

Prostate cancer

For many older men, prostate cancer may be present but never cause symptoms or problems and men will die with their prostate cancer rather than of their prostate cancer. The younger you are, the healthier you are and therefore the longer your life expectancy, the greater the chance that prostate cancer will come against you during your life span. Therefore although prostate cancer is much less common in younger men, it is very important to make a diagnosis in younger men.

For further information on screening and early detection of prostate cancer, see the section on this Website entitled Screening for Prostate Cancer

Conversely, the older you are and the more other diseases or medical conditions that you have, the less likely prostate cancer is to be a significant problem for you. As all treatments for prostate cancer have significant potential complications, each man must weigh up for himself in conjunction with his doctor whether he wishes to be tested for prostate cancer. It is the attitude of the Urological Society of Australasia that men should discuss the issue of early detection of prostate cancer with their doctor and be informed of the implications and benefits of testing.

If you have been found to have an elevated serum PSA

If you have attended your doctor for a blood test for a check-up, you may have had a blood test called a serum PSA (prostate specific antigen). In this setting, the test has been done to assess your risk of having prostate cancer. It is important to understand that this is not a specific cancer test. Serum PSA can be elevated in other situations such as benign prostate enlargement, urine infection or prostate infection. Where the test is elevated, however, it does mean that further assessment of the prostate is required usually by your Urologist. The Urologist will ask you about your general health and specifically any troubles you have had with passing urine and will then perform a rectal examination to assess the prostate. This test is unpleasant to think about, but is certainly not painful. The idea is to see whether the prostate is smooth, symmetrical and soft which are good things, or hard, irregular and asymmetrical which are bad things.

If abnormalities are found in either the serum PSA or the rectal examination of your prostate, then you may be advised to have a prostate biopsy. In this test, an ultrasound probe approximately 2cms in diameter, is passed up into the rectum and ultrasound pictures are taken of the prostate. Ultrasound pictures alone do not usually given any particular helpful information about the risk of cancer, but allow the Urologist to systematically sample the different areas of the prostate and calculate the size of the prostate. A small needle is passed up through the ultrasound probe and samples are taken from different areas of the prostate. When the samples have been taken, a loud click will be heard and there is some discomfort. This procedure is usually performed as an outpatient procedure without any particular anaesthesia, but in some cases may be performed as a day case procedure under general anaesthetic. You should discuss this with your Urologist. Following this procedure, it is common to get bleeding from the back passage, but this usually settles over several days. There may also be blood in the urine for several days and there may be blood in the semen for several weeks. None of these are anything to be concerned about and almost always settle by themselves. Because a needle is being passed across the wall of the bowel which always contains bacteria, there is a small risk of infection getting into the prostate or blood stream. You will therefore usually be given antibiotics which decrease this risk. A follow-up appointment to discuss the results of the biopsy will usually be scheduled.

If you have just been told you have prostate cancer

The most important thing to remember is that you have plenty of time. There is absolutely no need to rush the decision, as a delay in treatment of weeks or months will certainly not make



any difference to your prognosis. It is important that you reschedule another appointment with your Urologist to further discuss things. It is advisable to get other information such as through this Website and to see your referring general practitioner. A man with newly diagnosed cancer faces a difficult decision deciding on treatment due to problems of defining the risk or threat to a man's life from a particular cancer; and also in trying to estimate an individual man's life expectancy. Both of these are very important as some cancers may be regarded as significant cancers, but if you are not going to live long enough for that cancer to come against you, then it does not pose a threat. For younger men with a long life expectancy (say 15-20 years), then almost any cancer will progress over time and pose a threat to them.

Prostate cancer can be broadly divided into localised disease and advanced disease.

Localised disease is defined as a cancer confined (limited) to the prostate gland. Trying to establish whether this is the case, your Urologist will use factors such as digital rectal examination of the prostate (DRE), serum PSA grade (aggressiveness of the tumour, usually expressed as a Gleason score). If it is thought the cancer is more advanced, then further investigation such as a bone scan, CT scan or sampling of the lymph glands may be suggested. The combination of these factors is used to define what is called a clinical stage, ie, an estimate of how far the cancer has progressed or the likelihood of it having progressed beyond the capsule of the prostate or into the adjacent lymph glands or more distant areas. This staging system is called the TNM System.

