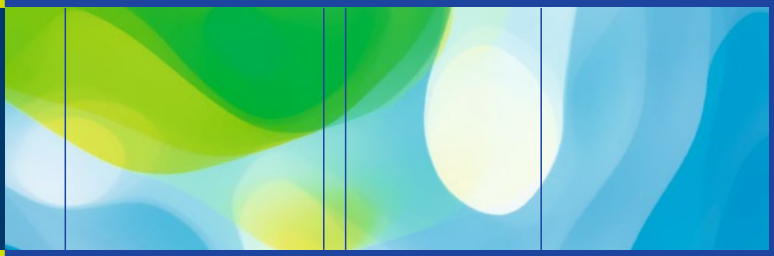
René Sotelo · Juan Arriaga
Raed A. Azhar · Inderbir S. Gill
Editors



Prostate Cancer
A Patient's Guide

Springer

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René Sotelo • Juan Arriaga
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Prologue

You are reading this book probably because you or your loved one has been diagnosed with a prostate-related disease or cancer. Understanding prostate diseases may seem overwhelming at first. For instance, information on how to screen for, diagnose, and treat prostate cancer varies by methodology and resources available. Newspapers, television, and web searches will bring up many topics ranging from scientific studies to inspirational stories about cancer survivors to rumors and myths about the treatment of prostate cancer. How does anyone who has never thought about cancer before make sense of all of this?

The information in this book is intended to help you know and understand the current medical standards; it is advice based on our professional experience. This book is written to help newly diagnosed patients with prostate-related diseases have a better overall understanding of their condition and know what to expect.

In every chapter, we have done our best to give you what you really need to know in a highly concise format. Our comments are intentionally presented in a practical manner so as to enhance understanding. If after reading this book, you feel a little less apprehensive and a lot more confident about the journey that is in front of you, we would have achieved our goal. Knowledge is power…and we seek to empower you.

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Chapter 1
Introduction

René Sotelo

What is the prostate?
Where is the prostate?
Size and weight
What does the prostate do?

What Is the Prostate?

The prostate has become a ghost that lurks within the male psyche. However, the truth is that when we deepen our understanding about this gland, which exists only in men, the aura of mystery begins to disappear (Fig. 1.1).

It is a male organ that is located in front of the rectum and below the bladder. It is formed of cells specialized in the production of fluid that makes up part of the semen, which protects and nourishes the sperm. It is formed of two parts. The external portion represents 30 % of the organ. It is constituted by fibro-muscular tissue and is covered by what is known as the capsule, which is a delicate membrane of

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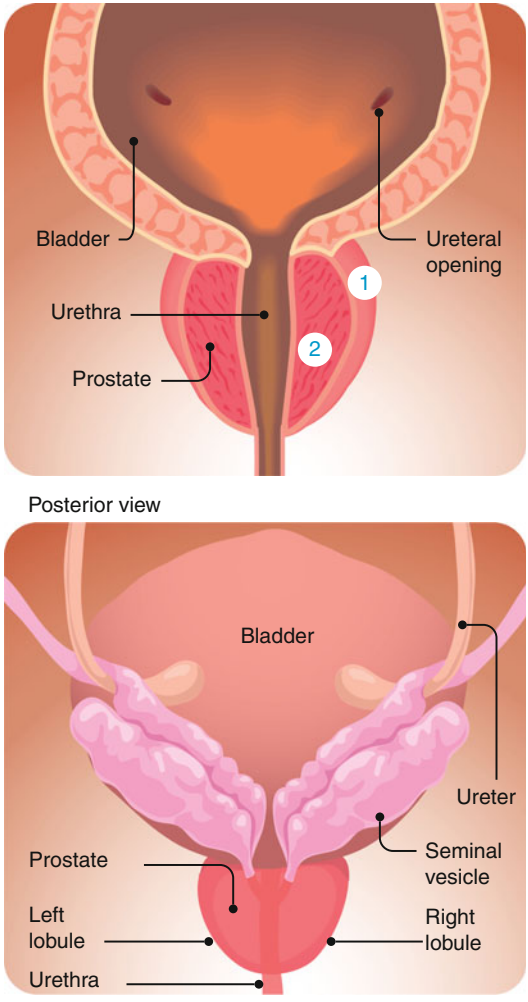

FIGURE 1.1 Prostate

fibrous tissue. The internal portion, formed by glands and ducts, constitutes the other 70 %. It is divided into two lobes, right and left, which are separated by a midline furrow or

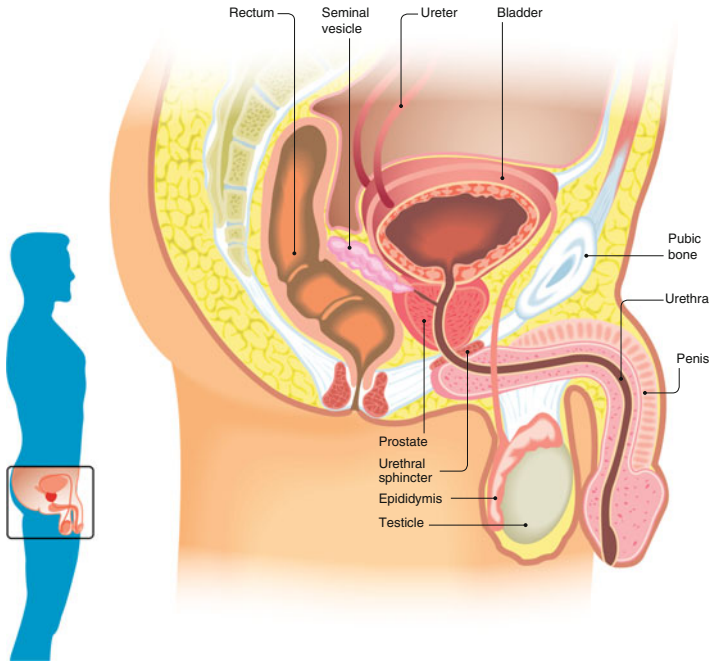

FIGURE 1.2 Male reproductive organs

depression, which is palpable by means of a digital rectal examination.

Where Is the Prostate? (Fig. 1.2)

The prostate is located below the bladder, behind the pubic bone and in front of the rectum. It surrounds the first part of the urethra, the duct through which urine and semen are expelled. On both sides there are nerves and blood vessels. Below the prostate there is a set of circular muscle fibers that constitute the urinary sphincter; those muscles prevent the release of urine when we cough, laugh, move, or perform physical activity.

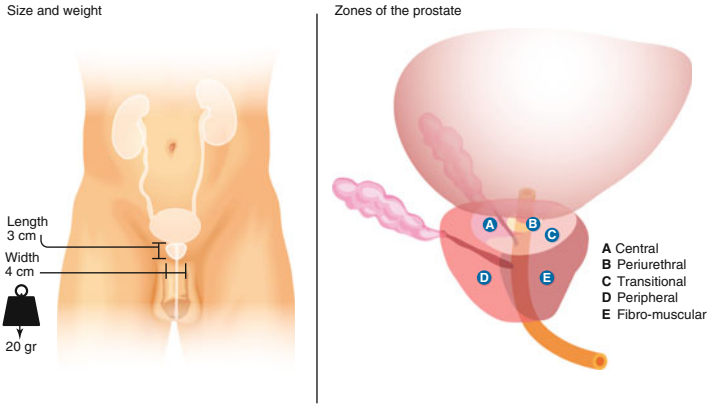

FIGURE 1.3 Size and weight

Size and Weight

One characteristic of the prostate is that during several stages of life it increases in size. At birth it is the size of a bean. Throughout childhood and adolescence it continues to grow until it reaches adult dimensions, when it measures approximately 3 cm in length, 4 cm in width, 2 cm in thickness, and weighs around 20 g. It maintains this volume until a man reaches approximately 45 years of age, when it begins to grow again; this can cause a narrowing in the lumen of the urethra and thus create difficulties in urinating. For its study, the prostate is divided into five zones: the central, the periurethral, the transitional, the peripheral, and the fibro-muscular zones (Fig. 1.3).

What Does the Prostate Do?

The prostate has two important tasks: (1) producing fluid that makes up part of the semen and (2) creating nutritive substances that are vital to the sperm, thus to reproduction.

Relationship with the reproductive system

The prostate forms part of the route that semen must follow during ejaculation (the expulsion of semen through the urethra to the outside of the body). The sperms, which originate in the testicle, travel through the vas and then through the urethra, which, like a tunnel, goes through the prostate. The seminal vesicles produce a fluid, which also drains into the prostate. The urethra carries the semen to the outside of the body. During orgasm the prostate fluid is mixed with that of the seminal vesicle and joined with the sperm to form semen. The contractions of the prostate muscle and the pelvic muscles enable ejaculation.

Relationship with the urinary tract

Once the kidneys filter the blood to cleanse it of impurities, they produce urine that is stored in the bladder and then travels through the urethra to the outside. It is precisely because the urethra passes through the prostate that any growth of this organ will compress it and cause difficulties in urinating. As with all organs of the human body, the prostate can be affected by various diseases. Among the most frequent are inflammations of various origins (prostatitis), the benign growth that produces obstruction (benign prostatic hyperplasia, or BPH), and cancer.

Fact

Another important characteristic of the prostate: it is an organ that can be easily accessible with a rapid and simple examination by way of the rectum. Your urologist may be able to diagnose many of the above-mentioned problems if you schedule periodic visits. Early detection and treatment may also avoid the deterioration of other organs and the advancement of disease.

Chapter 2
An Appointment with the Urologist

René Sotelo and Juan Arriaga

Does the urologist work only with men's diseases?
When should the urologist be consulted?
Symptoms of prostate disease
Why should you have a prostate examination?
Diagnostic Tests

Does the Urologist Work Only with Men's Diseases?

The urologist is a specialist in the diseases of the urinary tract, which includes the kidneys, ureters, bladder, and urethra, all present in both men and women. Therefore, the urologist

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works with both men and women. This specialist also deals with men's genital diseases—specifically those that affect the penis, testicles, or prostate—and those related to the male sexual function.

When Should the Urologist Be Consulted?

Whenever illness of the urinary tract is suspected—such as in the form of infections, calculi (stones), incontinence, or tumors, among others—a urologist should be consulted. As for prostatic diseases, the first consultation should take place at 50 years of age regardless of a suspected illness, unless the patient has a higher risk of prostate cancer, such as African Americans and those who have direct family members (brother, father, or grandfather) who have had this disease. In these latter, high-risk cases it is advisable to have the first consultation at age 40.

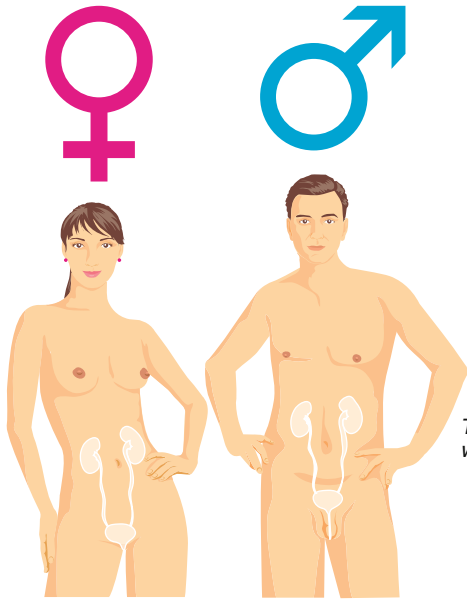
The consultation with the urologist is the first part of the evaluation. The urologist will ask about the personal data of the patient—such as age, previous illness, and health history of family members—as well as specific questions about the suspected urological disease, with emphasis on urinary discomfort. This is followed by a complete physical examination. Based on the findings, the urologist will order the relevant laboratory tests and imaging studies (Fig. 2.1).

Symptoms of Prostate Disease

In general, prostate disease symptoms are divided into two categories: irritative and obstructive.

The irritative symptoms include:

Dysuria (burning with urination): This is the presence of pain and/or burning during urination. It can occur at the



The urologist can work with both men and women

FIGURE 2.1 Men and women

beginning of urination, at the end of urination, or during the exit of the entire urinary stream. The presence of dysuria might mean an infection of the urinary tract, among other possibilities.

Urinary frequency: This is a pattern of urinating frequently, and often in small quantities. It may be accompanied by a sensation of incomplete emptying, which is related to the inability of the bladder to empty completely and expel all of the urine.

Urgency: A sudden, compelling urge to urinate is often, though not necessarily, associated with incontinence of urine (inability to control urination).

The obstructive symptoms include:

Straining: This is the inability to achieve spontaneous voiding of urine, so abdominal muscles must be employed to push one or more times before initiating urination.

Weakness of the urinary stream: This is the decreased caliber and force of the urinary stream, a sign that is usually gradual and imperceptible such that after some time the patient may think the thin and powerless stream is normal.

Post-void dribbling: This is the leakage of a few drops of urine after the patient has completed voluntary urination.

Nocturia (urinating several times a night): This may occur with a gradual or sudden increase in the number of times the patient has to urinate at night. This may occur because the bladder does not empty itself completely during daytime urination and continues emptying itself at night.

Scale of prostate symptoms: Besides asking about the previous symptoms, the urologist uses certain questionnaires designed to gather information about particular problems. These questionnaires are developed and validated by international scientific organizations and make it possible for all urologists to standardize selection and delivery of treatment options.

Subjective data is gathered and converted into numeric variables, which permit measurement and quantification in a more precise and objective manner. This numeric scale, in addition to quantifying the initial condition, makes it possible to objectively measure the effects of the treatment. The following is a questionnaire that evaluates the degree of urinary obstruction due to prostate disease and is known as the International Prostate Symptom Score (IPSS)

IPSS Scale of Prostate Symptoms

International Prostate Symptom Score (I-PSS)

Patient Name: Date:	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your Score
1. Incomplete emptying Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
2. Frequency Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
3. Intermittency Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
	None	1 Time	2 Times	3 Times	4 Times	5 Times or more	
7. Nocturia Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5	
Total I-PSS Score							

Quality of Life due to Urinary Symptoms	Delighted	Pleased	Mostly Satisfied	Mixed – about equally satisfied and Dissatisfied	Mostly Dissatisfied	Unhappy	Terrible
If you were to spend the rest of your lide with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6

The International Prostate Symptom Score (I-PSS) is based on the answers to seven questions concerning urinary symptoms, Each question is assigned points from 0 to 5 indicating increasing seventy of the particular symptom. The total score can therefore range from 0 to 35 (asymptomatic to very symptomatic).

Although there are presently no standard recommendations into grading patients with mild, moderate or severe symptoms, patients can be tentatively classified as follows: **0–7 = mildly symptomatic; 8–19 = moderately symptomatic; 20–35 = severely symptomatic.**

The International Consensus Committee (ICC) recommends the use of only a single question to assess a patient's quality of life. The answers to this question range from "delighted" to "terrible" or 0 to 6. Although this single question may or may not capture the global impact of BPH symptoms on quality of life, it may serve as a valuable starting point for a doctor-patient conversation.

For patients with erection dysfunction, there is a specific male sexual health form called the ***Sexual Health Inventory for Men*** **(SHIM).** This is a scale widely used in clinical practice for the detection and diagnosis of erectile dysfunction and its severity,

as well as for evaluating the response to treatment. With regards to male sexual performance, the following are some of the symptoms the urologist may ask about, when necessary.

Premature ejaculation (early expulsion of semen)
This is the involuntary and early expulsion of semen a common disorder in young men. It occurs when a man ejaculates sooner during sexual intercourse than he or his partner would like.

Erectile dysfunction (impotence)
This is the permanent or recurrent inability to achieve penile erection, or to maintain it with sufficient rigidity to perform and consummate intercourse. Sexual Health Questionnaire for Men

1. How do you rate your confidence that you could keep an erection?

1	2	3	4	5
Very low	Low	Moderate	High	Very high

2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)?

1	2	3	4	5
Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always

3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?

1	2	3	4	5
Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always

4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?

1	2	3	4	5
Extremely difficult	Very difficult	Difficult	Slightly difficult	Not difficult

5. When you attempted sexual intercourse, how often was it satisfactory for you?

1	2	3	4	5
Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always

Why Should You Have a Prostate Examination?

The prostate can be the source of diverse illnesses, like with all organs of the human body. Among these, the most representative are those caused by inflammation (prostatitis), benign growth (benign prostatic hyperplasia), and cancer. Fortunately, the prostate is an organ that is easily accessible with a simple and rapid examination by way of the rectum. All of these diseases can be rapidly diagnosed if periodic follow-up visits are made to the urologist. Moreover, they can be treated in time to prevent the deterioration of other related organs and the advancement of the illness.

What means are available for prostate evaluation?
For the general prostate evaluation, two basic tools are available: a digital rectal examination and a blood test to measure a substance called prostate-specific antigen (PSA), which will be dealt with in a special chapter.

What is the digital rectal examination?
During digital rectal examination, the urologist inserts his index finger into the patient's rectum in order to palpate (feel) the back part of the prostate. This examination not only can give the physician information about abnormalities in the configuration of the gland, but also information about its size, consistency, and tenderness. It assists in diagnosing the growth of the prostate, specifically with a concern for prostatitis or suspected prostate cancer (Fig. 2.2).

Diagnostic Tests

After questioning the patient and performing the physical examination, the urologist generally carries out the following four tests.

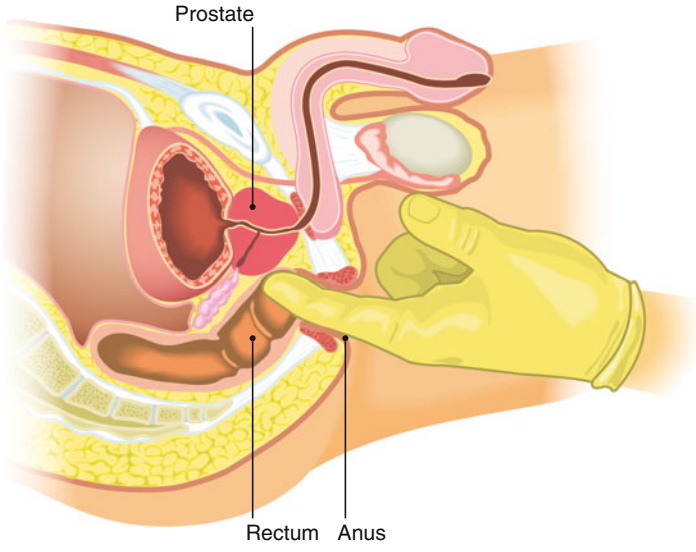


FIGURE 2.2 Exam

1. **Prostate-specific antigen (PSA) analysis**: This is a protein substance produced mainly in the prostate and measured in the blood. The results make it possible to estimate the possibility of the patient having prostate cancer. This test should be requested even when the findings of the digital rectal examination are normal, since there are many small, undetectable tumors that are only diagnosed on the basis of an elevated PSA value.
2. **Urine analysis**: Such analysis provides information about diseases and disorders of the kidneys and the urinary tract, and evaluates the presence of blood, proteins, and crystals in the urine, among other aspects. Blood in the urine may be due to calculi (stones), tumors, or infections in the urinary tract, and also is seen in some diseases that affect the functioning of the kidneys. The presence of crystals may be related to metabolic disorders that produce stones in the urinary tract, and the presence of proteins in the urine may be due to impairment of the kidney function.

3. **Urine culture**: This is a study used to confirm a urinary infection. A sample of urine is cultured in a special medium. If an infection exists, the infectious microorganism will grow and it is then possible to identify the drugs to which it is sensitive or resistant, thereby indicating the most effective treatment.
4. **Serum creatinine**: This is a blood test that is related to kidney function. A high level of serum creatinine allows medical professionals to infer that the kidney function is impaired. This might be the consequence of a prostate obstruction; although, other illnesses such as arterial hypertension and diabetes, which also cause damage to the kidneys, must be ruled out.

Depending on the circumstances of the patient, some of the other tests that might be requested are the following:

1. **Cystoscopy**: This is a relatively rapid and simple examination which consists of inserting a cylindrical instrument with a lens (cystoscope) into the urethra. It can be used to see inside the urethra, passing through the sphincter and the prostate and then up to the bladder for the purpose of studying the diseases of these structures. Before beginning the study, a local anesthetic gel is applied by way of the urethra to minimize pain and discomfort.

   A common tool employed for these tests are flexible cystoscopes: modern, thin-caliber, flexible instruments adapted to the natural form of the urethra so as to be inserted through the urethra and into the bladder. This results in less discomfort for the patient while providing excellent image quality (Fig. 2.3).
2. **Uroflowmetry**: This is a study that makes it possible to determine the speed at which urine is expelled. It is simple to carry out. The patient is asked to urinate into a container while flow sensors report the velocity with which the bladder expels the urine. Normal velocity is more than 15 ml/s. Lesser velocities might imply an obstructive situation or defects of the bladder itself that render it unable to pass the urine with sufficient pressure for elimination at a normal rate.

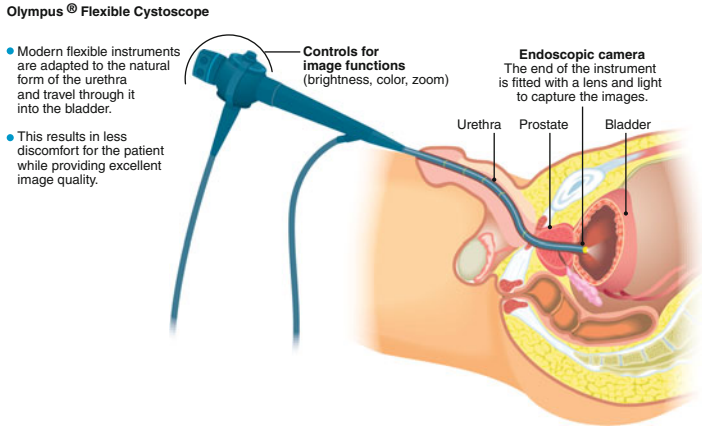


FIGURE 2.3 Cystoscopy

3. **Urodynamics**: This is a study that makes it possible to determine the functioning of the bladder and its capacity to expel urine. This study also evaluates bladder nerve coordination with the outlet duct, the urethra. This study involves placing catheters in the urethra and the rectum. This study is indicated when there is the suspicion that the symptoms are not due to the growth of the prostate but rather to impaired bladder function, such as is the case with neurological illnesses (e.g. strokes, diabetes mellitus).
4. **Post-void residual urine measurement**: This study allows medical professionals to determine the quantity of urine remaining in the bladder after the patient urinates. The normal amount should be less than 50 ml. Higher residual value implies an incomplete emptying, either because of an obstruction of the flow or because of the inability of the bladder to completely expel the urine. To obtain a measurement, a lubricated catheter is passed into the bladder or non-invasively by means of an ultrasound; although, in some cases, this latter method may give results different than the real values. The amount of residual urine enables the physician to estimate the seriousness of the problem, measure the response to treatments already started, and even evaluate the need for treatment.

5. **Intravenous urography**: This study involves a radiological examination. First the patient is injected with a contrast medium into the bloodstream. Later, after the kidneys eliminate the contrast medium, several X-rays are performed to show the passage of the liquid through the entire urinary tract. This diagnostic study, which has been a reference for many urological diseases, is now used less and less because of the advent of more modern techniques such as computerized axial tomography (CT scans) or magnetic resonance imaging (MRI scans). CT or MRI scans can provide the same if not more information than intravenous urography. They allow the entire urinary tract to be evaluated and permit the study of the characteristics of neighboring organs.
6. **Ultrasound**: To perform an ultrasound study, a transducer is placed on the skin and this transmits real-time images to a screen. It enables visualization of the urinary tract but does not provide data about kidney function. Ultrasound has the advantage that it does not require complex equipment nor does it expose the patient to any radiation. Nevertheless, it has the disadvantage that its interpretation depends on the training and experience of the radiologist to identify suspicious areas. Ultrasound is the best tool for taking biopsies of the prostate. This is fully explained in the later chapter dedicated to that subject.

Chapter 3
Prostate-Specific Antigen (PSA)

René Sotelo, Raed A. Azhar, and Mario Jesus Saldaña Guajardo

PSA analysis
Elevated PSA
Total PSA compared to free PSA
Future tumor markers for prostate cancer

The epithelial cells of prostate tissue produce a protein known as prostate-specific antigen (PSA), whose function is to liquefy the ejaculated semen and convert it into an adequate medium in which the sperm can move freely. It is also believed that another of its tasks is to dissolve the vaginal and

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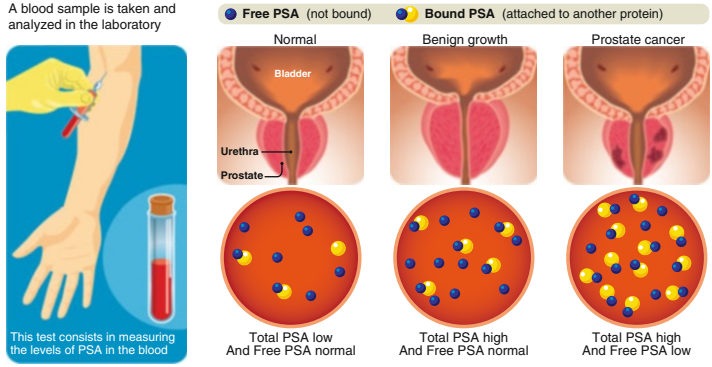

FIGURE 3.1 PSA test

cervical mucus in order to facilitate the entry of the sperm, allowing them to reach their destination. It is a protein substance that initially was discovered in the seminal fluid; it has now also been found in other tissues such as pancreas and breast tissue, though in minimal quantities.

The prostate-specific antigen is produced in the prostate and circulates in the blood throughout the whole body. The amount circulating in the blood can increase for different reasons, among which are: prostate cancer, the benign growth of the gland (relating to aging), and certain infectious processes that affect the prostate (Fig. 3.1).

The prostate-specific antigen was discovered in 1979, but its clinical utility was not identified until a decade later. Until this was known, urologists used only the digital rectal examination and a few indirect blood tests, such as the prostatic acid phosphatase, when prostate cancer was suspected. Today, the PSA is the tumor marker most widely used in contemporary medicine, and along with the digital rectal examination and transrectal prostate ultrasound, it's the best means of identifying patients with a high risk of suffering from prostate cancer, especially in the early stages when the possibilities of cure are greatest (Fig. 3.2).

In developed countries, it is estimated that three out of every four men older than 50 have had a PSA study at some point, which has made it possible to diagnose and treat patients with prostate cancer in early stages and thereby diminish mortality from prostate cancer.

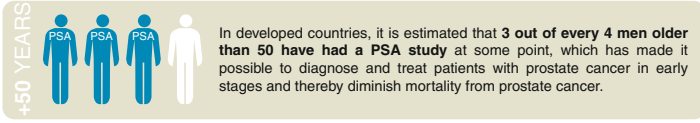

FIGURE 3.2 Men older than 50

Fact
Tumor markers are those substances that can be detected in blood, urine, or tissues, and whose presence in a higher than normal concentration can indicate the existence of a cancerous tumor. Although that abnormal concentration may suggest the presence of cancer, it is not itself sufficient to diagnose it, and for this reason its utility is reduced to providing a clue for diagnosis or for evaluating the evolution of a tumor already detected by other procedures. Most tumor markers can also be produced by normal cells and thereby give false positives. Likewise, some non-cancerous diseases can cause the levels of certain markers to rise.

PSA Analysis

We already know that PSA can be produced either by a benign prostate cell or from a cancerous prostate cell. For this reason it is very important to know how to interpret the presence and the characteristics of the antigen detected in the blood. Because of this, and due to the fact that up to 25 % of all cancers do not alter the PSA concentration, it is important to distinguish between the behavior of this substance in cancer and its behavior in other benign diseases of the prostate.

The results of the PSA analyses indicate its concentration in the blood. It is not necessary to fast before the laboratory test. The results are generally reported in nanograms of PSA per milliliter of blood (ng/ml) and can vary somewhat from one laboratory to another.

Some drugs, such as Finasteride and Dutasteride (used to treat benign prostate disease), certain infectious disorders such as prostatitis, and even urethral trauma (such as from placement of catheters or dilators, or such as occurs in high-performance

cyclists) can modify the PSA values. It's important to take into account that ejaculation in men over 50 years of age momentarily increases the levels of both the free antigen as well as the total. These return to their normal values in 24 h. For this reason, patients should refrain from intercourse for at least 2 days before the extraction of blood for the study. Contrary to what was believed for many years, the digital rectal examination does not significantly alter PSA levels.

All of the circumstances described above show that an abnormal analysis does not necessarily indicate that a prostate biopsy should be performed or that there is cancer; nevertheless, the higher the PSA concentration the greater the probability of a malignant tumor.

Since the discovery of the prostate-specific antigen, several of its isoforms have been isolated and studied. The most common are bound PSA (which is bound to a plasma protease inhibitor) and free PSA (which circulates without being attached to any other molecule.) Together they add up to the total PSA.

