particular who should be tested and which treatment presents the best chance of a cure. These critical decisions can change the complications experienced and perhaps the course of the disease.

Although it is not possible to really know what would have happened if another course were taken, a sense of feeling uninformed, misled, or not adequately cared for can justifiably cause anger and regret.

"When I originally asked my then GP about the test for prostate cancer, I was firmly rebuffed with a convoluted explanation about why a man should not be tested, if he had no symptoms ... to this day, I remain convinced that had I had a PSA test when I asked about it, I would have had a reasonable chance of an early detection, and a good chance of effecting a cure. This is what made me particularly angry."

Increasingly, health professionals are aware that men with prostate cancer need to be involved in the major testing and treatment decisions. The clinical practice guidelines covering PSA testing[88] and treatment[89] are clear on this, and increasingly practical guides and information are becoming available to help in making decisions.[90] These days, doctors have an important role in informing patients so that they can make these major decisions together.

There is no substitute for first-hand experience. Many men with prostate cancer have helped others by documenting their experience and in peer support groups by talking with other men about living with prostate cancer. Undoubtedly, the actions of these individuals have helped men who are seeking a good outcome by providing guidance and help. Peer

support of this type can help improve the experience of prostate cancer. See the Resource section for contact details for peer support groups.

10.4 When things seem beyond repair: depression and anxiety

For men who are going through a difficult period anyway, a prostate cancer diagnosis or a recurrence can seem like the final straw. It may seem impossible to understand and come to terms with the condition. Others deal well with the immediate issues, but see their enjoyment of life sliding away as time progresses, lacking motivation, an ability to enjoy life or the energy to take on their normal tasks.

For some men, these feelings are very intense or persist over a long time. The word 'depression' is often thought to mean sadness or a low mood. However, depression is more than just a low mood—it is an illness for which effective treatments are available. Having a depressed mood can extend beyond the issue of cancer and into all areas of a person's life. Men with depression can find it hard to carry out their normal daily activities.

Depression is very common.[91] About one in eight men will experience the condition during their lifetime. Men with prostate cancer are nearly twice as likely to experience depression[92] and partners of men with prostate cancer are also at higher risk of experiencing it.[91] The risk of depression is higher if a man has experienced depression before, or if his health condition makes it more difficult to remain active and connected with family and friends. Anxiety (worry and nervousness) and depression can be closely linked.

Men who are on androgen deprivation therapy may also be at increased risk of mood swings and depression because of changes in their testosterone levels. These men may also notice weight changes, tiredness, that they are more forgetful and they have trouble concentrating or making decisions. These changes are similar to the common signs of depression and so it can be hard to distinguish the two.

Being alert for depression is important because it can be managed with effective treatments. These include cognitive-behavioural approaches (changing ways of thinking), talking or interpersonal therapies, and medications. Appendix 7 includes a checklist from the *beyondblue* depression fact sheet that may be helpful.

More information on anxiety and depression is available from the *beyondblue* website and their fact sheets (*see Resources*). If you are not sure whether you have a depressive illness, it is important to consult a health professional. A GP, psychologist, psychiatrist, social worker or occupational therapist in mental health can help, although they may have different treatment approaches. There are Medicare rebates for these services when referred from a GP or other doctor. The *beyondblue* website and your state/territory Cancer Council may also be able to provide information on mental health professionals in your local region, particularly those who have experience in working with people with cancer. To find out more, call the Cancer Council Helpline on 13 11 20.

10.4.1 Tips for managing depression and/or anxiety

(*taken from beyondblue Fact Sheet 34*[91])

- Speak to a doctor about your concerns and discuss treatment options.
- Accept help, support and encouragement from family and friends.
- Reduce isolation by becoming involved in social activities.
- Exercise regularly (*see Appendix 4, beyondblue Fact Sheet 8—Keeping active*)
- Get enough sleep (*see beyondblue Fact Sheet 7—Sleeping well*)
- Allow yourself time to relax and reduce your stress (*see beyondblue Fact Sheet 6—Reducing stress*)
- Limit alcohol intake (*see beyondblue Fact Sheet 9—Reducing alcohol and other drugs*)

- Eat healthily and include a wide variety of nutritious foods. (*See beyondblue Fact Sheet 30—Healthy eating for people with depression, anxiety and related disorders*).

10.5 Resources and further help

National phone helplines

beyondblue Infoline: 1300 22 4636

Cancer Council Helpline: 13 11 20

Carers Australia: Counselling, advice, assistance 1800 242 636
Local services listed at www.carersaustralia.com.au

Life line: 13 11 14

Mensline Australia: 1300 789 978; www.menslineaus.org.au
National telephone support, information and referral service for men with family and relationship concerns

Multicultural Cancer Information Services: contact Cancer Council Helpline at 13 11 20

Prostate Cancer Foundation of Australia: 1800 22 00 99.

Support groups

Cancer Council Helpline: 13 11 20

Lions Australian Prostate Cancer Website: www.prostatehealth.org.au

Men's Sheds: www.mensheds.com.au

Prostate Cancer Foundation of Australia: 1800 22 00 99

Prostate Cancer Foundation of Australia affiliated peer support groups: www.pcfa.org.au or phone 1800 22 00 99

Bulletin boards, internet chat

New Prostate Cancer Infolink: prostatecancerinfolink.ning.com

Prostate Pointers: www.prostatepointers.org

Helpful books

Ashfield, J. Taking Care of Yourself and Your Family: a resource book for good mental health. 2008, Adelaide: Peacock Publications. 311. Available free from *beyondblue* infoline: 1300 22 4636, or online at www.beyondblue.org.au

Cancer Council New South Wales. Living with advanced cancer: a guide for people with advanced cancer, their families and friends. 2007, Sydney. Available from (02) 9334 1900 or online at www.cancercouncil.com.au

Additional resources

beyondblue website: www.beyondblue.org.au
Includes interactive checklists, fact sheets on anxiety, depression, information on available treatments, how to help someone with depression, how to reduce stress, sleeping well and many others.

beyondblue info line: 1300 22 4636
Order *beyondblue* resources, ask questions about signs, symptoms and available treatments or where to get help in your area.

Chapter 11: Partners, Families and Carers: Your Concerns

11.1 Key points

- Partners and carers of men with prostate cancer can find themselves on a long and difficult course. The following suggestions can make this easier:
- Maintain open communication with your partner, particularly on important issues. If this is difficult, this chapter includes ways to help.
- Maintain open communication with the specialist caring for your partner. Strategies that can help include attending consultations, taking notes, listing questions, asking for a longer consultation.
- Develop a communication plan with family and friends. One family member may offer to communicate with others. Accept offers of help—it can mean you have help, for example with household tasks, at critical times.
- You may take on new roles that can be stressful, both psychologically and physically. There is help available if needed through your doctor and respite care. Support groups can help you feel you are not dealing with this burden alone.
- Look after your self physically if you can—keep up as many of your normal activities as possible.
- If decisions are difficult or there are disagreements, try setting up a forum, for example with a trusted doctor or nurse, to discuss them.
- If you feel one of you needs psychological support, this chapter includes suggestions, and if it is your partner, some ways to discuss it with him.

As the partner of a man with prostate cancer, or a family member caring for a loved one, you may increasingly take on a new role—that of carer. This role has its own emotional, psychological and practical stresses. This chapter provides a brief overview of some of them and includes a Resources section.

11.2 Talking and communicating

11.2.1 With your partner

"He won't talk to me.'What do I say to make him feel better?"

Many people say that talking about the cancer with their partner is very difficult. This can be for a number of reasons. Withdrawal is a common way of coping with a problem that seems overwhelming. It may simply mean a person is thinking through the implications of the situation and needs time to do so. Alternatively, he may feel that talking about it may worry his partner and make things worse. Both the carer and the person with cancer may try to protect each other by avoiding topics that cause anxiety or are hard to discuss.

On the other hand, others may pine for life to be 'normal' again and want to exclude the cancer from daily conversation. Some say it becomes a shadow that intrudes on every conversation.

It is worth looking for ways to discuss what is happening, even though it is difficult. Putting thoughts into words can help you to see the situation in a different perspective and regain a sense of control. In doing this you can establish a communication process that will be invaluable in the future as new decisions have to be made.

"Even through the worst times, we've been reassured by what we have together and we hang onto the fact that we have a good relationship and we are not going to let this beat us."

If communication has not been strong point for you both, try to establish a forum for discussion. You can use outside expertise to do this. Carers may not be aware that they have access to social workers, psychologists and other allied help. Your GP could be a place to start. He or she can explain a lot of the uncertainty about the disease, as well as answering questions from both of you.

Some couples decide to have 'cancer-free days' where they don't mention the disease. This helps restore normal life, and it is reassuring to find that while this problem may be a part of your life now, it need not dominate.

11.2.2 With the doctor

Sometimes, if you don't go to the consultation with your partner, you may feel out of the information loop. Trying to understand the true situation can be frustrating. This is particularly true of sons and daughters of men with prostate cancer.

Not all specialists are good communicators, and even if you do attend, they may use terms you don't understand or speak too quickly for you to follow. A good doctor will check that the person with the illness understands, but there also are some things you can do to minimise this type of problem.

Before you visit the doctor, write down your questions (in case you forget them in the rush of the consultation). You can ask the doctor to write down the key points you need to know.

- Ask if you can audiotape the conversation. Some doctors are happy for consultations to be recorded, particularly if they are discussing treatment options.
- Take notes during the consultation.

- It is better if two people attend the consultation. If possible, accompany your family member when he visits the doctor. A support person can remind him later of things the doctor said that he may have forgotten or misunderstood.
- If you have lots of questions, ask for a longer appointment. It may help to do some research beforehand, particularly if there are words or terms you don't understand.
- Take an active role in the consultation. You have a crucial role in respecting and supporting the person you care for, so you need to feel confident about understanding the illness, the treatment, its impact and overall, and what to expect.
- Ask your doctor if there are any information resources, such as booklets or websites, which are trustworthy and relevant to your questions.
- Remember that 'framing' and viewing things from a different perspective can make a big difference. For example, 'Its cancer, but it can be treated' versus 'It's cancer, he's going to die'; 'This is a challenging project to be managed' rather than 'This is a miserable situation to be endured'.

11.2.3 With family and friends

You may find that you are fielding many phone calls and visits from family and friends and that this is becoming stressful and time-consuming. If someone offers to help, you can ask the person to take on this role, perhaps emailing a list of people who want to be updated.

Deciding when and how much to tell family members can be difficult, particularly if they live overseas or interstate. Decisions about when to come home can be very hard for family members who don't live nearby. Good communication with the doctor about prognosis can help make decisions like this.

When people ask if they can help, remember that you may need support from time to time, including respite for a day, help with driving, meal preparation and so on (*see Chapter 10*).

11.3 Emotional and psychological stresses

11.3.1 Changing roles

You may notice that the roles of you and your loved one are changing. This can affect both partners and children. In particular, you may notice a change in the way decisions are made. The carer may need to take on a decision-making role that previously belonged to their partner or father, especially on family issues. Nevertheless, the person himself may need to retain the decision-making role in relation to his illness and treatment to maintain his sense of autonomy and a sense of being in control of his life.[93] The man's need for privacy can also be a big issue and hard for the carer to negotiate. Some men have asked their partner not to tell the family. This can have the unintended consequence of cutting off sources of support for their partner. It is important to discuss the needs of both patient and carer.

If making decisions is causing stress, talk to your partner about what decisions need to be made now and which ones can be left until later. Listing the pros and cons of decisions that need to be made now, and discussing them from each of your perspectives, can help you make progress. Sometimes you may need to compromise. If necessary, decisions can be revisited later.

Carers often say they have no training for their new support roles and this can be stressful.

"Dad's supposed to be able to solve everything."

Family members may need to manage the finances, which they have never done before. Similarly, partners may feel isolated and alone in dealing with grief and anxiety, and adult children who until now have always deferred to their parents may need to take on the role of lead decision maker.

11.3.2 Grief and distress at the cancer's return

After treatment for prostate cancer, the regular program of PSA testing can be a source of tension and anxiety.

"We've been clear for years, but every time the test comes up, he goes a little bit quiet. It's the thing we dread and we just hope for zero."

In Chapter 10, we discuss the emotions men experience after the cancer returns. These apply equally to their partners or carers. If there is a recurrence, often years after the original treatment, some say that it is even more stressful than the original diagnosis.

"When you manage to get over it and it looms again, you withdraw. The challenge of facing it again can be harder than the first time."

The treatments and their side effects, pain, and changes in the appearance of a loved one can be very hard for partners or family members to witness. The situation may seem relentless. You may also feel angry at the demands placed on you and the need to give up things that are important to you. The demands of caring may be so physically demanding that you wonder how long you can keep it up. Manual assistance can include showering, toileting and moving a person.

"It's all right to feel miserable if you're not coping."