If based on these factors, it is thought that there is a high probability that the cancer is confined to the prostate then this is called localised disease. If it is felt that the cancer has progressed outside the prostate to the surrounding structures or lymph glands, then this is called locally advanced disease. If it is felt that the cancer has spread more widely, usually to the bones, then this is called advanced prostate cancer or metastatic prostate cancer.

Treatment options for localized cancer of the prostate

- Watchful waiting
- Radical prostatectomy
 - o retropubico perineal
- Radiation therapy
 - external beam
 - brachytherapy

The decision on a treatment option for an individual man with prostate cancer remains difficult due to uncertainties as to how a particular cancer will behave, uncertainties as to the future health and life expectancy of an individual man, and also difficulty in interpreting the data from various clinical trials on the success of various treatment options and their side effects. This must be seen on a background of a cancer which tends to behave in a non-aggressive way compared to many other cancers and for which few even untreated men with localised prostate cancer succumb to the disease within five years of diagnosis and only a small number within 10 years. Nevertheless, prostate cancer remains the second leading cause of cancer death in Australian men.

Further detailed information can be obtained from the National Health and Medical Research publication, 'Evidence Based Recommendations for the Management of Localised Prostate Cancer'.

Having decided to have active treatment, the decision for younger men in reasonable health rests between considering surgery or radiation therapy. There are no truly objective criteria on which this decision can be made, however, men should have a full discussion of both treatment options with their Urologist prior to making a decision.



Watchful waiting

Watchful waiting is essentially a no treatment or treatment deferred option. Behind it is the concept that many older men with prostate cancer will die of other causes before their prostate cancer can cause harm. Watchful waiting is suitable for older men (over 70 years of age) or men who have significant other diseases that are likely to limit their life expectancy or render them not fit enough to undergo more aggressive treatment options. Watchful waiting is mostly used in men who have biopsy-proven prostate cancer, but may be used in men who have an elevated serum PSA or abnormal digital rectal examination in whom an assumption is made that they almost certainly have prostate cancer and a decision is made not to proceed with a biopsy.

Watchful waiting usually involves a regular set of serum PSA measurements in conjunction with regular examinations of the prostate. This monitoring is usually carried out by a Urologist but may be carried out by your general practitioner on advice from the Urologist. The checks are usually at six monthly or yearly intervals. This may at first glance seem like quite a long time, but we know that prostate cancer almost always progresses slowly.

That therefore is the watching part of it, so what is it that we are waiting for?

What we are looking for is to see if there is a sudden change or progression in the prostate cancer such that it is felt that problems may occur. Just because the serum PSA is slowly rising, does not mean that something immediately can or needs to be done. Often the PSA will rise slowly over many years without any particular problems occurring. However, at some point, if your Urologist feels that problems may occur, more active treatment may be introduced. This is usually in the form of hormone therapy.

Radical prostatectomy

The aim of this surgery is to remove the entire prostate and the adjacent seminal vesicles (where the semen is stored prior to ejaculation). After removal of the prostate there is a gap between the bladder and the urethra. The bladder is then pulled down and funnelled, and joined back onto the urethra. A catheter is then placed up through the penis into the bladder which stays in for a variable period after the operation. By necessity, the operation is extremely close to the pelvic nerves which are travelling to the penis and which allow an erection to occur, very close to the rectum itself and very close to the sphincter muscles which control urinary continence.

Advantages of surgery are that if the cancer is truly confined within the prostate and the prostate is removed, then the patient is cured. As the prostate is removed, this allows the whole prostate to be examined by a pathologist and determine the exact clinical stage and whether any follow-up treatment is required.

Following radical prostatectomy, the PSA should fall to essentially zero (strictly less than 0.1), and if it does not, then this indicates some residual prostate tissue. In this setting, the options are then either following the PSA or considering follow-up radiation therapy or hormone therapy. After surgery, the PSA can be followed sequentially and if there is no rise in the PSA, then there is no cancer activity (recurrence).

Clearly if the cancer is removed and you are cured and there are no particular side effects, then there would not be a problem.