Total PSA

The total PSA is the result of the sum of the antigen that circulates freely and the antigen that circulates bound to proteins. It is estimated that normal values are around 0.7 ng/ml in men under 50 years, 0.9 ng/ml in men between 50 and 60 years of age, 1.2 ng/ml in men from 60 to 70 years, and 1.5 ng/ml in men older than 70. Clearly the natural aging process increases the size of the prostate gland and consequently raises the quantity of total PSA in the blood (Fig. 3.3).

Benign-growth prostate cancer
The natural aging process increases the size of the prostate gland and consequently raises the quantity of total PSA in the blood.

Bound PSA (attached to another protein)
Patients with prostate cancer have less free PSA and therefore have a diminished PSA ratio (PSAR).

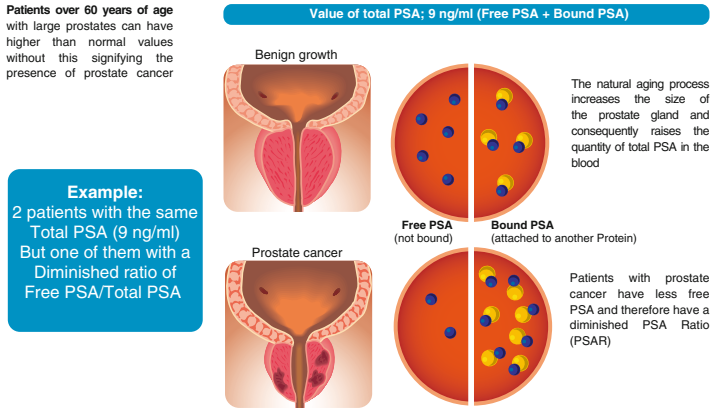

FIGURE 3.3 Value of total PSA

Total PSA Compared to Free PSA

Approximately 5–35 % of the total PSA is found in the free form; that is, it circulates in the blood without being bound to any protein. Patients with prostate cancer show less free PSA because most of the antigen is bound to proteins while it circulates. This detail is extremely important since it can help distinguish between a patient with cancer and one with benign growth of the prostate. Both have a high total PSA, but the one with cancerous cells shows less free PSA.

Free PSA includes at least three isoforms currently under study. Those studies will probably increase the possibility of making more trustworthy diagnoses in the future.

Besides the concentrations of total PSA and free PSA, other characteristics of the antigen are also analyzed for diagnostic purposes. These characteristics or "indicators" are as follows:

1. **Static indicators**

   PSA density (PSAD): It is known that each gram of healthy prostate tissue liberates a certain quantity of PSA into the blood. Therefore, it is expected that patients with prostates of a larger volume have a total PSA higher than normal.

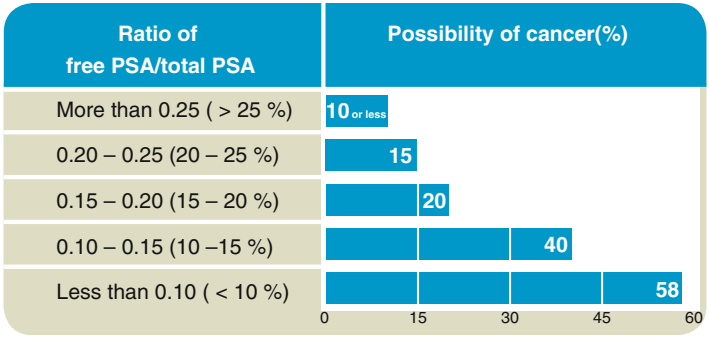

FIGURE 3.4 Ratio of free PSA/Total PSA

The density of the prostate-specific antigen (PSAD) is the relation that exists between the total PSA and the size of the prostate. Its value is obtained by dividing the total PSA by the weight in grams of the prostate. It is necessary to take into account that the larger the prostate gland, the more PSA-producing cells it will have and this will result in a larger value; but if the gland is not so large and has a high PSA, there is a greater possibility that this increase is due to a cancer, because the cancerous tissue produces more PSA than normal tissue. Current statistics determine that a man with a PSAD higher than 0.15 is at greater risk for cancer than the general population. On the other hand, patients with large prostates, larger than 80 g, may have a high total PSA but a PSAD lower than 0.10.

PSA ratio (PSAR): This percentage is found by dividing the value of the free PSA by the total PSA. The lower the result the greater possibility of prostate cancer, especially when it is lower than 0.15 or 15 %. This is because when there is cancerous prostate tissue, most of the circulating antigen is bound to proteins and there is very little free PSA, thus the PSAR is also diminished (Fig. 3.4).

2. **Dynamic indicator**

PSA velocity (PSAV): This is an evaluation of the PSA over time, requiring at least three studies over 18 months.

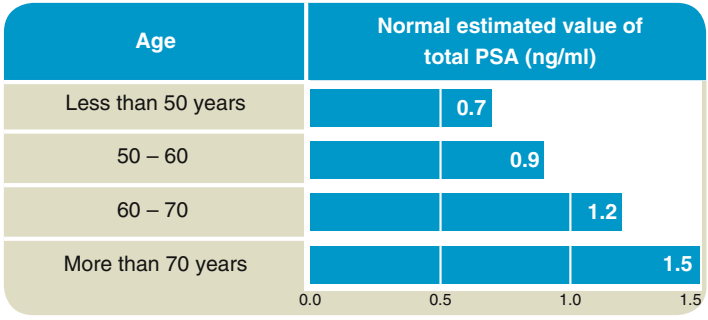

FIGURE 3.5 PSA normal estimated value

It is accepted that the PSA may rise up to 0.25 ng/ml per year in men between 40 to 59 years, 0.4 ng/ml per year in men from 60 to 70 years, and up to 0.75 ng/ml per year in men older than 70. Antigen increases greater than these values; and if persistent at any age, increase the suspicion of prostate cancer (Fig. 3.5).

Future Tumor Markers for Prostate Cancer

The discovery and development of new tumor markers for prostate cancer is a great challenge for medical science. Although there are constantly new advances, their application tends to take time. One needs only to remember that more than a decade had to pass after its discovery before PSA was applied in modern clinical settings, and in the same way a decade later it is recognized that it's still not the ideal tumor marker. New bodily substances identified as playing a role in the functioning and/or disease of the prostate, often at a molecular level, must be developed to permit the differentiation of degrees of tumor aggressiveness and with this information, discover the best treatments.

At present, many research projects are underway that are concentrating on studying different bodily substances that

might become future tumor markers for prostate cancer. Here are some of the most important:

Isoforms of PSA: Free PSA is comprised of at least three varieties of isoforms that have shown diagnostic utility in prostate cancer. The most important are ProPSA (pro-prostate-specific antigen) and the BPSA (B-prostate-specific antigen). The presence of the isoform ProPSA is related to aggressive varieties of prostate cancer. Diagnostic tests that detect it might in the future diminish the need to do biopsies. The BPSA isoform traditionally represents benign prostate tissue, so that the ratio between ProPSA and BPSA helps improve the timely detection of prostate cancer.

AMACR (*alpha-methylacyl-CoA racemase*): This is an enzymatic substance expressed in practically all types of prostate cancer. It is detected by special histopathological stains and is currently used to confirm the diagnosis in tissue samples obtained through biopsy.

Autoantibodies (AA): Recently, multiple specific antigens for prostate cancer have been discovered, as well as the corresponding autoantibodies, in the plasma of patients whose cancer has already been diagnosed.

PCA3 (prostate cancer antigen): This is a gene detected in the urine obtained after a digital rectal examination. It is estimated that in patients with prostate cancer, the concentration of this gene is up to 95 % greater than in patients with healthy prostate tissue; thus it promises to be a very sensitive test in the timely detection of prostate tumors.

Fact

Although the measurement of PSA is used principally for the early detection of prostate cancer, it is also clinically useful in other situations; for example, in patients with prostatitis who present initially with a high PSA but then receive medical treatment, the PSA levels tend to decrease as the treatment takes effect and the symptoms of the inflammation of the gland improve. Likewise, patients with prostate cancer who

have already undergone surgery, radiation therapy, or other treatments and who continue the PSA tests as part of a follow-up screening are more likely to accurately determine whether the treatment has been successful or whether there is a relapse of the disease, taking into account that the PSA takes 4–6 weeks to fall to its definitive level. These and other details will be explained at length in the following chapters.

Chapter 4
Prostate Biopsy

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What is a prostate biopsy?
Who needs this procedure?
Who performs the biopsy?
How many samples are needed for a diagnosis?
What should be known about the biopsy procedure?
What should be done before the biopsy?
How is the procedure performed?
What should be done after the biopsy?
What are the possible complications after the biopsy?
What are the possible results of the biopsy?

What Is a Prostate Biopsy?

It is obtaining a small amount of prostate tissue with a needle. This tissue sample is analyzed under the microscope in order to make a diagnosis.

Who Needs This Procedure?

It is recommended for those patients in whom there is suspicion of prostate cancer, either because they have an elevated prostate-specific antigen or because the digital rectal exam revealed a suspicious area in the prostate.

Who Performs the Biopsy?

The biopsy is performed by a urologist. The procedure also involves the use of an ultrasound to guide the needle to take the sample. The biopsy is typically performed under local anesthesia.

How Many Samples Are Needed for a Diagnosis?

In the cases of patients with tumors that are not palpable during rectal examination, and those in which there is only a suspicion of cancer because the prostate-specific antigen is

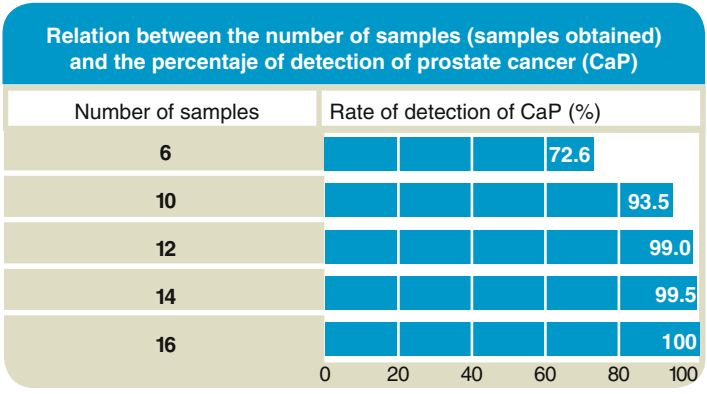

FIGURE 4.1 Number of samples in prostate biopsy

high, the method of sextant biopsy is used. This involves taking six fragments from each of the two lobes (right and left), extracting 12 in total. In the cases where the prostatic biopsy is negative but the patient has an increasing level of prostate antigen in successive follow-up tests, a new biopsy is performed in which additional samples are taken from each lobe (Fig. 4.1).

What Should Be Known About the Biopsy Procedure?

The trans-rectal ultrasound and prostate biopsy is a procedure that can be somewhat uncomfortable for the patient, first because of worry about the possibility of cancer; then due to the need to use an unusual means of access, by way of the rectum; and, finally, because of the potential risks of the procedure. Even with all of this, it must be understood that this diagnostic procedure is always carried out taking all of the measures to reduce the risk of complications and that it is the only way to obtain an early diagnosis of prostate cancer.

What Should Be Done Before the Biopsy?

1. Stop use of aspirin and anticoagulants 7–10 days before the biopsy.
2. Eat a light meal the night before the biopsy and have no breakfast or liquids on the day of the biopsy.
3. In the morning, attempt a spontaneous bowel movement and immediately thereafter administer a rectal enema to complete the emptying and cleansing of the rectum so that the procedure will be safer.
4. Begin taking antibiotics the day before the biopsy and continue for a total of 3 days, including the day of the biopsy.

How Is the Procedure Performed?

The only way to definitively diagnose prostate cancer is by examining a sample of that tissue under the microscope. In these cases a biopsy is performed, using the ultrasound device. As mentioned earlier, in this procedure a needle is inserted in equidistant areas of the prostate.

The prostate is divided into various zones; the most external, or peripheral, is where cancer is found most frequently and, therefore, is the area most focused on when taking the biopsy. The ultrasound makes it possible to scan the entire prostate gland and guarantee that tissue is taken from all of the regions. In the past it was thought that ultrasound could help distinguish cancerous areas from the noncancerous; however, ultrasound can only approximate and direct the needle to each of the different areas for sampling and offer a greater possibility of finding the affected region. There will be occasions when, despite the experience of the urologist, samples are taken of non-cancerous tissue, though cancer is present in the prostate (Fig. 4.2).

The needle, by means of the ultrasound, will extract fragments that will then be preserved in formalin to be examined later by the pathologist. The pathologist prepares the final report of the findings. These fragments are of a cylindrical shape

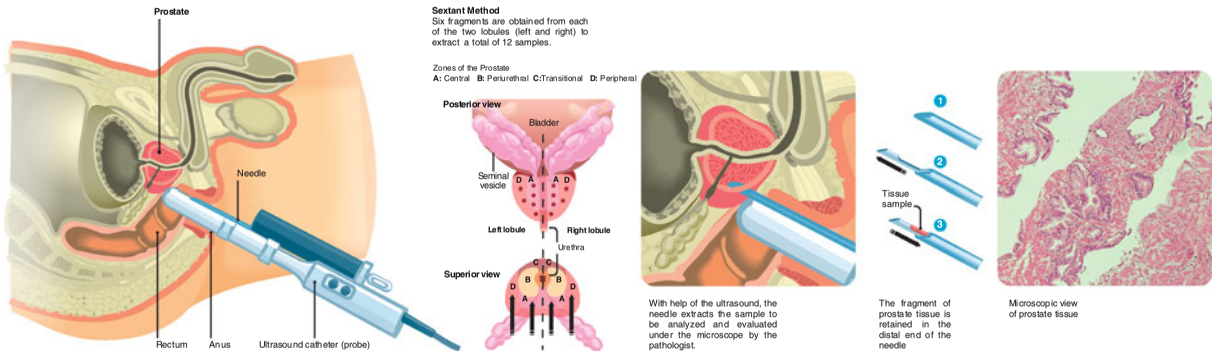

FIGURE 4.2 Sextant method

and each measures approximately 0.4 mm in width by 12–15 mm in length. On the basis of the examination of each one, the pathologist will report the number of cylinders that are positive for cancer and the percentage of tumor they contain. Depending on the results of the biopsy, the urologist can project the course of the illness and plan the most appropriate treatment.

Shortcomings of ultrasound-guided prostate biopsy

During the PSA era, general management of prostate cancers may have over-diagnosed and over-treated clinically unimportant cancer, and misdiagnosed and under-treated clinically important cancer. Now as a standard, trans-rectal ultrasound (TRUS) image guidance is used worldwide at the time of biopsy. However, TRUS is used as a general guide to insert the needle into the prostate organ and take random tissue samples without experienced efforts to specifically target suspicious areas for cancer within the prostate.

Currently in general practice prostate biopsies are typically performed in a random "image-blind" fashion, as described above. Since the clinician dose not know where exactly the cancer is, the image-blinded, random nature of general biopsy may result in missing the location of clinically important cancer.

Novel technologies for precise "image-guided targeted biopsy" now exist. The following innovative techniques are available only in highly specialized centers in the world. They include:

Doppler ultrasound: Cancerous lesions likely have neovasculature that feeds the cancer cells. Doppler ultrasound study can demonstrate the increased blood flow in the cancer lesion. Doppler signals represent the movement of blood or ultrasound enhancer (contrast agent) in the region of interest. Overlaid image of Doppler study onto the gray-scale ultrasound may enhance the diagnostic accuracy of prostate cancer. Nevertheless, the use of Doppler ultrasound is still controversial in the diagnosis of prostate cancer.

Ultrasound elastography: Since cancer is a mass of the prostate epithelium, stiffness of the cancerous lesion may actually be higher than normal prostate tissue. Elastography can demonstrate this differential stiffness of the cancer region in a color-coded, multi-parametric ultrasound with

integration of gray-scale, Doppler, and Elastography to provide a new diagnostic opportunity to suggest the location of the cancerous lesion within the prostate.

Histo-scanning: Computer-assisted diagnosis is now available for identifying prostate cancer lesions. These novel algorithms may provide the diagnostic precision beyond the ability of a medical professional's naked eye to interpret the ultrasound image. Even when the cancer is not visible on an ultrasound image, the computer-algorithm can suggest the cancer likelihood, which can then be overlaid on the actual ultrasound image to allow for potentially more precise targeting.

Magnetic resonance imaging (MRI) of the prostate: MRI is being used increasingly to identify areas within the prostate that are suspicious for cancer. MRI has greater accuracy if the suspicious area is of a larger size (0.5 cc volume) than if it is smaller. Many centers in the United States currently are beginning to perform MRI as a routine part of the diagnostic evaluation for prostate cancer. There are four types of MRI images available: T2 weighted ADC (Apparent diffusion co-efficient), DCE (Dynamic contrast enhanced), and spectroscopy. These types are used in combination to maximize the diagnostic yield.

MRI/TRUS fusion: To increase the targeting accuracy of needle biopsy, the MRI image can be fused and overlaid onto the ultrasound image, thus allowing a new opportunity to precisely target the cancer lesions. 3D volume data of the MRI performed before biopsy is registered onto the intra-operative real-time 3D TRUS image. This MRI/US-fused image is used to guide the delivery of the biopsy needle into the prostate to the suspicious lesion in a targeted manner.

What Should Be Done After the Biopsy?

1. Rest. You should remain at home with little physical activity for 24 h. You should not ride a bicycle, motorcycle, or horse, nor make any long trip for a week.
2. Take antibiotics. Oral antibiotics will be prescribed for you. The treatment should be completed as prescribed in order to avoid infections.

3. Take painkillers. Depending on the case, the most appropriate painkiller will be prescribed to avoid or reduce the pain. Generally, a few days after the biopsy, the pain will diminish and little medication will be required.
4. If medicine is taken for blood pressure, this should not be suspended.
5. It is normal for blood to appear in the urine or stool for 2 or 3 days, and even in the semen.
6. If fever or chills appear, you should immediately contact a physician.

What Are the Possible Complications After the Biopsy?

First, it is important to clarify that a prostate biopsy cannot disseminate the cancer, if it does exist. Although the appearance of blood in the stool and/or the urine is considered normal, continuous bleeding from the rectum or in the urine is considered a complication and the physician should be immediately informed.

Likewise, a persistent fever should also be brought to the attention of the doctor for proper treatment, especially if it is associated with chills and weakness, since an infectious process known as *bacteremia* might be involved; appearing in up to 7 % of patients, it is produced by the transfer of bacteria from the rectum to the bloodstream at the moment when the biopsy is taken. This phenomenon may progress and turn into a severe infectious process known as *sepsis*, which in some cases can be life threatening, though this phenomenon occurs in less than 1 % of all biopsy patients. The estimated mortality for the procedure is less than 0.05 %.

What Are the Possible Results of the Biopsy?

Although the great majority of biopsies are requested because of suspected prostate cancer, the procedure can also

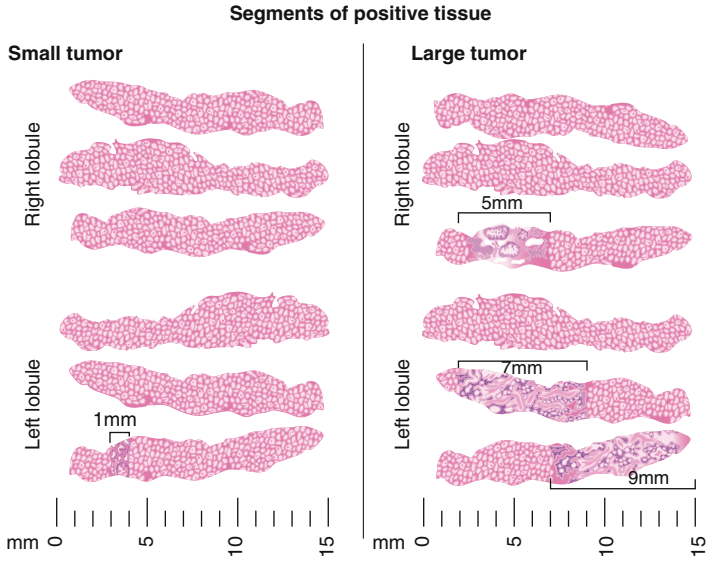

FIGURE 4.3 Segments of positive tissue

diagnose other diseases, such as certain inflammatory or infectious processes. Once the urologist receives the report of the test, the most appropriate possibilities for treatment may be discussed. The following are some of the possible results:

1. **Positive for cancer**
   A biopsy reported as positive means there is cancer in the prostate. The degree of aggressiveness of the tumor is different in each patient; to determine this, the report must include a series of elements that help determine the prognosis and subsequent treatment. Until now, the most important element has been and continues to be the Gleason histological grade (Fig. 4.3).

   Gleason histological grade: In 1974 Dr. Donald F. Gleason publicized findings referring to the changes a prostate cell undergoes when affected by cancer; today these findings are still considered a key factor in the prognosis of the disease.

The Gleason grade is based on the changes the cancerous tumor has developed with respect to the normal structure of the prostate cell. If the prostate tissue examined has undergone few changes in comparison with normal tissue, then a low-risk tumor is involved. On the other hand, if the tissue examined has undergone many changes as a result of tumor activity, this indicates that a high-risk prostate cancer is involved. The pathologist identifies the predominant characteristics of the tissue and assigns a score to the two most prevalent patterns. Thus, number one (1) refers to tumors with lowest risk and the score rises to five (5), which indicates the more aggressive varieties of the tumor. In this way, the Gleason Sum or Combined Gleason Scale is defined by the sum of both predominant histological patterns and can vary in a range from 2 (1 + 1) to 10 (5 + 5). In present form of the Gleason system, prostate cancer of Gleason pattern 1 and 2 are almost never seen, and by definition are almost never seen on biopsy. Gleason pattern 3 is by far the most common. Thus a Gleason score 3 + 3 = 6 cancer is to be regarded as LOWEST grade seen in practice, and indeed these cancers usually have rather good prognoses (Fig. 4.4).

2. **Prostatic intraepithelial neoplasia (PIN)**
   This result indicates that the prostate cells have undergone a growth on their surface similar to that present in cancer. It is not prostate cancer but probably a precursor. In approximately 50 % of the patients with this finding, prostate cancer is found in biopsies performed within the following 5 years.
3. **Atypical small acinar proliferation (ASAP)**
   This is the proliferation of small groups of prostate cells with characteristics that differ from the normal and are similar only to cancerous cells, but in very small quantity. As with the prostatic intraepithelial neoplasia, this pathological finding may require a second opinion from another pathologist; according to the reports from two pathologists, the urologist may suggest another biopsy.

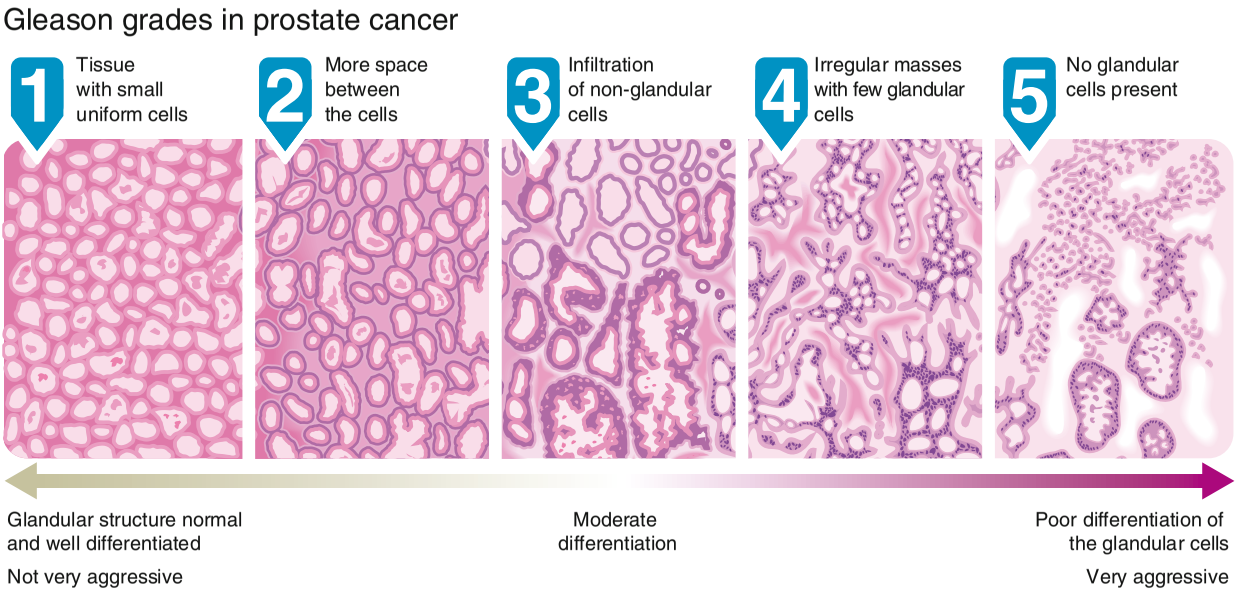

FIGURE 4.4 Gleason grades

4. **Review of slides**
   Because the cellular changes in PIN and ASAP are similar to those present in prostate cancer, in these cases it is advisable a pathologist who is an expert in prostate cancer review the biopsy slides. An experienced pathologist may be able to confirm a diagnosis of cancer, or who may decide to perform an additional pathological study called immunohistochemistry, which makes it possible to identify antigen markers within the cells and corroborate the diagnosis.

Chapter 5
Prostatitis—Pelvic Pain

René Sotelo and Jeannette Potts

Type I prostatitis
Type II prostatitis
Type III prostatitis
Type IV prostatitis
NIH Chronic Prostatitis Symptoms Index (NIH_CPSI)

Prostatitis is an inflammation of the prostate that can be produced by various agents, principally bacterial infections. The diagnosis of prostatitis is complex and can be frustrating, both for the patient and for the physician, since in many cases the symptoms are non-specific and hard to control. There are several types of prostatitis, according to the symptoms and their origin (Fig. 5.1).

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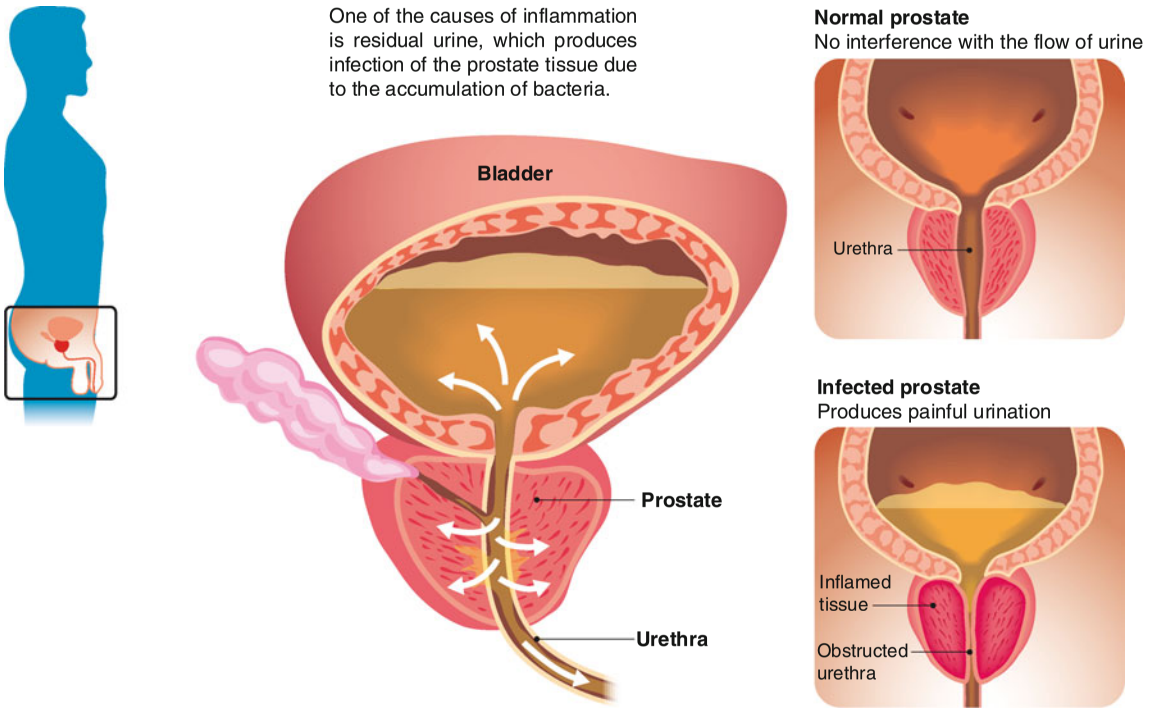

FIGURE 5.1 Prostatitis

Type I Prostatitis

In general, this is an infection of the prostate appearing suddenly, that is, in an acute manner, caused by bacteria present in the urine. The patient may have burning pain while urinating, an increase in the frequency of urination, fever, pelvic pain, or urinary retention.