Things that may help:

- Do not hesitate to seek help with caring tasks. Help is available through your GP, your palliative care team and carer's services (*see Resources*).

- A good strategy is to try to keep as much of your normal life going as possible. Enlist the help of friends or family who have offered to help.
- Participate in activities that both you and your partner enjoy, for example, take a day off from caring for both of you—have a 'cancer-free day'.
- Support yourself physically and emotionally (*see Chapter 10*).

If the demands are overwhelming, there are people to support and help you, particularly if you have involved a palliative care team (*see Chapter 12*). Do not hesitate to discuss this with them or with your doctor.

11.3.3 Prostate cancer care issues

The treatments for advanced prostate cancer, particularly hormone therapy, can affect a man's emotional state, his levels of energy, his body shape and his libido. These can have profound effects on your lifestyle together.[94] Symptom control is discussed elsewhere in this guide, however every family has a different experience of this illness. It is important that you and your partner have a member of your medical team who you feel has some empathy and with whom you can talk frankly. If you don't have such a person, consider contacting your nearest palliative care team, the Carer's Association of Australia, or the relevant help lines (*see Resources section*).

As his illness progresses, his needs will change and you may have to rearrange the house so it remains comfortable. This could involve getting a chair for the shower or repositioning the bed so it is easier to lift and wash him. You may have to learn new skills along the way. Various programs such as palliative care and community nursing services can help you with this (*see Resources*).

Decisions about further treatment are not always straightforward. Some treatments may come with considerable side effects and there

may be times whether the patient and partner do not agree about the desirability of a particular treatment. Honouring the patient's wishes can be complicated, especially when other members of the family also have a view. *Poor communication on these very important issues can lead to misunderstandings and long-term feelings of exclusion and hurt*. If you need to, set up a forum to discuss these matters. You can draw on your doctors and other health professionals, such as oncology nurses, to assist you in these discussions.

One way to try to avoid this situation is to have a family talk, at an early stage of the disease, long before decisions have to be made at short notice. It is also a good idea for the family member with cancer to have a living will (*see Resources*) in which he can express his wishes clearly (*see Chapter 12 and Appendix 8*).

11.3.4 If the doctor says 'There is nothing more I can do.'

Sometimes a doctor may signal the end of his/her phase of care by saying, 'There's nothing more I can do.'

"He simply said: 'I am afraid that I can do no more for you.' That appeared to be the end of the matter ... with no word of the next steps, who would take over my care, such as pain control, palliative care, counselling, radiotherapy, etc. ... and around whom I should base that care."

While this may signal the end of one doctor's involvement, it is important to remember that this does not mean the end of treatment and care. As we said in Chapter 3, different types of doctors step in at different stages and take over the main role in care.

For example, you may see a medical oncologist, a urologist, radiation oncologist and palliative care specialist, each of whom can take over care which targets cancer control and symptom control at different times. If

you are not sure who is coordinating your care, discuss your treatment plan with your GP or any of your specialist doctors.

"That a doctor could not make some suggestions about where I could find help, or what action I could consider, absolutely astounded both of us. It was certainly left to us as to what we could do about any further action."

A strategy to avoid this situation is to have a treatment plan which you discuss with the doctor. The three goals—cancer control, symptom control and quality of life—are part of that plan. You can bring in different services, specialists and approaches at different times to provide support in meeting these goals. It can help to discuss things that are working and not working with the doctor, and treatments such as complementary therapy. We know that good cancer care is multidisciplinary—different types of specialists together develop a plan for you.

11.3.5 As a carer, you need to look after yourself

It goes without saying that looking after your own health is important for both you and your family member with cancer.

Keep well. Eat healthy foods and treat yourself occasionally. Exercise if you can. With some forms of exercise, such as yoga and tai chi, you don't need to leave the house once you have some training. Take breaks and get good sleep if possible. Meditation, relaxation and guided imagery can be helpful. Limit your alcohol intake and avoid other drugs.

Develop coping skills. Ask for assistance with tasks and meals from friends and family who have offered it. Set realistic goals. If something seems overwhelming, break it down into smaller tasks and take one step at a time. Don't forget to make time for other loved ones.

Manage your emotions. Find ways to blow off steam—physical activity, writing a journal, talking. Find a counsellor or support group, people who

can celebrate the ups with you, and support you through the downs. Some people seek spiritual advice. Don't forget to pat yourself on the back. Look for the symptoms of depression and anxiety in yourself and seek help at the earliest sign.

"It's taught me that whenever someone has something wrong with them, it can be a stressful time. You don't know how long it's for. It's important for carers to have a contact—someone to talk to."

Find respite. Make a plan early on for this—allow yourself time to relax and participate in enjoyable activities. Plan activities like social outings and time away. Nourish your spirit by engaging in activities that comfort you. Find ways to ease the load, for example, arrange help from your family and friends or take carer's leave from work.

"Maybe once you know how to care, you can do it again, even if the illness is different."

11.3.6 If you feel that one of you needs psychological support

It is not unusual for the experience of a chronic or terminal illness to trigger depression in some men and their carers. If, as a carer, you feel overwhelmed by the problems and see no end to it, it may affect your continuing mood. Depression can be experienced as a persistent loss of interest or pleasure in normal activities, or feeling sad, down or miserable most of the time.[87]

As we discussed in Chapter 10 and Appendix 7, there are questions you can ask which can help you work out whether you're experiencing a 'normal' part of the cancer progression, or whether you may be experiencing depression or anxiety. Your local doctor, the Cancer Council Helpline, and the *beyondblue* information line and website can help you talk about your concerns, and get help.

If it is your partner who is feeling down, it may be difficult to raise the issue. The free *beyondblue* book: *Taking care of yourself and your family* offers tips and suggestions:

- Talk to the person about how they are feeling.
- Listen to what the person is saying—sometimes when a person wants to talk, he/she isn't always seeking advice, but just needs to talk about his/her concerns.
- Use open-ended questions such as 'So tell me about...' which require more than a 'yes' or 'no' answer.
- If your conversation becomes difficult because the person you are talking to gets angry, stay calm, be firm, fair and consistent, admit if you're wrong. Don't lose control.
- Often just spending time with the person lets them know you care and can help you understand what they are going through.
- Encourage the person to seek professional help from the family doctor or a mental health worker.
- Take care of yourself. Supporting someone with depression can be demanding, so make sure you take time to look after yourself.

Changes in personality, such as becoming excessively withdrawn or uncharacteristically angry, may also be difficult to cope with and may be a response to either the condition or its treatment.

This may be a difficult burden for you, particularly if you too have continuing health problems or other issues. Don't hesitate to talk to your local doctor or specialist about such changes.

The *beyondblue Guide for carers* provides useful information about caring for people who are experiencing depression or anxiety and about caring for yourself (*see Resources section*).

The booklet *Reactions to prostate cancer: how to manage them* provides a more detailed account of the psychological stresses experienced by couples facing prostate cancer and how to manage them (*see Resources section*).

11.4 Resources and further help

National phone helplines

beyondblue Info line: 1300 22 4636

Carers' Association Helpline: 1800 242 636

Cancer Council Helpline: 13 11 20

Commonwealth Carelink: 1800 052 222

Life line: 13 11 14

Multicultural Cancer Information Services: 13 11 20

Prostate Cancer Foundation of Australia: 1800 22 00 99

Respite care

Commonwealth Respite and Carelink Centre 1800 052 222

Palliative care: 1800 660 055
To find a palliative care service in your area (or discuss it with your GP or specialist)

Support groups

Cancer Council Helpline: 13 11 20

Lions Australian Prostate Cancer Website: www.prostatehealth.org.au

Prostate Cancer Foundation of Australia: 1800 22 00 99

Prostate Cancer Foundation of Australia affiliated peer support groups: www.pcfa.org.au or phone 1800 22 00 99

(Partners are welcome at all PCFA support groups)

Further resources

beyondblue website: www.beyondblue.org.au
Interactive checklists, fact sheets on anxiety, depression, information on available treatments, how to help someone with depression, how to reduce stress, sleeping well, and many others.

beyondblue info line: 1300 22 4636
Order *beyondblue* resources, ask about signs, symptoms and available treatments or where to get help in your area

Bulletin boards, internet chat

New Prostate Cancer Infolink: prostatecancerinfolink.ning.com

Prostate Pointers: www.prostatepointers.org

(Both sites have partner/family chat groups)

Books

Ashfield J. *Taking Care of Yourself and Your Family: a resource book for good mental health*. 2008, Adelaide: Peacock Publications. 311. Available free from the *beyondblue* info line: 1300 22 4636 or website: www.beyondblue.org.au

beyondblue Guide for carers—supporting and caring for a person with depression, anxiety and/or a related disorder. Available free from the *beyondblue* info line: 1300 22 4636 or website: www.beyondblue.org.au

Cancer Council New South Wales, *Living with advanced cancer: a guide for people with advanced cancer, their families and friends*. 2007, Sydney: Available from www.cancercouncil.com.au, (02) 9334 1900

Cancer Council New South Wales, *Caring for someone with cancer*. 2007, Sydney. 48. Available from www.cancercouncil.com.au, (02) 9334 1900

Department of Veterans Affairs. *Carer's Booklet: assistance for the Veteran Community*. 2005. Available from 133 254 anywhere in Australia

Perlman G and Drescher J. *A gay man's guide to prostate cancer*. 2005: Haworth Medical Press, Birmingham NY.

Reactions to prostate cancer: Information on depression and anxiety for men living with prostate cancer and their partners. Available from *beyondblue* infoline: 1300 22 4636; Prostate Cancer Foundation of Australia 1800 22 00 99; or downloadable from their websites.

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Chapter 12: Palliative and End-of-Life Care

12.1 Key points

- Palliative care teams are experts in managing symptoms so that the patient is comfortable and pain free. They can offer care at any time in the progression of prostate cancer when management of complex symptoms is needed.
- Palliative care teams can arrange equipment and nursing and other services for those being cared for at home.
- Palliative care can be accessed through your doctor or you can self-refer. Call 1800 660 055 to find a local service.
- Pain control is an important part of care. Pain has many contributors which all need to be addressed. Do not put up with pain.
- Different types of medications are used for different levels of pain. Make sure you have at least one week's supply at all times.
- You and your partner can help to ensure pain relief is effective by keeping a record using a pain thermometer. This helps your doctor respond to breakthrough pain by changing your medication plan.
- We describe ways to deal with other symptoms such as weakness, lack of appetite, nausea and constipation.
- Many complementary therapies such as guided imagery, mediation, progressive relaxation can help you stay comfortable.
- Advance care plans can ensure that your wishes are implemented if you are unable to make decisions (*see Appendix 8*).
- Do not hesitate to let others—family, friends and your care team—take on things that have become a burden.
- Your palliative care team will support family members and carers throughout this time.

In this chapter we discuss the nature of palliative care, approaches to symptom control and some of the planning you can do and services which are helpful.

"Nothing in life is to be feared. It is only to be understood."
Marie Curie

Every cancer takes a different course at this stage and so care can be very different from one person to another. There may be different types of health professionals providing your care. A medical oncologist or urologist may be coordinating your care and you may have occasional treatments from a radiation oncologist. If problems such as availability develop with a particular specialist, it is not unusual to go back to your primary carer (GP) or seek help from another specialist. It is important at this stage to have someone with whom you feel comfortable and with whom you can discuss your overall treatment.

Your care continues to be aimed at controlling metastases where they occur, preventing complications and treating symptoms. Managing complications and symptoms can become quite complex. Palliative care physicians and nurses are experts at this, and can help with the management of symptoms both in hospital and at home. We are fortunate that Australia has excellent palliative care services in each state (*see Resources*).

12.2 Palliative care

If your prostate cancer or its treatments causes you to experience unpleasant symptoms such as pain, difficulty sleeping, nausea, tiredness, constipation, the approach used to control and manage these problems is called palliative care.

Palliative care can be provided to you at any time during your treatment for advanced prostate cancer and alongside other treatments.

The World Health Organization (WHO) describes palliative care as:

"An approach that improves quality of life for patients and families facing the problems associated with life-limiting illness, through the prevention of suffering by the early identification and impeccable assessment and treatment of pain and other symptoms, physical, psychological and spiritual."

Palliative care:

- works with you to provide relief from pain and other symptoms
- uses a team approach to address your needs
- offers support for your family
- offers a support system that encourages you to live as actively as possible until death
- affirms life and regards dying as a normal process
- intends neither to hasten nor postpone death

Palliative care is successful when you and your family feel comfortable and supported.

12.2.1 Coming to terms with what is happening for you

It is important to know that you can request palliative care at any time in your experience with advanced prostate cancer. It means that suffering can be prevented or managed so that you can better cope with what is happening to you. For example, most men are anxious about the effect of their cancer on those closest to them.

"My biggest worry was my wife's reaction when I was told that the cancer had progressed. The palliative care nurse was able to help her a lot."

