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Mr PHIP No. 5
Hormone treatment for prostate cancer

Hormone treatment controls cancer growth by reducing the effects of male hormones.

Key points

- Prostate cancer cells require male hormone for development.
- Treatment to remove male hormone activity can control cancer growth wherever it is in the body.
- Hormone treatment is usually given by injection, but may also include tablets. It may last many years.
- Side effects of hormone treatment can include hot flushes, lack of interest in sex, tiredness and bone loss. Exercise can minimise these effects. It is important to keep up calcium intake and vitamin D levels.
- Drugs called bisphosphonates may help with bone loss.
- Hormone treatment can stop working after some years. Treatment then includes chemotherapy, new types of hormone treatment and new agents.

Introduction

Hormone treatment is the major treatment option for cancer that has spread beyond the prostate region or has recurred following initial treatment. It is also sometimes used with radiotherapy for the initial treatment of high risk prostate cancer. Here we describe what hormone treatment is, its effects and the long term outcome.

What is the male hormone and what does it do?

Male hormones (also called androgens) are important for the development and functioning of the male reproductive system. Men rely on normal levels of male hormones to have adult sexual function and fertility. The level of male hormone in the body is precisely controlled by several factors, the main one being the normal secretion of stimulatory hormones from the hypothalamus and the pituitary gland, two structures at the base of the brain. Testosterone is the principal male hormone. It is released from the testicles and is important for prostate growth. Both normal and cancerous prostate cells are stimulated to grow in the presence of male hormones.

What is hormone treatment?

Prostate cancer cells that have left the prostate and are growing in other areas of the body (metastases) are stimulated to grow by male hormones. A common treatment for metastatic prostate cancer is to lower the levels of male hormones in the body to control this growth. Prostate cancer cells typically die when the hormone levels are lowered. Unfortunately, not all prostate cancer cells die, and with time, often several years later, the cancer growth returns. Nevertheless, men receiving hormone treatment may get good cancer control and a symptom-free life for many years.

Hormone treatment is also called androgen ablation or androgen deprivation therapy.

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When is hormone treatment used?

Hormone treatment is normally used for men whose cancer has not been cured by surgery or radiotherapy. The timing of hormone treatment in response to a rising PSA level varies. It is based to some extent on the speed of tumour growth and its location.

Hormone treatment is the principal therapy for metastatic prostate cancer – when the prostate cancer cells have escaped from the prostate to grow in other sites of the body. The treatment may be started soon after this diagnosis is made. On occasions a delay in starting does not pose serious risk to the patient.

Hormone treatment may also be used to shrink a tumour before or together with radiotherapy. There is evidence that this hormone therapy is beneficial when used with external beam radiotherapy as a treatment for high risk localised prostate cancers. Once the radiotherapy is complete, the hormone treatment may continue for months to several years. PSA tests are used to check on the tumour control.

What does hormone treatment involve?

There are two ways of reducing male hormones:

- by surgery, where the testicles are removed (orchidectomy)
- by medication, either in the form of regular injections and/or tablets.

Both are effective.

Surgery (orchidectomy)

The testicles provide over 95% of the male hormonesand so surgery to remove the testicles reduces the blood hormone levels. This occurs very quickly after the operation.

An advantage of surgery is that the inconvenience and cost of regular medications is avoided.

The operation is usually done as day surgery. The scrotum (pouch of skin that holds the testes) remains and the testes are removed through a small incision. The operation, called an orchidectomy, is permanent.

Medication

Medications are available as an alternative to orchidectomy. Some are injected and others taken as tablets.

Injectable drugs act on the brain to reduce the production of male hormones in the testicles. They currently last from 1–6 months per injection. This means that regular monthly or 6-monthly injections are required to control the cancer cell growth. Should these be stopped in men with metastatic cancer, the cancer will start to grow again when male hormone levels begin to rise (after several months).