Sometimes the difficulty in urinating may be so severe that it is necessary to insert a catheter by way of the urethra up into the bladder in order to drain the urine. In those cases where it is not possible to introduce the catheter through the urethra, it may be necessary to place it through a small opening in the abdominal wall, a procedure called cystostomy. The treatment requires hospitalization and the administration of antibiotics, either intravenous or intramuscular. Once the fever recedes, the treatment should continue 4–6 weeks with oral antibiotics.

Although this type of prostatitis often occurs spontaneously, the probability of it appearing due to certain urological procedures is also known, such as the insertion of a catheter or carrying out diagnostic tests such as cystoscopies or prostate biopsies. It is often seen in men with conditions that predispose them to this problem, such as diabetes or narrowness of the urethra.

The infection can be recurrent since the bacteria are retained in the prostate despite treatment. Repeated episodes are more common if antibiotics are taken for less than 4 weeks or if the patient is suffering from other diseases of the urinary tract.

If recovery is delayed or if the fever returns or persists, other studies should be performed, such as a trans-rectal ultrasound or a CT scan, to evaluate the pelvis and determine whether other complications, such as a prostate abscess, exist.

In some cases, prolonged treatments with antibiotics and/or surgery to drain the abscess are required. In other situations a transurethral resection of the prostate may be required, similar to that done in cases of benign prostatic hyperplasia.

Type II Prostatitis

This refers to a long-standing (i.e., chronic) prostate infection. It can be the consequence of acute prostatitis, generally seen in older patients and commonly caused by the same bacteria. In general, this infection only makes itself known when it causes problems in urinating. The diagnosis is confirmed by the symptoms described above and a urine culture, which shows the presence of the microorganism causing the infection. For this, urine samples must be taken before and after a prostate massage, that is, after performing a digital rectal examination and gently massaging the gland. The samples are incubated in the laboratory to compare the growth of the bacteria. If the concentration of the microorganism is higher in the urine obtained after prostate massage, the conclusion is that the prostate harbored the bacteria and is the cause of the urinary tract infection. If the infections are very frequent or very severe, a long-term treatment with a low dose of antibiotic daily and indefinitely should be considered. It is important to rule out calculi (stones) or problems such as urinary retention or narrowing of the urethra, which predispose patients to these infections.

Type III Prostatitis

This type of prostatitis is also chronic, but it is not related to a bacterial infection. It could be described as *chronic pelvic pain*. This category represents more than 90 % of the cases diagnosed as prostatitis.

The majority of the patients are younger than 50 years old and suffer from symptoms such as pain in genitals, pelvis, or perineum; discomfort while urinating; and, sometimes, sexual dysfunction, including pain after ejaculation. In many cases the patient feels a great anxiety caused by this discomfort.

Lack of strength of the pelvic muscles is the cause of the pain, which sometimes is described as a stabbing or burning pain in places like the scrotum, anus, or groin. These problems are analyzed by means of a detailed examination of the

abdomen, genitals, and pelvic muscles, which are palpable in an anorectal evaluation.

For some men the pain is not located in the area of the prostate but in more distant places, generally in muscles contracted in the back or inside the pelvis, but which are in relation to the nerves close to the prostate area.

These muscles are more vulnerable to the development of what is known as *trigger points*, that is, specific points which when stimulated provoke the pain, which is exacerbated in people who remain seated for a long time. Posture and repeated trauma perpetuate the discomfort of the muscle and its irritability.

Urinary problems like burning, urinary retention, and increase in the frequency of urination also can be signs of contraction and tension of the pelvic muscles due to the abnormal activity of the urinary sphincter. It is not rare that many patients also show intestinal disorders, constipation, and discomfort during evacuation.

Some men note a change in their sexual life because of the symptoms. Sexual desire diminishes due to anxiety and physical discomfort. These factors also alter the quality of the erection and increase anxiety and lack of confidence during the sexual act, provoking a vicious circle in which the patient expects the discomfort to appear, with the consequent anxiety and muscular contraction. Moreover, at the moment of orgasm, a spasm occurs, triggering great discomfort and lessening desire. Obviously this increases tension and stress, and affects couples.

Although the cause is not known with certainty, it has been observed that some of these symptoms, along with others attributed to prostatitis, are resolved when a special program of exercises for the back and pelvis is carried out.

It is important to take into account that this illness can appear with other disorders, such as inflammation of the colon, chronic fatigue, depression, and migraines. Emotional support is also fundamental.

It is necessary to get expert advice for exercises for posture and exercises to strengthen and relax the muscles of the body, especially the pelvis. Emotional support is also fundamental.

Likewise, other recommendations will include rest, guidelines to improve the diet, and suggestions for stress management. One of the treatments used is called myofascial release therapy, a specialized procedure that uses various forms of massage and precise pressure to release certain points in the back that trigger spasm. The treatment is more efficient, and offers long-term relief, if it is carried out together with a program for relaxation.

Type IV Prostatitis

Type IV prostatitis is an inflammation of the prostate that is diagnosed incidentally through laboratory tests or from tissue samples sent for pathological study. The patients affected show no symptoms. Sometimes during fertility evaluations, inflammatory cells appear in the semen, which can indicate an infection even though the patient continues without symptoms. On other occasions, the result seems to be an inflammation whose origin cannot be explained, as it is a longstanding process. In samples from biopsies or tissue extracted in surgery during a prostatectomy, these changes due to chronic and acute inflammation can also be observed frequently.

For many decades these symptoms have been attributed to infections but it has been proven that only between 5 and 7 % of these cases are really associated with bacterial action. Unfortunately, for the majority of these patients, antibiotics were prescribed for extended periods. It is a reason for concern that many of the cases diagnosed as prostatitis are not really caused by problems of the prostate but by muscular problems. Consequently it is important to consult the urologist when these symptoms are present or when they persist after treatment.

The following questionnaire, called the National Institutes of Health (NIH) Chronic Prostatitis Symptoms Index, gathers objective information from the patients and assigns to it distinct numerical values in order to obtain quantifiable results, allowing a more precise evaluation of the response to a specific treatment.

NIH Chronic Prostatitis Symptoms Index (NIH_CPSI)

Pain or Discomfort

1. In the past week have you experienced any pain or discomfort [Yes/No] in the following areas:

   (a) Area between rectum and testicles (perineum)
   (b) Testicles
   (c) Tip of the penis (not related to urination)
   (d) Below your waist, in your pubic or bladder area

2. In the past week have you experienced:

   (a) Pain or burning during urination
   (b) Pain or discomfort during or after sexual climax ejaculation

3. How often have you had pain or discomfort in any of these areas over the past week?

   Never
   Rarely
   Sometimes
   Often
   Usually
   Always

4. Which number best describes your AVERAGE pain or discomfort on the days that you had it over the past week?
   1 2 3 4 5 6 7 8 9 10
   No pain Pain as bad as you can imagine

Urination

5. How often have you had a sensation of not emptying your bladder completely after you finished urinating over the past week?

   Not at all
   Less than 1 time in 5
   Less than half the time
   About half the time

More than half the time
Almost always

6. How often have you had to urinate again less than 2 h after you finished urinating over the past week?

Not at all
Less than 1 time in 5
Less than half the time
About half the time
More than half the time
Almost always

Impact of Symptoms

7. How much have your symptoms kept you from doing the kinds of things you would usually do over the past week?

None
Only a little
Some
A lot

8. How much have you thought about your symptoms over the past week?

None
Only a little
Some
A lot

Quality of Life

9. If you were to spend the rest of your life with your symptoms just the way they have been during the past week, how would you feel about that?

Delighted
Pleased
Mostly satisfied
Mixed (about equally satisfied and dissatisfied)
Mostly dissatisfied
Unhappy
Terrible

Chapter 6
Benign Prostatic Hyperplasia

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Symptoms
Diagnostic methods
Medical treatment
Alpha blockers
Secondary effects
5 alpha reductase inhibitors

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DOI 10.1007/978-3-319-05600-5_6,

Impaired kidney function
Acute urinary retention
Bladder stones
Recurrent or severe bleeding
Unstable bladder with urge incontinence
Hernias
Surgical treatments
Other minimally invasive procedures

During the first two decades of a man's life, the prostate gland grows constantly until it reaches the size of approximately 20 cm^3. Between the ages of 20 and 40 this growth stops, and then starts again around the fifth decade of life. From then on, it will continue growing.

This process is known as benign prostatic hyperplasia (BPH) and, as its name indicates, it is not related to prostate cancer, but it can become a health problem. The greatest risk is obstruction and the resultant difficulty in urinating. Nevertheless, both the age at which this growth occurs as well as the size the prostate can reach vary from person to person (Fig. 6.1a).

Besides age, other factors have been related to prostate enlargement. Among these are alcoholism and liver cirrhosis, two conditions which increase the concentration of estrogen, a hormone of the blood that stimulates prostate enlargement. Likewise, family history can be another factor indicating risk of benign prostatic hyperplasia, since the sons of patients who have shown this disorder have a risk up to four times greater than other men of developing the disease. In many of these cases, BPH appears at an early age (sometimes before 50 years of age) and the gland can reach a large volume: eight out of every ten men between 60 and 80 years of age will have prostate growth that surpasses 20 cm^3 (Fig. 6.1b).

Symptoms

Increase in the size of the prostate does not necessarily cause the same symptoms in all patients, since it has been shown that the appearance of difficulties in urinating is not directly related to its size. That is, there are patients with great difficulty in urinating whose prostate does not show a considerable

growth, while others with a noticeable growth of the gland do not develop this problem (Fig. 6.2).

In general, benign prostatic hyperplasia symptoms include: thinning and weakening of the urinary flow, difficulty in starting to urinate, and/or intermittent urination or dribbling at the end of the urination. Likewise, there may be an urgent or frequent need to urinate, an increase in urination during the night (nocturia), or the sensation that the bladder does not completely empty after urinating.

There are various explanations for what triggers these symptoms. One of them is that the prostate capsule, which covers the gland like a shell, begins to compress the rest of the organ, causing an increase in the pressure inside the prostate with the consequent difficulty in urinating.

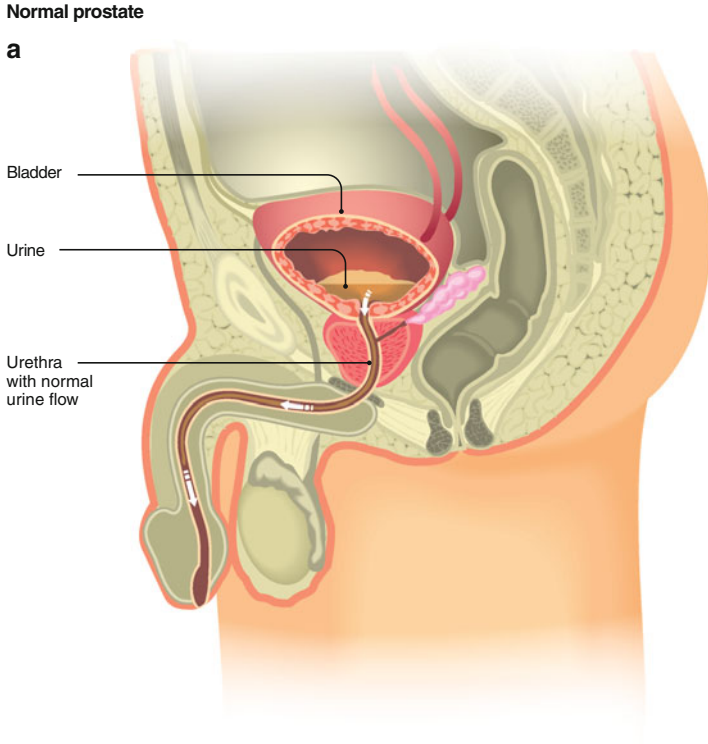


FIGURE 6.1 (**a**) Normal prostate. (**b**) Enlarged prostate

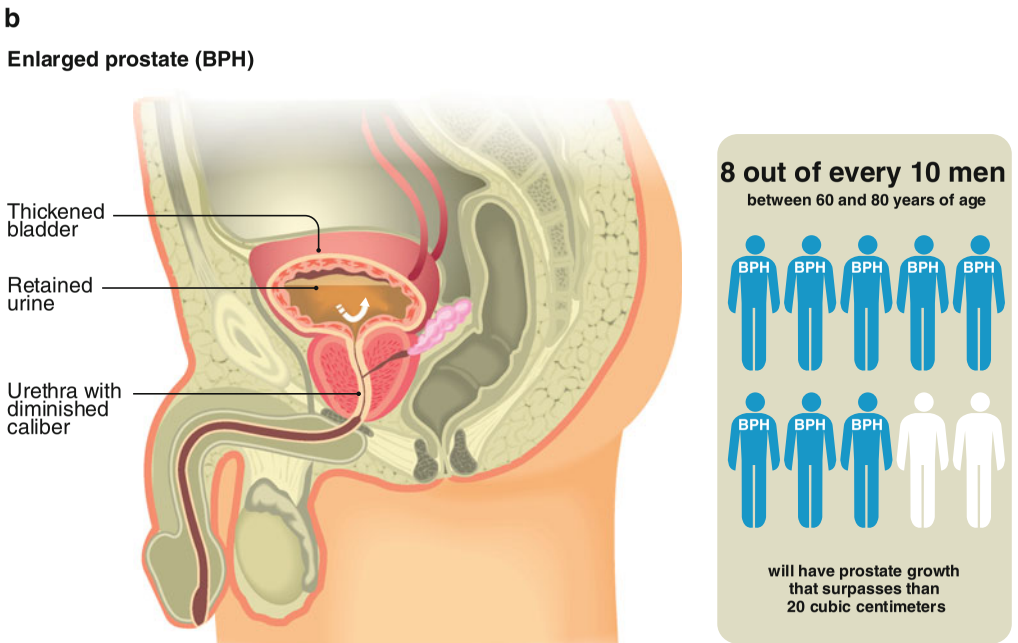


FIGURE 6.1 (continued)

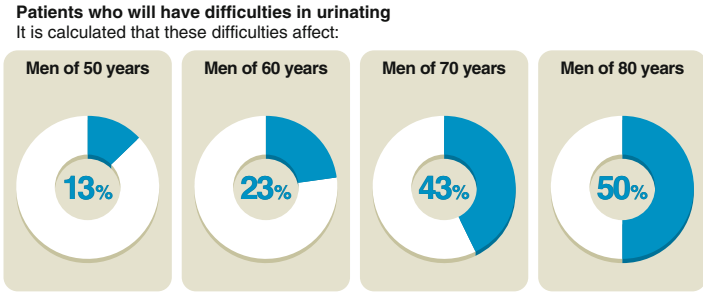


FIGURE 6.2 Urinary symptoms

Likewise, the problems have also been attributed to a change in the characteristics of the muscle and fiber cells forming the prostate. The interaction of these cells causes a constant pressure called active and passive tone, which determines the elasticity of the gland. An increase in this pressure, which is transmitted throughout the organ, can also interfere with the flow of urine.

Urinary obstruction can have disastrous consequences, since to compensate for this and to be able to function, the bladder reacts with an increase in the thickness of its walls so as to be able to expel the liquid with greater pressure. Because of this thickening, microscopic changes may appear; these may include the accumulation of fiber or decreased nerve sensitivity, which lead to altered organ function. *Storage* (*filling*) symptoms may begin to appear, characterized by the need to urinate more times during the day as well as urinary urgency.

In time, the bladder deteriorates to such a state that it is no longer capable of expelling the urine with sufficient pressure, leading to *voiding* symptoms: weak urinary stream, the need to push to urinate, etc. A substantial amount of residual urine may remain inside the bladder. This can cause complications such as the growth of bacteria and the resulting urinary infection, or the appearance of bladder stones.

Additionally, the kidneys may also be affected when there is a deficient elimination of urine. In this case, these organs may become dilated (known as hydronephrosis) and their function may deteriorate (chronic renal failure).

Diagnostic Methods

In the presence of symptoms like those described above, it is necessary to consult a specialist, who will inquire about the time of symptom evolution and intensity. The physician will investigate the presence of other symptoms or signs as well, such as: blood in the urine (which might indicate bladder stones or a tumor in the bladder); fever (which may be an indication of a urinary infection); pain in the lower part of the abdomen or behind the testicles (which might be due to prostatitis); a history of urethritis or urethral injury (which could lead to narrowness of the urethra); or a history of neurological disease such as diabetes, stroke, or Parkinson's disease (that may cause bladder malfunction).

Medical Treatment

One of the things the doctor will try to establish is the degree to which the symptoms are having an impact on the quality of life of the patient, since this will be important at the time of determining the treatment. Also, as of this first consultation, the physician will indicate the laboratory studies and will carry out the explorations considered necessary to learn about the condition of the prostate. These procedures are explained in detail in Chap. 2.

Once benign prostate hyperplasia has been established as the origin of discomfort, it is necessary to follow the treatment as indicated by the physician. The severity of the symptoms will determine the guidelines to follow.

Nevertheless, in those patients with mild symptoms that do not imply an important deterioration in the quality of life, it is possible to simply remain under the observation of the specialist, without needing to take medication. In these cases the patient will need to undergo regular medical checkups (generally every year) to follow the evolution of the symptoms.

The doctor may offer a series of recommendations, such as limiting nighttime intake of liquids, which will help reduce the number of times it is necessary to urinate at night. Also it

is advisable to reduce the consumption of certain irritants, such as coffee and alcohol, which can worsen the storage symptoms (urinary urgency and urinating an increased number of times each day). In half of these cases, the symptoms remain stable, without worsening.

As can be seen, the decision to begin a treatment with medication does not depend on the size of the prostate, since this is not necessarily correlated with the inconvenience it produces. In those cases where the symptoms begin to be bothersome, the patients can begin taking medications. These can improve the quality of life and prevent damage to organs such as the bladder and kidneys. However, it must be taken into account that these medications, except in a few cases, do not cure prostate enlargement but only alleviate the symptoms, so if the treatment is suspended, the symptoms will reappear almost immediately.

Alpha Blockers

The symptoms of benign prostate hyperplasia can be related to the contraction of the muscle cells found in the prostate. Like all the cells of the body, those of the prostate have receptors in order to be able to take orders sent by the nervous system. In this case, the order which indicates to the cells that they should contract is received by means of a receptor found on the surface, known as alpha 1 a.

There are medications that block or suspend the activity of this receptor, called alpha blockers. These relax the muscle tone of the prostate and allow the urine to pass easily through the urethra, which is freed from the pressure exercised by the prostate.

At present there are several alpha blockers available on the market. Some commonly prescribed alpha blockers include: Terazosin, Doxazosin, Alfuzosin, Tamsulosin (Flomax), and Rapaflow® (silodosin). The dose prescribed is one tablet once a day, which generally should be taken at night. Alleviation of the symptoms usually begins 48 h after starting the medication. The best possible response is achieved after 2 weeks.

Secondary Effects

In less than 10 % of people taking these drugs, episodes of vertigo, weakness, and dizziness may occur when they make sudden changes in position, such as getting up after having been lying down. One of the effects of the alpha blocker medications is that they can cause a deficiency in the regulation of the blood pressure. The exceptions are Tamsulosin, Alfuzosin, and silodosin, which do not tend to produce this type of alteration.

Alpha blockers do not interfere with erections or with sexual appetite. In less than 10 % of cases, Tamsulosin and silodosin may induce retrograde ejaculation, that is, the semen is not expelled outward but is sent to the bladder and then comes out with the urine. This happens because the drug, which acts on the receptors of the urinary system, keeps the neck of the bladder open during orgasm, causing the sperm from the seminal vesicles and the prostate to take a different path and head toward the bladder rather than outward.

5 Alpha Reductase Inhibitors (5ARIs)

The growth of the glandular cells that cause benign prostatic hyperplasia occurs because of the action of *testosterone*. However, the real influence on this process occurs from the combined action of the hormone with a protein called 5 alpha reductase, which results in a form known as dihydrotestosterone.

A group of drugs exist to block that protein. When taken, they can reduce the size of the prostate and thereby alleviate the symptoms of the patient. This symptomatic relief is usually more evident in the second month of the treatment.. The greatest reduction in the prostate volume is seen after 6 months. The patients who most benefit from the treatment are those with a prostate volume greater than 40 cm^3. The dose is one tablet per day. Some secondary effects reported are diminished sexual interest (4 % of cases), ejaculation disorders (2.7 % of cases), and difficulties with erection (between 1.7 and 3 % of cases).

Fact

Which treatment is more effective to alleviate the symptoms, alpha blockers or 5-ARIs? There are studies that indicate the greater benefit can be obtained with the first group, with observable differences after the seventh day of treatment. This finding can be explained by the fact that 5-ARIs bases its action on the reduction of prostate volume, and, as mentioned, the volume is not correlated with the severity of the symptoms. A recent study suggests that the combination of 5-ARIs plus an alpha blocker is more effective than the use of either one of the drugs alone, but this improvement is achieved only after 1 year of treatment and in patients with large prostate volumes and severe symptoms. Furthermore, this combination has a high cost.

Impaired Kidney Function

When the bladder remains full for long periods and does not empty completely with urination, the pressure increase in the urinary tract can cause alterations in the function of the kidneys, which are forced to filter the urine against the pressure generated in the bladder.

This can cause irreversible damage to the kidneys, especially when the symptoms have been present for a long time. For this reason, an intervention is required to free the obstruction of the urinary tract. If this cannot be done, the problem must be solved by introducing a catheter through the urethra so that urine can be released without resistance.

Acute Urinary Retention

This is the inability to urinate when the bladder is full. It may occur due to various prostate diseases such as benign prostatic hyperplasia, prostatitis, certain infections of the prostate, or also because of prostate cancer. It also occurs because certain medications can contract smooth muscle fibers of the prostatic tissue, causing urinary tract obstruction, or through

the action of certain drugs that inhibit bladder muscle contraction. Treatment for this condition is the placement of a catheter through the urethra to drain the retained urine. This emergency procedure should be done by a urologist, who will also decide on further treatment.

Fact
Urinary tract infections may be associated with the amount of urine left in the bladder after urination, which favors the growth of bacteria in the urinary tract.

Bladder Stones

The accumulation of solids in the urine, known as solutes, gives rise to mineral formations called calculi, or stones. Some of these calculi can be treated with medical therapy, especially those composed of uric acid, for which it would be necessary to neutralize the acidity of the urine. However, this would not solve the obstruction of the urinary tract exit caused by benign prostatic hyperplasia.

Recurrent or Severe Bleeding

This can occur in various clinical situations, such as in cancer anywhere in the urinary tract or in the prostate, and always requires immediate treatment. The cause of bleeding in prostatic hyperplasia can be the growth and dilation of the veins surrounding the urethra, which can break because of the obstruction and the straining to urinate.

This clinical picture occurs more often in people who take medications that alter the clotting process, such as acetylsalicylic acid (Aspirin®) and other anticoagulants. Bleeding usually occurs during urination and stops after a few days, though in some cases it persists and causes urinary retention because of the presence of clots.

Unstable Bladder with Urge Incontinence

Many men with prostatic hyperplasia may eventually develop what is known as bladder instability, which describes the situation where the bladder is activated independently of the desire to urinate, causing in some cases urine leakage.

This occurs due to changes experienced by the bladder muscle, due to the effort to overcome the resistance of the prostate to the expulsion of urine. As time passes, these changes may become more severe and there is increased risk of them becoming irreversible, damaging the bladder completely.

These changes cause symptoms of irritation, which occur with greatest intensity during the night. The most significant is urge urinary incontinence: a sudden need to urinate, often such that there is not even time to get to the bathroom.

Hernias

Patients with obstructive symptoms tend to contract their abdominal muscles to increase the force of the urinary stream and thus have a more complete emptying; this may promote the development of abdominal hernias or the growth of existing ones. These patients should first be evaluated and treated by the urologist to resolve their prostate disease, since, if the hernia is corrected without first freeing the urinary obstruction, the patient will continue straining to urinate and the hernia may recur.

Fact

Because of longterm obstruction of the flow of urine by the prostate, it is possible that the bladder muscle has become so weak that even when prostate surgery is performed and the obstruction is removed the bladder muscle is unable to contract enough to empty the urine completely.

When this is suspected, a study called urodynamics should be carried out; it will evaluate these changes before the surgery and thereby predict the response of the patient afterwards.

Surgical Treatments

Although surgery is the most effective therapeutic option for prostatic hyperplasia, it is also the one with the most possibility of complications. Even so, the percentage of patients who present them is very low. However, when certain health conditions such as uncontrolled diabetes, liver failure, and/or significant pulmonary or cardiovascular problems are present, surgical treatment is not recommended; rather, a more conservative treatment is advised. An operation is also contraindicated when there are severe psychiatric or mental disorders that impede adequate postoperative control (Fig. 6.3).

1. **Transurethral resection of the prostate (TURP)**: This is the most common prostate surgery and is practiced in about 95 % of patients with benign prostatic hyperplasia of less than 60 g (grade I–II).

   During the operation, once the patient is in an appropriate position and under anesthesia, the surgeon inserts a thin instrument called a resectoscope by way of the urethra and employs certain metallic elements known as loops, which produce sections and coagulation of tissues. In this way, the prostate tissue causing the obstruction is removed (Fig. 6.4a).

   Upon completion of the procedure the fragments of prostate tissue are extracted and sent for pathological

Classification according to the estimated size of the prostate		
Grade I	**Grade II**	**Grade III**
Between 20 and 40 g	Between 40 and 60 g	Greater than 60 g

Figure 6.3 Classification size of prostate

study. After the procedure, there must be continuous irrigation with sterile fluid using a urethral catheter to avoid the formation of blood clots, since there can be bleeding after the procedure. This irrigation is usually removed the day after the surgery. The patient should remain with a catheter in place, usually for a few days, and will be discharged from the hospital 2 days after the surgery if there are no complications (Fig. 6.4b).

What can happen if the patient decides against the operation? The urine retained in the bladder by the obstruction from the enlarged prostate will cause repeated urinary infections that will worsen with time, and depend-

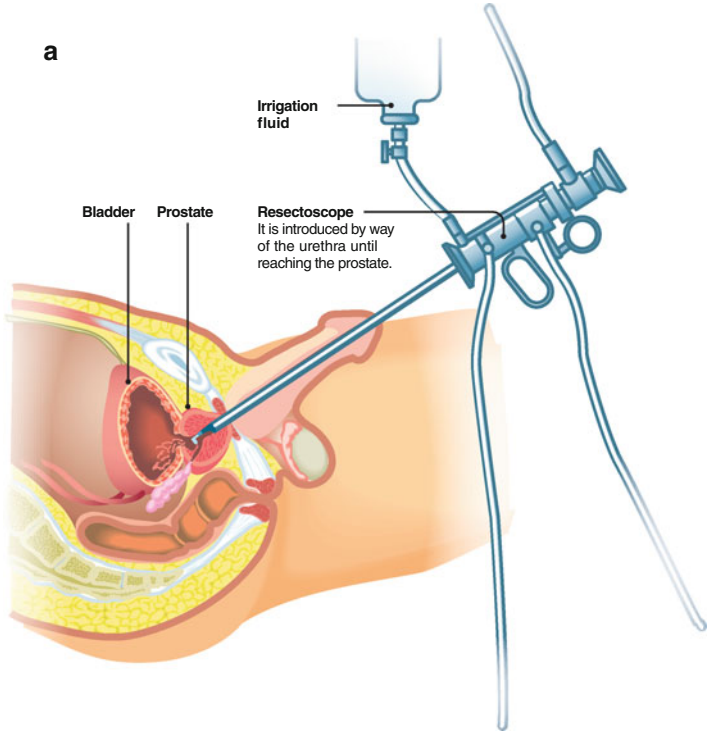
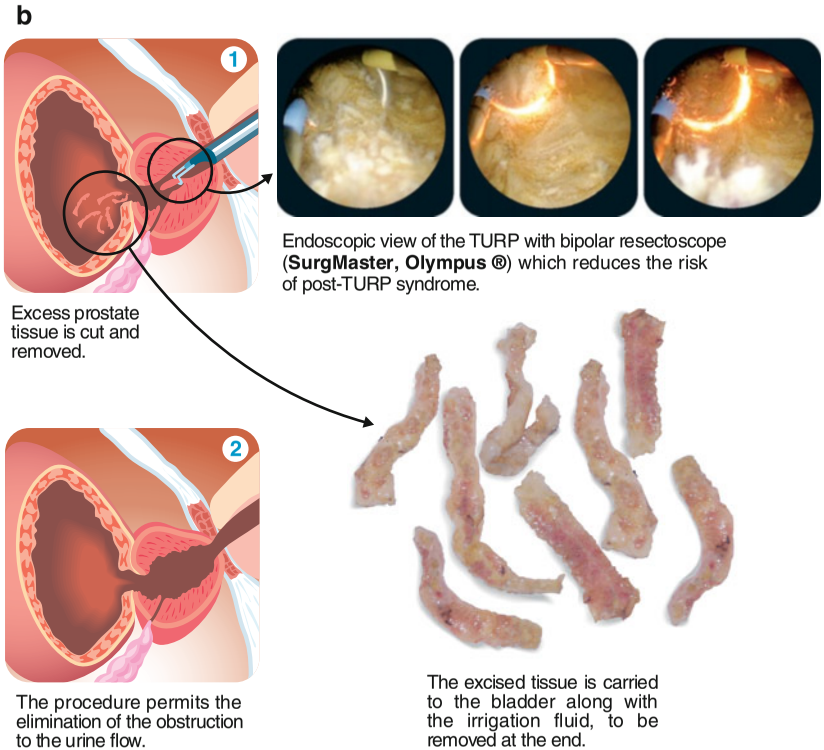


FIGURE 6.4 (**a**) TURP surgery. (**b**) TURP in detail



- Although the transurethral resection is considered a safe operation, there is a possible complication known as **post-TURP syndrome.**
- It is characterized by changes in the state of consciousness and visual alterations caused by the absorption of the liquids used during surgery through the resected tissue.
- While this complication can be very dangerous, it occurs in approximately **1 of every 50 patients** who undergo the operation and when it is identified in time, it can be successfully treated.