The news that treatments are not working or are too risky can be disturbing. This is the time that palliative care can be most helpful to you. It can help you understand what to expect, how to prevent unpleasant symptoms and how to live a life that provides meaning and value for you. For some men, stopping anti-cancer treatments can provide a sense of relief from treatments that are unsuccessful, unpleasant and sap energy.

Because palliative care has the ability to enhance your quality of life it can also positively affect the course of your illness.

Although you may have gone through grieving since your diagnosis, this may be a time that deepens your grief and you may become withdrawn as you process your thoughts. This is a normal response. Your palliative care team is available to help if you are unable to progress to a calmer state of mind.

The palliative care team can assist you in making end-of-life decisions such as how to ensure you are not given treatments you do not want, and in making directions about the treatments that you would like to have as part of your medical care (*see Appendix 8*).

12.2.2 Coming to terms with what is happening for your partner, family and friends

Family members and carers also need information and support at this stage. They now have equal access to a care team that:

- encourages contact with spouses and family members
- discusses how family carers may provide care for you if you are no longer able to do everything for yourself
- provides your partner/family and carers with information and education about your care and your health progress

- coaches them through any problem that may occur for them or you (*refer A Caregiver's Guide p.7. See Resources.*)
- advises your carer/partner and monitors their wellbeing
- suggests when and how to get the supports you may need, such as equipment aids, help with showering etc

"Without palliative care I don't think I would have coped caring for Phil." A carer

12.2.3 When to access palliative care

Whenever there are symptoms such as pain, anxiety, depression, fear, spiritual distress, difficulties in deciding about treatments that are offered or family issues related to the illness, it is a good time to be in touch with palliative care. If things are just not right and you cannot explain it, the palliative care nurse or doctor can help you work through your problems and suggest helpful ways to proceed.

When you or your family are not coping with your symptoms and needs, it is a good time to access palliative care.

12.2.4 Is there a time limit to palliative care?

Palliative care is often required for short periods of time to help solve different issues that occur as a result of your cancer. The issues can be yours or your family's. Once the matter is addressed you will be referred back to your GP and/or specialist for the appropriate cancer-specific treatments and ongoing care. Sometimes you will have treatments such as radiotherapy whilst being cared for as a palliative care client. You can receive palliative care whenever you need it.

The level of care and support you and your family need is generally available in your own community.

12.2.5 Accessing palliative care

Usually your treating doctor or GP will refer you to the local palliative care service. However, family members and patients can self-refer to the local palliative care service. To find a service near you call 1800 660 055 or ask your doctor to refer you to your local palliative care service (*see Resources*).

It is a good idea to contact a palliative care service early. Once the service has your details, it can be quicker to initiate care when it is needed. The palliative care team will work with your usual doctor.

12.2.6 Providers of palliative care

Palliative care is an integral part of the standard clinical care delivered by health professionals. However, if a more specialised approach is needed or your needs are not being met by your usual treating team, your urologist, GP, oncologist, radiation therapist or visiting nurse can refer you to specialist palliative care.

Palliative care is most successful when a team approach is adopted. Your palliative care team may include any of the following:

- specialist palliative care doctors and nurses
- your general practitioner
- specialist doctors, such as urologist, radiation oncologist, cardiologist
- pharmacists
- physiotherapists
- psychologists, social workers, grief and bereavement counsellors
- occupational therapists
- pastoral care workers

12.2.7 Where is palliative care practised and delivered?

Where possible, palliative care is delivered where the person wants to be—at home (70% of Australians), in hospital (some have special palliative care units), hospice or aged care facility. Family, relatives and friends are the main caregivers for the majority of people with cancer throughout the course of the illness. Evidence shows that involvement of palliative care services also improves the life and health of caregivers [21].

12.2.7 What is a hospice?

A hospice is a place devoted to the care of people with life-limiting illnesses. Hospices are staffed by specially trained doctors, nurses, social workers, physiotherapists and volunteers who offer total care for patient and family. Hospice admission may be needed for a time to manage symptoms that have proved difficult to control. It can provide respite for a carer who needs a break, or who has become ill or exhausted. It is common for people to be discharged to home from hospices if their healthcare needs can be met at home. If your community does not have access to a hospice, the local hospital is usually able to provide palliative care on a short- to medium-term basis.

12.2.8 Aged care facility

Staff in aged care facilities have palliative care training and resources that allow people to receive excellent end-of-life care without having to relocate. When necessary, specialist palliative care teams can visit and consult to ensure the most appropriate and effective care is provided for you and your family.

12.2.9 Supportive care at home

Your palliative care team can organise the equipment you need and services that can help you to be cared for at home. This can include walking and lifting aids, or help with showering, for example.

12.2.10 Role for family and friends

You may find that drawing on family and friends to help with tasks can free you from some which are more physically difficult at this stage. Remember that having something to do can be particularly helpful for those who care deeply for you. Assigning tasks to friends or family can make them feel able to play a practical role in helping you. If family are overseas or remote, communication can be difficult, and one family member can take on this role. Your partner or close family member will also need support and someone to talk to. Consider talking to your medical and palliative care team to ensure that this is in place.

This is also a time to enjoy the company of children and grandchildren when you are feeling well. Some men find that taking the time to do something enjoyable and meaningful with those who are important to them and maintaining ‘normal’ activity as much as possible is important to their quality of life.

A sense of autonomy in decision making and a long history of keeping medical information private may make it difficult for some men to involve family members in their illness. If this occurs and becomes a problem, particularly for a carer, an open discussion about the extent of information sharing can be helpful, so that each person can understand and respect the other’s wishes while recognising their own needs.[93] Partners and carers face their own stresses, responsibilities and information needs that can go unrecognised.[95]

12.2.11 Symptom control at home

Pain

Not all men with advanced prostate cancer experience pain, but in common with other advanced cancers, pain occurs in about 70% of people. We have discussed the role of radiotherapy and bisphosphonates in controlling pain from bone metastases. Pain may

occur from other sources as well as these and its control is important in advanced prostate cancer.

The approach to pain control can vary depending on the intensity and duration of the pain as well as its cause (see Table 12.1). The first step in pain management is to have your pain professionally assessed.

Questions that your healthcare professional may ask when assessing your pain concern:

- the intensity of the pain (see below)
- the site of the pain
- the description of the pain eg, an ache, a stabbing pain, a burning pain, a spasm of pain etc.
- how long does the pain last?
- what brings it on or makes the pain worse?
- does the pain prevent you sleeping, eating, walking? Etc.
- what helps relieve the pain?
- apart from making you hurt, how does the pain make you feel?

Understanding the level of pain

There are several measures that help the doctor to understand the level of pain. One of these is the 'pain thermometer'—a 10-point scale shown beginning with 0, no pain at all to 10, the worst possible pain you can imagine.

Table 12.1: Types of treatments appropriate for different levels of pain.

Level	Description	Treatment	Names of drugs
0	No pain at all	None	
1–2	Annoying but bearable like a common headache	Over-the-counter remedy or even ignore the pain	paracetamol, ibuprofen
3–4	Too painful to ignore; you will look for a remedy	Prescription medicine	codeine,* oxycodone*
5–6	Interferes with your ability to focus on normal activities: stronger relief needed	Larger doses of prescription medications, if needed; long-acting prescription medication You require pain control that is continuous	oxycodone* morphine* fentanyl*
7–9	Pain is almost unbearable. Dealing with pain has taken over your life. You cannot do normal activities	May require hospitalisation. Intravenous medications ramped up to find effective dose and use of medications that work on specific pain mechanisms in combination with the pain-specific drugs such as morphine, etc.	morphine*, oxycodone*, fentanyl* Drugs that may be added at any time in your pain experience, according to the cause (eg nerve irritation): – antidepressants – steroids – anticonvulsants – local anaesthetic (called adjuvant pain control)
10	Worst pain you've ever had; unbearable	Increased and/or multiple drugs, surgical or invasive options	Combinations of the above and constant attention from a trained health care professional until your pain is relieved

* *prescription only* Table drawn from Institute for Continuing Health Care Education: Living with advanced prostate cancer[96]

Medications that give relief from pain are called analgesics. Two types of analgesics are called opioids and non-opioids by the WHO. Non-opioids include over-the-counter medications such as paracetamol and ibuprofen. Opioids are used for moderate to severe pain and include morphine, fentanyl and oxycodone. Note that all opioids have the potential to cause constipation—laxatives are normally required to be taken on a regular basis to control constipation.

Some useful things to remember about pain control:

- You may have other symptoms or circumstances that contribute to pain such as nausea, worry, fear, boredom and loneliness, which should also be addressed.
- Depending on these factors, your doctor may recommend a particular treatment or medication and way of taking it (tablets, injections, patches, suppositories are possible).
- It helps to keep a record or journal of the medication, any positive or negative side effects, and the level of pain while you are on it. If you experience a return of pain before the next dose is due, this is called 'breakthrough pain'. Keeping a record helps with ensuring your treatment plan is effective.
- Whenever you have pain that is present around the clock, your pain medication needs to be formulated for continuous relief. All opioids can be administered in this way either as tablets, infusions or patches.

Taking opioids (such as morphine) for cancer pain does not cause addiction—your pain medication is part of your treatment.

You have an important role in achieving good pain control!

- Communicate your pain levels to your care team. Recording your pain levels and medication is an excellent way of letting the team know your pain status and the effectiveness of the plan to date. Your partner or family member can help with this. Do not be afraid to contact your care team and ask for assistance if the plan needs to be updated. For example, you are experiencing breakthrough pain and need to modify dosages or delivery methods.
- Mild pain is easier to control than severe pain, so keep to your pain medication schedule even if you are not feeling pain. This may involve setting an alarm to wake for medication at night. However, long-acting medications are available to such disturbances. It also means that you should report pain and not 'tough it out'.
- 'Multimodal' methods or using several approaches at once can be most effective. Many of the complementary therapies—progressive relaxation, guided imagery, meditation, heat, ice, gentle exercise and hypnosis—can help to control or modify the pain. Your carer can help you with much of this. We recommend the chapter on complementary care in *A caregiver's guide* (*see Resources*) for details of how to use some of these.
- Be prepared. Make sure you have at least one week's supply of medications at all times. Make sure you have contact details and know who to contact on your care team should the situation change.
- Continue with your life—the activities that give you distraction, purpose and joy. In their booklet *Living with Advanced Prostate Cancer*, the US-based Institute for Continuing Health Care Education states: 'Athletes, soldiers, artists and volunteers know that when you are involved and engaged in pastimes and goals that are important to you, you tend to be less aware of pain'.

What you can do if your pain is not controlled and the care provider (doctor or other) is not responding to your distress

If your pain disables you, ask your carer to do the following for you. Do not give up until there is an acceptable response and you (and your carer) feel comfortable and supported.

- Contact your health care professional again
- Describe your pain/distress
- Describe the effect of your pain medication or the pain you are experiencing
- Request an urgent reassessment

People receiving palliative care services need to feel comfortable in contacting their professional care providers at any time because there is a clear understanding that issues affecting your comfort are paramount and can occur at anytime.

Your palliative care service provider will make sure you have a 24-hour number to call and a plan for this type of emergency. Palliative care service providers plan for the worst whilst hoping for the best!

12.2.12 Other symptoms

Symptoms such as pain and tiredness can be caused by the cancer or arise out of treatments or complications (new conditions) caused by the cancer or treatments. Some of these symptoms are shown in Table 12.2.

Table 12.2: How to manage symptoms

Symptom	Description	Ways to manage
Fatigue	Persistent feeling of tiredness or a complete lack of energy that is unrelieved by rest or sleep Fatigue is a common symptom in advanced cancers and may not have an identifiable other cause	Ask your doctor or nurse to assess your fatigue for any reversible causes such as depression, anaemia, worry/anxiety, treatment side effects, infection etc. - Plan activity when energy levels are best - Prioritise your activities - Do not do too many activities in a short period of time - Try mild exercise such as walking to help you feel more energised - Establish good sleep habits - Avoid stimulants such as coffee and alcohol before bed - Practice relaxation techniques There are some medications such as low dose corticosteroids and psycho stimulants that may help—your doctor can discuss and advise you.
Weakness	Loss of strength Tiredness after activities that were once easy, eg moving about, moving in bed, dressing, bathing	Managing weakness is similar in many ways to managing fatigue. The treatment for this symptom is to reverse the reversible and find a balance between rest and activity that is restorative, calming and healing. Consultation and assessment with your doctor and nurse are important in managing this symptom.