Drugs given as tablets are called anti-androgens. They block the action of the male hormone in the reproductive organs and are not as effective as injectables in controlling cancer growth. Treatment with both injectables and tablets is called combined androgen blockade. Sometimes doctors start with a tablet, then 2–4 weeks later give an injectable medication. This is to control a brief increase in testosterone activity (called 'flare'), which passes with time.

The effectiveness of hormone treatment can be checked with a blood test for testosterone. Its effectiveness in controlling the cancer can be checked with a PSA blood test (see Mr PHIP No. 1 and 2), although this is not always reliable.

Sometimes hormone treatment may be given in cycles (i.e. started and stopped repeatedly). This type of treatment is called intermittent hormone treatment. Typically, the treatment is continued for several months until the PSA has reached a low level, then the hormone treatment is stopped.

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Table 1: Medications available in Australia

Injections		Tablets
Common name (technical name)	Injection site	Common name (technical name)
Lucrin (leuprorelin)	Into muscle	Anandron (nilutamide)
Zoladex (goserelin)	Under skin	Androcur (cyproterone)
Eligard (leuprorelin)	Under skin	Cyprone (cyproterone)
Diphereline (triptorelin)	Into muscle	Cyprostat (cyproterone)
		Cosudex (bicalutamide)
		Flutamin (flutamide)

The PSA then gradually rises. Once it rises to a particular level (and this can take many months), hormone treatment is restarted. The main benefit of this approach is reduced side effects (see the next section) without a significant reduction in tumour control. Trials suggest that cancer control is similar with both continuous and intermittent therapies[1].

What medications are available in Australia?

A list of current medications available in Australia is shown in Table 1.

What are the side effects of hormone treatment?

Many of the side effects of hormone treatment are related to the low levels of male hormone in the body and occur whether you choose orchidectomy or medications. These are summarised in Table 2.

Most men have poor or absent erections (impotence) and a lack of interest in sex (reduced libido). Your voice will not change. Some men notice a change in their body hair: a different texture and growth on previously bald areas. Tiredness is common and is related to the main 'male fuel' being suppressed.

Hot flushes are very common in the early stages of treatment but may decline after several months of treatment. Medications can reduce the intensity of this symptom if required. Over many months or years there may be a decline in muscle strength and some tenderness or enlargement in the breast area. Hormone treatment may also increase the risk of diabetes[2].

Before beginning treatment, it is helpful to discuss the possibility of side effects with your wife or partner. Good communication is important in dealing successfully with these changes and maintaining your close relationship.

What you can do to minimise side effects

Recent research has shown that exercise, particularly resistance exercise, can reverse some of the side effects of hormone treatment. This kind of exercise builds up muscle mass and muscle strength in the body. Examples include chest presses ('push-ups'), leg presses and lifting weights. They have been shown to increase muscle strength, reduce fatigue, improve mood and reverse some of the changes in the body that predispose to diabetes[3]. Further information is given in the 'Advanced prostate cancer: A guide for men and their families' (see Resources). Check with your doctor regarding an exercise program that is suitable for you.

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Table 2: Common side effects of hormone treatment

Poor erections or impotence	Weight gain
Reduced libido	Reduced muscle strength
Altered body hair and skin texture	Breast changes
Fatigue	Changes in appetite
Sweating	Dry eyes
Hot flushes	Mood swings
Memory problems	Balance problems
Reduced ability to concentrate	Insomnia
Reduced bone strength (osteoporosis)	

You may notice changes in energy levels and sexual interest.

Do not hesitate to discuss distressing symptoms such as hot flushes with your doctor as there are medications and supplements that can help.

Intermittent hormone treatment can also reduce the effects for periods of time off the drugs.

A word about hormone treatment

The removal of male hormone or its effects means that a man will experience changes in the way he feels, his attitudes and his sex life. While this can be distressing, and it means communication with your partner is particularly important, it does not change who you are. It does not change your identity as an individual and your ability to direct your own life. Some men feel a need for a change in focus in their lives at this stage, and they may take up activities that are more meaningful to them. According to these men, the years that follow can be rewarding and productive.