FIGURE 6.4 (continued)

ing on the velocity of growth of the patient's prostate, could cause complete urinary obstruction with irreversible damage to the kidneys. This could lead to catheter use indefinitely to deal with the obstruction.

2. **Open simple prostatectomy**: Generally, this type of surgery is only performed if the prostate is excessively large, that is, more than 60 g (grade III), as determined by digital rectal examination or transrectal ultrasound. It is referred to as open because the surgeon makes an incision of some 8–10 cm in the lower part of the abdomen to get to the prostate, instead of entering through the urethra as in the transurethral resection, because the prostate is so large that a long time would be required in the operating room to extract so much tissue in small fragments, as is done in TURP.

   There are two types of techniques: transvesical open prostatectomy, in which the obstructive part of the prostate is extracted through the bladder, and the open retropubic prostatectomy, in which the obstructive part of the prostate is extracted through the overlying cortex (capsule) without opening the bladder.

   Upon completing the procedure, a sterile plastic drain is placed to one side of the surgical incision in order to remove the urine and blood left in the site of the surgery. The drain is generally removed after 3 or 4 days. On some occasions a catheter is placed from the bladder to the abdominal wall to help emptying the urine, and is withdrawn 3 days after surgery, always before removing the catheter from the penis, which is done 4 or 5 days after the operation. The patient remains in the hospital 2–4 days after the procedure and should rest for approximately 2 weeks (Fig. 6.5).

Fact

The technique for the laparoscopic excision of the adenoma (that part of the prostate gland which has grown and is producing the obstruction) requires the urologist to undergo a special training so it is not very widespread. It is the specialist who will indicate the procedure to follow, according to his own knowledge and the conditions of the patient.

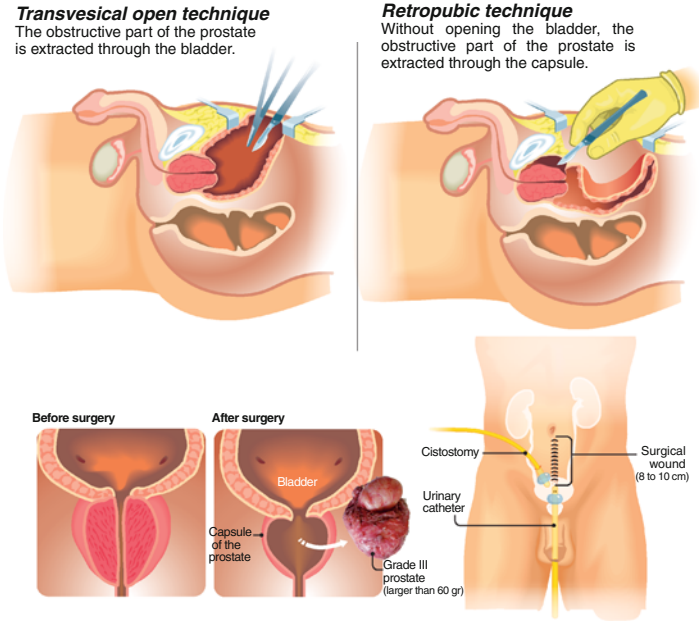


FIGURE 6.5 Open prostatectomy

3. **Laparoscopic simple prostatectomy**: Laparoscopy instead of open surgery can be used to remove the prostate if it reaches more than 60 g. Laparoscopy in the urological field has been gaining popularity in recent times because of its advantages. Among these are reduced pain, smaller scars and a faster recovery time.

   The procedure requires the use of five cylindrical instruments, called trocars, measuring between 5 and 12 mm in diameter each, which are inserted strategically in the abdominal wall through orifices of those same dimensions. The surgeon then inserts forceps and other instruments by way of the trocars and is able in this way to access the prostate; once it has been identified, the obstructive portion is extracted and placed in a special bag that is withdrawn

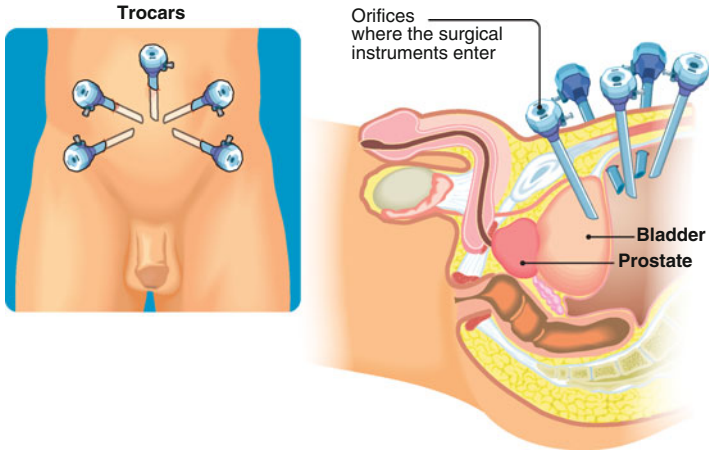


FIGURE 6.6 Laparoscopic prostatectomy

through the umbilicus. Finally, a catheter is inserted through the urethra, a thin latex drain is placed, and the wounds are closed. The urinary catheter is withdrawn 4–5 days after the operation (Fig. 6.6).

One of the advantages of the laparoscopic technique is that on producing a much smaller wound, in comparison to open surgery, the recovery is much faster. The patient can consume food much sooner and, in the majority of the cases, can go home the day after the procedure. Moreover, there is usually less bleeding during the operation since the pressure of the gas used during surgery acts as a clamp on the blood vessels and stops them from bleeding. Because of the instruments used, it is possible to see the tissues magnified, allowing for greater precision in the reconstruction of the urinary tract.

4. **LESS (Laparo Endoscopic Single-Site Surgery) Prostatectomy** This type of minimally invasive surgery is part of the evolution of conventional laparoscopy. It is performed through a 3 cm single suprapubic incision through which a single trocar with multiple valves is inserted. This in turn provides

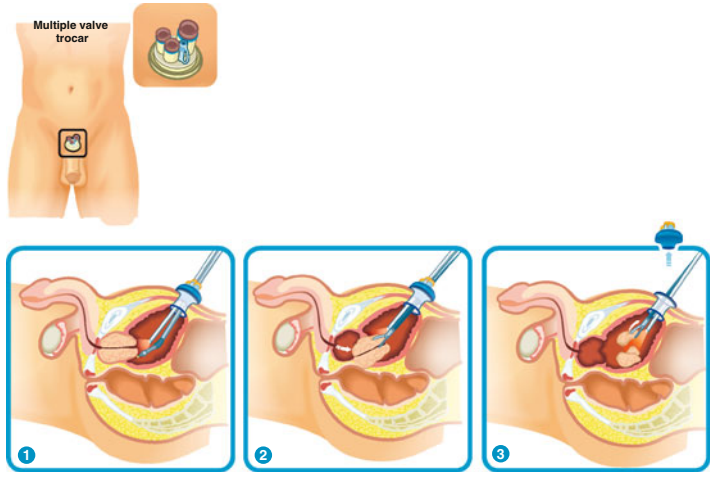


FIGURE 6.7 LESS prostatectomy

access to a modern flexible camera and other devices to allow the trained surgeon to perform the extraction of prostate adenoma with the same safety and efficacy when performed by open or laparoscopic surgery. This also implies rapid postoperative recovery and early return to daily activities (Fig. 6.7).

5. **Robotic simple prostatectomy**: Technological advances, like improvements in the audiovisual devices (which permit capturing images in three dimensions) and the ability to manage remote instruments, have resulted in the creation of auxiliary robots for surgery.

   Robotic surgery is also part of what is called "minimally invasive surgery," because, like conventional laparoscopy, it needs only small incisions through the abdominal wall to carry out the procedure, with the difference that through these, the arms of the Da Vinci surgical robot (by Intuitive Surgical®) are inserted (Fig. 6.8).

   The advantage of the modality: It permits a wider variety of maneuvers than even the human hand, as well as greater precision and detail in the surgical movements.

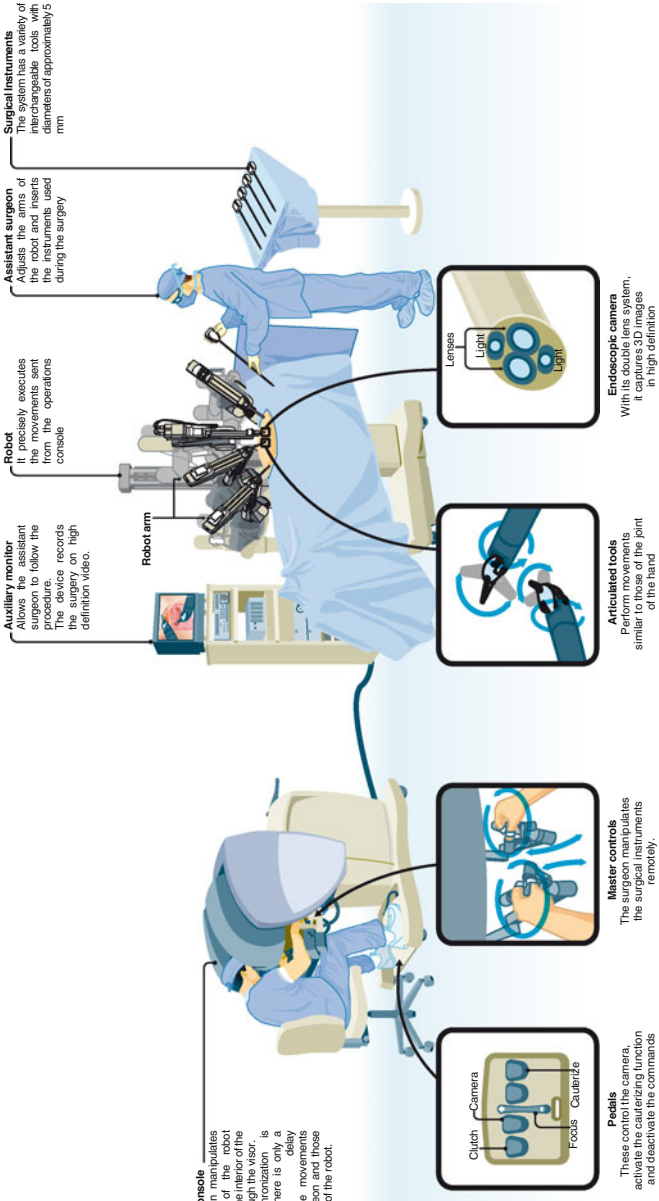


FIGURE 6.8 Robot

Contraindications: In spite of its advantages, laparoscopic and robotic surgery is not for all kinds of patients, since, as was mentioned, in order to have good visibility inside the abdomen, it is necessary to pump in gas, principally CO_2 (carbon dioxide). This gas can impact the heart, the lungs, and the abdominal organs, which are affected by the pressure of the gas. For this reason, patients who have any kind of previous pulmonary disease or whose cardiovascular function is less than optimal are not good candidates for this type of intervention.

Fact
Laparoscopic and robotic techniques have been shown to be safe, with excellent results in comparison to open surgery. They have the advantages of a minimally invasive procedure, such as better control of bleeding, less pain in the postoperative period, and a faster recovery.

6. **Other minimally invasive procedures**
Newer studies are being published about minimally invasive procedures for the treatment of benign prostatic hyperplasia. These studies are optimistic and seem to provide a favorable solution for patients with large prostates, those at high surgical risk, and those for whom a minimally invasive procedure would be preferable. In the many cases, hospitalization is either not required or is overnight.
   A. **Green light laser prostate surgery**: This technique uses a type of laser known as a KTP (potassium-titanium-phosphorus), which is guided to the prostate through an elastic optical fiber by way of the urethra to direct the laser to the prostate tissue. High temperatures are achieved that vaporize the tissue and at the same time cauterize the sites of bleeding. The surgeon must direct the light only toward the affected tissue so as not to damage neighboring tissue.

      Pros and cons of the green light vaporization of the prostate: The laser vaporizes prostate tissue at the same time that it seals the nearby blood vessels, thus reducing the risk of bleeding and the need for transfusion (Fig. 6.9).

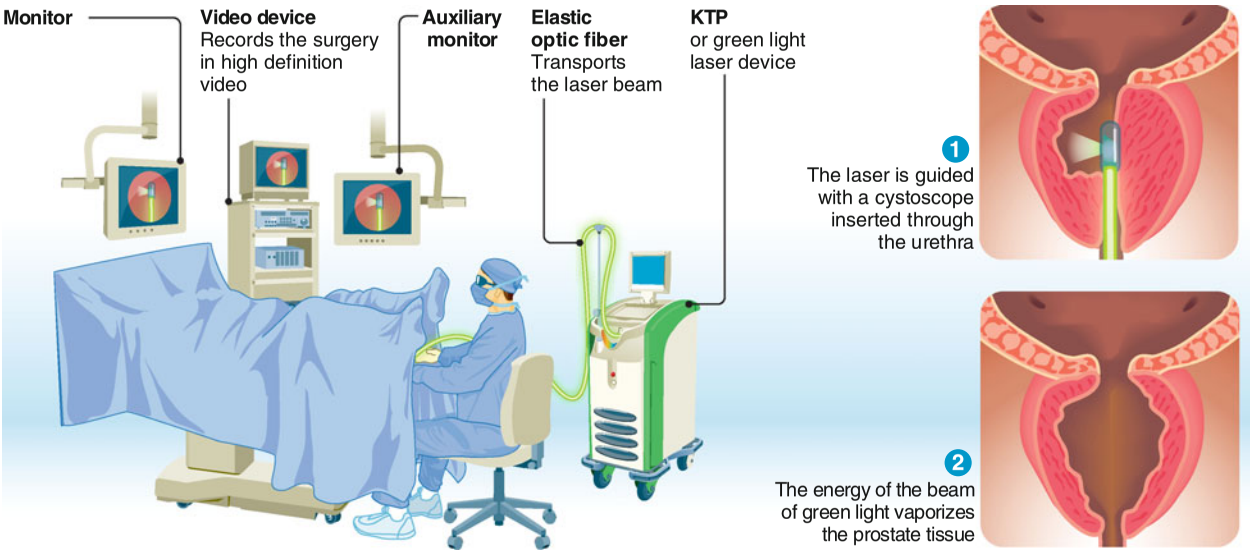


FIGURE 6.9 Green light laser

Patients who undergo this surgery are hospitalized for a short time and the catheter can be withdrawn earlier than in patients who undergo TUPR. Compared to conventional TURP, some men may experience symptoms of urinary irritation following the procedure for a longer period of time. Other complications such as urethral stricture, incontinence, and erectile dysfunction are rare, similar to TURP.

These procedures require the urologist to undergo a special training. Moreover, the high cost of laser therapy also has hindered studies from being carried out in a larger number of hospitals. One disadvantage is that the laser permits removal of 1 g of tissue per minute, thus requiring somewhat longer time in the operating room for men with large prostate glands. Finally, it is not possible to obtain a sample of tissue for a pathological study, for example when cancer is suspected.

B. **Holmium laser prostate surgery (HoLEP)**: This technique involves the use of another type of laser known as Holmium: YAG (Ho: YAG). This surgical procedure is typically performed on larger prostates, wherein, instead of ablating the tissue, this high-energy laser removes the core of the prostate from inside the gland to create an open channel, which is then cut into smaller pieces using a machine called a morcellator and then flushed with irrigation fluid. It provides results similar to TURP, but with less chance of bleeding and a shorter recovery time. Therefore, HoLEP is preferable for patients with bleeding problems or multiple other health conditions. One of the benefits of HoLEP is that the procedure preserves removed tissue for microscopic examination unlike the green light surgery that vaporizes the tissue. This procedure requires specialized skills and training, which has limited more widespread adoption of this technique.

Other Treatments

Phytotherapy
Extracts of vegetable products have also been utilized to alleviate the symptoms of prostate hyperplasia. Some of the therapies have been known since the fifteenth century B.C. Phytotherapy is relatively popular in Europe. The products can be obtained without medical prescription in natural food stores, often as nutritional supplements. These are usually extracts from roots, seeds, or fruit.

Serenoa repens (saw palmetto)
This is the product most known to doctors and patients. It is extracted from the dwarf palm of North American origin, and can be obtained with different brand names. Since it is considered a nutritional supplement, the manufacture and efficacy are not regulated like pharmaceutical products, which leads to doubts about its quality and effectiveness (Fig. 6.10).

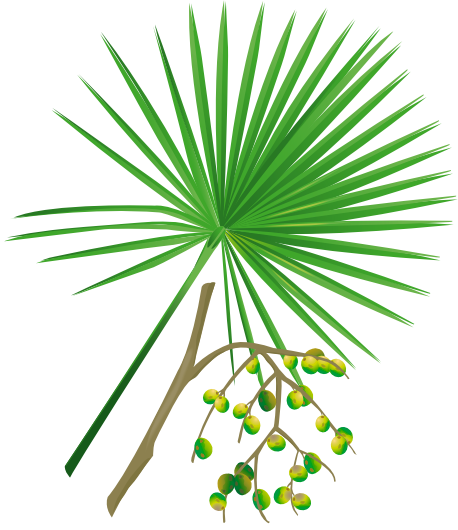


FIGURE 6.10 Saw palmetto-plant

The mechanism of action is apparently based on the inhibition of the 5 alpha reductase enzyme. Like Finasteride, it stimulates the death of cells within the prostate and has anti-inflammatory and anti-estrogenic properties. Remember that estrogens stimulate the growth of the fibrous and muscle tissue of the prostate. Secondary effects occur infrequently and are related to fatigue, headache, insomnia, vomiting, and loss of libido or sexual desire.

Fact

The benefit obtained from phytotherapy seems to be, in the best of cases, moderate. There are many doubts about the trustworthiness of these compounds, seeing as they are fabricated without rigorous standards due to the lack of supervision by official agencies. More clinical studies are needed, involving a large number of patients with longterm follow-up, before recommending the formal use of these therapies in daily practice.

Chapter 7
Prostate Cancer

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What is prostate cancer?
Prevention
Symptoms
Surgical treatments
Preparation prior to surgery and aftercare
Pathological interpretation of the prostate removed during surgery
Biopsy results
Prognosis
Complications of radical prostatectomy

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Sexuality and prostate cancer
The diagnosis of prostate cancer—what to do, what to know?
Relationship between the treatment for prostate cancer and erectile dysfunction
Alternative treatments for erectile dysfunction
Erectile dysfunction secondary to radical prostatectomy
Urinary incontinence secondary to radical prostatectomy
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Testimonial

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What Is Prostate Cancer?

This is the presence of cancerous cells in the prostate gland. As in the rest of the organs, when cancer develops in the prostate the cancerous cells begin to multiply in an uncontrolled manner such that in time they can spread from the prostate to other parts of the body, especially to the bones and the lymph nodes near the gland (Figs. 7.1 and 7.2).

Epidemiology

Prostate cancer is the most common cancer diagnosed in North American men, excluding skin cancers. Prostate cancer is now the second leading cause of cancer death in men, exceeded only by lung cancer. It accounts for 29 % of all male cancers and 9 % of male cancer-related deaths.

Predisposition
Before 50 years of age, it's rare that men develop prostate cancer, so efforts to diagnose it are usually intensified after that age. Although it is not known with precision what triggers prostate cancer, several factors that might be related have been described, including:

Age
This is one of the determinants. On the average, the diagnosis is made beginning at 71 years. Fewer than 1 % of the cases of

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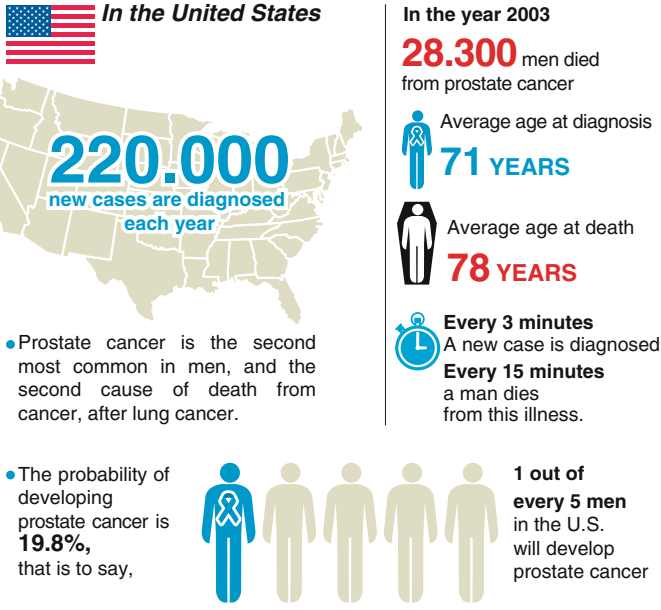


FIGURE 7.1 USA epidemiology

prostate cancer are detected in men under 50 years of age, and only 16 % in men between 50 and 64 years of age. However, with the development of new technologies, the diagnosis in young men has increased.

Hormonal factors

Hormonal action is without doubt another trigger of the disease. It has been observed that the men suffering from a failure of the pituitary gland, those who have had their testicles removed, or those suffering from a hormonal problem that decreases androgen levels are less prone to develop this type of cancer. Similarly, the appearance of this disease in young men has been related to the use of testosterone.

Hereditary factors

It has also been shown that a man whose father or brother has developed prostate cancer has twice the risk of occurrence

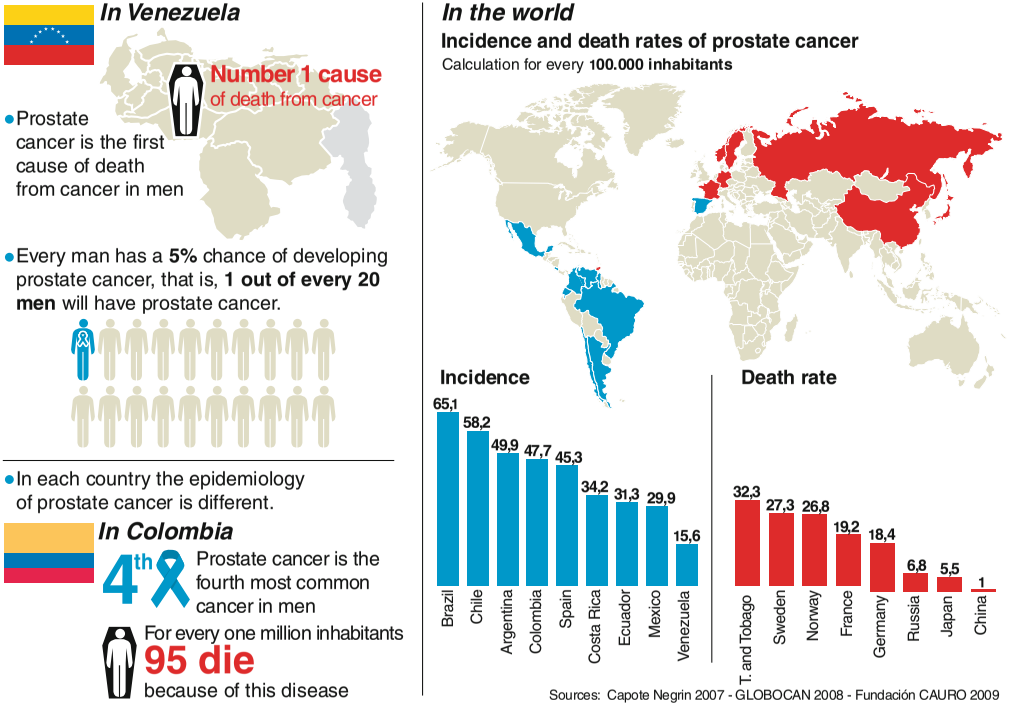


FIGURE 7.2 World epidemiology

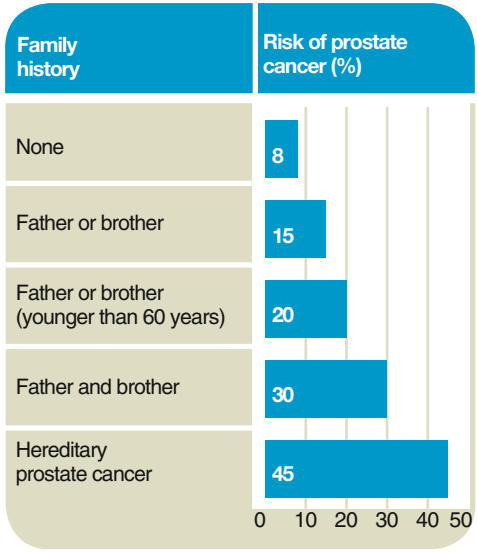


FIGURE 7.3 Family history

of the disease compared to that of the average man. For this reason it is recommended that if there is any family history of prostate cancer, examinations such as the digital rectal examination and the prostate-specific antigen should be carried out at early ages, starting at 40, and a urologist should be seen at least every 6 months after the age of 50. Between 11 and 15 % of the patients with prostate cancer have a family history of this disease (Fig. 7.3).

Genetic susceptibility

Studies of the human genome and more recently of the proteins that form part of the human DNA (that is, all of the genetic information of the species) have described several mutations or changes in certain chromosomes that generate cellular alterations, thereby accelerating the appearance of cancer. In the very near future, new markers that have been studied will be the gateway to new perspectives in the prevention and treatment of prostate cancer.

Diet
This also plays an important role. It is known that people who are overweight or have problems with fat metabolism tend to develop more prostate cancer than those who follow a balanced diet. Several research studies have been conducted to study the effect of selenium, vitamin E, as well as the isoflavonoids found in various food products on prostate cancer prevention. However, at this time there is not enough conclusive evidence that any of these agents can effectively prevent prostate cancer.

Geographic location
It appears that men who live in countries with less exposure to the sun are more likely to suffer from prostate cancer because of their low levels of vitamin D.

Tobacco use
Important, though not conclusive, studies indicate that smokers may be at greater risk of developing prostate cancer. It appears that nicotine, which is highly toxic, might generate some cellular and hormonal change that favors the disease.

Exposure to cadmium
Cadmium is a mineral found in cigarettes as well as in alkaline batteries. It interferes with zinc, a chemical element vital to many activities of the human cells, including some of those processes that occur in the prostate. Patients with prostate cancer have been found to have low levels of zinc in the body.

Vasectomy
This common procedure used for birth control in men (comparable to tubal ligation in women), may play a role in the predisposition to prostate cancer; however, there is no evidence suggesting a direct relation between prostate cancer and vasectomy (Fig. 7.4).

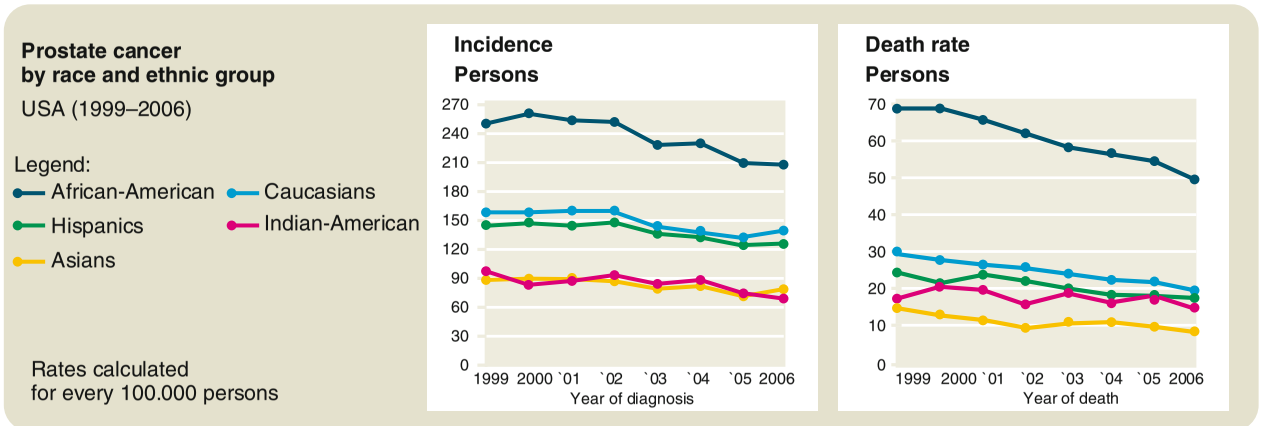


FIGURE 7.4 Race and ethnic group

Prevention

Screening

One of the great controversies in preventative medicine is whether the prostate-specific antigen test should or should not be part of the periodic health examination. To answer this question it should be taken into account that prostate cancer is the most frequent of the lethal tumors and the leading cause of death by cancer in men.