The first problem is that in 20-40% of patients, the cancer extends to the margin or edge of the specimen removed and therefore the possibility of cancer remaining behind exists. This does not always, however, translate into recurrent cancer and future problems.

The second problem relates to the side effects of surgery.



Side effects of radical cancer surgery

The first complications are those of any major operation. These include the possibility of blood transfusion (5-20%), and pulmonary embolism (clots in the lungs) 1%. There is a small risk during the operation of damage to the rectum which can usually be repaired at the time of the operation, but may require further surgery. After a prostate operation when the catheter is removed, there will usually be an initial period of short term incontinence and men will often need to wear pads during this period. The risk of long term minor incontinence has been reported at 5-20% and the risk of long term severe incontinence requiring further surgery has been reported at 1?5%. The other major long term complication is erectile dysfunction (inability to achieve an erection sufficient to have sexual intercourse). This has been reported in 30-80% of some series, but with newer nerve-sparing techniques rates of 20-40% are now being reported, especially in younger men. Other more rare complications include narrowing at the join between the bladder and the urethra (stricture formation) requiring further surgery and faecal incontinence (loss of bowel control) which has been reported at rates of between 2 and 10%.

Radical prostatectomy can either be performed by a perineal approach with a cut behind the scrotum, or a retropubic approach with a lower abdominal incision. The results and the incidence of complications are essentially similar for both procedures. Advantages of the retropubic approach are that larger volume prostates can be removed, the lymph glands can be sampled at the same time and the risk of faecal incontinence in some series has been lower. Advantages of the perineal approach are that it is a less invasive procedure with a lower risk of transfusion. The early rate of incontinence is also lower, however the rate of erectile dysfunction may be higher.

Following surgery, five year survival rate ranges from 74-97%.

Radiation therapy

This can either be delivered as an external beam or with radioactive seeds implanted into the prostate (brachytherapy).

External beam radiation therapy

The principle of external beam radiation therapy is to deliver high powered radiation to the prostate and the areas immediately surrounding the prostate. Clearly the most obvious situation in which radiotherapy is a better option than surgery is for patients who are poor candidates for surgery because of other medical risk problems. Patients who do not wish to accept the risks of surgery are also candidates for radiation. Patients with lower stage and lower PSA (as with surgery), will do better with radiation therapy usually takes approximately six weeks with a "fraction" of the total radiation dose being delivered usually four days of each week.

Advantages of radiation therapy are that there is no surgery and no anaesthesia and there is no risk of bleeding or transfusion. Rates of incontinence are very low (less than 5%). Disadvantages are a 10% possibility of radiation damage to the bladder and/or rectum. The rate of long term impotence is approximately 30-50%.

Ideally, following radiation therapy, PSA levels should fall down to approximately 1.0. If this occurs, then control of prostate cancer appears to be approximately equivalent for surgery for at least up to 7-10 years. One disadvantage of radiation therapy is that the prostate remains inside the patient and therefore the exact pathology of the prostate cancer cannot be determined. It has been difficult to compare radiation therapy and surgical series as it is



difficult to know the precise stage of patients who underwent radiation therapy. Patients with higher stage (more advanced disease) are traditionally included in radiation therapy series.

Gleason score

If you have had a prostate biopsy and been found to have cancer, the pathologist will have given the cancer what is known as a Gleason Score or sum. This is an attempt to categorise the aggressiveness of the cancer, ie, its potential for invasion and spread through the body. This system is based on the fact that the prostate is a gland (that produces semen). The Gleason system recognises five levels of increasing aggressiveness -

Grade 1 tumours consist of small uniform glands which are almost normal Grade 2 tumours, though slightly larger glands, are still separated but more closely arranged Grade 3 tumours (the most common grade of cancer) show marked variation in gland size and organisation. The tumour infiltrates or invades the adjacent prostate tissue Grade 4 tumours show fusion or joining of the glands and the glands are much less defined Grade 5 tumours are characterised by solid sheets or cords of tumour with no attempt to form glands.

Because tumours are often composed of cancers of different grades, the two most prominent grades are added together to produce the Gleason Score or sum which is a score out of 10.