Hormone resistance: What if the treatment stops working?

The ability of hormone treatment to continue controlling your cancer over the years is quite variable. Some men (approximately 1 in 5) have recurrent cancer growth within a year from starting hormone treatment. Others have no sign of recurrent disease after 10 years of treatment.

For men with metastatic disease (cancer present in areas of the body remote from the prostate), the average time to active cancer growth (hormone resistance) is about 3 years. This stage is sometimes called 'castrate resistance'.

When resistance to hormone treatment occurs, it is usually indicated by rising PSA while testosterone levels remain low. Symptoms typically occur months to years after the rising PSA. Symptoms caused by growth of the cancer in the pelvic region may include blood in the urine and reduced ability to pass urine. Symptoms caused by growth of the cancer at distant sites such as the bones may include pain in the bones, pelvis and back.

Treatment options for hormone-resistant cancer

1. Changing the type of hormone treatment. Even when one type of drug ceases to work, others may remain active. The order in which you have drugs can also change their effectiveness. Consequently different types and combinations of drugs may be effective. This is called 'secondary hormone manipulation'.

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2. Chemotherapy for prostate cancer is an area of research. A range of newer agents and methodologies are showing promise. Docetaxel is a chemotherapy agent used successfully for other cancers. It has been shown to extend life and reduce pain for prostate cancer[4]. Discussion regarding pros and cons of chemotherapy options usually involves a medical oncologist. This should occur early on when considering approaches to treating hormone resistant prostate cancer.
3. Radiotherapy may alleviate pain and control cancer growth at sites away from the prostate. It is usually delivered by external beam although agents which are injected are sometimes used.
4. Steroids such as prednisolone to control pain and reduce tumour growth.
5. New treatments and clinical trials. Trials of drugs including one called 'Abiraterone' are currently underway in Australia. You can search for trials on the ANZ Clinical Trials Registry website listed under Resources, or ask your doctor about clinical trials that could be helpful to you.

Protecting the bones

Hormone treatment is known to weaken bones over time and increase the risk of a break or fracture. A DEXA scan for bone strength is a common investigation for men on or beginning hormone treatment. This is safe and readily available.

To maintain bone strength, it is wise to have an active exercise program and to maintain a balanced diet with adequate calcium intake. Exposure to sunlight stimulates the production of vitamin D, which is also important to bone health. A supplement of vitamin D and calcium is often recommended.

Prostate cancer may spread to the bones, where metastases can lead to bone pain and fractures. Your specialist(s) may recommend drugs known as bisphosphonates. Studies show regular use of this drug by men with secondary prostate cancer in the bones reduces bone fractures and bone pain[5]. These drugs help to retain bone density but they have side effects. It is important to talk to your doctor about these. The drugs can be taken orally or by injection.

Radiotherapy is also used to effectively control bone pain and metastases.

What about complementary therapies?

There are non-medical therapies that can help with your quality of life, which we have not covered in this series. Information about these is available from the cancer organisation in your state and prostate cancer support groups (see Resources). Looking after your health through improving your diet, undertaking active exercise and managing stress is a good way to begin. It is wise to advise your medical team if you are taking additional non-conventional therapies.

Who is taking care of me?

Different kinds of doctors care for men on hormone treatment:

- a urologist specialises in disorders of the urinary tract and reproductive system, and so they will probably be the first specialist you see
- if radiotherapy is an option, you will be referred to a radiation oncologist, who will discuss, plan and deliver this treatment. Then you may return to your urologist
- sometimes a medical oncologist, who specialises in the treatment of cancer with chemotherapy, may also be involved
- a palliative care doctor will focus on symptom control and quality of life.

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If you are ever unsure about who has overall responsibility for your care, discuss this with the doctor you are currently seeing and your GP – our system of care can be confusing, and your GP can act as your guide as needed.