The use of the prostate-specific antigen has contributed to increased detection of prostate cancer. Now more than ever prostate cancer is diagnosed. At the same time, the death rate has decreased. Men with localized prostate cancer have a 20–60 % chance of dying from this cause if they do not receive treatment. For example, at present in North America about 60 % of the tumors detected at the initial PSA screening are localized, making it possible for the urologist to offer the patient a treatment that will cure the disease.

In the past 10 years, thanks to screening programs, the diagnosis of prostate cancer in advanced stages has declined significantly.

Fact

Screening, according to the World Health Organization, is the application of a simple test in a healthy population to identify those individuals who have some related pathology but who do not as yet show symptoms. In the case of prostate cancer, the screening is directed toward men 50 years of age or older and those 40 years and older if they are of African descent or have a first-degree relative who has been affected.

Primary prevention

Current information about the risk factors for prostate cancer suggests that some cases can be prevented. One possible risk factor that can be changed is the diet. The risk of prostate cancer can be reduced with a diet low in fats and high in vegetables, fruits, and cereals.

The American Cancer Society recommends eating a variety of health foods, with emphasis on those of vegetable origin and limiting the consumption of red meat. It also suggests the daily consumption of fruit and products with fiber, such as bread, cereals, and rice. These nutritional suggestions also help reduce the risk of other types of cancer.

Tomatoes, citric fruits, and watermelon are rich in lycopenes. These substances, similar to vitamins, are antioxidants, which can help prevent mutations of the DNA and, therefore, reduce the risk of prostate cancer. The effects of vitamin E and selenium as preventatives have also been studied.

Several studies associate daily use of nonsteroidal, anti-inflammatory drugs, such as Aspirin®, with a lower incidence of prostate cancer in men 60 or more years old.

It should be taken into account that the exact cause of prostate cancer is unknown and that there are risk factors such as age, race, or family history that cannot be controlled.

Secondary prevention

Early treatment through early detection reduces morbidity and mortality associated with the disease. In the United States and Europe, studies have been carried out in the past few years to clarify whether screening with the prostate-specific antigen reduces mortality from prostate cancer or not. Up until now, screening in healthy men has proved to be useful, in spite of criticism of some of the studies. What is found in medical literature suggests that it is a useful tool and it reduces mortality.

One of the most recognized studies is that of Tyrol, an Austrian city where screening with the prostate-specific antigen began in the 90s. The research showed that there was a reduction in mortality from prostate cancer in the period analyzed (between 1999 and 2003) in comparison with other cities where the antigen tests were not performed.

The effect of the screening programs depends on the sensitivity and the specificity of the detection method, but also on the effectiveness of the therapy applied in the cases detected. In Tyrol, the majority of the patients underwent

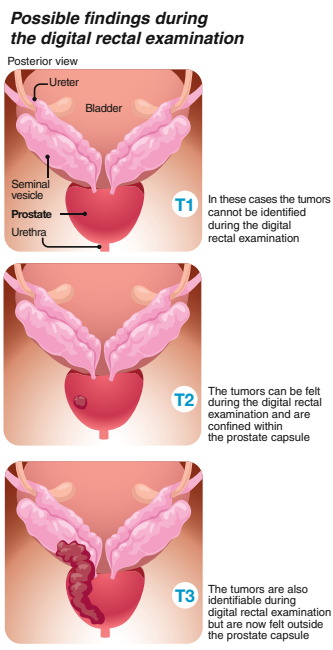
surgical removal of the prostate and seminal vesicles (radical prostatectomy) with good results.

In the United States, the most important study of screening for the detection of prostate cancer showed that the diagnosis has increased drastically since 1988, but then demonstrated controversy about the benefits of the program. One study compared two groups of men, one in which the prostate-specific antigen was tested and the other group in which it was not. After 10 years of follow-up, a very low death rate was found, without any significant difference between the two groups. The European study, mentioned above, showed a mortality reduction of 20 % in patients subjected to the screening 8 years after starting the program.

A recent and important study carried out in Sweden compared two groups of 10,000 men between 50 and 65 years old. What was found was a higher incidence in the group of men who underwent PSA testing, as there was a diagnosis of prostate cancer in 12.7 % of these men. In the second group (without PSA), the diagnosis was reduced to 8.2 % of the participants. This means there were 1.6 times more diagnoses of prostate cancer in those who underwent the test regularly. They concluded that screening with PSA reduces mortality from prostate cancer by half.

Symptoms

Prostate cancer rarely causes symptoms, and when it does, most probably it is a tumor in an advanced stage. This is because the majority of the tumors grow in the peripheral zone of the prostate, that is, far from the urethra, so they can continue growing without causing any discomfort. When the tumor grows near the urethra or the neck of the bladder, then it can cause symptoms of irritation or obstruction (see Chap. 2), which do not arouse much suspicion of cancer because they also occur in other prostate diseases. Prostate cancer with local invasion can grow and affect the bladder



TNM Classification of Prostate Cancer

T: *primary tumor*	
Tx	The primary tumor cannot be evaluated
T0	There is no evidence of the primary tumor
T1	**Tumor not clinically evident,** not palpable nor visible with imaging techniques
T1a	Tumor detected fortuitously **in less than 5% of resected tissue**
T1b	Tumor detected fortuitously **in more than 5% of resected tissue**
T1c	**Tumor identified by means of a needle biopsy** (because of an elevated PSA)
T2	**Tumor limited to the prostate**
T2a	The tumor affects **half or less than half of one lobule of the prostate**
T2b	The tumor affects **more than half of one lobule but not both lobules**
T2c	**The tumor affects both lobules**
T3	Tumor which **extends through the prostate capsule**
T3a	**Extracapsular extension unilateral or bilateral**
T3b	Tumor which **invades the seminal vesicle**
T4	**Tumor is fixed or invades adjacent structures** other than seminal vesicles: bladder neck, external sphincter, rectum, levatorani muscles, and/ or pelvic wall
N: *Regional lymph nodes*	
Nx	Cannot be evaluated
N0	Metastasis not shown in regional lymph nodes
N1	Metastases in regional lymph nodes
M: *Evaluation of distant metastasis*	
Mx	Cannot evaluate distant metastasis
M0	There is no distant metastasis
M1	There is distant metastasis
M1a	The cancer has spread to lymph nodes beyond the regional ones
M1b	The cancer has spread to bone
M1c	The cancer has spread to other sites (regardless of bone involvement)

Ohori M, Wheeler TM, Scardino PT "The New American Joint Committee on C and International Union Against Cancer TNM Classificaton of Prostate Cancer Clinicopathologic Correlatons" Cancer 74 (1994):104-114

FIGURE 7.5 Classification

floor and, thus, occlude the emptying of urine from both kidneys, leading to total obstruction and kidney failure.

Other symptoms, such as pain in the bones and anemia associated with renal failure, suggest metastatic prostate cancer (Fig. 7.5).

Surgical Treatments

Radical prostatectomy

This is the name given to surgery used to remove the prostate in patients with cancer. It involves the removal of the entire prostate gland, together with the seminal vesicles, and the bladder is then reconnected with the urethra, the channel

through which the urine flows from the bladder through the penis to the exterior. In special cases, the surgeon might also remove the regional lymph nodes to evaluate them and determine if the cancer has spread beyond the prostate (Fig. 7.6).

An important consideration is that after surgery, the patient will no longer ejaculate due to the removal of the prostate and the seminal vesicles, which store the seminal fluid; although this happens, the patient will conserve exactly the same sensation of pleasure during orgasm. In the case where the patient wishes to have children after the procedure, some assisted reproductive techniques to achieve fatherhood will be needed, such as those that involve the extraction of sperm from the testicles with subsequent injection into the female reproductive cells (as such is the case with in vitro fertilization) (Fig. 7.7).

Indications

In general, a radical prostatectomy is recommended only for men who have clinical, biochemical, and/or radiological evidence of the cancerous disease located only in the prostate, as well as being in good health in general, with a life expectancy of 10 years or more. An exception to this are young men with suspicion of a localized advanced disease, who could benefit more from a combined treatment including radical prostatectomy, radiotherapy, and hormonal blocking (as opposed to just receiving radiotherapy and hormonal blocking). The urologist can make use of certain normograms, like those shown in the table, to estimate the risk of extraprostatic disease and evaluate the pros and cons of surgery.

Diagnostic studies currently available do not make it possible to precisely evaluate whether the prostate tumor has extended beyond the prostate. This can only be known after surgery, once the pathological examination has been completed. Furthermore, on rare occasions (less than 3 % of patients), it happens that even when the results of the pathological study indicated that the disease was limited to the prostate, the prostate-specific antigen begins to rise after

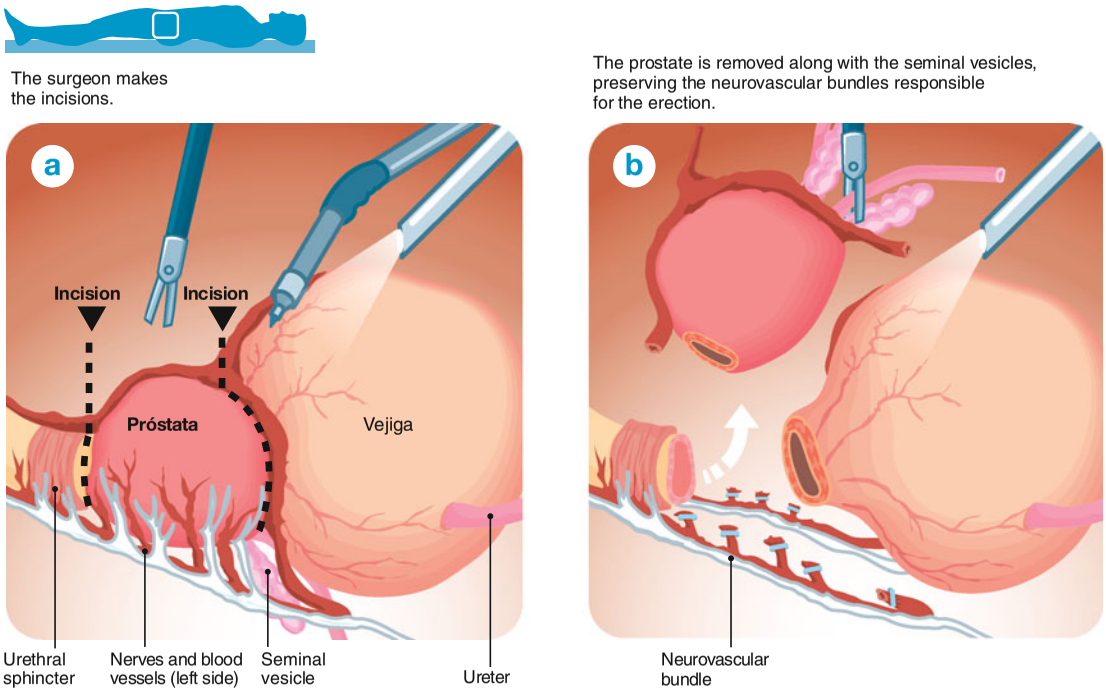


FIGURE 7.6 (**a**, **b**) Radical prostatectomy

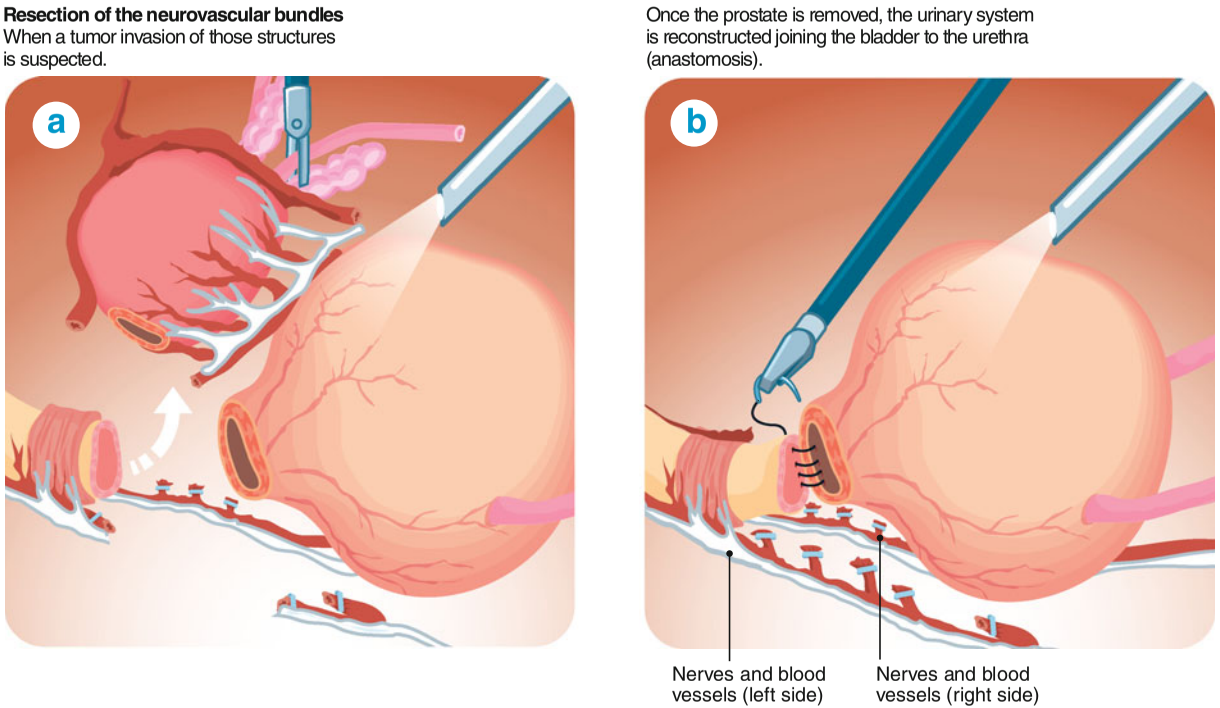


FIGURE 7.7 (**a**, **b**) Radical prostatectomy

Risk groups for clinically localized prostate cancer			
RISK	**TNM stage**	**Gleason**	**Pre–operative PSA**
Low	T1c – T2a	Up to 6	Up to 10 ng/ml
Moderate	T2b – T2c	7	10 – 20 ng/ml
High	T3	8–10	More than 20 ng/ml

Prostate Cancer Guidelines NCCN Clinical Practice Guideline in Urology, 2011

FIGURE 7.8 Risk groups

surgery, revealing that possibly cancerous cells still remain at the prostate bed or has entered the bloodstream and disseminated in the body. For this reason, patients who have undergone this operation, even when according to the biopsy the disease was contained, must continue annual control during at least 10 years after surgery.

Lymphadenectomy
This is the removal of lymph node chains near the prostate (iliac and obturator nodes) to determine the presence of cancer cells in them. It is indicated for patients who are considered medium to high risk, as shown in the table (Fig. 7.8).

Types of radical prostatectomy
The purpose of surgery is to eradicate the prostate cancer, attempting to protect the nervous and vascular structures responsible for erection without compromising the cancer control goal, and delicately separating the area of the urinary sphincter to re-establish urinary continence.

The neurovascular structures responsible for erections are located along the sides of the prostate and in close contact with it. Therefore, on occasion, if it is suspected that the cancer may be on the edge of the prostate, the total or partial removal of these structures is indicated in order to increase the possibility of the complete extraction of the cancer.

At present, the use of certain statistical analyses of the results of patients operated on under similar conditions makes it possible to create tables of probabilities. When the results of a specific patient are situated within these tables, it is possible to know the risk of the disease extending beyond the prostate, and even the possibility that the regional lymph nodes are affected. The analysis of these probabilities, the results of the biopsies, and the digital rectal examination (sometimes a nuclear magnetic resonance is added), along with the intra-operative findings, condition the surgeon's decision to remove or preserve the nerves linked to erection.

The operation can be carried out in different ways, with various methods of incision. The preservation of the healthy nerves is possible in any of the techniques, and success depends more on the expertise of the surgeon than on the method used.

Minimally invasive laparoscopic techniques, with or without robot, offer the advantage of very small incisions with more rapid recovery (and return of the patient to normal activities), as well as lower risk of complications from surgical wounds, such as infections or hernias, since only five incisions, between 5 and 12 mm in length, are made. However, it should be taken into account that robotic surgery in the hands of non-experts is not better than open surgery in expert hands.

Some publications report that, in addition to these advantages, robotic surgery enables a faster return to urinary continence and erectile function. Furthermore, there are surgeons, experts in open surgery, who have decided to start operating with the robot and have reported more than 2,000 cases in which the results with positive margins (indicating that tumor tissue was left) are fewer with the use of the robot (Vanderbilt University). However, another series of studies reports similar results in the hands of experts, independent of the technique used.

There are different approaches to a prostatectomy. Some can be carried out with regional anesthesia, others require general anesthesia. On the average, the surgery lasts about 3 h.

Radical retropubic prostatectomy: This is the most common approach. Regional anesthesia can be used and it is a conventional open surgery. The incision in the skin extends from the umbilicus to the pubis. Bleeding is a known complication to this procedure. The surgeon will remove the prostate gland, taking care to preserve the nerves that control erections on either side of the prostate. The surgeon may also remove the lymph nodes nearby, if advanced disease is suspected.

Radical perineal prostatectomy: In this procedure, the surgeon makes an incision in the skin between the anus and the base of the scrotum (perineum). Due to the location of the incision, it is difficult to remove the regional lymph glands. The perineal surgery has less risk of hemorrhage and normally takes less time to complete than the retropubic procedure.

Radical laparoscopic prostatectomy: This procedure is carried out in specialized medical centers. This type of technique requires general anesthesia, and in place of a single large incision, the surgeon makes various small incisions of between 5 and 12 mm each in the abdominal wall. Through one of them, gas (carbon dioxide CO_2) is fed into the abdominal cavity, creating a working space between the wall and the abdominal viscera. Then a special tube with its own light source and video camera (laparoscope) is introduced; this helps observe inside the abdomen, with the possibility of amplifying the view of the operating field with optimal quality in high definition (HD). Into the other incisions (up to four) other working instruments are introduced, such as forceps and scissors, used for performing the surgery. One of the difficulties in carrying out this procedure is that the surgeon must learn and have adequate training in a series of maneuvers that will allow for an adequate angle for cutting or suturing while using these instruments. The air in the abdominal cavity compresses the veins and thus reduces the bleeding. With this technique it is also possible to preserve the nerves around the prostate and remove the lymph nodes. Clearly the recovery of the patient and his reincorporation into his daily life is much faster than in any of the open surgery techniques.

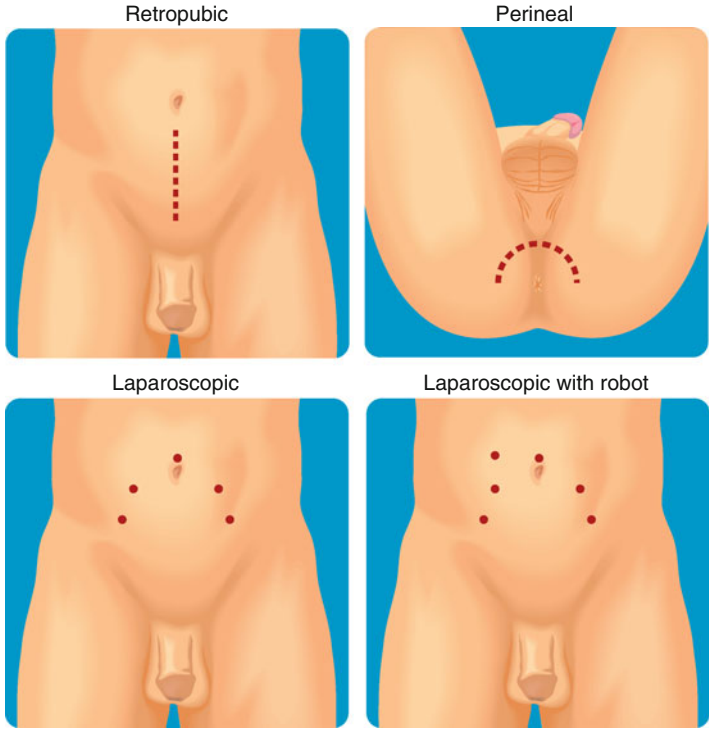


FIGURE 7.9 Prostatectomy incisions

Robotic laparoscopic radical prostatectomy: Today, this is the most frequently employed prostate cancer surgery in the United States, and is used in very specialized centers. It follows the same oncologic principles as the previous techniques and can preserve the nerves for erection as well as obtain lymph nodes, when necessary. The air in the cavity and the points of access to the abdomen are obtained in the same way as in the laparoscopic technique, but through them the robot arms of the Da Vinci® system are introduced. The robot arms give the surgeon finer and more precise control for certain tasks, such as preservation of nerves. Visual amplification like that in laparoscopy is used (Fig. 7.9).

Another difference between laparoscopy and robotics is that the forceps used in laparoscopy are manipulated directly

by the hands of the surgeon, where as in robotics the surgeon is seated at a control console from which the movements of his hands are transmitted to the hands of the robot, which are inside the patient's abdomen.

In laparoscopy, the surgeon has the indirect sensation of touch between the organs and his forceps, a sensation not experienced by the surgeon who uses the robot. Also, the robotic camera has one lens for each eye, which when fused give the surgeon a three-dimensional view similar to normal human vision, in contrast to the laparoscopic technique. The robotic procedure just like the laparoscopic technique requires general anesthesia and the time in surgery is a bit longer than with open techniques, but just like laparoscopy the recovery and the reincorporation of the patient into his daily activities are faster.

One important difference is that for surgeons the learning curve to use the robot is faster than with conventional laparoscopy, since three-dimensional vision and the movements of the ends of the instruments are similar to those of the human hand. Both procedures, laparoscopy with or without the robot, require a learning process estimated at over 250 cases to achieve the best oncologic results.

In the United States today there are more than a 1,000 robotic systems employed in surgery, and statistics show that robotic surgery is more frequent than traditional open surgery. Of course, one drawback to the use of these complex technologies is the cost: besides the price of the robot, approximately three million dollars, there is the cost of maintenance and replacement of the instruments, since each pair of forceps can be used in only ten procedures.

The advance of these technological platforms is evolving. At present, the most modern robot has two consoles; at one is the surgeon, and at the other the expert professor who guides him in order to accelerate the learning curve. Additionally, a series of simulators are available where the surgeon can practice. Moreover, a robot is being developed that will enter through a single orifice and will deploy a series of forceps internally, reducing further still the number of punctures needed for the surgery.

Preparation Prior to Surgery and Aftercare

Ten days before surgery: All treatment with Aspirin® or other anticoagulants should be suspended (Warfarin, Plavix®, etc.). All of the preoperative examinations should be done: laboratory exams, chest X-ray, and cardiovascular evaluation. If diabetic, stop taking tablets of the oral hypoglycemic type (Glibenclamide, Metformin, etc.) 48 h before surgery.

The day before surgery: Have a light breakfast at 9 am. Starting at noon, take one-half of a bottle (50 ml) of undiluted oral laxative (Fleet Fosfosoda®) followed by several glasses of sweetened juice, which will help relieve the salty and unpleasant taste of the laxative. Three hours after taking the first dose, take the remaining half of this laxative, also followed by the sweetened drinks. This oral laxative will cause an increase in bowel movements in order to clean the intestine for the day of the operation.

For supper, have clear liquids such as water, juice, or tea; consuming liquid is acceptable, if thirsty, until midnight. Antihypertensive drugs should not be suspended nor should the times they are habitually taken be altered. Even on the morning of the day of the surgery, this medication should be taken with a small quantity of water (just a sip).

Finally, pack luggage for the hospital stay: take comfortable pants with an elastic waist, a shirt with buttons (which can be opened in front), and a bathrobe.

The day of surgery: A full fast all day is required. If necessary, take only the anti-hypertensive medication with a sip of water.

The first hours after surgery: In the first hours the patient might feel cold, as an effect of the anesthesia, as well as some pain at the incision sites. This is easily controlled with painkillers.

A very common feeling is the discomfort produced by the presence of the catheter inside the urethra of the patient; generally this is perceived as an irritation or an intermittent desire to urinate without being able to, but the sensation is

mild and transitory. This is a normal effect due to the surgery and catheter in the urethra and bladder. The feeling disappears completely after a few hours. Family members and persons accompanying the patient play an important role in the first hours after the operation to help control anxiety. If more intense discomfort occurs, the medical personnel should be notified.

Fact

One of the principal advantages of laparoscopic surgery is that usually there is less bleeding. Only 3 % of the patients require a transfusion of 1 or 2 units of blood. At 6 and 24 h after surgery, blood tests are performed to determine hemoglobin levels.

Aftercare—getting up progressively: After surgery, remain quietly in bed for 2–3 h without talking. Gradually begin to move in bed, then raise the bed to a sitting position. It is recommended that you try to get to your feet during the first 6–8 h after operation. Obviously this should be a slow process: progressively the head of the bed should be raised. If you tolerate this without feeling dizzy, after 10–15 min you can sit up. Having achieved this, wait about the same time and finally try to stand beside the bed. Then you should try to take a few steps in the room. It is very important that this be done after the doctor's evaluation.

The possibility of being able to get up soon afterward is one of the principal benefits of laparoscopic and robotic surgery. This will prevent complications such as pneumonia, intestinal paralysis, and thromboembolic disorders.

Early initiation of the diet: After 4–6 h, try a few sips of water. If this is tolerated adequately (no nausea or vomiting), try some juice (non-citric) or jell-O, and begin a complete diet in the following hours. Likewise, this is done as per the recommendations of the doctor.

Care of the urinary catheter: The catheter performs a fundamental role during the postoperative period. It will remain

in place for a period of 7–10 days, as decided by the doctor. Consequently, it is very important that it not be tugged or pulled at. The presence of the catheter can cause a burning feeling and the desire to urinate without being able to do so, but this is normal and will disappear spontaneously. The catheter has an internal system that prevents it from coming out of place. However, if this should occur, the medical staff should be notified immediately. Also, it might happen that from time to time a little urine escapes outside the catheter; this is normal if the quantity is small. The bag for collecting the urine, which is connected to the catheter, should always be below the level of the abdomen. Therefore, when in bed, should be hung in side and not rely on the mattress (Fig. 7.10).

Similarly, when you walk, you can carry it in your hand, with your arms extended downward. There is no need to worry about the fact that the urine has a reddish color, since it is normal for it to be mixed with a little blood during the first days after the operation. Mainly it turns reddish when walking or having a bowel movement. All of this subsides spontaneously during the first days after the operation and the urine assumes a normal color more quickly if you drink plenty of clear fluid (water, crystalline drinks, etc.) On occasion when passing stool, a few drops of blood might appear on the penis, around the catheter. This is usually a non-alarming sign. Also it is important to verify that urine is coming out adequately thorough the catheter. For this it is necessary to empty the urine-collecting bag every 2 h, thereby being able to confirm that it fills up regularly.

Usually a cream is prescribed to apply at the tip of the penis around the catheter, to avoid inflammation of the skin.

At home, after surgery: The great majority of prostate patients who have undergone surgery by laparoscopy or robot are released from the hospital the day after the operation and are sent home in good condition to continue their convalescence. The following is indicated for them:

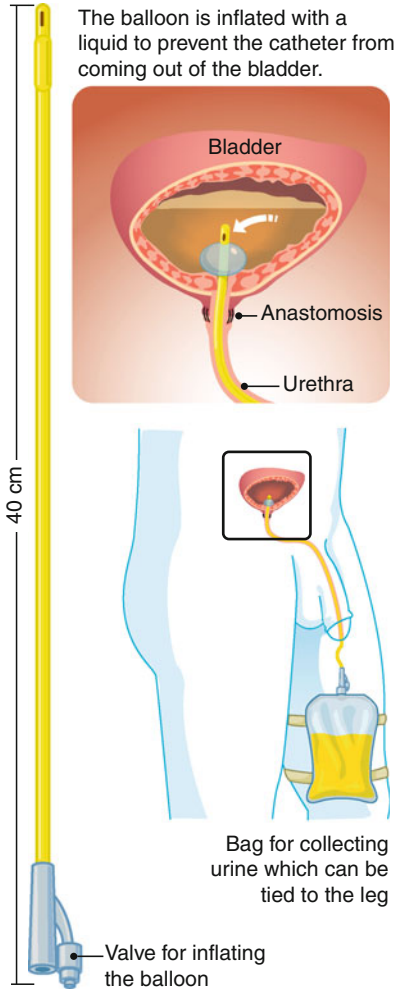


FIGURE 7.10 Catheter

Take antibiotics: If instructed by the doctor, take antibiotics after leaving the hospital. This treatment must be completed as indicated in order to avoid infections.