Tumours with a Gleason score of less than or equal to 4 are what are described as well differentiated and have only a 25% chance of local progression within 10 years with only a 4-7% chance of dying within 15 years of diagnosis. By contrast, if the Gleason Score is between 8 and 10, this is described as being poorly differentiated and there is a 75% chance of local progression over 10 years with a 60-80% chance of death from prostate cancer within 15 years. Most patients, however, fall within a Gleason 5-7 Score which is described as moderately differentiated. In this group there is an approximately 50% chance of progression over 10 years.

PSA

PSA stands for Prostate Specific Antigen. This is a protein which is produced in the prostate and released into the semen where its major function is in turning the coagulated semen into a liquid which helps movement of sperm within the female reproductive tract. Somewhat by chance small amounts of PSA are released into the bloodstream and can be measured. Here we are most concerned about changes in the PSA that occur in prostate cancer but it must be remembered that many other non-cancerous conditions will cause a rise in the PSA level. Rises in the PSA level occur with cystoscopy (telescope examination up into the bladder), prostate biopsy and vigorous prostate massage. Small and less sustained rises in PSA have been recorded after bicycle riding, prostate ultrasound and ejaculation. Certainly urinary tract infection, passage of a kidney stone and prostatitis (inflammation or infection in the prostate) will cause a rise in the PSA. It is important to remember that also benign enlargement of the prostate or BPH can also cause significant elevation of PSA. This is because the larger the prostate gland, the more PSA will be produced and released into the blood. When a man goes to the doctor for a PSA test to assess the risk of prostate cancer, the presence of the above conditions must be excluded before a PSA test can be used to determine the risk of prostate cancer. In the absence of the above conditions, the PSA is quite a reliable test to determine the risk of prostate cancer but it must be remembered that PSA is not a cancer test and a high PSA does not prove that a man does have cancer. Correspondingly, even a low PSA does not prove that a man does not have cancer; nonetheless, it is the first step in deciding whether further investigation should be performed.

If the PSA level is over 10, more than 30% of men will have cancer. However, of patients with known benign enlargement of prostate, 25% will have a PSA in the range 4-10.



The commonly used cut-off is a level of 4 with further investigation or referral to a Urologist being recommended for levels above this. There is evidence, however, that the upper limit of normal should be lower for younger men and the suggested upper limit of normal for men less than 50 is 2.5 and for men 50?60, 3.5.

Efforts are being made to improve the use of PSA some of which are listed below.

PSA velocity -- measures the rate of change in PSA over time. A steadily rising PSA was though to indicate a higher risk of cancer, and perhaps may be of help in men with PSA levels in the 4-10 range. However, recent studies have shown PSA and variations of up to 20% in consecutive daily measurements, so PSA velocity is not yet of proven value. PSA density -- rates the PSA level against the volume of the prostate as measured by transrectal ultrasound. Since large benign glands cause a rise in PSA, it was hoped that adjustment for prostatic volume would improve specificity, but this has not been confirmed. It may still be help in assessment of those men with a raised PSA but previously negative biopsy.

Age-related PSA -- is sometimes used to adjust for the natural increase in BPH with age, and the resultant PSA rise. Levels for those over 70 or 75 are therefore higher, but few groups recommend screening of men over 70. This relates to their other competing risks and reduced remaining lifespan. In men under 60, some proposed a lower cutoff in PSA with consideration of biopsy for PSA levels of >2.5 or 3. This aimed to reduce the numbers of localised cancers being missed, but will necessarily increase the numbers of men requiring biopsy. It has not been universally adapted.

% free PSA -- the majority of PSA is bound to alpha-1-antichymotrypsin. For unclear reasons, men with BPH have a higher proportion of PSA that is unbound (% Free PSA) than do men with cancer. PSA measurement techniques previously measured both free and bound PSA, but it is now possible to measure both components separately. Patients with a %Free PSA less than 20% have a higher risk of cancer. This may enable some men to avoid unnecessary biopsy, but may risk a small number of cancers being missed.

Neural networks there is a commercially available index (Prostasure*) which derives from calculations including the PSA level, Prostatic Acid Phosphatase, Creatinine phosphokinase enzymes, and the man's age. Though this has been publicised in some areas in Australia, the published data is preliminary and only applicable to PSA levels in the 4-10 range. The test is unproven in the Australian population.