Table continues next page

Table 12.2: How to manage symptoms (continued)

Symptom	Description	Ways to manage
Lack of appetite (anorexia)	Absence of interest, desire or energy to eat Your doctor and nurse can provide valuable insights and guidance for dealing with anorexia	Medical assessment and treatment of reversible causes - Check that dentures still fit correctly - Provide nutritional support, especially orally (refer to *A Caregiver's Guide* in *Resource* section) - Ensure any food is taken in the normal social setting if possible, even if only small amounts are consumed - Don't focus on quantity as much as balance and enjoyment - Don't overwhelm with a large array of 'special' foods—it is better to eat serves of well-liked, nutritious foods - Small serves are less off-putting - Check that the smell of the food is not off-putting—prepare food where cooking smells can be lessened where possible Lack of appetite can be more upsetting for family and caregivers than for you, however it is a normal part of the end stage of advanced cancer.
Constipation	When you have a bowel motion a stool is passed. Constipation means difficulty passing a stool	Common causes of constipation include not drinking sufficient fluids or eating enough food, lack of fibre in the diet, insufficient physical activity, slowing of your gut cased by medications such as morphine, codeine, oxycodone, etc. and certain diseases. - Try and correct any of the above that you can - Take laxatives if you are on opioids—your doctor or nurse can advise the best ones for you and your problem If you have no appetite, weakness and fatigue, do not eat high-fibre foods unless you can easily drink sufficient water. Call for help if you notice blood in or around the anal area or in the bowel movement.

Table continues next page

Table 12.2: How to manage symptoms (continued)

Symptom	Description	Ways to manage
Diarrhoea	The passing of loose or watery bowel movements 3 or more times a day	Treatment is aimed at ensuring the body's fluid and chemical balance is maintained and keeping the bowels moving. Diarrhoea may be overflow of liquid bowel movement around hard bowel movement and is a consequence of untreated constipation. Take fluids often when diarrhoea is present. Avoid foods that have a stimulating effect on the bowel such as whole grains, fried and greasy food, raw fruit/ juices/vegetables, carbonated drinks, strong spices and herbs, caffeine, alcohol and tobacco products when diarrhoea is present. Call your doctor/nurse if you: - have six or more loose bowel movements for two days or more - notice blood in or around the anal area or in the bowel movement - at any time if the diarrhoea makes life unmanageable for you or your carer
Mouth sores, funny taste	Little cuts or ulcers in the mouth	Possible causes: chemotherapy, radiation therapy, infection, lack of fluids, poor oral hygiene, oxygen therapy, alcohol and tobacco use and some medications. - Check inside the mouth twice a day for ulcers, white patches (thrush) - Report changes in taste sensations to your doctor or nurse - 30 minutes after eating clean teeth and rinse mouth with water or weak solution of ½ teaspoon salt, 1 teaspoon bicarbonate of soda and 4 cups water. Use a soft toothbrush. Only use commercial mouthwashes ordered by your doctor
Pins and needles, numbness	Occurs when the cancer affects bones in the spine and pressure is placed upon the nerves in the spine	Back pain is often the first sign of spinal cord compression. If back pain, pins and needles or numbness occurs medical treatment is needed urgently to prevent paralysis (usually steroids and radiation treatment).

Table continues next page

Table 12.2: How to manage symptoms (continued)

Symptom	Description	Ways to manage
Difficulty sleeping	Inability to go to sleep, waking after a couple of hours or less, restlessness, disturbing dreams that wake you	Being relaxed as possible at bedtime helps, (warm bath, warm milk, relaxation techniques) can all help at this time and it can be helpful, and it is quite OK, to take sleeping pills. If you have a lot on your mind it is good to speak with someone about anything that is worrying you—this is half way to solving any problem.
Incontinence	Incontinence is the accidental or involuntary loss of urine from the bladder (urinary incontinence) or bowel motion, faeces or wind from the bowel (faecal or bowel incontinence) (Continence Foundation of Australia definition)	Treat causes where possible. Continence needs to be controlled to maintain your dignity, provide comfort and prevent the breakdown of skin. There are many ways this can be achieved—your doctor and nurse will be able to work with you to provide the best solution. For skin comfort there are many creams that are water-repellent and soothing. Leakage that is not sufficiently contained using pads and other products may require a urinary catheter or a condom with a drain attached.
Nausea or vomiting	Feeling sick with or without vomiting Anyone who has been sea-sick knows how overwhelming this feeling can be	Nausea and vomiting can have many causes, including illness, medication, irritation of the digestive system, infection, constipation or movement. Sometimes it may have no connection to advanced prostate cancer and could be influenza or food poisoning. In life-limiting illness, nausea and vomiting may be more severe and so if present need prompt assessment and treatment. Anti-emetics (drugs to prevent vomiting) such as Maxolon® or Stemetil® may be prescribed. - Keep a record of nausea (present/absent) and the amount and appearance of vomit in your record. - Notify your doctor or nurse immediately if blood or material that resembles coffee grounds is in the vomit. - Try and sip fluids or ice chips to maintain hydration while you are awake. - Notify the doctor or nurse if you cannot keep medications down.

Your palliative care team can discuss any symptoms with you and your partner and the best approach to managing them. Often specialist nurses, such as a palliative care nurse or continence nurse, can help if problems arise. Contact details are given in the Resources section.

12.3 Things you can do for the future

A new idea that has been developed recently is to leave thoughts and messages for family members and loved ones. Most people prepare a legal will to pass on their material possessions but many want to leave more than just things. They want to leave a sense of themselves, of their love, their beliefs, their memories and their experiences. They want to leave a will from their heart, a heart will.

This is not difficult to do and can take any form you like. You could leave letters for your loved ones, record a tape, make a video, compile a CD of your favourite songs, create something online or just buy a notebook from the newsagent and put down thoughts, bits of family wisdom or life advice for the next generation. You could get a shoe-box and fill it with significant photos and cards for special birthdays in the future. You can use your own creative ideas to leave behind a lasting gift of love. A heart will is a way to be heard when your voice is still.

12.4 Advance care planning

In most states and territories you can make advance plans for your care that can be implemented if you are unable to make your own decisions. These plans are known by various names: wills, enduring powers of attorney, guardianship orders, advance directives, living wills, medical powers of attorney, etc. Some of these terms are taken from applicable legislation; others are standard terms in everyday use. See Appendix 8 for descriptions of these terms, how to implement them, and other legal and financial topics.

12.5 Conclusions

In this chapter, we have described some of the care options and resources that can help you to be comfortable and active as long as possible. Planning and preparation can help deal with some of the issues that may arise. It is a time to let others—family, friends and your care team take on things that have become difficult.

Your loved ones can also draw on your care team should they need them. Palliative care professionals understand fully the participation of your family in providing you with support and care and it is their goal to make sure your family is treated with understanding and compassion for as long as is needed.

12.6 Resources

Palliative care organisations

Nationwide contact telephone number is 1800 660 055

Palliative Care Council of NSW
T: 0403 699 491
E: info@palliativecarensw.org.au
W: ww.palliativecarensw.org.au

Palliative Care Council of SA
T: (08) 8291 4137
E: pallcare@pallcare.asn.au
W: www.pallcare.asn.au

Palliative Care Queensland
T: 07 36330096
E: info@pallcareqld.com
W: www.palliativecareqld.org.au

Tasmanian Association for
Hospice and Palliative Care
T: 03 6234 7577
E: enquiries@palliativecareqld.org.au
E: tahpc@associationoffices.com.au

Palliative Care Victoria
T: 03 9662 9644
E: info@pallcarevic.asn.au
W: www.pallcarevic.asn.au

Palliative Care ACT
T: 02 6273 9606
E: actpc@bigpond.com

Palliative Care WA
T: 08 9212 4330
E: pcwainc@palliativecarewa.asn.au
W: www.palliativecarewa.asn.au

Palliative Care NT
T: 08 8922 8824
E: moq13026@hcinternet.com.au

Books and guides

A caregiver's guide: a handbook about end-of-life care. Palliative Care Council of SA Inc. 2007. 202 Greenhill Rd, Eastwood, 5063

Food and cancer: a guide to nutrition for people with cancer. Cancer Council NSW. Available at www.cancercouncil.com.au/editorial.asp?pageid=192

Managing Cancer Pain, Pain Relief Foundation. Available at www.painrelieffoundation.org.uk

Overcoming and controlling cancer pain. Booklet from Cancer Council NSW available at: www.cancercouncil.com.au/html/patientsfamiliesfriends/livingwithcancer/cancerpain/downloads/overcoming_cancer_pain.pdf

Understanding palliative care: a guide for people with cancer, their families, carers and friends: Cancer Council NSW. Available at: www.cancercouncil.com.au/editorial.asp?pageid=1957

What is anorexia? Canadian Virtual Hospice: www.virtualhospice.ca

Other resources

Aged Care Australia: www.agedcareaustralia.gov.au
Commonwealth Government's Aged Care Website

Caresearch: www.caresearch.com.au/Caresearch/Default.aspx
Website for information on all aspects of palliative care

Peer Support

Prostate Cancer Foundation of Australia affiliated peer support groups: www.pcfa.org.au or phone 1800 22 00 99

Appendix 1: Staging and the TNM System

'Staging' refers to finding out how far the cancer has spread.

This is investigated in a number of different ways. Initially, at the digital rectal examination, the surgeon notes whether he or she can feel the tumour as a nodule or irregularity on the prostate, and if so, whether it extends beyond the prostate itself. This is referred to as clinical staging. However, the exact stage is not easy to determine from a clinical examination. Sometimes the number of biopsy cores with cancer in them is reported by the pathologist, and gives an indication of the extent of the cancer. If surgery is completed and the prostate removed, staging can be determined more precisely by pathological (using a microscope) examination of the prostate tissue and surrounding organs that have been removed. This is called pathological staging.

TNM system

This is a system for recording how far the cancer has spread. 'T' refers to tumour, 'N' to node and 'M' to metastasis. The system is used around the world to stage cancers that develop as tumours and metastasise. In the TNM system for prostate cancer, this more detailed version shows the stages for advanced prostate cancer. Prostate cancer does not necessarily progress in a sequential manner, as this implies, however.

- Stage T1–T2c—Organ-confined disease
- Stage T3a—Extracapsular extension of the tumour
- Stage T3b—Invasion of the seminal vesicle(s)
- Stage T4—Tumour fixed or tumour invading adjacent structures other than seminal vesicles (eg, bladder neck, external sphincter, rectum, levator muscles, and/or pelvic floor)
- Stage NX—Regional lymph nodes cannot be assessed
- Stage N0—No regional lymph node metastasis
- Stage N1—Regional lymph node(s) metastasis
- Stage MX—Distant metastasis cannot be assessed.
- Stage M0—No distant metastasis
- Stage M1—Distant metastasis
- Stage M1a—Distant metastasis other than regional lymph nodes
- Stage M1b—Metastasis to bone(s)
- Stage M1c—Other site(s)
- Stage pM1c—Metastasis to more than one site

Appendix 2: The Gleason Grading System

Grading systems score how abnormal the tissue looks under the microscope. This is also related to how fast the cancer is likely to grow. Sometimes a pathology report refers to tissue as 'poorly differentiated'. This is another way of saying that the tissue does not look like the normal tissue (fully differentiated).

The main system for grading tissue taken at biopsy is the Gleason grading system. The higher the Gleason score, the more aggressive the cancer, and the faster it is likely to grow. The pathologist identifies the two most common tissue patterns and gives them a score from 1 (most normal or differentiated) to 5 (most abnormal or poorly differentiated). The Gleason score is given as two numbers added together to give a score out of 10 (for example, 3 + 4 = 7). The first number is the most common pattern seen under the microscope and the second number is the next most common. This means that a Gleason 4 + 3 is more aggressive than 3 + 4. A total Gleason score of less than 6 is rarely reported.

Gleason scores reflect the 'risk' posed by the cancer.

- Low risk: low grade, well-differentiated tumour, Gleason score 2–6
- Intermediate risk: intermediate grade, moderately differentiated, Gleason score 7
- High risk: high grade, poorly differentiated, Gleason score 8–10

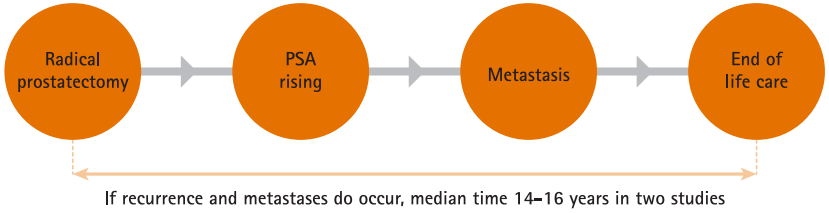
These risk categories are those adopted in the American Urological Association 2006 Clinical Practice Guidelines for Localised Prostate Cancer and the National Cancer Control Network Practice Guidelines in Oncology version 2.2009 Prostate Cancer: www.nccn.org/professionals/physician_gls/PDF/prostate.pdf

Appendix 3: PSA rising—What Does It Mean?