Take painkillers: The doctor will indicate the most adequate painkiller to avoid and alleviate the pain. Generally, a few days after the operation the requirements for painkillers are low, and these should be taken according to how the patient feels and the guidelines from the doctor.

Rest: Remain at home, resting. During the first 5–7 days it is acceptable to go to the bathroom, take a shower, eat while seated at a table, and carry out normal activities that do not require much physical effort. It is advisable to sit on soft surfaces or on a pillow while the catheter is still in place. After 2 weeks, begin to do more activities, such as driving an automatic car for short distances, carrying out light office work, etc. as long as your are not having pain the require the use of narcotic pain killers, but do not return to demanding jobs such as masonry, gardening, or plumbing; do not engage in any physical exercises or sports. After 30 days it is acceptable to fully return to work, sports, and other daily routines. Sexual activity can also be renewed a month after the operation, either with natural erections or with the treatment recommended to improve them, which can be through intracavernous injection or oral medication (see a more detailed discussion later in this chapter). However, until 3 months after the operation, do not ride a bicycle, motorcycle, or horse.

Clean the wounds: It is only necessary to wash the wounds with soap and water during a daily bath. The wounds can be left uncovered; it is not necessary to cover them with bandages or dressings.

The drain is a small rubber hose placed in the abdomen of the patient, extending to the exterior through one of the holes used in the laparoscopy. It facilitates the drainage of any liquid that may accumulate inside the abdominal cavity (blood, urine, serous fluid, etc.)—a routine occurrence after surgeries.

Care of the drain

Generally, the doctor removes the drain between the second and forth day after the operation, but in some cases it may be

necessary to maintain it in place a few days longer. In these situations, the patient should clean it just like the other wounds and arrive punctually at the appointment made by the doctor to remove it. For this appointment it is recommended to measure the quantity of liquid collected in the reservoir during the past 24 h, to help the doctor with the decision to remove the drain (Fig. 7.11).

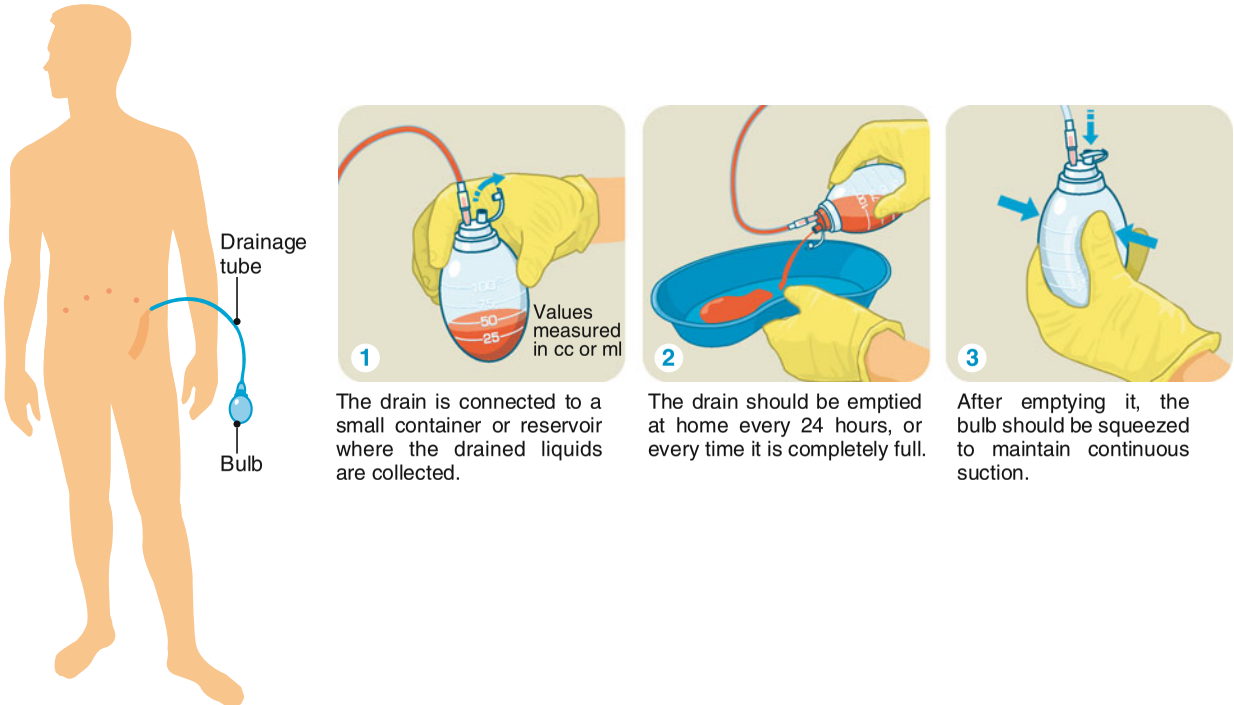
Medical visit for catheter removal

Approximately between 7 and 10 days after the operation, you should see the doctor for evaluation and removal of the catheter. Typically, this appointment will be made by the doctor. There will be a certain degree of incontinence when the catheter is removed, something which is normal and will disappear in time. Therefore, you should take an adult diaper to the appointment. The duration and severity of the incontinence is variable and depends on many factors, so it is necessary to be patient and understand that it is part of normal convalescence. Statistically, more than 50 % of the patients have complete continence when the catheter is removed; after 3 months, that figure goes up to more than 85 %; and at 6 months, almost all (95 %) recover urinary continence.

Diet at home

Upon returning home from the hospital, eat a regular, healthy diet. Drink abundant clear fluids (eight to ten glasses a day) to keep the urine clear. Also, it is good to eat easily digestible food like vegetables, salads, fruits, greens, and broth. The diet should be rich in fiber to ease bowel movements and include food like cereals, wheat germ, wheat bran, bran, vegetables, prunes, prune yogurt, etc.

The overall diet should also have low-fat content, and give preference to meats like chicken or fish (as opposed to red meat), either grilled or baked. Those patients who previously suffered from constipation and who were taking laxatives (Sennosides, Plantago Psyllium, etc.) should start taking them again.



The drain is connected to a small container or reservoir where the drained liquids are collected.

The drain should be emptied at home every 24 hours, or every time it is completely full.

After emptying it, the bulb should be squeezed to maintain continuous suction.

FIGURE 7.11 Drainage

Whole milk is not recommended nor are citric fruits, fried eggs, or alcoholic drinks. This diet is oriented toward controlling constipation, since it is normal for patients to not evacuate up to 4 or 5 days after the operation. This is basically because in the first days there is hardly any intestinal content, a result of the cleansing done by the enema prior to surgery, and also because surgery produces a certain degree of slowing of the intestinal movements, which reduces the frequency of the bowel movements.

Resumption of previous treatments
Patients who suffer from any type of illness, which requires daily medicine, can restart their treatments after the operation. In cases of diabetes mellitus, oral hypoglycemic agents should be resumed once the patient resumes his regular diet and the functions are back to normal. Treatments with anticoagulants or Aspirin® should be suspended until the catheter is removed.

Sleep
Undergoing surgery causes certain discomfort and generates some anxiety in some patients; thus, there may be some difficulty in sleeping. During the first and second weeks after the operation the patient is in a period of convalescence, which requires a greater expenditure of energy. For this reason he should take a nap during the day to restore his strength.

Pathological Interpretation of the Prostate Removed During Surgery

The specimen obtained from surgery consists of the prostate and seminal vesicles. When advanced disease is suspected, the lymph nodes are also included. The specimen is studied to identify certain parameters that will determine whether cancer treatments are necessary after surgery. These parameters are established by the Gleason grade, the histological features of the surgical margins, which show if the disease has

extended outside the prostate, whether it has reached seminal vesicles, and if there is metastasis to the regional lymph nodes.

The information obtained from this analysis is used to predict the evolution of the illness, measure the probability of biochemical recurrence, and calculate long-term survival. It is also useful to indicate or select the adjuvant therapy, radiotherapy, or hormone therapy.

The three dimensions of the prostate are measured and it is weighed without the seminal vesicles. It should be immediately immersed in a solution of 10 % formalin to prevent self-destruction of the tissues. This process must be completed in full, prior to proceeding to its study. The specimen should be immersed in a volume at least 20 times greater. The time depends on the size. One hour per millimeter of thickness of the tissue is estimated. Usually it takes at least 24 h. Then the outer surface is stained with different colors for topographical identification of the tumor and precise determination of the surgical margins. It is cut into thin slices in order to begin the microscopic examination.

The number of histological slides of each specimen varies, with an average of 20 per case. In selected cases the entire piece is included, which means up to 60 slides for study, which explains why it takes several days to get the final result of the biopsy.

Histological examination of the apex, which corresponds to the tip and the base of the prostate, is essential for the evaluation, in addition to the margins of resection, which are considered positive if the tumor is in contact with the stained surface.

Biopsy Results

Positive margins of resection

The positive surgical margin is defined as the extension of the tumor to the outer surface of the specimen, which is manifested by the contact of the tumor cells with the painted surface of the prostate.

The average rate of positive margins in radical prostatectomy specimens is 28 %, with values that can range between 0 and 53 %. The possibility of positive margins appearing is related to various factors, including the value of the pre-operative prostate-specific antigen (PSA), the clinical stage, the tumor volume, the percent of cancer in the biopsy and its Gleason number (Chap. 4), the pathological processing of the specimen, and even the surgeon's experience.

Today the incidence in positive margins is progressively diminishing because the majority of prostate cancers are diagnosed and operated on in an early stage. Moreover, more surgical experience has been acquired and new techniques continue to be perfected (Fig. 7.12).

The treatment for positive margins is different in each patient. It depends basically on the quantity of tissue affected. In patients with only one positive millimetric margin identified, the choice can be to conduct observation and close monitoring according to the value of the prostate-specific antigen (PSA); if this tends to rise, complementary treatment will be started, such as radio therapy or hormone blockade. In the case of patients who show an extensive zone or multiple zones with positive margins, the urologist may decide to start early adjuvant treatment in conjunction with the radiation oncologist and medical oncologist to prevent the spread of the disease.

It should be understood that every patient is different and will receive the most adequate therapies in a personalized way, since not only is the number of millimeters of tumor in contact with the surface important but the Gleason histological grade present is also taken into account, which is what determines the aggressiveness of the tumor.

Negative resection margins

A negative surgical margin means there is no evidence of contact between the tumor and the surface of the cutting edge of the surgery, suggesting that it has not extended beyond the prostate; therefore, there is a better prognosis.

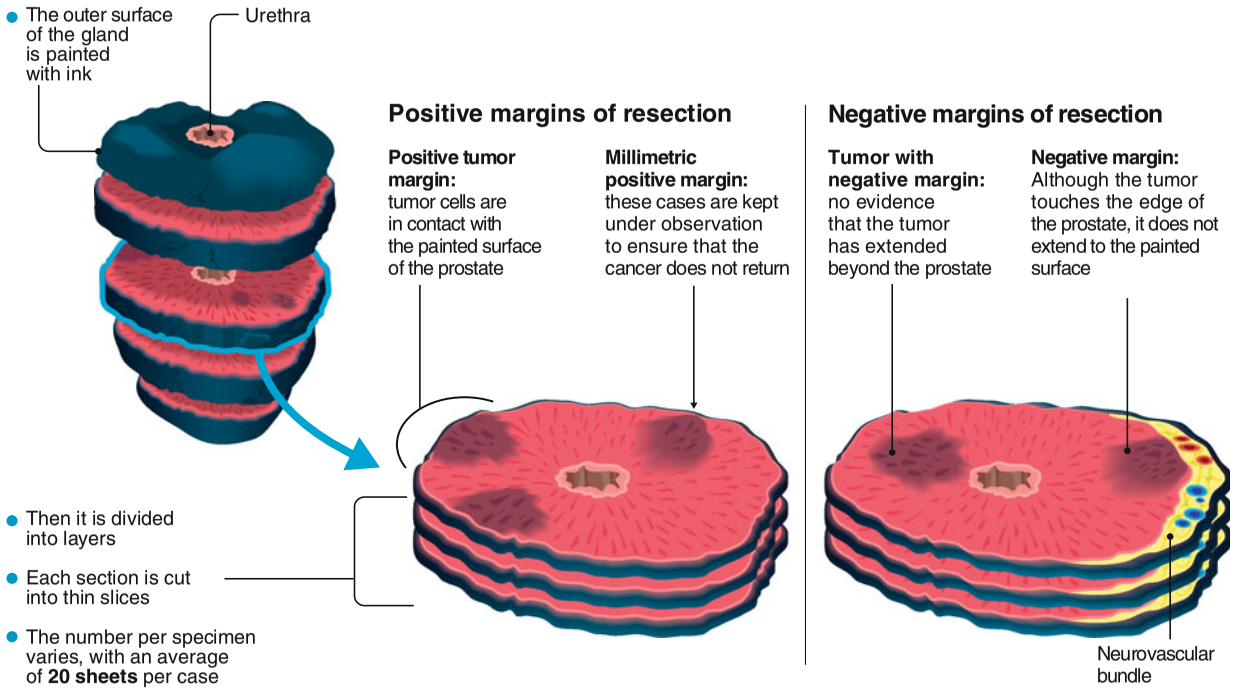


FIGURE 7.12 Positive margins

Prognosis

The surgery should eliminate all cancerous cells. Even so, small tumor cells may have escaped before surgery without being identified. Therefore, the doctor will keep close watch on the patient for some time to be sure the cancer does not reappear. The patient will have to undergo regular checkups, including blood tests for the prostate-specific antigen and urine cultures. Generally the followup will be every 3 months during the first 2 years, then every 6 months for three more years, then annually.

Complications of Radical Prostatectomy

Traditionally, this has been a greatly feared operation because of the complications and consequences associated; however, thanks to research in recent years, it has been possible to describe the anatomical details and exact location of the blood vessels and nerves (neurovascular bundles) that are responsible for both urinary continence and for the erection. Now that the anatomy of the region is known perfectly, the technique has evolved and surgery can be performed while respecting each of these important structures and minimizing the associated risks. These risks are inherent in the general condition of the patient and the surgical procedure itself. They can be classified into general and specific risks.

1. **General**: These are the same complications as for any other surgery, and include the following:
    - Allergic reactions: Allergies may occur to any drug, including anesthetics, as well as to operating room materials such as gloves, sheets, etc.
    - Infection: Of specific concern is the surgical wound but infection may also present itself in the lungs (pneumonia), in the abdominal cavity, in the bladder, or in the kidneys.

- Pulmonary problems: Atelectasis (lung volume reduction), pneumonia, pulmonary thromboembolism.
- Hemorrhage: Bleeding, at the time of surgery or afterwards, that warrants transfusion or reoperation.
- Cardiovascular problems: Heart attack or stroke during or after surgery.

2. **Specific**: These are the complications related to the specific surgery used in the treatment of prostate cancer.

   Intestinal injury: This is the most dangerous of all; it consists of fecal material leaking into the abdominal cavity due to the opening of the colon or rectum during surgery. This complication is very rare, but in very specific cases, such as inflammation of the prostate, history of multiple biopsies of the prostate, locally advanced disease, and a salvaged surgery after failure of brachytherapy or radiotherapy, it becomes difficult to separate the rectum from the prostate, thereby increasing the risk of injury. If it occurs, the important thing is to diagnose it. Generally, when repaired by suture, there is no additional complication. If not diagnosed or if the repair fails, a rectovesical fistula may occur.

   Rectovesical fistula: This is a communication between the rectum and the location where the bladder was joined to the urethra (anastomosis site). This condition is manifested by the outflow of fecal matter through the urinary catheter, and/or the outflow of urine through the rectum. This complication is rare and is reported in the United States in 1 % of patients who undergo open retropubic prostatectomy.

   Urinary incontinence: This is the involuntary loss of urine, requiring the use of diapers. Usually it is transient. The patient progressively notes his recovery. First, at night, he is aware that he can get up and go to the bathroom. Then, during the day, he will perceive that the loss between urinations decreases and that he requires fewer diapers. Then he substitutes the diapers for sanitary napkins or towels for protection, and so on until he loses only a few drops when exerting himself, doing exercises, or drinking alcohol.

Generally, 1 year after surgery, 96 % of the patients have restored urinary continence. Not all patients are incontinent. In fact, more than half are fully continent when the catheter is removed. One factor that influences this is age. Young patients with more muscular strength of the perineum recover urinary continence rapidly. A later discussion in this chapter is dedicated to the review of urinary incontinence secondary to radical prostatectomy.

Erectile dysfunction: The difficulty to achieve and maintain erections, due to the loss of the blood vessels and nerves responsible for erection. It may result from unintentional injury or intentional resection during surgery.

The way the patient is affected depends on age and the condition of the erections before surgery, in addition to general health conditions and risk factors such as smoking, diabetes, and others having to do with the microcirculation in the penis. Similarly, the upcoming discussion on erectile dysfunction secondary to radical prostatectomy is devoted to this probable complication and its treatment.

Urethral stricture: Narrowing of the urethra due to scarring. This can occur anywhere along the urethra, from the tip of the penis to the site where the urethra joins the bladder. One of the triggers is the body's inflammatory response to the urethral catheter (which is left in after surgery). This is also seen in patients with catheters placed for other reasons.

Additionally, the stricture can occur at the site where the connection was made to the bladder; i.e., the site where the prostate used to be. If the patient notices that progressively after surgery the caliber of the urinary stream is declining, he should consult the doctor to rule out a stricture in the neck of the bladder. Another reason for this to occur, though rather rare, is that the body rejects some of the clips used in the operation and does so at the site where the continuity of the urine flow has been restored; i.e., at the site of the anastomosis.

Sexuality and Prostate Cancer

Sexuality

To understand how sexuality is affected in a man with prostate cancer, we must understand some basic principles about the human sexual response and principally about the erection.

Professors Alonso Acuña and Pedro Guerrero, the first a urologist and the second a psychiatrist, defined sexuality as the group of thoughts, emotions, attitudes, and behaviors that govern the exercise of the sexual function; and this, in turn, is the conscious activity of the genital system for the purposes of pleasure and, secondarily, reproduction.

Human sexuality was initially studied by Dr. William Master and Mrs. Virginia Johnson in their book, *Human Sexual Response*, in which they established the basis for what we know today about human sexuality. With later contributions from the psychiatrist Helen Kaplan, we divide this response into three stages or phases; they are the phases of desire, excitement, and orgasm.

Sexual desire

This is the first stage of sexuality, which we might define as the wish to have sexual activity. Desire, besides depending on a series of circumstances or situations that we experience every day, in which the relationship with our partner, family, economic, and work situations are involved, depends directly, both in men and in women, on certain hormones called *androgens*. In men they are produced mainly in the testicles and also in other organs such as the adrenal glands; in women, androgens are produced in the adrenal gland and the ovaries, though in lesser quantities than in men.

The principal androgen is *testosterone* and, therefore, it is principally responsible for sexual desire.

Excitation

This is the second phase of sexual response, manifested in men by the erection and in women by vaginal lubrication.

The erection is produced as a reflex action to a series of erotic stimuli, which can be internal or external. The principal internal stimuli are due to androgens and manifest themselves as fantasies or erotic thoughts. External erotic stimuli can be visual, auditory, olfactory, gustatory, or tactile, and, depending on the person, some can be more important than others.

Orgasm

This is the exquisite and intense pleasure obtained at the culmination of the sexual act. The orgasm originates in the brain and is perceived most intensely in the genitals and the areas that surround them and is accompanied by pleasurable sensations in the whole body.

The stimuli that produce arousal, both internal and external, are concentrated in a region of the brain called the limbic system, where certain brain nuclei in the presence of testosterone cause a neurological impulse that travels by way of the spinal cord to the nucleus of Onuf in the lower part of the cord. From here the impulse goes through the pelvic nerves, primarily through the cavernous nerve, to the penis.

The penis consists of different parts: the corpus spongiosum, inside of which is the urethra, ending at the glans, and two corpora cavernosa, which are the main actors of the erection. These columns consist of erectile tissue containing blood vessels and muscles, which are surrounded by a thick layer called albuginea. The penis receives blood through the penile arteries and cavernous arteries, which are responsible for erections.

When the penis is flaccid, the arteries are contracted, as is the erectile tissue. When there is adequate sexual stimulation, these arteries dilate and grow in size, increasing blood flow to the penis; simultaneously, the erectile tissue of the corpora cavernosa relaxes, allowing the accommodation of the increased blood flow. Substances called neurotransmitters, which facilitate the erection, mediate this whole process.

While the penis fills with blood, another phenomenon takes place in which the veins (which are responsible for removing the blood from the penis) are compressed, avoiding the release of the blood and maintaining the erection. In summary then, to produce an erection, you need an erotic stimulus, a neurological brain impulse to the penis, and adequate dilation of the penile arteries; also needed is relaxation of the erectile tissue and compression of the penile veins to prevent the blood from exiting. If any of these factors does not work, there will be a failure in the erection process.

Erectile Dysfunction

This is defined as the repeated or permanent incapacity to achieve or maintain an erection that enables penetration and satisfactory sexual activity. Knowing the elements that produce the erection, we can therefore understand why a patient with prostate cancer may have problems with his sexuality. Population studies in various parts of the world show that half of men over age 40 have some degree of erectile dysfunction.

In some patients, the risk of erectile dysfunction is greater than in healthy men, such as in diabetics, those with high blood pressure, those who have high cholesterol and/or triglycerides and those suffering from depression, etc.; even some treatments such as anti-hypertensives, antiandrogens, and antidepressants may also affect the quality of the erection.

Thus, a sexual function already diminished before the illness can make its treatment after prostate cancer treatment more difficult.

The Diagnosis of Prostate Cancer—What to Do? What to Know?

When a man receives the news that he has prostate cancer, it is natural that he loses control over his state of mind:

he feels sad, furious, or frightened, all moods that can worsen his erections and his sexual activity.

The first thing to understand is that this disease is common, and the older the person the greater the risk of being affected. Prostate cancer advances slowly, is a long process, and the urologist is the best person to accompany a patient during this process.

Fact

The prostate is a gland whose primary function is to produce part of the semen, so it is important for the man's reproduction, but it has no relation to sexual response, in general, nor to the erection in particular.

Prostate cancer is not sexually transmitted, so the sexual activity you engage in will not worsen your situation; intercourse will not make your partner sick. In fact, sexual activity is recommended because it improves the oxygenation of the penis, avoids scarring of the corpora cavernosa, and prevents erectile dysfunction. No relationship has been shown between sexual activity and prostate cancer. However, the anxiety and depression that can occur when you are aware of the diagnosis of prostate cancer can cause erectile dysfunction, because in these states the brain releases substances that hinder the relaxation of the erectile tissue of the corpora cavernosa. If this happens, your doctor can prescribe a treatment for anxiety and depression, and probably will prescribe a medicine for erectile dysfunction. Remember that the primary objective is to obtain sexual pleasure, that the erection is a reflex response to an erotic stimulus, and that problems are not helpful stimuli. Set them aside for the moment and enjoy.

The treatment of prostate cancer can, in varying degrees, affect the erection. Note that whatever treatment is chosen, we now have a variety of effective therapies for erectile dysfunction.

Relationship Between the Treatment for Prostate Cancer and Erectile Dysfunction

There are three classes of possibilities in the treatment of prostate cancer:

1. **Observation**: In this case, do not forget that sexual activity will not affect the evolution of the cancer. Intercourse should be enjoyed. If, due to age or some other health problem the erection is not satisfactory, talk to your doctor in order to begin treatment as soon as possible. This prevents further damage to the erection.
2. **Palliation (symptom management)**: However, if your situation is different and it was decided to begin hormone therapy to suppress testosterone production, then the desire for sexual activity will be affected. If there is no interest in sex, there will be no erections. Some men, however, retain their erections and their sexual activity, but this is highly individual.
3. **Surgery and radiotherapy**: Among the alternatives to try to cure cancer localized within the prostate are surgery and radiotherapy. The surgery that takes place is called a radical prostatectomy. Radiotherapy is performed externally or internally; this latter approach is applied directly to the prostate and is known as brachytherapy. Each of these treatment modalities (surgery and radiotherapy) has a risk of causing erectile dysfunction, because they can affect the nerves and blood vessels (arteries and veins) to the penis that are responsible for erections.

The frequency of erectile dysfunction after radiotherapy varies between 25 and 58 % and depends on many factors; among the most important is the type and quality of the machine used for the radiotherapy. Damage to the arteries responsible for producing an erection is progressive, and the longer the time after the radiotherapy, the more

erectile dysfunction is noted. Conformational radiotherapy has the best results, as it allows delimitation of the radiation field with greater precision. The results of the new forms of radiotherapy, such as proton and intensity-modulated radiotherapy, are yet to be known.

Brachytherapy
This treatment specifically causes erectile dysfunction with similar frequency, that is, between 30 and 50 %. Like external radiotherapy, radiation damages the blood vessels and nerves that produce the erection; the more time that passes, the more this phenomenon is noticed.

Radiation therapy
This treatment does not affect the desire for intercourse unless it is used at the same time as drugs that reduce or block the production of testosterone. This particular hormone therapy produces a decrease in the sex drive, further affecting the erection.

Radical prostatectomy
This treatment can also cause erectile dysfunction, depending on whether during surgery it is possible to spare the nerves and vessels that produce the erection. When the tumor is very large, it's probably not advisable for the urologist to retain the neurovascular bundle, because of the risk of leaving fragments of cancer in this area. The urologist will decide this before or during surgery.

The risk of erectile dysfunction after radical prostatectomy varies between 30 and 90 %, depending on the preservation of the neurovascular bundles. One factor in this is the quality of the erection that existed before surgery. Another important factor is the experience of the urologist, because those with more experience in this type of surgery achieve better results.

The recovery of erections after surgery can be slow; studies even indicate that it can take up to 4 years, but this

process can be accelerated with drugs that promote erections early after surgery. In any case, if a long time passes without an erection, the penis loses its elasticity and the possibility of recuperating the erection is less. For this reason it is important to have early strategies to recuperate the erection.

Among the strategies to recuperate the erection more rapidly, one might consider a drug injection in the penis to act on the blood vessels (vasoactive) and produce an erection. There are various types of this drug: alprostadil, papaverine, and phentolamine, or mixtures thereof.

Ideally these drugs are applied as soon as possible after removing the catheter. For this, a short, thin needle is used so as not to cause pain in the penis. The first erection may be somewhat painful, depending on the drug used; there may be a burning sensation within the penis when it becomes erect, but this will decrease rapidly with the weakening of the erection. This pain occurs in 30 % of patients who used alprostadil and is less frequent in patients using the papaverine-phentolamine mixture.

Alternative Treatments Erectile Dysfunction

There are different ways to treat this condition. Depending on the situation of each patient, the urologist will choose the best alternative. The treatments noted below will be reviewed fully later in this chapter.

Oral therapy: This is the first line of treatment and includes five phosphodiesterase inhibitors (Sildenafil, Vardenafil, and Tadalafil), which are all safe and effective medications.

Vacuum devices and injections: The second line of therapy includes the vacuum devices, which are effective and easy to use, and injections into the corpora cavernosa of the penis, the effectiveness of which makes both of them a great alternative.

Penile prostheses: Finally, the third line of treatment is represented by penile prostheses, which have proven highly effective and produce good levels of satisfaction in both patients and their partners.

Today we have all the resources to produce an erection in patients with erectile dysfunction. In the twenty-first century we have effective resources to treat erectile dysfunction with efficacy, but the future is more promising, since novel options are being explored with new drugs, gene therapy, and tissue bioengineering.

Also, remember that your partner is very important in the decision process, so involve that person in your treatment discussion. Patients with prostate cancer can have an active and pleasurable sex life. Ask your urologist to recommend the best available options that best suite you and your partner.

Erectile Dysfunction Secondary to Radical Prostatectomy (Fig. 7.13)

Although erectile dysfunction is one of the most feared situations for patients who undergo a treatment for prostate cancer, it is good to know that there are different alternatives for its management; these are highly effective and include sex therapy, oral medications, medications for local application, mechanical vacuum devices, injections to strengthen and exercise the cavernosum muscles, and even penile prostheses. Each one is recommended according to the needs of each patient, trying always to go from least to most invasive.