Sources

1. Heidenreich A, et al. Guidelines on prostate cancer. The Netherlands: European Association of Urology, 2011.
2. Saylor PJ and Smith MR. Metabolic complications of androgen deprivation therapy for prostate cancer. Journal of Urology, 2009;13:13.
3. Galvao DA, et al. Exercise can prevent and even reverse adverse effects of androgen suppression treatment in men with prostate cancer. Prostate Cancer Prostatic Disease, 2007;10(4):340–6.
4. Berry WR. The evolving role of chemotherapy in androgen-independent (hormone-refractory) prostate cancer. Urology, 2005;65(6 Suppl):2–7.
5. Michaelson MD and Smith MR. Bisphosphonates for treatment and prevention of bone metastases. Journal of Clinical Oncology, 2005;23(32):8219–24.

For more information

Mr PHIP series available online at: www.prostatehealth.org.au

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1. Prostate cancer: Should I be tested?
2. Interpreting the PSA test for prostate cancer
3. After a diagnosis of prostate cancer: Choosing a treatment for localised prostate cancer
4. Life after treatment for localised prostate cancer
5. Hormone treatment for prostate cancer
6. Sexual function after treatment for prostate cancer
7. Useful resources / Glossary

Internet

- www.prostate.org.au Prostate Cancer Foundation of Australia
- www.prostatehealth.org.au Lions Australian Prostate Cancer Website
- www.andrologyaustralia.org.au Andrology Australia

Phone

National Cancer Helpline: 13 11 20

Resources

Advanced prostate cancer:
A guide for men and their families

Cancer Council 2010. Available free of charge from Cancer Council Helpline: 13 12 00, Andrology Australia 1300 303 78 or download from www.prostatehealth.org.au

Your guide to prostate cancer:
The disease, treatment options and outcomes (paperback) 2010

Dr Prem Rashid, Publisher: Uronorth Group, Port Macquarie 02 6581 3456

A primer on prostate cancer:
The empowered patient's guide

(Paperback) by Stephen Strum, MD Donna L. Pogliano Publisher: Life Extension Foundation 2005

Dr. Peter Scardino's prostate book:
The complete guide to overcoming prostate cancer, prostatitis and BPH

(Hardcover) by Peter Scardino, Judith Kelman. Penguin Group NY, 2010

Websites

ANZ Clinical Trials Registry: lists all registered trials underway in Australia and whether they are still recruiting www.anzctr.org.au

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Prostate Cancer Foundation of Australia Support group network. Find a group near you. http://www.prostate.org.au/articleLive/pages/Support-Groups

You Are Not Alone! This site has a strong patient input and is very supportive. It has stories from family members as well as men themselves, http://www.yananow.net/

Lions Australian Prostate Cancer Website. Download or search the consumer guide: Advanced prostate cancer: A guide for men and their families, in the resource section. www.prostatehealth.org.au

PSA Rising: Prostate cancer information and support with sections on eating well, recipes, stories and more. http://psa-rising.com/

Prostate Pointers: This site has email lists where men on different types of treatments and their families can discuss issues. www.prostatepointers.org

National Centre for Alternative and Complementary Medicine. You can search for trials of complementary treatments on PubMed from this site. http://nccam.nih.gov

Support

The Cancer Council Helpline: 13 11 20 for information on treatments, including complementary therapies, counselling and support.

More resources

See the Mr PHIP prostate cancer resource list in this series

Disclaimer

This information sheet is not intended to take the place of medical advice. Information on prostate disease is constantly being updated. We have made every effort to ensure that information was current at the time of production; however your GP or specialist may provide you with new or different information that is more appropriate to your needs.

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About Mr PHIP

This information has been developed by the Urology Unit at the Repatriation General Hospital, in consultation with men who live with prostate cancer, their families and friends. In addition other health professionals and community agencies have contributed to their production. We are grateful to all of these individuals and organisations who have been so generous with their time and willingness to assist.