After surgery or radiotherapy for localised prostate cancer, the PSA usually stays low for many years or indefinitely. But if it starts to rise again, some men say they wonder what it means. 'Does it mean I'll be dead tomorrow?' they ask. The answer is definitely 'No'. In fact a low PSA, even if rising, usually means the cancer is still at an early stage, and it can be many years before it progresses to the next stage. Several studies have looked at this question

One study of men undergoing radical prostatectomy found that at 15 years, 82% of them remained free of metastasis. For those men who did develop metastases, the median time after the first signs of PSA rising to the development of metastases was 8 years.[6] Two other studies found that for men who did ultimately died from prostate cancer, the median time this occurred after surgery was 14–16 years (median means 50% experienced longer, 50% shorter times).[7, 97]

This means there is often ample time to make changes in lifestyle and undertake the treatments that may alter the course of the disease. We discuss these in Chapters 4, 5 and 6.



Median = mid point
Half of the patients take longer, half take shorter time

For those who are interested in prognosis, a number of nomograms are available. These are statistical equations that assess the likelihood of an event given your particular clinical details. Some of these can be accessed online at www.mskcc.org/mskcc/html/10088.cfm. You can download a worksheet, which you and your doctor can complete, then feed this information in to the program to calculate your risk of PSA recurrence and other outcomes after surgery and radiotherapy.

Appendix 4: Resistance Exercises

Resistance or strength training aims to develop the size and strength of skeletal muscle by performing effort against an opposing force. These exercises increase muscular fitness and muscle mass. Additional benefits include improving bone density and functional capacity (ability to enjoy activities requiring strength such as gardening).

A workout aims to work all the major muscle groups and so may have as many as 8–10 exercises (*see Figure A4.1*). A biceps curl exercises the muscles at the front of the upper arm and a triceps extension the back of the upper arm and so on.

A repetition maximum (RM) is the maximum weight you can lift once. It is always safer to warm up, rather than go straight to the maximum training intensity, so we recommend that you begin with 12–15 repetitions at just under half your RM. Then increase that to 60–70% of your RM and repeat it 8–12 times. In a complete workout, you would do 2–3 sets of these repetitions for each muscle group and aim to workout at least twice a week.

This is just an example however. It is important for you to choose the level that best suits you and wise to do it in consultation with your doctor or an exercise professional.

The table shows examples of resistance exercises that you can do in your own home. For each muscle group:

- Step 1: work out your Repetition Maximum by gradually increasing the weight to be lifted until a maximum weight is identified
- Step2: warm up with 12–15 repetitions at 40–50% of your RM
- Step 3: exercise with 8–12 repetitions at 60–70% of your RM
- Step 4: do two to three sets of Step 3.

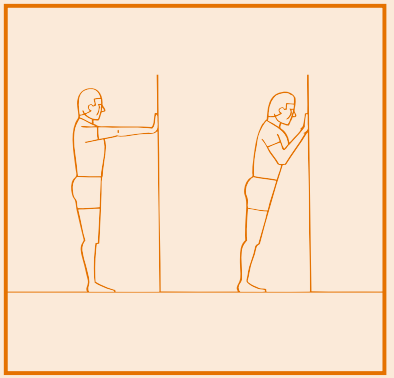
Ask your doctor for guidance in choosing the right type and amount of exercise for you. If you have unstable bone lesions (areas of bone weakness) or other medical problems such as cardiovascular disease you may not be able to do all kinds of exercise.

Figure A4.1: Examples of resistance exercises

Body part: Upper body
Exercise: Chest Press

Description:
Hands in front of the chest. Elbows bent. Straighten the arms against resistance.

Home exercise alternative:
A push up. Start with a standing one: hands against the wall; progress to hands on the floor.



Body part: Lower body
Exercise: Leg Press

Description:
Reclined sitting. Feet placed on a foot plate. Push out, extend the legs. Slowly return.

Home exercise alternative:
Squat. Back against the wall. Slide your back down the wall until knees are at a 45 degree angle.

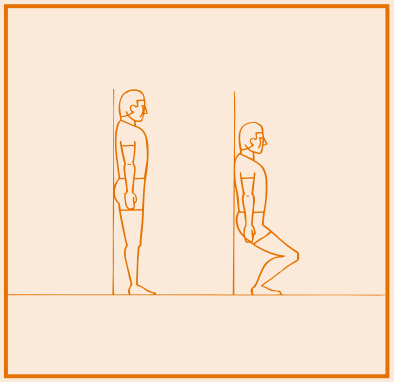
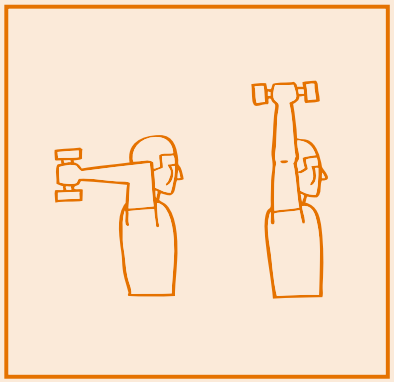


Figure A4.1: Examples of resistance exercises (continued)

Body part: Upper body
Exercise: Triceps Extension

Description:
Holding a weight behind your head with the elbow bent. Straighten your arm against the resistance / weight, towards the ceiling.

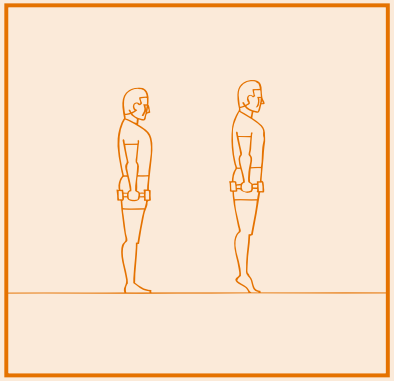
Home exercise alternative:
Sitting in a chair or resting with your backside against a bench. Push up through your arms. Raise your body up from a chair or bench.



Body part: Lower body
Exercise: Calf Raise

Description:
Rise up on to your toes. Push up against resistance though the shoulders or push out against a foot plate whilst sitting.

Home exercise alternative:
Stand on the edge of a step. Hold a rail for support. Rise up to the tips of your toes and then lower down.



Body part: Upper body
Exercise: Shoulder Press

Description:
Sitting or standing. Start with the hand next to the shoulder holding a weight. Push upwards until the arm is straight.

Home exercise alternative:
Hold a weight and extend the arm directly upwards, palms towards the ceiling.

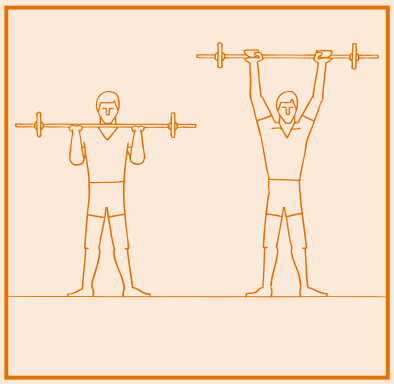
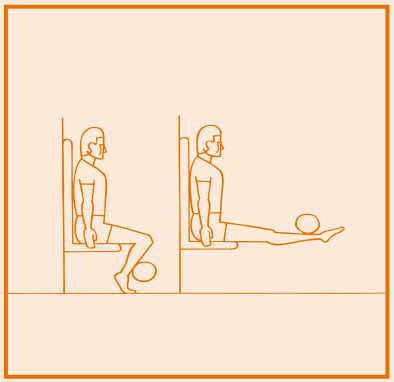


Figure A4.1: Examples of resistance exercises (continued)

Body part: Lower body
Exercise: Leg Extension

Description:
Sitting with knees bent. Straighten your knee against resistance.

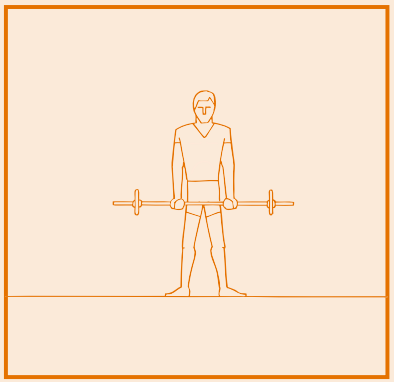
Home exercise alternative:
Start with a bent knee. Place a weight on or against your shin. Straighten your leg / knee.



Body part: Upper body
Exercise: Biceps Curl

Description:
Sitting or standing. Holding a weight in your hand with the elbow straight, bend the elbow bringing the hand upwards.

Home exercise alternative:
Sitting or standing. Holding a weight in your hand with the elbow straight, bend the elbow bringing the hand upwards.



Body part: Lower body
Exercise: Leg Curl

Description:
Standing or lying on your stomach with your knee straight. Bend your knee against some resistance.

Home exercise alternative:
With a weight around your ankle, bend the knee. Bring the foot behind you towards your backside.

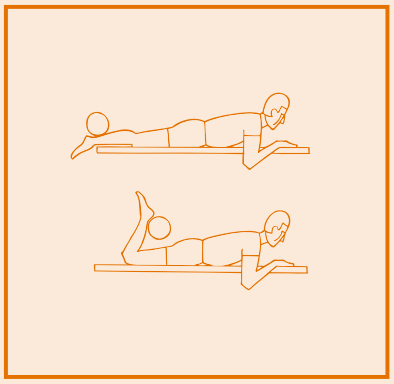


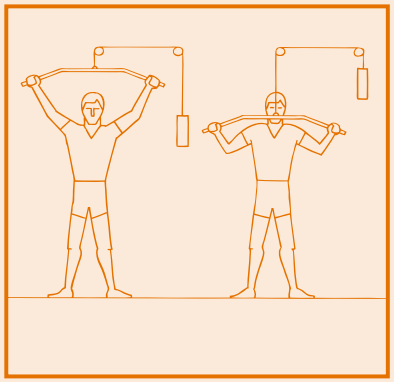
Figure A4.1: Examples of resistance exercises (continued)

Body part: Upper body

Exercise: Lat Pull Down

Description:
Whilst sitting pull downwards on a pulley from above your head towards chest height.

Home exercise alternative:
Tie an elastic band to something above your head height and pull downwards on it.

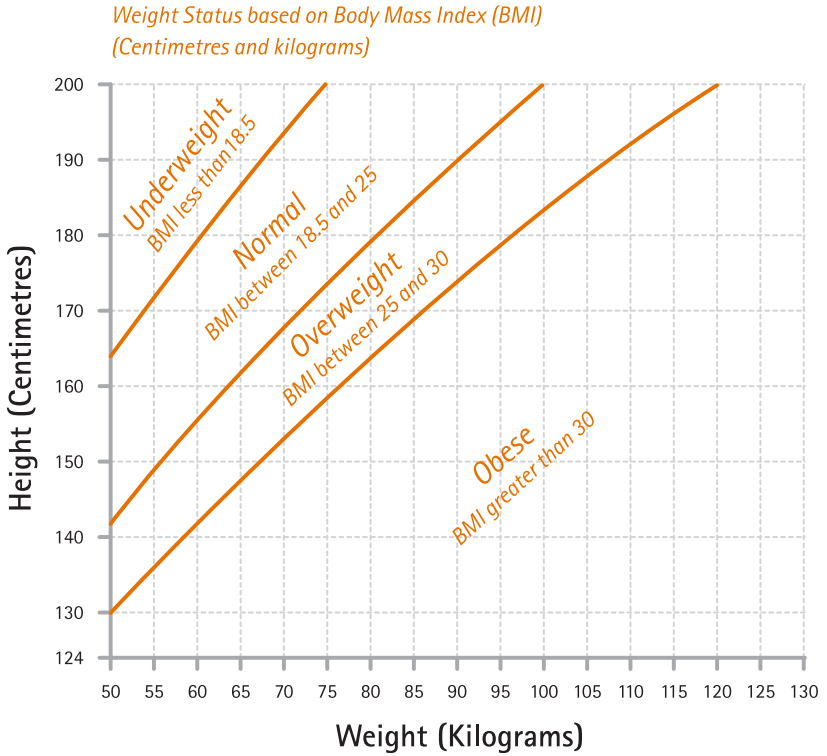


Source: American College of Sports Medicine (ACSM) Recommendations and Position Stand, www.exrx.net/WeightTraining/Guidelines.html
Author: Tim Morris, Physiotherapist, Repatriation General Hospital

Appendix 5: Body Mass Index (BMI) Calculator

The graph below (*Figure A5.1*) provides a simple way of determining if you have a healthy body weight for your height. Just measure your height (cm) and weight (kg) and see which category you are in—underweight, normal, overweight or obese. Many Australians are overweight or obese—if you are in either of these categories talk to your doctor about losing some weight.

Figure A5.1: Weight status based on BMI



Source: www.chartsgraphsdiagrams.com/HealthCharts/bmi-status.htm
Permission received 26.3.09 josephbcasey@gmail.com

Appendix 6: Models of Resistance to Androgen Deprivation Therapy

Understanding the events that occur in the cell at the molecular level can be helpful in understanding why prostate cancer stops responding to Androgen Deprivation therapy despite low-circulating testosterone levels. A protein in the prostate cancer cell, called the androgen receptor is active at every stage in the progression of prostate cancer.

We are not sure of the exact way in which the cell continues to function without normal circulating levels of testosterone, but the following models have been proposed.[98] All suggest that changes occur in the way the androgen receptor in the prostate cancer cell operates. These are shown in the diagram and explained below.