1. **Sex therapy**: *Sex therapy* is the name given to a set of measures whose purpose is to bring peace of mind to the patient and complement the effect of the drugs used in the treatment of erectile dysfunction. Although they are not a

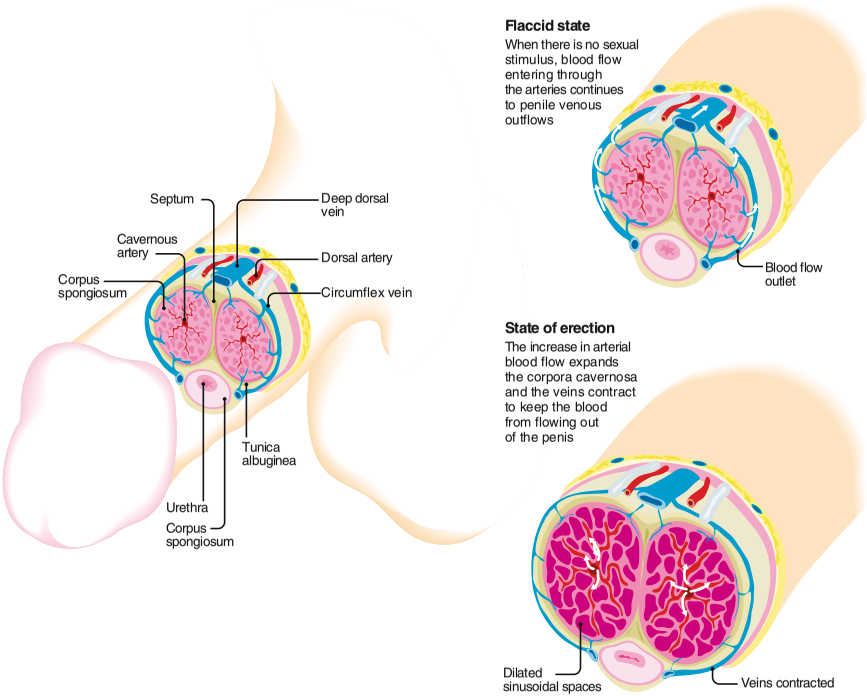


FIGURE 7.13 The erection

treatment as such, these measures consist of techniques and strategies that help reduce anxiety, improve communication with the partner, and strengthen the emotional support as well as recognize the body as a focus of pleasure in itself. The trust that exists in a good doctor-patient relationship is the key to better understand the situation and to determine the appropriate therapy for each case.

2. **Oral medications**: This group of drugs is called "inhibitors" of the five phosphodiesterase enzyme (PDE-5 inhibitors). These drugs are thought to protect the lining of the blood vessels. There are studies that show that these medicines can actually increase the amount of smooth (involuntary) muscle in the penis. This muscle is responsible for trapping the blood during an erection. This group includes Sildenafil (commercially known as Viagra®), Vardenafil (commercially called Levitra®), and Tadalafil (commercially known as Cialis®).

Sildenafil (Fig. 7.14a)

Viagra® should be taken 1 h before intercourse, on an empty stomach (because food interferes with its absorption). Its time of action is about 4 h, during which time you can have intercourse. The most common side effects of this drug are headache, facial flushing, nasal congestion, heartburn, and occasionally altered vision. About 7 % of patients taking these drugs may have some side effects. If you have any of them, do not become distressed; when the drug wears off, these symptoms will disappear.

Vardenafil (Fig. 7.14b)

Levitra® is a powerful drug that should be taken half an hour before intercourse. You can eat foods low in fat and drink in moderation, because it has little interaction with food or alcohol and its period of action is 4–5 h. The most common side effects are headache, nasal congestion, and facial flushing. These problems also disappear when the drug wears off.

FIGURE 7.14 (**a**) Sildenafil, (**b**) Vardenafil, (**c**) Tadalafil

Tadalafil (Fig. 7.14c)

Cialis® should be taken 2 h before intercourse; you can eat and drink moderately, because it does not interact with food or alcohol, and its period of action is up to 36 h, approximately. The main side effects are headache, nasal congestion, facial flushing, and back pain or muscle pain, and again these symptoms generally **disappear** as the effects of the drug **wear** off.

The usual dose is 20 mg. However, there is also a 5 mg dose, which is taken every night, regardless of whether or not you will have intercourse, in order to maintain a constant level of medication to facilitate spontaneous erections every day. At the same time, this low dose decreases the occurrence of side effects.

In the near future, new drugs in this same group, like Udenafil, Avanafil, and Mirodenafil, will be available in the market and are likely to have greater benefits and fewer contraindications and side effects.

Contraindications to phophodiesterase type 5 inhibitors: We can affirm that this group of drugs is very safe. However, they are contraindicated in patients taking drugs for the treatment of angina pectoris or heart attack (called nitrates), as the simultaneous use of both drugs can cause significant drops in blood pressure and cause cardiovascular emergencies. They are also contraindicated in men for whom strenuous physical activity is inadvisable due to cardiovascular risk factors. Well-known is the case of the patient with prolonged sexual inactivity, who, when he uses these drugs, achieves a powerful erection and then dies at the moment of intercourse, not because of the medication but due to the previous incapacity of the heart to make such efforts.

Fact

It is advisable to always use original non generic drugs. The patient can try different substances and compare them to know which is more effective with fewer side effects, and once identified, can compare the same substance with the generic prescription and choose the one to use.

3. **Drugs for "local application"**: These are medicines that present in a gel or cream form. The composition comprises prostaglandin E1 (alprostadil), a substance that promotes blood supply to the corpora cavernosa of the penis and thus helps erection. However, these drugs are not very potent and are short-lived, though they are in constant development and future versions of the drugs promise to be more effective.
   Intra-urethral medication: Another local application, intra-urethral therapy involves inserting a pellet of Alprostadil inside the urethra. To date, this therapy has not proven completely effective to achieve or maintain adequate erections. The undesirable effects include penile pain (32 %) and urethral pain or burning (12 %).
4. **Vacuum erection devices**: The vacuum device is a tube that surrounds the penis. This apparatus rests against the pubic bone in such a way that no air enters. At the other end of

the tube is a mechanism, manual or automatic, that sucks air from the tube, producing a vacuum inside that causes increased blood flow into the penis thus causing an erection. To maintain this erection, a ring or elastic band is placed at the base of the penis, which retains the blood in the corpora cavernosa, making it thus hold the position of erection. Some patients report a short lasting erection and an uncomfortable feeling of coldness at the tip of the penis. In addition, by using this device the patient may not experience an ejaculation, due to the obstruction that the ring itself produces (Fig. 7.15).

5. **Intracavernous injections**: Intracavernous therapy involves the injection of drugs directly into the corpora cavernosa of the penis as a treatment for impotence. In the setting of post radical prostatectomy erectile dysfunction, there is scientific evidence indicating that it helps restore erections faster than oral medications. This is because after surgery, when there is some numbness of the nerves, injections are more rapid in promoting the blood supply to the penis. Once some degree of spontaneous erection is achieved without injection, the treatment continues with oral medication, which completes the erection until it is sufficient to achieve penetration. Until spontaneous partial erections are achieved, intracavernous injections must be continued. The agent most widely used and approved by the Food and Drug Administration (FDA) is prostaglandin E1 (alprostadil). This drug is used alone or in combination with other drugs. According to the amount of the substances used and the proportions used they are given different names, as shown in the table (Fig. 7.16).
   Dose of treatment: The dose should be the minimum amount necessary to achieve sufficient rigidity for an adequate time and to allow for penetration, thus reducing the risks of a prolonged erection; in general, the lower the dose, the fewer the risks. Usually the treatment starts with low doses and these are increased until the desired effect is achieved, and not vice versa. The doses are different for each man, depending on his health status (age, diabetes, etc.)

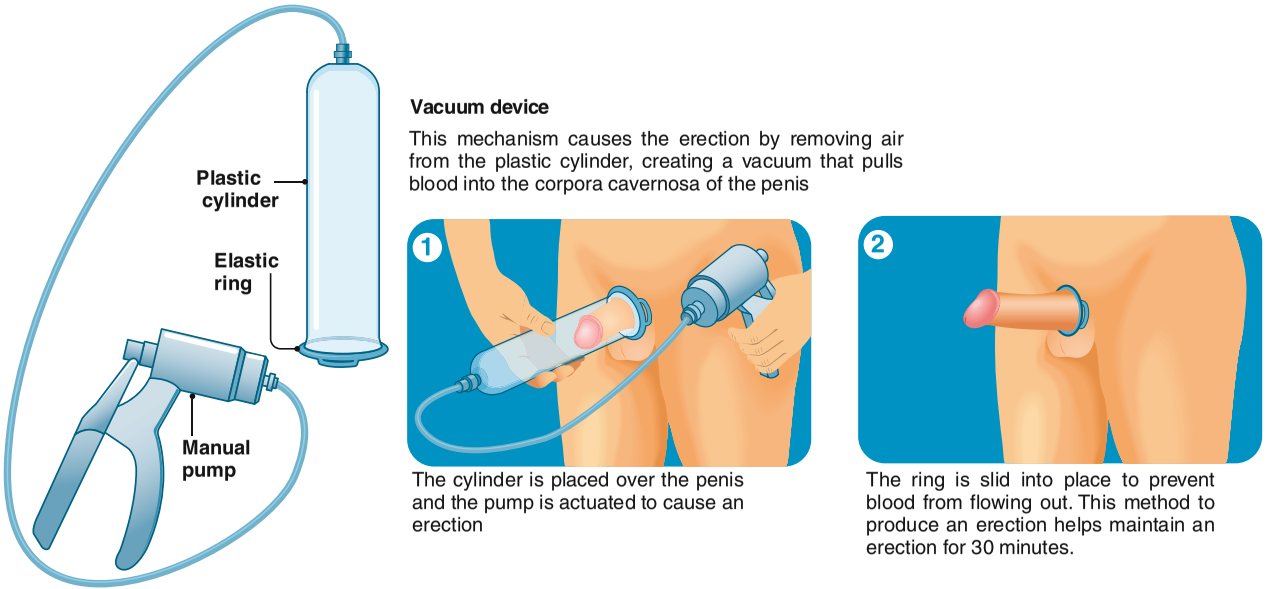


FIGURE 7.15 Vacuum device

Medication	Papaverine	Phentolamine	Alprostadil (Prostaglandin E1)
Caverject ®			10 and 20 mcg
Bimix ®	30 mg	0.5 mg	
Bimix Plus ®	30 mg	1 mg	
Trimix ®	30 mg	1 mg	10 mcg
Trimix Plus ®	30 mg	2 mg	20 mcg
Super Trimix Plus ®	30 mg	2 mg	40 mcg

FIGURE 7.16 Intracavernous dose

and the mixture of substances in the drug to be injected (Fig. 7.16).

Mode of treatment administrations: To administer medication, the same type of syringe as that used to administer insulin to diabetic patients is employed. It has the capacity of up to 1 ml and a small, thin needle at the tip. Once the injection is given, the puncture site must be compressed with a wet alcohol swab; the pressure must be applied for 5 min to prevent a hematoma from occurring, as this could promote fibrosis in the area and compromise the functioning of the corpus cavernosum (Fig. 7.17).

In the event that the injection is painful, it is important to determine whether the pain is from the puncture or from the liquid. If it is from the puncture, the patient should be trained to correctly apply the injection; if the pain is caused by the drug itself, the drug can be diluted with a local anesthetic to decrease the irritant effect and improve the erection.

In the event of an erection lasting more than 4 h, the patient should seek an urgent medical treatment to reverse the drug effect.

Complications: they occur most often in patients who administer a dose greater than recommended or who apply more than one injection in a 24-h period.

- *Fibrosis*: This refers to a hardening of the corpora cavernosa. It may occur in between 0.5–31 % of patients and appears to be related to the number of injections applied. To prevent this, the patient should compress

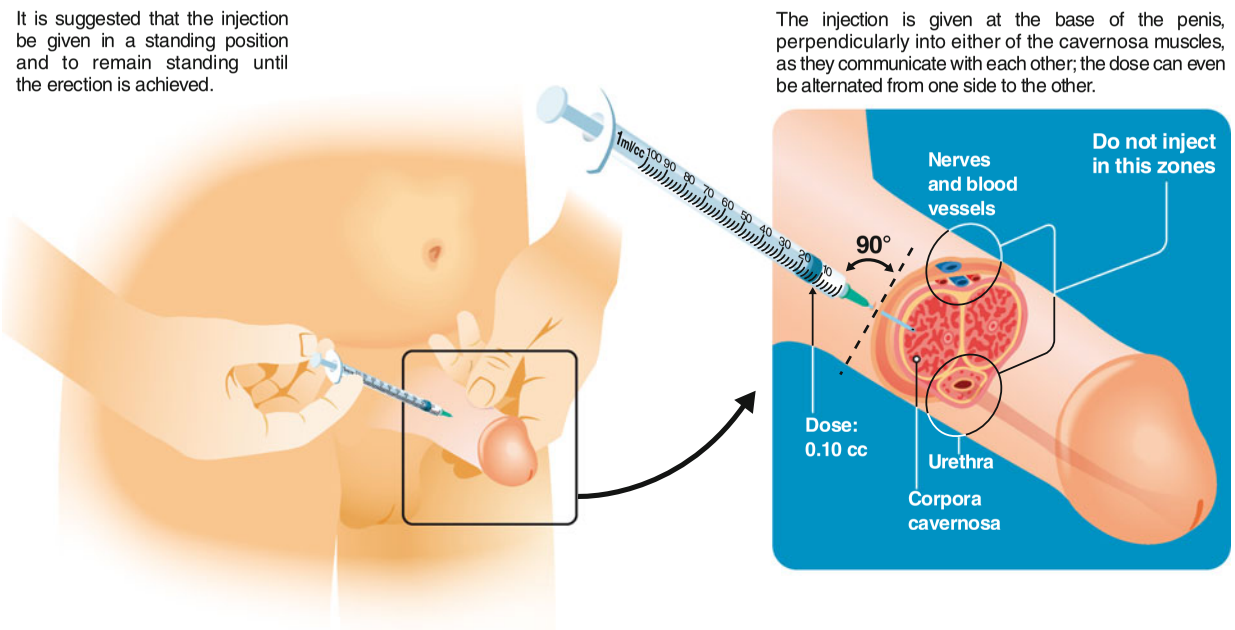


FIGURE 7.17 Intracavernous injection

the injection site for 5 min (up to 10 min in men taking blood thinners). In the majority of cases, the nodules disappear within the first months after discontinuing the treatment.

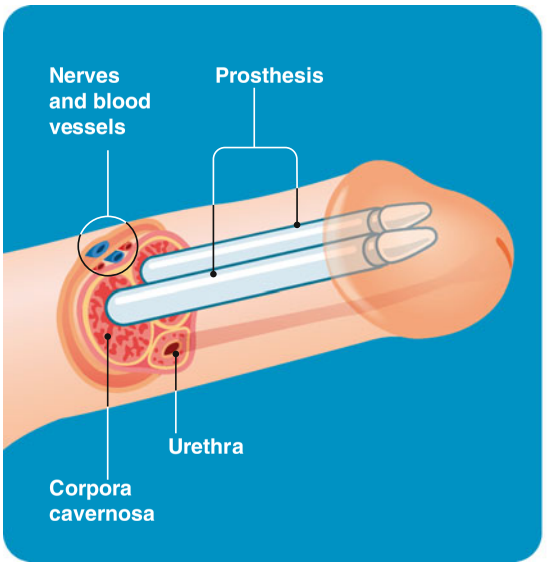
- *Priapism*: It is a persistent and painful erection that can compromise the functioning of the penis. It occurs in 1 % of the patients receiving this treatment. Any man with an erection that persists for more than 4 h after application of the injection should first apply ice locally to try to decrease the erection. He must see a doctor urgently for phenylephrine-based treatment to counter the effect of the drug. An erection lasting more than 6 h can produce irreversible scarring in the corpora cavernosa of the penis and cause complete loss of the erectile function. Because of these potential side effects, the physician should prescribe the lowest effective dose.

Contraindications: Intracavernous injection therapy is contraindicated in patients with sickle cell anemia and in patients with schizophrenia or other psychiatric disorders.

6. **Penile prosthesis**: In third-line therapy are the penile prostheses or implants. These have been used for 40 years and have proven to be effective and provide an active, satisfying sex life. There are several kinds of these implants, but the ones currently used are malleable prosthesis (mechanical) and the inflatable prosthesis (hydraulic). Both devices consist of two cylinders, one of which occupies each corpus cavernosum, and are permanent.
   Malleable prosthesis: The semi-rigid malleable prostheses are easier to use; the penis remains rigid and can be bent by hand upward and forward during sexual activity and down or sideways after sexual intercourse. These devices can cause some discomfort, as when using a bathing suit or playing sports (Fig. 7.18).
   Inflatable prosthesis: These prostheses have several components. There is a sterile liquid reservoir that is positioned behind the pubic bone and a valve is placed in the scrotum (next to the testicle), by which, when pressed in one direction, the fluid travels to the devices that are within the

Semi-rigid bar prosthesis

Two silicone rods are placed in the corpora cavernosa of the penis.



The flexibility of the prosthesis allows manually direction in the erection position

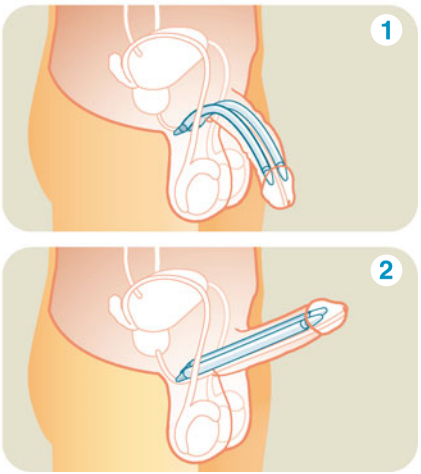


FIGURE 7.18 Semi-rigid prosthesis

penis and thus erection occurs; pressing the valve in the opposite direction, the liquid returns to the reservoir, and the penis returns to its empty and flaccid state.

In either of the two types of prostheses, the surgery is not painful. Through a small incision in the scrotum and/or above the pubic bone, implants are placed within the corpora cavernosa. Anesthesia can be general, regional, or local in some cases. In any form, it is considered low-risk surgery and provides a high degree of satisfaction for those who have these devices and their partners. Surgery is ambulatory. The patient leaves surgery with a urinary catheter, which is removed within the week. Patients are able to have intercourse 6 weeks after surgery (Fig. 7.19).

Complications: The main complication is infection, which may occur in 6 % of the patients who undergo this operation, and to prevent it, the patient is given antibiotics before surgery and continues them a few days after. If there is an infection, usually it is necessary to remove the implant. Infection is more common in diabetic patients, so they require special care.

The body's rejection of the prosthesis is uncommon and the erosion of the implanted material outside the corpus occur in fewer than 3 % of the patients. The operating mechanism of the inflatable prosthesis may eventually fail, which would require changing the part that does not work or changing the complete prosthesis (the latter occurs in fewer than 1 % of patients). The main problem of the prosthesis is its cost, which tends to be high.

Urinary Incontinence Secondary to Radical Prostatectomy

Urinary incontinence, or involuntary loss of urine, is a disorder, as defined by the International Continence Society, that has been classified as a social and hygienic problem deserving attention of doctors and patients. It is not a rare condition, since it can affect between 3 and 19 % of the general masculine population and up to 19 % of men over 60 years of age.

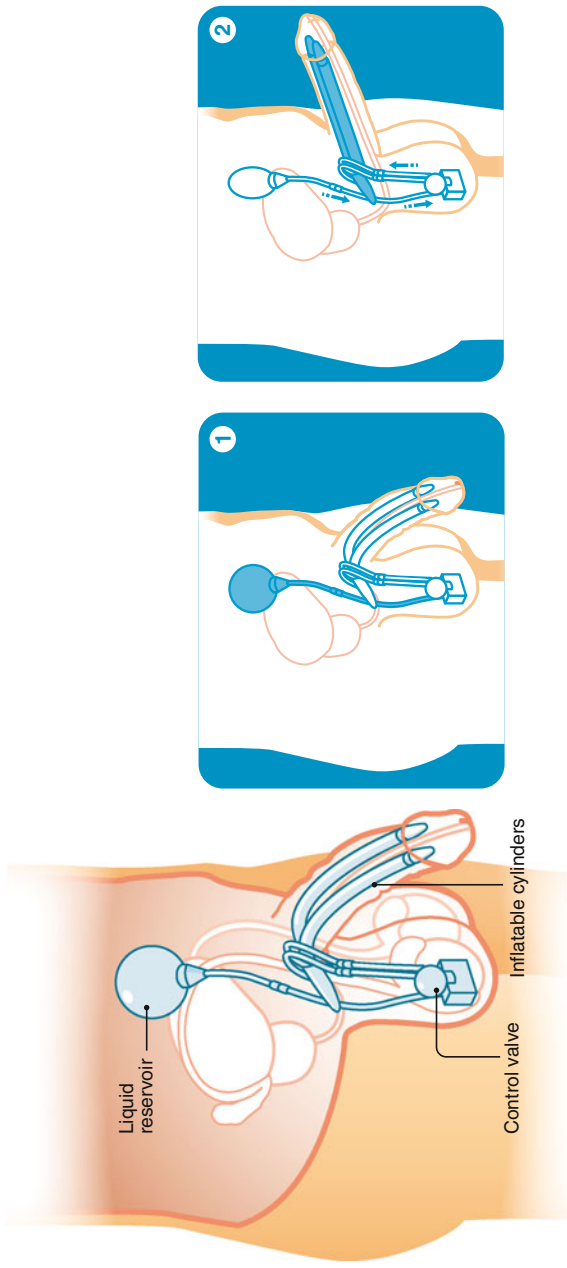


FIGURE 7.19 Inflatable prosthesis

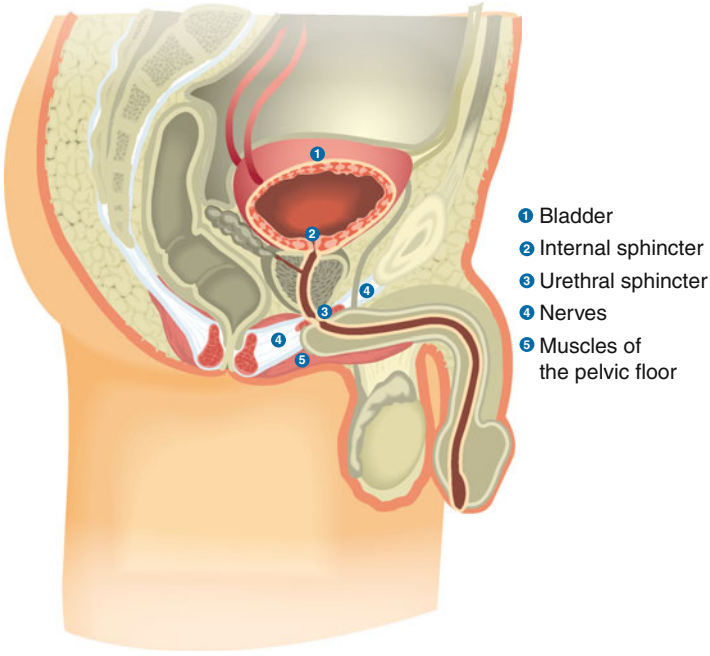


FIGURE 7.20 Urinary organs

It can occur during physical exertion such as coughing, sneezing, straining, heavy lifting, walking, or even during sex. In such cases, it is called *stress urinary incontinence*. When leakage of urine occurs, associated with a strong desire to urinate (sudden and difficult to defer), it is known as *urge incontinence*. If both types of incontinence are present, that is both stress and urge incontinence, a ***mixed urinary incontinence*** occurs.

Then there is *overflow incontinence*, which is what happens inadvertently to the patient, unrelated to effort and without symptoms of urgency. Clinically it is manifested as a steady loss of small amounts of urine, and is usually caused by an impaired ability of the bladder to contract. This must be distinguished from continuous urinary incontinence, which refers to involuntary and permanent leakage of urine, usually related to a deficit of the sphincter function, either from neurological or muscular injuries (Fig. 7.20).

Organs responsible for control of the urine:

1. The bladder: Thanks to the elastic property of its muscle fibers, the bladder can adapt to increasing volumes of urine. In order to achieve this, it has the quality to gradually distend.
2. The sphincter: This specialized muscle surrounds the urethra, at the bladder outlet. The muscle must be kept closed while the bladder is filling and must relax (to open) during urination. There is an internal sphincter, with an involuntary control mechanism, and an external sphincter that responds to voluntary control
3. The pelvic floor muscles: This is a group of muscles that are in the lower portion of the pelvis. The muscles are responsible for providing support to the bladder, urethra, and related organs.
4. Nerves: These special nerves exit from the lower spinal cord and go to both the bladder and the sphincter and pelvic floor muscles. They are responsible for sending nerve signals that relax the bladder during bladder filling and cause the sphincter to remain contracted, and then during urination allow the contraction of the bladder, with simultaneous relaxation of the urinary sphincter. All this runs under the coordination of the higher neurological centers: the brain and the brainstem (Fig. 7.21).

Diagnosis of Urinary Incontinence

To make the diagnosis, evaluation must be made by an urologist, who will determine the type of incontinence and the cause; thus, the most appropriate treatment can be provided for each type of patient.

A urinary tract infection must be excluded by performing a urine test and/or a urine culture. Urinary tract infections cause inflammation of the bladder mucosa, resulting in increased frequency with which the patient goes to the bathroom to urinate, the feeling of urgency, and, occasionally, involuntary leakage of urine.

The causes of urinary incontinence are numerous in both sexes. It may be due to congenital malformations, neuromuscular diseases, infections, accidents or due to ceratin medications, among other things. In this chapter we will indicate the ones that are related to prostate cancer treatment.

The appearance of symptoms of incontinence after surgery is highly variable.
It depends on the age of the patient, the degree of continence prior to surgery, the type of surgery used and the degree of expertise of the surgeon. Multiple studies indicate that incontinence occurs between 1% and 12% of patients who have been subjected to radical prostatectomy with different surgical techniques. The statistics also vary according to the definition of incontinence which is used (stress, urge, etc...).

The realization that there is a possibility of urinary incontinence after radical prostatectomy or other treatments for prostate cancer can be very discouraging. However, when it occurs, the patient should know that there are many alternatives to treat it successfully.

FIGURE 7.21 Causes of urinary incontinence

There are several diagnostic tools that help pinpoint the type of incontinence that affects the patient. The evaluation begins with an interview, which makes it possible to determine several aspects, including:

- Frequency and severity of the incontinence.
- The effect of incontinence on the quality of life and daily activities of the patient, specifically in the areas of work, social, and personal relations.
- Other associated problems or to rule out other causes of the urinary incontinence.

Similarly, a physical examination is performed to assess whether there are irritative lesions on the skin from contact with urine, and to examine the sensitivity of the reflexes as well as the muscle tone of the anal sphincter and pelvic muscles.

The voiding diary is a record of your fluid intake, voiding, and urine leakage. This is a very important diagnostic tool because it allows evaluation of the relationship between the amount of liquid ingested, the frequency urination and, more

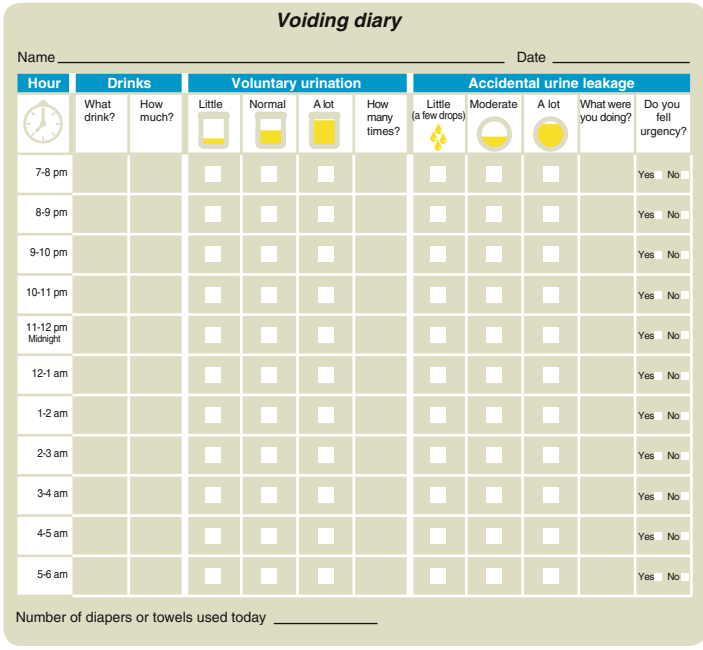


FIGURE 7.22 Voiding diary

importantly, the frequency and severity of urine leakage, as well as its relation to stress or urgency.