Bone scan

Advanced prostate cancer frequently spreads to the bones particularly of the spine and pelvis. This may sometimes be picked up on ordinary x-rays but the bone scan has a higher pick-up rate.

In this test, a radioactive tracer is injected which is selectively taken up by areas of increased bone activity (such as in secondary deposits in the bone). Hotspots or suspicious areas are therefore diagnosed. These, however, are not automatically areas of cancer spread and frequently comparison with ordinary bone x-rays will need to be made.

(CT Scan (Computerised Tomography)

This is an x-ray test which usually involves an intravenous injection of contrast. During the test you lie on the table and the table slowly moves through a circle which takes x-ray pictures in three dimensions. In the context of prostate cancer, this is sometimes useful for diagnosing enlarged lymph nodes.

TNM System

Primary Tumour Tx Primary tumour cannot be assessed



T0 No evidence of primary tumour

T1 Clinically unapparent tumour not palpable or visible by imaging

T1a Tumour incidental; histological finding in 5% or less of tissue resected

T1b Tumour incidental; histological finding in more than 5% of tissue resected

T1c Tumour identified by needle biopsy (eg. Because of elevated PSA)

T2 Tumour confined within the prostate1

T2a Tumour involves one lobe

T2b Tumour involves both lobes

T3 Tumour extends through the prostatic capsule2

T3a Extracapsular extension (unilateral or bilateral)

T3b Tumour invades seminal vesicle(s)

T4 Tumour is fixed or invades adjacent structures other than seminal vesicles; bladder neck,

external sphincter, rectum, levator muscles and/or pelvic wall

1. Tumour found in one or both lobes by needle biopsy, but not palpable or visible by imaging, is classified as T1c.

2. Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2.

Regional lymph nodes Nx Regional lymph nodes cannot be assessed N0 No regional lymph node metastasis N1 Regional lymph node metastasis

Distant metastasis Mx Distant metastasis cannot be assessed M0 No distant metastasis M1 Distant metastasisM1a Non-regional lymph node(s) M1b Bone(s) M1c Other site(s) Note: when more than one site of metastasis is present, the most advanced category should be used.

Further information:

Books

"Your Prostate, Your Choices" G Hirst & S Wilde 1999 Bantam Books ISBN 1 86471 027 6

"Your Prostate - Questions Answered" P Rashid, G Walters ISBN 983-808-068-3 Published by authors: 3 Highfields Circuit Port Macquarie, NSW, Australia 2444

Queensland Cancer Funds Prostate Cancer Resources:

A Guide to Treatment for Localised Prostate Cancer: Understanding Treatment for Localised Prostate Cancer

Copyright Queensland Cancer Fund (Video, 20 minutes and Booklet)

Description: This video has been designed as a guide for men who have been diagnosed with localised prostate cancer and are in the process of deciding what they should do about it. The video describes three treatment choices; close observation, surgery called radical

prostatectomy and radiation therapy, and includes presentations from both clinicians and men who have received each treatment. The booklet complements the video.



Availability: Video and booklet are available free of charge* through the Queensland Cancer Fund on 1300 361 366 or by email: CISS@qldcancer.com.au

A Guide to Treatment for Advanced Prostate Cancer: Understanding Treatment for Advanced Prostate Cancer

Copyright Queensland Cancer Fund

(Video, 33 minutes and Booklet)

Description: This video has been designed as a guide for men who have been diagnosed with advanced prostate cancer and who are considering hormone treatment. This video discusses the main types of hormone treatments and includes presentations from clinicians and interviews with men who have received hormone treatments. The booklet complements the video.

Availability: Video and booklet are available free of charge* through the Queensland Cancer Fund on 1300 361 366 or by email: <u>CISS@gldcancer.com.au</u>

Prostate Cancer: Sexual Function after Treatment

Adapted from Prostate Health Improvement Project Materials Repatriation General Hospital, South Australia

(Patient Information Sheet)

Description: Topics covered include: Normal sexual function, What causes sex drive, Why are erections affected by treatment to the prostate gland, Medications to achieve erections, Vacuum erection devices.

Availability: Video and booklet are available free of charge* through the Queensland Cancer Fund on 1300 361 366 or by email: <u>CISS@gldcancer.com.au</u> and the Anti-Cancer Foundation of South Australia on 131120.