Free testosterone in the circulation enters prostate cells and is converted to dihydrotestosterone (DHT) by the enzyme 5 alpha-reductase. DHT then binds to the androgen receptor (AR), a protein that resides initially in the cytoplasm of the cell (the jelly-like substance that surrounds the nucleus). The AR complex is then 'translocated' or moved to the nucleus where it activates genes responsible for cell growth and survival (AR genes).

There are currently five models of changes which happen during the prolonged absence of testosterone and DHT that can lead to cancer re-growth.

a. Hypersensitive. The AR gene is 'amplified' (so that there are many copies) resulting in more AR receptor protein in the cytoplasm. This causes increased sensitivity to low levels of testosterone or DHT.

b. Promiscuous. The AR gene becomes 'mutated' so that AR protein can bind steroid hormones other than testosterone. Cells with this mutation survive and grow normally even if testosterone levels are low.

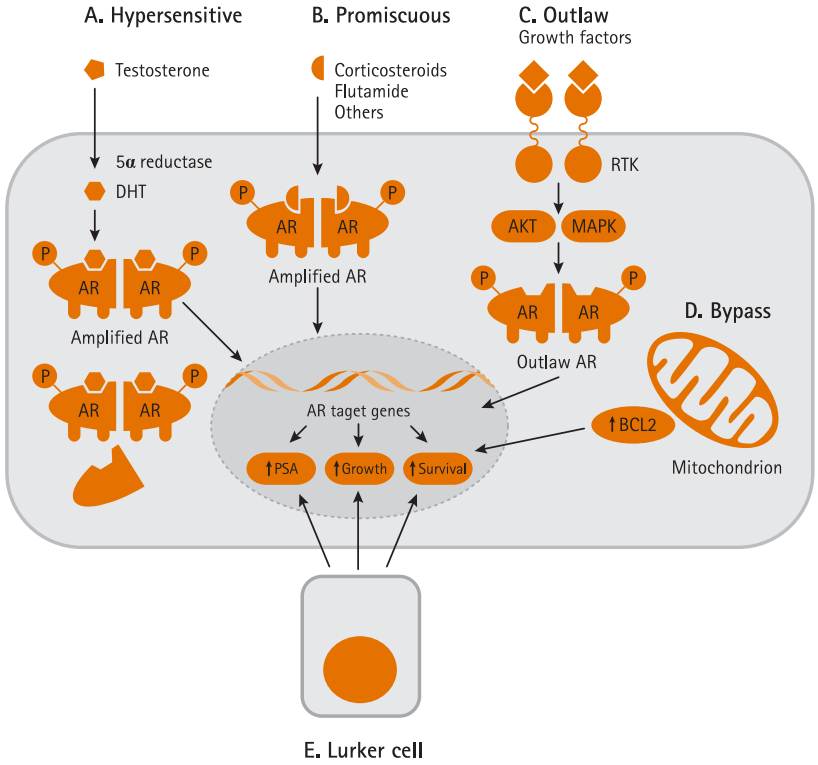
c. Outlaw. The AR can be 'short-circuited' into an active state by other pathways such as by growth factors and cytokines (proteins that serve as messengers between cells).

d. Bypass. Prostate cancer cells that are deprived of androgens develop new ways in which to make, accumulate or prevent degradation of testosterone, thus bypassing the dependence on circulating levels produced by the testes.

e. Lurker cells. Altered expression of 'co-activators' or 'co-repressors' of the AR. A very large number of molecules within the nucleus can influence activity of the AR. Changes in the level of these co-regulators may lead to a super-active AR and contribute to androgen independence.

There is some evidence supporting all of these mechanisms. Understanding these pathways can lead to the development of drugs which target key steps in the process. For example a new drug, abiraterone, is currently being trialed with some success. This drug targets a key enzyme necessary for the synthesis of androgens in cells, including in cancer cells (mechanism d).[98]

Figure A6.1: Models of androgen independence



The androgen receptor (AR) is shown in the cytoplasm of the cell. When an androgen such as DHT (comes from testosterone) binds to it, the AR enters the nucleus of the cell and combines with 'target genes' on the DNA in the nucleus that trigger cell growth and multiplication.

With androgen independence, this may happen in many different ways, shown as a) to e) in the diagram and explained in the text.

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Reference: Feldman, B. and D. Feldman, The development of androgen-independent prostate cancer. Nature Reviews Cancer 2001. 1(October): p. 34–45.

Appendix 7: Do I Have Depression?

In its fact sheet 34 on Prostate Cancer and Depression/Anxiety, *beyondblue* gives the following check list:

You may be depressed if for more than TWO WEEKS you have

- Felt sad, down or miserable most of the time
- Lost interest or pleasure in most of your usual activities

If you answered 'YES' to either of these questions, complete the symptom checklist below. If you did not answer 'YES' to either of these questions, it is unlikely that you have a depressive illness.

Have you:		Tick ☑ if 'yes'
1	Had a change in weight? Or Had a change in appetite?	☐
2	Experienced sleep disturbances?	☐
3	Felt slowed down, restless or excessively busy?	☐
4	Felt tired or had no energy?	☐
5	Felt worthless, excessively guilty OR	☐
	Felt guilt about things without a good reason?	☐
6	Had poor concentration OR	☐
	Had difficulties thinking? OR been very indecisive?	☐
7	Had recurrent thoughts of death?	☐
Add up the number of ticks for the total score		

What does your score mean?

Assuming you answered 'YES' to questions 1 and/or question 2

4 or less: You are unlikely to be experiencing a depressive illness

5 or more: It is likely that you may be experiencing a depressive illness

It's important to note that scores provide only a rough guide as to whether you may have depression. If you have ticked five or more of these statements, consult a health professional as you may have a depressive illness

Source: beyondblue Fact Sheet 34: Prostate cancer and Depression/Anxiety www.beyondblue.org.au

References: American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed (DSM-IV). Washington, DC: APA,1994; and, International classification of diseases and related health problems, 10th revision. Geneva, World Health Organization, 1992–1994.

Appendix 8: Planning Ahead

It is important to prepare for decision-making regarding your care if you are unable to make your own decisions. The various options for this are described below. This appendix also describes some of the legal, financial and care matters you may need to consider while you are feeling well. It can be helpful to plan these at an early stage, so you don't need to be bothered if the cancer progresses.

Decision making—advance care planning

This section will briefly outline the basic sorts of plans that you can make. You will need to check the state of the law where you live—your local palliative care association, your GP, aged care provider or palliative care team can help you do this. It is important to discuss your advance care plans with those who are close to you so that they understand why you have made certain decisions—this can help lessen confusion or conflict later.

Guardianship

When you are not able to make decisions for yourself, for example, about your lifestyle, your healthcare and your daily needs, an appointed guardian can make these decisions on your behalf. Your guardian may need to exercise these powers for several years if you live a long time without the capacity to make informed choices about your lifestyle, financial and healthcare needs.

In some places you can appoint your own guardian in advance, and this is recommended whenever possible. In most states and territories a court or a board convened by government applicable to where you live, will appoint a guardian, when required, if you have not already appointed one in advance

Advance care directive

In some states and territories advance directives are known as 'living wills' or 'anticipatory directions'. Using an advance directive you can specify the medical care you would like when you are dying and unable to make or communicate your decisions. People commonly direct that they want futile medical treatments withdrawn at this time. Some make general statements eg. 'I do not want any treatment that will delay my dying process,' while others provide details e.g. 'I do not want artificial feeding'.

Not all states and territories have legislation governing the use of these documents. In some places you can register your advance directive or medical power of attorney with a central office, which then makes this information available to doctors and other healthcare providers. It is important that your professional caregivers and your spouse/partner have copies of your advance directive.

If in doubt about what you need to do ask your health care professional who will have knowledge of local courses of action and availability of contacts.

Medical power of attorney

There is wide variation between Australian jurisdictions on how to appoint a 'medical agent' or a 'medical attorney'—the name itself is different in various parts of the country and the medical agent's legislated powers also differ. The basic concept is that you are able to appoint in advance a person or people who are empowered to make healthcare decisions on your behalf when you are no longer to able to make those decisions for yourself. You can also specify conditions which your agent or agents must observe when they make decisions.

Typically a medical agent would be your spouse or partner, a son, daughter or other family member or a close friend who is familiar with your wishes. Doctors will ask this person to make decisions about your healthcare if you are unable to make those decisions yourself and in this case it is legitimate for medical agents to refuse futile medical treatments on your behalf when you are dying, consistent with your expressed wishes.

Legal and financial matters

Enduring Power of Attorney

An Enduring Power of Attorney is a document that appoints a person to act on your behalf in financial matters if you become unable to act for yourself. In some Australian states and territories you are able to complete a simple pro-forma document to appoint your 'financial attorney'. In others it's best to consult with a solicitor or accountant to ensure the format of the document is valid and correct.

When completing an Enduring Power of Attorney you must be of sound mind, alert and be able to make decisions—a document completed by a person who does not understand the implications of the appointment is invalid and anyone acting on the Power of Attorney order is acting without authority.

Will

A will is a plan, made while you are alive, which stipulates what should happen to your property after you die. If you die without a will—this is called 'intestate'—your state or territory government, working through the office of the Public Trustee, will divide your property according to set formulas.

'Make your own will' kits are available in many places and if your plans are simple or straightforward, these will suffice. If your plan or financial situation is more complex, it's probably best to consult with a trusted professional advisor about your will—this could be a solicitor or an accountant. It's also helpful to discuss your will with those around you.

In Australia there are reputable Public Trustees that can assist. See local guides/phone books/Google for your area.

When you appoint an Executor to see your wishes are carried out after your death, this person or persons has (have) no powers to speak or act on your behalf until after your death.

A Will can also be a place where you write down specific wishes for your funeral.

Financial aid

There will be costs attached to many of the services that you can access as you receive palliative care. Don't be afraid to ask any member of your healthcare team about the costs of services: it's better to know in advance than to receive a bill you weren't expecting! In some cases you may be able to negotiate a cost reduction if you feel your circumstances warrant it. If you are having financial difficulties, a social worker can give you advice.

What financial support is available?

There are two Australian government-funded support payments that you may be able to access. Centrelink administers both:

Carer Allowance

You may obtain a Carer Allowance if you personally provide care and attention on a daily basis to a person who needs a lot of additional care due to a severe medical condition. To qualify, the care can be provided in either your home or the home of the person. The payment of Carer Allowance is not income or asset-tested, and is not taxable. Carer Allowance can be paid in addition to Carer Payment or any other Centrelink payment. The condition of payment is that the person would otherwise require full-time nursing care, should a carer not be available to provide this.

Carer Allowance may be backdated for up to 12 weeks prior to the claim being lodged.

Carer Payment

Carer Payment is an income support payment for carers who, because of the demands of their caring role, are unable to support themselves through substantial paid employment. This payment is income and assets tested both for the carer and the person being cared for.

A doctor or health care professional must also assess the person you care for.

Carer Payment is granted from the date the claim was made with Centrelink.

Note: If you currently get an income support payment from Centrelink you need to decide which payment is best for you. If you need advice on which payment is best for you call Centrelink on 13 2717.

- If you get a Carer Payment, you can work, train or study for up to 25 hours per week, including travel time.
- You can also get a Pensioner Concession Card that entitles you to low cost medicines and you may also be entitled to Rent Assistance, Telephone Allowance and Utilities Allowance.
- To claim Carer Allowance and/or Carer Payment, you and the person you care for must be Australian residents.
- You can access forms from your GP or from the visiting nurse, domiciliary care or community health service and also from Centrelink on 13 2717.
  www.centrelink.gov.au/internet/internet.nsf/forms/sa336.htm

Tax free lump sum superannuation

The federal government has announced that it will allow tax-free treatment of lump sum payments from both taxed and untaxed funds paid to persons with 'terminal medical conditions'—this applies to payments after July 2007.

www.ato.gov.au/superprofessionals/content.asp?doc=/content/00132334.htm&mnu=46101&mfp=001/149

Equipment costs

Equipment can be made available through most domiciliary and community health care services who may charge fees for services, but these may be waived if financial hardship is assessed. In many cases if your domiciliary equipment provider cannot supply the equipment needed, private hire agencies that charge reasonable fees can be recommended.

Medications

Some prescribed medications are not available from the local community pharmacy. In extreme circumstances a hospital may supply what is needed with the help of a palliative care doctor or specialist. In the case of more expensive medications, the doctor, visiting nurse or palliative care worker may help you find a supplier who charges less than the local pharmacy or you may also be able to negotiate the cost with the local pharmacist. Don't hesitate to discuss medication costs if they are proving to be a financial burden. Your visiting nurse or GP can make suggestions and investigate options that are more financially accessible in your case.

Doctor's visits at home

General practitioners

Some GPs will visit at home, patients who are unable to attend their surgery.

Many will bulk bill for the visit, but some may charge a fee in excess of this amount.

You need to check with the doctor about their billing arrangements.

Specialists

In certain circumstances a specialist will undertake a home visit and you will need to check what the cost will be.

Visiting Nurses

Most visiting nurse services will charge a Health Service Fee to all clients eligible to pay. The fee is a contribution towards the costs of services provided and is usually a set amount per 28 days.

Private home nurses

Fees vary between agencies. Some health insurers will cover the cost of a visiting nurse service which may include overnight nursing care when needed. With permission, contact can be made with the patient's health insurer to find out if a palliative care financial package is available. However, the person or family may wish to use his or her own funds for these services. Please ask your palliative care team member for a referral to a service that is experienced in palliative nursing care.

Other financial help

In South Australia the Palliative Care Council has some funds available for specialised home nursing. In your area check with your visiting nurse for availability of other funds to help you care at home.

Eligible veterans and war widows can seek assistance from the Department of Veterans' Affairs for services, equipment and, in some cases, medications.

Your visiting nurse or palliative care team member can organise this for you.

Commonwealth Government Carer Respite

Commonwealth Carer Respite Centres coordinate access to respite services in your local area. They can give you advice about respite services and find the service closest to you. They can also help get the right respite services. Commonwealth Carer Respite Centres work with carers to plan sensible approaches to respite and other support needs and also arrange 24 hour emergency respite care.

Telephone 1800 059 059 from anywhere in Australia.

Bereavement Payments

Centrelink, on behalf of the Commonwealth Department of Family and Community Services, help people coping with bereavement. Payments can be in the form of Bereavement Payments, Bereavement Allowance and Widow Allowance.

People may also be able to claim a supplementary payment such as Rent Assistance, Remote Area Allowance, Pharmaceutical Allowance and Telephone Allowance. For more detailed information, contact Centrelink Tel. 13 2300

Internet: www.centrelink.gov.au/internet/internet.nsf/site_help/az.htm to check the payment required.

Access to the deceased's bank accounts (other than joint accounts) is not available until probate has been granted. However, banks will release funds to meet funeral expenses (contact your bank to understand their requirements). The executor must sign a statutory declaration and the bank will pay the money directly to the funeral director.

Appendix 9: What Questions Could I Ask?

The following questions were contributed by one of our consumer members and may help you raise issues with your care team.

- What is best for me at this stage?
- Tell me the risks of no further treatment.
- Is further treatment likely to be any advantage to me?
- If no further treatment is undertaken, how is the disease likely to affect me?
- What is the estimated rate of progression of the disease?
- Can rate of progression be retarded?
- How much longer do I have to live?
- What, if any, are the choices of treatments available?
- What complications are likely to arise, and what are the likely effects from treatment thereof?
- What are the likely effects on quality of life, and how may I maintain such quality of life?
- Are co-morbidities (or existing illnesses) significant in the proposed treatment of advanced disease?
- What about pain management?
- Are there any clinical trials in which I could participate?

Carers/family

- Who will look after them when I am unable to look after myself?
- How do I prepare them for the last stages of my life? (assuming death from prostate cancer)
- How do they manage their stress?

Palliative/hospice care

- Who identifies the critical point in my care, particularly when hospice care is necessary?
- Who will be involved in this stage?
- How much time is there to make this decision?
- Is there any counselling or literature available to help my family?

Appendix 10: Steering Committee and Reviewers

Steering Committee for the Guide to Advanced Prostate Cancer

We are grateful to members of the steering committee who generously volunteered their time to develop this Guide:

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Past and present members of the Support and Advocacy Committee of the Prostate Cancer Foundation of Australia

Don Baumber

Trevor Hunt (dec)

Bill McHugh

Max Shub

Reviewers

We are grateful to the following people who provided very helpful feedback on the content.

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Professor Villis Marshall, Chair NHMRC Clinical Practice Guidelines on Locally Advanced and Metastatic Prostate Cancer Steering Committee

Abbreviations

AA	Anti-androgens
ADT	Androgen deprivation therapy
CAB	Complete androgen blockade
CT	Computerised tomography
EBRT	External beam radiotherapy
HIFU	High-intensity focused ultrasound
LHRH	Leuteinising hormone releasing hormone
LH	Luteinising hormone
LUTS	Lower urinary tract symptoms
MDC	Multi-disciplinary care
MRI	Magnetic resonance imaging
NHMRC	National Health and Medical Research Council
ONJ	Osteonecrosis of the jaw
PBS	Pharmaceutical Benefit Scheme
PBAC	Pharmaceutical Benefits Advisory Committee
PIN	Prostatic intraepithelial neoplasia
PSA	Prostate-specific antigen
TRUS	Trans-rectal ultrasound
TURP	Trans-urethral resection of the prostate

Glossary

Most of the words listed here are used in this guide; others are words you are likely to hear used by doctors and other health workers.

ablation	The destruction of tissue by surgical means or some form of energy such as heat, cold or radiation.
adjuvant therapy	A treatment given in conjunction with or shortly after another treatment to enhance its effectiveness.
adenocarcinoma	A cancer originating in glandular tissue. Glandular tissue is part of a larger tissue category known as epithelial tissue, which includes skin, glands and a variety of other tissue that lines the cavities and organs of the body.
advanced prostate cancer	Prostate cancer that has spread outside the prostate. If it has spread outside the prostate but not to distant tissues, it is called 'locally advanced'.
anaesthetic	A drug given to stop a person feeling pain. A local anaesthetic numbs part of the body; a general anaesthetic causes temporary loss of consciousness.
androgen independent prostate cancer	This is an old term that refers to the ability of prostate cancer cells to continue to develop despite withdrawal of circulating testosterone. It is no longer preferred because there is evidence that the cancer is not hormone resistant—there is still a variety of hormones, including androgens, available to stimulate growth within the cancer cells. The cancer cells have developed their own ways of making testosterone available.

androgen receptor	A complex of proteins within the cell that binds androgens (male hormones such as testosterone), translocates into the nucleus and regulates genes controlling prostate cell growth and reproduction.
androgen withdrawal therapy	Also called androgen ablation, androgen deprivation or hormone therapy. Treatment to remove the male hormone, testosterone or its effects.
androgens	Male sex hormones. The most active male hormone, testosterone, is produced by the testicles. Other male hormones are produced by the adrenal glands.
angiogenesis	The formation of new blood vessels to support tissue. Angiogenesis enables tumours to develop their own blood supply, which helps them to survive and grow.
anti-androgen withdrawal phenomenon	A reduction in tumour growth caused when anti-androgen drugs are discontinued. It may be caused when these drugs change from being an 'off switch' to an 'on switch' due to changes in the androgen receptor.
anti-androgens	Drugs which slow the growth of prostate cancer by blocking the action of the male hormone, testosterone, in the prostate.
anus	The opening at the end of the rectum through which faeces pass to the outside.
apoptosis	A type of cell death in which the cell uses specialised cellular machinery to kill itself. Also called programmed cell death.

autologous (blood)	Where the donor and recipient are the same. You can donate your own blood before prostate surgery so that it is available if you need a transfusion.
benign	Not cancerous.
benign prostate enlargement	Non-cancerous enlargement of the prostate. An overgrowth of normal prostate tissue. It is caused by a condition known as benign prostate hyperplasia.
biopsy	Removal of small pieces of tissue for examination. When prostate cancer is suspected, tissue samples are taken from different areas of the prostate then examined under the microscope to see if they are cancerous.
bisphosphonate	A class of drugs that can slow pain and bone loss due to prostate cancer bone metastases.
bladder	The hollow organ that stores urine.
bone scan	A test in which a radioactive chemical is injected, then x-rays trace its path throughout the body. The chemical goes to parts of the bone that are abnormal, such as areas of cancer, infection or arthritis. Bone scans can be unreliable, and so are often used to give guidance, rather than answers, to a problem.
brachytherapy	Radiotherapy given from within the prostate. Low-dose brachytherapy involves the insertion of radioactive seeds directly into the prostate, which are retained. High-dose brachytherapy involves the temporary insertion of radioactive substances into the prostate.

castrate-resistant prostate cancer	Cancer that continues to grow despite treatment to lower the levels of testosterone. Old terms for this condition are 'androgen-independent' or 'hormone-resistant' prostate cancer
catheter	A hollow, flexible tube through which fluids can be passed into the body or drained from it.
cells	The 'building blocks' of the body. A human is made of millions of cells, which are adapted for different functions. Cells are able to reproduce themselves exactly, unless they are abnormal or damaged, as are cancer cells.
chemotherapy	A treatment of cancer cells with cytotoxic chemicals (cytotoxic means toxic to cells).
clinical staging	Staging of prostate cancer by digital rectal examination.
clinical trial	A trial of a new treatment, conducted by medical researchers on patients who have agreed to take part. Clinical trials must be conducted ethically and in keeping with internationally accepted principles.
CT scan	A CT (computerised tomography) scan uses x-rays and computers to produce an image of a cross-section of the body. This image allows your doctor to check for swollen or enlarged lymph nodes, which might mean that cancer has spread. Also called CAT scan.
confined to	In the example of prostate cancer, when we say that the cancer is 'confined to' or 'confined within' the prostate, we mean that cancer cells have not spread from the prostate gland into other tissues or organs.

conformal radiotherapy	A type of radiotherapy where the beams of radiation are shaped so that the area where they overlap follows the same shape as the prostate.
cryotherapy	A method of killing cancerous cells by freezing the tissue.
cystoscopy	A procedure in which an instrument is introduced into the urethra under local anaesthetic, to view the bladder and prostate.
cytotoxic	Any substance that affects cells in a negative way. This term is commonly used to describe special medications that are used to kill cancerous cells in the body.
DEXA scan	Dual energy x-ray absorptiometry, or DEXA scanning, a widely used method to measure bone mineral density in men considering hormone treatment.
digital rectal examination (DRE)	An examination of the prostate through the wall of the rectum. The doctor inserts a finger in the rectum and feels the shape of the prostate. Irregularities may be caused by cancer.
doubling time	The time taken for the PSA level to double, for example from 4ng/ml to 8ng/ml. It is a measure of how fast the cancer is growing.
dry ejaculation	After a radical prostatectomy, a man may achieve orgasm, but produce no ejaculate (fluid). This is because the glands that produce much of the fluid in the ejaculate are removed. See also reverse ejaculation.
dysuria	Difficult or painful urination.

ejaculate	Fluid produced at ejaculation, which contains sperm and secretions from the prostate, seminal vesicles and testicles.
epididymis	a long tube that lies atop each testicle and functions as a reservoir of sperm produced by the testes.
erectile dysfunction	Inability to achieve an erection firm enough for penetration.
erection	The sexually active state of the penis, when it is enlarged and rigid.
external beam radiation (EBRT)	Radiotherapy given from outside the body.
fertility	The ability to conceive children naturally.
five-year survival rate	A scientific measure used to determine the success of a treatment, because it is hard to know if someone is cured or not. It measures the number of people alive five years after a particular treatment. It does not necessarily mean you will only live for five years after having treatment.
flare	When an LHRH agonist is first started, it paradoxically causes a rise in the pituitary hormone LH. The LH rise stimulates the testicles to make testosterone during the first 5–12 days after initiation of the LHRH agonist. This increase in testosterone stimulates prostate cancer cell growth and is termed flare. It can be prevented by taking an antiandrogen—a drug which blocks the testosterone receptors for two weeks prior to LHRH therapy.
fractionation	The delivery of a radiation dose in several small doses or 'fractions'.
free to total PSA ratio	In both healthy men and those with prostate cancer, the prostate specific antigen (PSA) in the bloodstream 'latches' onto protein. In men with benign prostatic enlargement (BPE), there tends to be more 'free' or 'unbound' PSA. This test compares the ratio of unbound PSA to total PSA in the bloodstream.
gene	The tiny factors that govern the way the body's cells grow and behave. Each person has a set of many thousands of genes inherited from both parents. Genes are found in every cell of the body.
Gleason score	A way of grading cancer cells. Low-grade cancers (Gleason score 2, 3, 4) are slower growing than high-grade (Gleason scores 8, 9, 10) cancers. The pathologist identifies the two most common tissue patterns and grades them from 1 (least aggressive) to 5 (most aggressive). The Gleason score is given as two numbers added together to give a score out of 10 (for example, 3 + 4 = 7). The first number is the most common pattern seen under the microscope and the second number is the next most common.
grade/grading	A score that describes how abnormal the cancer cells look, and consequently how aggressive or fast-growing the cancer is likely to be. The most commonly used grading system is the Gleason score, which ranges from 2–10 (see above).
Gray (Gy)	The international system (SI) unit of radiation dose expressed in terms of absorbed energy per unit mass of tissue.

HIFU	High Intensity Focused Ultrasound. A method for killing cancer cells. The high intensity ultrasound is focused in the prostate causing heat that kills the tissue.
hormone resistance	Prostate cancer cells are dependent on testosterone or male hormone for growth. Withdrawal of male hormone by surgery or by means of drugs is therefore a means of controlling its growth. However cancer cells may develop which do not need testosterone for growth. The cancer is then said to be `hormone resistant'.
hormone therapy	In prostate cancer, treatment with drugs that minimise the effect of testosterone in the body, which can slow or stop the growth of prostate cancer.
hormones	Natural chemical substances that are produced by one body organ, and travel through the bloodstream to other organs where they exert their effects. A well-known example is insulin, which regulates the blood sugar level.
hot flush	A sudden rush of heat to the face, neck, sometimes chest and back. It can be associated with hormone therapy for prostate cancer.
impotence	See erectile dysfunction.
incontinence	Involuntary passing of urine (urinary incontinence) or faeces (faecal incontinence).
indolent	Means 'lazy', usually referring to the type of cancer cells which grow only slowly.
infertility	Inability to conceive naturally.

intermittent hormone therapy	Hormone therapy that is started and stopped in cycles. Typically, it is continued for several months until PSA has reached a low level, and then discontinued. Once the PSA level in blood rises to a particular level again (and this can take many months), hormone therapy is re-started. The main expected benefit in this approach is reduction in side effects.
laparoscopic surgery	Minimally invasive surgery to remove the prostate. Small cuts are made in the abdomen. Surgery is conducted using telescopic instruments inserted through these cuts.
leuteinising hormone releasing hormone (LHRH)	Stimulates leuteinising hormone production by the pituitary.
leuteinising hormone (LH)	Stimulates testosterone production by the testicles.
libido	Sex drive.
localised prostate cancer	Prostate cancer that is at an early stage, and has not spread beyond the prostate gland.
locally advanced prostate cancer	Prostate cancer that has spread beyond the prostate capsule and may include the seminal vesicles, but is confined to the prostate region. Stage T3, or C.
locally recurrent	Cancer that has recurred (come back) after treatment, but which is confined to the prostate or nearby tissues only.

lower urinary tract symptoms (LUTS)	Symptoms related to the flow or passing of urine, such as poor stream, frequent urination, needing to get up at night two or more times to urinate, incontinence and incomplete emptying of the bladder. They are often caused by benign enlargement of the prostate, but can also be caused by advanced prostate cancer.
leuteinising hormone releasing hormone (LHRH) agonist	a substance that resembles LHRH which controls the production of sex hormones. The LHRH agonists keep the testicles from producing hormone (testosterone).
lymph nodes	Also known as lymph glands. Small, generally pea-sized pieces of tissue found all over the body but easier to feel in the neck, armpits and groin. They act as filters for foreign substances and commonly become inflamed if there is an infection nearby. They can also harbour cancer cells that have spread from elsewhere.
lymphoedema	Swelling in the limbs caused by blockage of lymph nodes and lymph drainage system. In prostate cancer, blockage in the pelvic lymph nodes can cause swelling in the legs and ankles.
magnetic resonance imaging (MRI)	A way of imaging the inside of the body using magnetic forces and without using x-rays.
malignant	Cancerous.
margin positive	After surgery to remove the prostate, if cancer cells are present at the cut edge (Margin) of the removed prostate, it is termed 'margin positive'.
medical oncologist	A specialist in the treatment of cancer using chemotherapy.

metastasis/ metastasise	The spread of cancer away from the place where it began.
metastatic prostate cancer	When small groups of cells have left the primary tumour site and started to grow in other parts of the body.
micro-metastases	Small deposits of cancer cells, not large enough to be detected by the usual means.
monitoring	The process in which patients are followed up after initial diagnosis and treatment. It may include clinical examination and/or the regular performance of tests.
MRI scan	Magnetic resonance imaging, a test that produces very clear pictures of the human body without the use of x-rays. Instead, MRI uses a large magnet, radio waves, and a computer to produce these images. It is used to distinguish benign and cancerous tissue.
nadir	The lowest PSA reading before it starts to rise, occurring some months after radiotherapy to cure prostate cancer.
neo-adjuvant therapy	A treatment given before another treatment to enhance its effectiveness.
nerve-sparing operation	Surgery for prostate cancer that aims to preserve the nerves which are needed for erections. These nerves are on either side of the prostate gland. The technique is not always possible because cancer can affect the areas around the nerves.
oncologist	A specialist in the treatment of cancer (see medical oncologist and radiation oncologist).
orchidectomy (also orchiectomy)	A type of operation that removes the testicles, but usually leaves the scrotal sac or scrotum.

osteoblasts	One of two cell types (with osteoclasts) that the human body uses in the creation and maintenance of bones. Osteoblasts are the cells that actually create bone.
osteoclasts	Osteoclasts are highly specialised cells that must work in perfect synchronisation with osteoblasts to maintain the skeletal system. Osteoclasts are the cells that resorb, or break down and absorb, bone tissue back into the body.
osteonecrosis of the jaw	Areas of dead bone, not covered by gum in the jaw (thought to be associated with treatment by drugs controlling bone loss called bisphosphonates).
osteoporosis	A condition that affects bones, making them thinner and weaker than normal and liable to fracture and break.
palliative care	Care of persons whose disease is not responsive to curative treatment. The goal of palliative care is to achieve the best possible quality of life for the person and their family.
paraesthesis	Tingling in the skin, often of the extremities. Also called 'pins and needles'.
pathologist	A doctor who specialises in the examination of cells and tissues removed from the body.
pelvic	The area of the body located below the waist and surrounded by the hip and pubic bones.
penis	Male reproductive organ consisting of a body or shaft which starts deep inside the body and extends externally to the end of the penis at the glans.

perineal (perineum)	Area of body between the anus and the scrotum.
Pharmaceutical Benefit Scheme (PBS)	An Australian government program designed to provide effective, subsidised drugs for Australians (see Chapter 9).
PIN	Prostate intraepithelial neoplasia. The cells are dividing more rapidly than normal cells but are not yet cancerous.
pituitary	Part of the brain that produces hormones which stimulate the testicles to produce testosterone (male hormone).
positive surgical margin	Where cancer cells extend to the cut margin of the surgically removed tissue. It implies that some tumour tissue may be left behind.
potency	The ability to have and maintain erections firm enough for penetration.
priapism	A painful, prolonged erection lasting 3 hours or more.
primary cancer	The original cancer. At some stage, cells from the primary cancer may break away and be carried to other parts of the body, where secondary cancers may form.
prognosis	The course and likely outcome of a disease, as estimated by a person's doctor or treatment team.
prostate cancer: localised	The cancer is confined within the prostate gland.
prostate cancer: locally advanced	The cancer is contained within the prostate region but extends beyond the prostate gland and may include seminal vesicles.

prostate cancer: advanced	The cancer has spread to adjacent organs such as bladder, rectum, pelvic wall.
prostate cancer: metastatic	The cancer has spread to distant parts of the body such as bone.
prostate gland	The gland that sits just below the bladder and opens into the urethra. It produces a fluid that forms part of semen.
prostate specific antigen (PSA)	A protein produced by the cells in the prostate, which is usually found in the blood in larger than normal amounts when prostate cancer is present. It can be used as a test for prostate cancer or to monitor its recurrence.
prostatectomy	An operation to remove all or part of the prostate.
prostatitis	Inflammation of the prostate. It can be caused by bacteria.
PSA bounce	Temporary rise in PSA reading that can occur during the first 24 months after radiotherapy to cure prostate cancer. It is commonly seen after seed brachytherapy.
PSA doubling time	The time taken for the PSA level to double, for example from 4ng/ml to 8ng/ml. It is a measure of how fast the cancer is growing
psychosocial	Referring to the emotional, psychological, social and spiritual aspects of life.
quality of life	Your overall appraisal of your situation and your wellbeing.

radiation	Energy in the form of waves or particles, including x-rays. This energy can injure or destroy cells by damaging their genetic material. This ability is 'harnessed for good' when it is used in radiotherapy.
radiation oncologist	A specialist in the treatment of cancer using radiation techniques.
radical prostatectomy	An operation that removes the prostate, part of the urethra, a small part of the vas deferens and the seminal vesicles. This is usually done through a cut in the lower abdomen.
radiotherapy	The use of radiation, for example, x-rays, to kill cancer cells.
rectum	The last part of the bowel, leading to the anus, through which faeces pass.
recurrence	The re-occurrence of cancer some time after it was first treated.
remission	(Also known as complete response) The term used when, after treatment, there is no sign of any cancer. It is not necessarily the same as 'cure', as some cancer cells may be hidden. In partial remission, signs of the disease process have partly resolved but have not disappeared completely.
response	A change in the size or extent of the disease due to treatment.

reverse ejaculation	Also called retrograde ejaculation. This may occur after surgery for benign conditions of the prostate. The ejaculate travels back into the bladder instead of exiting through the penis. This means a man is usually infertile (cannot produce offspring in the conventional way), but he can still achieve orgasm.
robotic prostatectomy	A form of laparoscopic surgery where telescopic instruments inserted through small cuts in the abdomen are controlled remotely by the surgeon with the aid of a computerised robot.
salvage treatment	Treatment, in prostate cancer usually radiotherapy, to try to destroy cancer cells that escaped the initial treatment.
screening	Testing an at-risk population for an illness, to find people who have the illness, although they don't yet have obvious symptoms.
scrotum	A pouch of skin that contains the testicles and some other parts of the male reproductive system. It hangs outside the body and behind the penis.
second line chemotherapy agents	Chemotherapy agents used to prolong remission after first line (initial) chemotherapy agents are no longer effective
secondary cancer	See metastasis.
secondary hormone manipulation	Treatments designed to reduce testosterone levels after primary (initial) androgen withdrawal (hormone therapy) ceases to be effective.
semen	The fluid ejaculated from the penis at sexual climax.

seminal vesicles	Glands that lie very close to the prostate and produce secretions that form part of the ejaculate.
spinal cord compression	Growth of cancer in the vertebra so that the nerves in the spinal cord are squeezed. It leads to symptoms such as pins and needles or numbness in other areas of the body. In extreme cases it can cause paraplegia.
stage/staging	The process of determining the extent of the disease. A system for describing how far the cancer has spread. The most common is the TNM system described in Appendix 1.
stent (urinary)	A specially designed hollow tube, made of a flexible plastic material inserted into a ureter to maintain flow of urine from the bladder.
stress incontinence	Uncontrolled loss of a small amount of urine as a result of any strenuous activity, laughing, coughing, sneezing or lifting heavy objects.
stricture	Scar tissue which obstructs fluid flow; in the case of a urethral stricture, urine flow is obstructed.
surgical margins	After a radical prostatectomy, the edges of the tissue that has been removed are examined to see if cancer cells are present. If they are not (negative surgical margins) the chance is higher that all of the cancer has been removed.
Survival (biochemical)	Biochemical survival refers to the proportion of people surviving without an increase in PSA levels (this can be defined in different ways) in a given time, such as five years.
Survival (disease-free)	Disease free survival refers to the proportion of people surviving without evidence of disease to a given time, such as five years.

survival (prostate cancer specific)	Prostate cancer specific survival refers to the proportion of people who do not die of prostate cancer in a given period, such as five years.
systemic therapy	Treatment which extends throughout the body.
testicles	Glands that produce sperm and the male hormone, testosterone. They are found in the scrotum.
testosterone	The major male hormone. It is produced by the testicles.
thrombocytopenia	Fewer clotting cells in blood caused by mild suppression of bone marrow, so that it produces of these cells.
tissue	A collection of cells.
TNM system	A system for staging cancer, depending on the size and invasiveness of the tumour, whether lymph nodes are affected, and whether there is metastasis. See Appendix 1.
trans-rectal ultrasound (TRUS)	A means of imaging the prostate in order to locate cancer. The ultrasound probe is placed in the rectum.
trans-urethral resection of the prostate (TURP)	A common operation for benign enlargement of the prostate, but only occasionally used to treat prostate cancer. An instrument is inserted, under anaesthetic, along the urethra (urine tube) and removes prostate tissue that may be blocking the flow of urine.
tumour	Any swelling. In the context of cancer, the word usually refers to malignant (cancerous) lumps.
TURP	Trans urethral resection of the prostate. An operation to remove prostate growth obstructing urine flow in the urethra (tube carrying urine from the bladder to the outside). See transurethral resection of the prostate.
urethra	The tube that carries urine and ejaculate along the length of the penis and to the outside of the body.
urinary retention	The outflow of urine stops due to a blockage in the outflow tube below the bladder (urethra) or between the bladder and kidneys (ureters). It can be temporarily relieved by insertion of a catheter, prior to removal of the blockage surgically or by other means.
urologist	Surgeon who specialises in treating urogenital tract diseases.
vas deferens	Ducts that take sperm to the urethra on ejaculation.
watchful waiting	Not treating a disease, but monitoring it to see whether or how fast it is worsening.
x-ray	A form of electromagnetic radiation.

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