Additionally, the need to use protective diapers or towels or changes of underwear is evaluated. Usually it is appropriate to make a record of 3–5 days. The patient is advised to maintain a normal fluid intake and, likewise, to carry out his usual daily activities; that is, to make no changes to normal habits while making this record. The more reliable the diary, the higher the quality of information obtained, which enables better decision-making (Fig. 7.22).

Other tests

Most of the time the clinical evaluation, the voiding diary, a complete physical examination, and urinalysis or urine culture are sufficient for an initial diagnosis and to plan the

Urethrocystoscopy
The insertion, under local anesthesia, of a small device, either rigid or flexible, equipped with a camera, which makes it possible to evaluate inside the urinary tract, the sphincter and the bladder.

Urodynamic study
Enables assessment of the behavior of the bladder in the two phases of the micturition cycle, that is, during filling and emptying. This can be done by simultaneously recording the activity of the sphincter by electromyography. This test permits one to know if the incontinence occurs from a bladder disorder, for example, hyperactivity of the bladder muscle, known as overactive bladder, or, if on the contrary, the incontinence is caused by problems of the sphincter.

Neurophysiological tests
Their purpose is to determine the functional status of the nerve pathways of urination. To perform these tests, two interconnected devices are used. One of them emits a low voltage electric current that travels to stimulate the nerves of the pelvic floor and then back to the originating device; the system records the speed of the current and the responsiveness of nerves and muscles to it. With this, the doctor can identify certain neurological disorders that affect the process of urination.

FIGURE 7.23 Other tests

treatment. However, in some cases the physician may require more thorough evaluations (Fig. 7.23).

Urinary incontinence treatment
A variety of treatments are available, including habit modification, exercises, drugs, catheters, penile clamps, surgery, male perineal slings, injectable agents, artificial sphincter, bladder pacemaker or neuromodulator, and radiotherapy.

1. Habit modification: This includes several aspects, such as:

   - Controlling the amount of fluid intake
     Try to ensure that fluid intake is maintained between six to eight glasses a day. This fluid intake must be balanced during the day, preferably before going to the bathroom, in small quantities, as tolerated. Try not to drink large quantities of fluids at night before bed.

- Controlling the type of fluid consumed
  Certain beverages are irritating to the bladder mucosa and cause the patient to go to the bathroom more often. Some examples are citrus, coffee (in excess), tea, alcohol, carbonated beverages (soda), and water with artificial flavor.
- Avoiding bladder irritants
  These include smoking, chocolate, foods with a lot of spices or smoked foods, and those containing chemical dyes.
- Getting used to maintaining a healthy urinary rhythm
  It's normal to go the bathroom every 2 or 3 h, but, of course, the rhythm will depend on the quantity and quality of the fluid consumed. At night, it is necessary to get used to going to the bathroom just before bedtime, because there will be less urine in the bladder, reducing the need to get up at night to urinate.
- Performing low-impact exercise (like walking or yoga or any recreational activity)
  This contributes to the general well-being, and also tones the pelvic muscles.
- Seeking to maintain proper body weight for height and build
  This not only contributes to overall health, but also prevents the increased pressure on the bladder and thus minimizes the risk of incontinence.
- Keeping an eye on bowel habits
  It's important to try to set up a daily routine. In case of constipation, consult a specialist (Fig. 7.24).

2. Exercises for strengthening the muscles of the pelvic floor: These are a series of exercises to be performed regularly to improve the tone and contractility of the muscles that give support to the pelvic organs and urinary sphincter. The first thing a person should do, before starting this workout, is to identify which muscles are involved. The doctor can help you to do so. Let's discuss some of these exercises now.

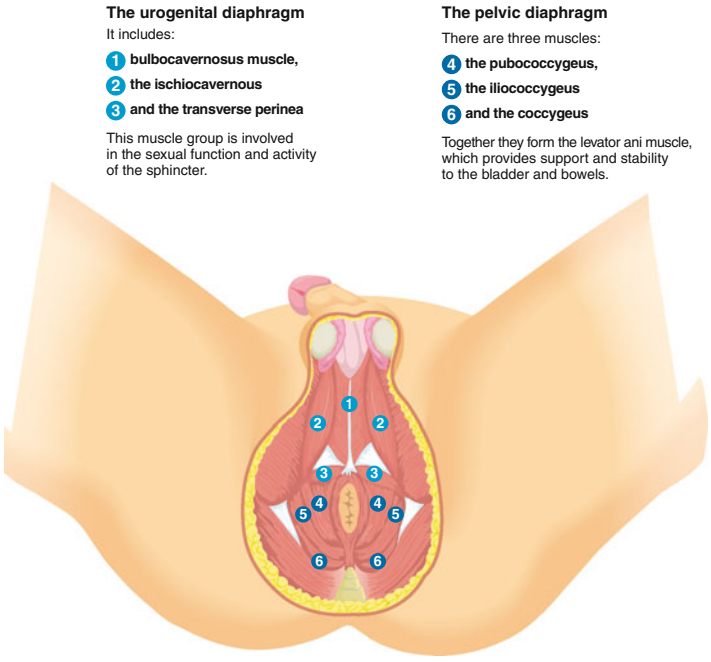


FIGURE 7.24 Pelvic muscles

Kegel exercises: Arnold Kegel was the first to propose exercises of contraction and relaxation of the pelvic muscles as a means for the non-surgical treatment of urinary incontinence. Originally the intention was for the patient to do as many of the exercises as possible, up to 500 times a day. Many patients contracted other muscles in addition to the pelvic muscles. Over time, the way of performing these exercises has changed substantially. The intention is that the abdominal muscles and buttocks remain relaxed while contracting the pelvic muscles.

The frequency and intensity of the contractions has also changed to avoid muscle fatigue. Additionally, breathing exercises are included to help improve the work of the muscles. The exercises are designed to work both the

fast-twitch muscle fibers (forming the striated sphincter) and the slow-twitch (which form much of the pelvic muscles that provide support for the bladder and rectum). Today, these are also known as the pelvic floor exercises (Fig. 7.25).

Exercises for the fast-twitch muscle fibers: These fibers are found mainly in the muscles that form the urogenital diaphragm and external sphincter (both urethral and anal). They are important to prevent loss of urine when sneezing, coughing, straining, or lifting.

Exercises for the slow-twitch muscle fibers: Slow-twitch fibers have more endurance than fast-twitch fibers, that is, they tire less quickly and, therefore, provide ongoing support to the pelvic organs. The pelvic floor muscles have mostly slow-twitch fibers, which support both the bladder and the urethra in the best position for continence.

While the exercise can be done in any position, it is recommended when the patient starts this therapy, to perform it in the supine (lying on the back) position with the legs semi-flexed, resting on a couple of pillows or sitting in a comfortable chair. This is for the purpose of keeping the abdominal muscles relaxed (Fig. 7.26).

Each training program is designed according to the needs and possibilities of each patient, taking into account his activity level, time availability, work hours, cognitive level, etc.

Biofeedback: Is a training technique that measures and displays information on a monitor about what is happening in the body with respect to the level of muscle tension in order to carry out the therapies correctly. Typically, the patient does not perceive the contractile activity of his pelvic muscles. Biofeedback allows the patient to become aware of such activity. This information helps improve the ability to contract certain muscle groups (Fig. 7.27).

Electro-stimulation: This therapy is based on the emission of alternating electric current of low-voltage (less than 1 V), which is applied by a transducer placed in a cavity (inside the anus for men) or by surface electrodes around

- You can do the exercises in any position. Initially, try to find a comfortable position.
- Focus on your breathing, keep a regular, soft breathing pattern

Strongly contract the anus for 2 or 3 s and then relax immediately

Do this 3 to 4 times.

- Make sure that the abdominal muscles, buttocks and thigh muscles (adductors) remain relaxed

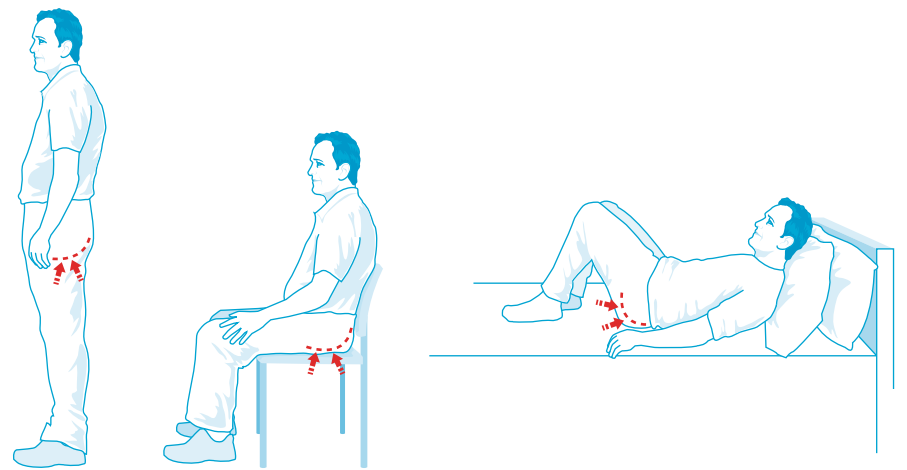


FIGURE 7.25 Kegel exercises 1

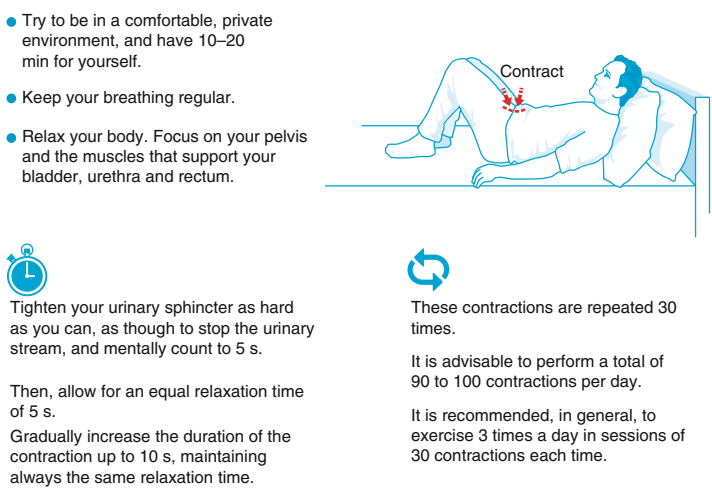


FIGURE 7.26 Kegel exercises 2

the anus. This therapy is designed to electrically stimulate the nerves and muscles involved, to exercise them and improve their strength so as to best contribute to achieving urinary continence. The current may be perceived by the patient as a tingling sensation, which does not become painful (Fig. 7.28).

3. Drugs: There are several drugs now used for urge incontinence when there are bladder contractions. For example, Hyoscyamine, Oxybutynin, and Tolterodine, which help control incontinence by relaxing and decreasing the bladder contractions. The side effects may include dry mouth, blurred vision, and constipation.
4. Catheters: If the contraction of the bladder does not occur with enough force to expel the urine, it will be necessary to place a catheter through the urethra. The catheter will not have to be used permanently. The doctor can explain how to use it intermittently, in case of need (self-catheterization). It is almost always recommended every 4–6 h to empty the bladder. In addition, the patient should receive information on how to wash and preserve these catheters.

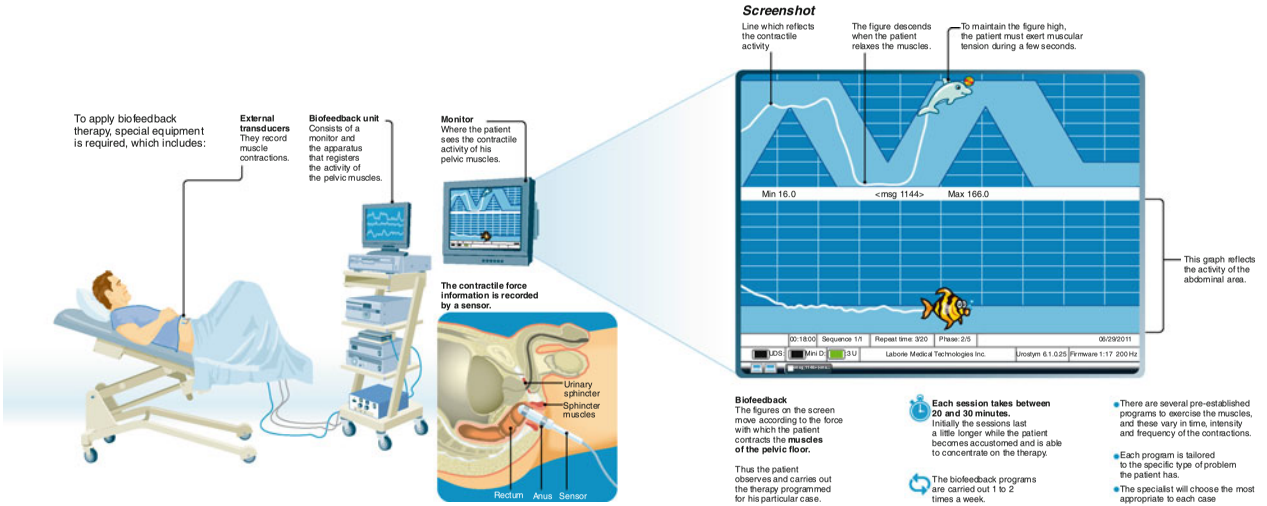


FIGURE 7.27 Biofeedback therapy

Indications of electro-stimulation

- Urinary stress incontinence.
- Urge incontinence or overactive bladder.
- Pelvic floor muscle weakness.
- Disorders of relaxation of the pelvic muscles.
- Urinary retention.
- Pelvic pain.

Contraindications

- Cardiac pacemaker.
- Metal prosthesis in the pelvic region or lower extremities.
- Ano-rectal bleeding.
- Perineal infections.
- Urinary tract infections.
- Ano-rectal lesions.
- Disorders of perineal sensation.

FIGURE 7.28 Electro-stimulation

5. Penile clamps (*Cunningham clamp*): This instrument secures the outer zone of the penis and closes the urethra to prevent leakage. It has the disadvantage that it may cause erosion of the skin of the penis and narrowing of the urethra (Fig. 7.29).
6. Surgery: If there are no signs of improvement and incontinence permanently alters the quality of life of the patient, surgery is recommended. This should only be carried out between 12 and 18 months after the prostatectomy. Surgical options include:

   A. Male perineal slings: These slings are placed beneath the urethra to provide support and improve continence. These represent another surgical option for treatment of urinary incontinence, particularly with the appearance of a new generation of materials that produce less rejection and have greater effectiveness, and which have reported success rates above 80 % and risks of complications of about 7 % (Fig. 7.30).

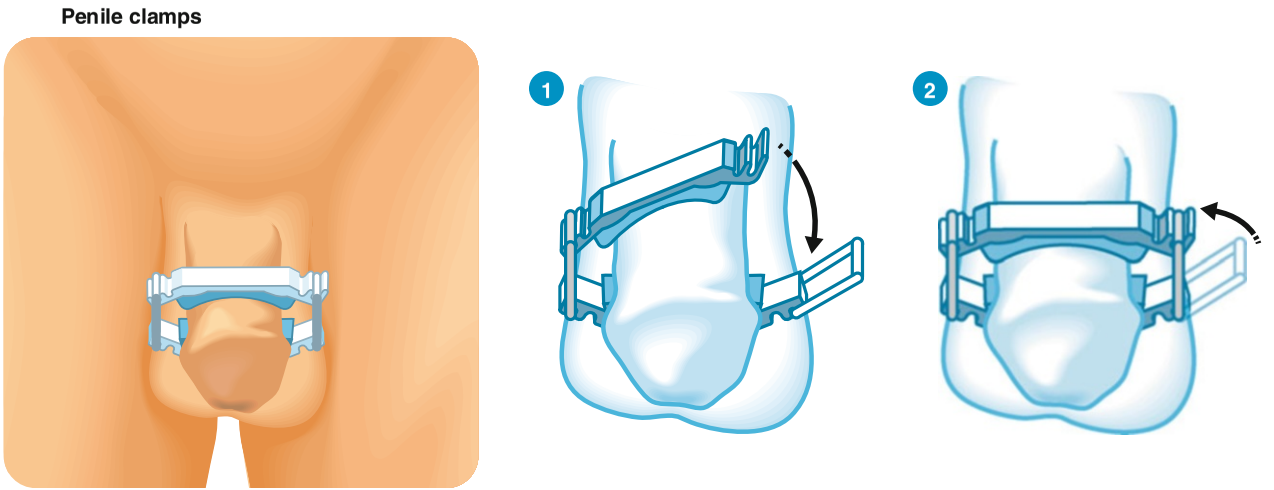


FIGURE 7.29 Penile clamps

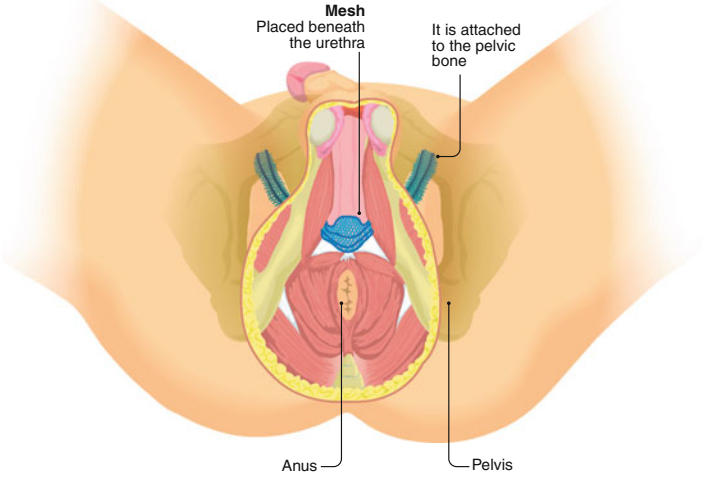


FIGURE 7.30 Mesh

B. Injectable agents that increase the volume of the bladder neck: This is a less invasive procedure. It is performed under sedation or with local anesthesia, and involves the injection of substances into the bladder neck to produce an increase in its volume, which partially occludes it and reduces incontinence. The substances most commonly used are bovine collagen, Teflon, or silicone polymers. With this technique, 50 % of the patients show a partial improvement and 30 % initially report total improvement. However, this type of material can be absorbed by the surrounding tissues, which would make necessary to undergo a new injection procedure. This technique is not recommended for patients with prior radiotherapy.
C. Artificial sphincter: This is the most effective procedure to treat stress urinary incontinence and consists of an inflatable silicone cuff, which is placed around the urethra. The cuff around the urethra is filled with a liquid. When this solution is not in the cuff, it remains in a reservoir that is located in the lower abdomen. To make

the liquid pass from the reservoir to the cuff, a pressure pump is placed in the scrotum. When activated, it enables the liquid to be deposited in the cuff, thereby occluding the urethra and preventing the leakage of urine. When the patient has the desire to urinate, he simply manipulates the device in the scrotum, which allows the cuff to empty and frees the obstruction of the urethra, thereby allowing the outflow of urine (Fig. 7.31).

D. Bladder pacemaker or neuromodulator: This is implanted in the spine, and generates electrical impulses to the nerves controlling the bladder. These impulses help reduce involuntary bladder contractions that cause incontinence.

Radiotherapy

Radiotherapy involves the application of electromagnetic waves in the form of X-rays or Y (gamma) rays, or subatomic particles such as protons, electrons, or neutrons. It is classified as "external radiotherapy" if the waves are released from an external device and "brachytherapy" if the waves are released from radioactive seeds implanted within the prostate. The amount of energy delivered is measured by a unit called a *gray*. Radiation acts through two mechanisms:

- It destroys water and oxygen, converting them into free radicals, compounds that destroy cellular DNA. In this way tumor cells do not multiply, or they do so in such a way that their offspring inherit genetic damage that will cause them to self-destruct.
- It triggers a chemical reaction within the cell that leads to programmed cell death called *apoptosis* (Fig. 7.32).

External radiotherapy

This treatment was first used more than 80 years ago, without encouraging results. At that time, the energy that could be released was low and, therefore, insufficient for healing

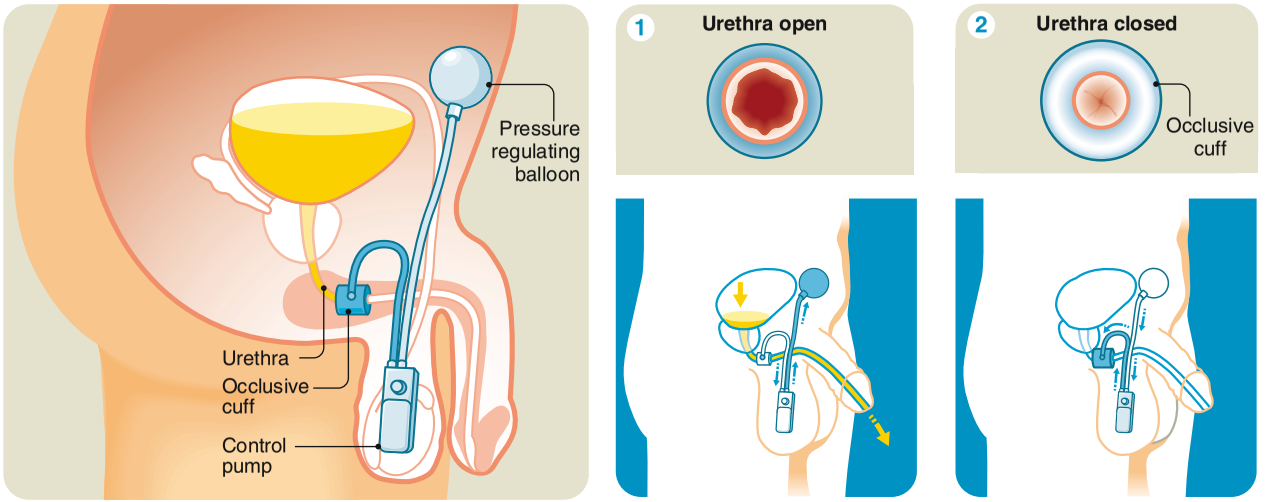


FIGURE 7.31 Occlusive cuff

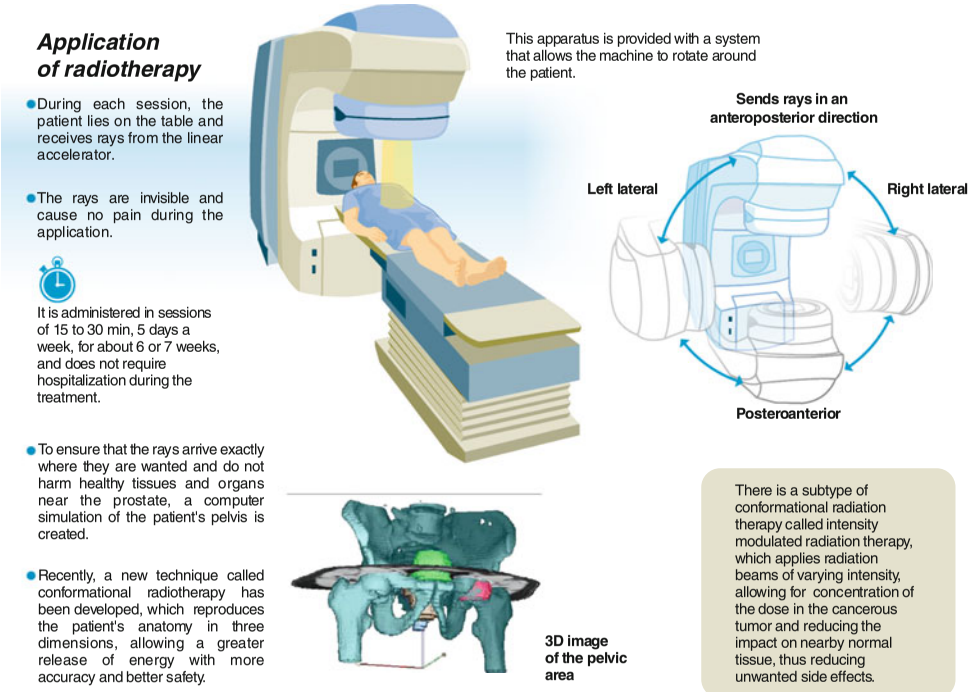


FIGURE 7.32 Radiotherapy

purposes. However, in the 1940s, a machine called a "linear accelerator" was introduced, and is still used, capable of releasing more energy without inducing excessive damage to tissues near the prostate. The X-ray waves are generated by mixing high-energy electrons with the nucleus of the mineral tungsten. This device revolutionized the use of radiotherapy and became one of the alternatives for curing prostate cancer.

Proton beam radiotherapy

This is a new type of radiotherapy that does not emit electromagnetic waves but a type of subatomic particles called protons. Thanks to its unique physical properties, a more precise localization of the radiation is achieved. Both intensity-modulated radiation therapy and proton beam radiation therapy allow the release of greater amounts of radiation with fewer side effects and greater chance of cure, and are referred to as high-dose radiotherapy.

Complications of radiotherapy

Radiation therapy is not free of complications. Such complications have been divided into two categories: acute and chronic. Acute complications are those that occur during the weeks in which the procedure is being carried out or during the first weeks after completion. Observed in 70–80 % of the patients (although somewhat less frequently if using the conformational technique), they consist of urinary symptoms (urgency to go to the bathroom often associated with incontinence, burning urination, bleeding in the urine, greater urinary frequency during the day and night) and/or gastrointestinal symptoms (diarrhea, bleeding with the bowel movements, painful bowel movements). Fortunately, in most cases, these symptoms resolve themselves within the first weeks after treatment.

Chronic complications are those that occur more slowly and which, unlike acute complications, may persist indefinitely. Approximately 15–30 % of patients have a sense of urgency

associated with urinary incontinence, which can be managed medically. In 5 % of the cases there is a persistence of the gastrointestinal symptoms mentioned among the acute complications. Additionally, between 25 and 58 % of the patients suffer a state of erectile dysfunction, caused by damage to the arteries that supply the penis, which decreases the oxygen and generates fibrosis in that organ. These changes can be produced slowly, thus erectile dysfunction may occur late, not appearing for months or years after the treatment (Fig. 7.33).

Radiotherapy Compared with Radical Prostatectomy

Unfortunately, no studies have compared the two therapeutic modalities in a serious manner. Only studies based on the medical records of patients undergoing surgery are available; these have shown that radiation therapy is equivalent to surgery in terms of curing the disease and in the side effects such as erectile dysfunction.

Benefits of external beam radiotherapy over radical prostatectomy: Anesthesia is not required. This makes it the first choice for patients suffering from diseases that increase surgical risk (for example, significant heart or lung disease).

It offers less risk of stress incontinence. It does not require hospitalization. It does not require the placement of a urinary catheter.

Disadvantages of external beam radiation over radical prostatectomy: It does not remove the prostate or the lymph nodes surrounding it. This prevents an exact pathologic diagnosis being carried out with regards to the microscopic characteristics of the tumor and its true extension. Some authors consider that because the organ is not removed there may be an increased risk of recurrence of the disease after many years of follow-up. Long term follow-up studies are needed to verify this possibility.

Radiation therapy produces more irritative intestinal and urinary tract symptoms. Due to changes generated in the

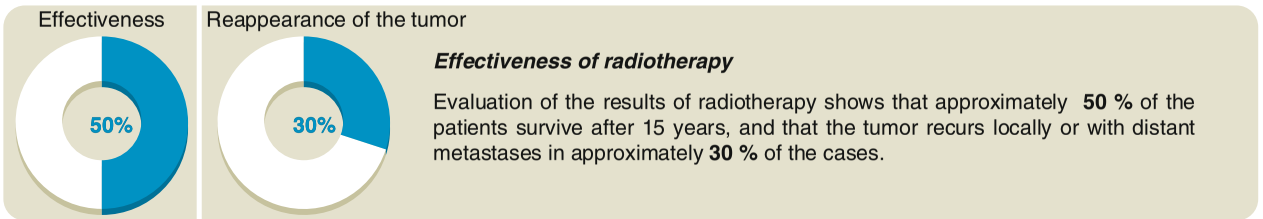


FIGURE 7.33 Effectiveness of radiotherapy

genetic content of the cells, radiation induces an increase from 0.5 to 1 % in the risk that the patient will have another malignant tumor in the pelvis. As mentioned, approximately 30 % of the patients have a recurrence of the tumor after radiotherapy. How is this diagnosed? Unfortunately, recurrence is usually asymptomatic, so that it is not enough to do a physical examination and a clinical interview. One option routinely practiced for many years was to perform a prostate biopsy after radiotherapy in order to assess tumor recurrence. This alternative has fallen into disuse for several reasons:

1. The presence of cancer cells in the biopsy does not indicate that tumor recurrence has occurred only locally (within the prostate), as many patients with positive biopsy have additional tumor cells elsewhere in the body (metastasis).
2. Tumor cells found in the biopsy may represent a tissue that is alive but seriously injured by the radiation therapy, and in the process of death. As described above, the radiation does not eliminate the tumor immediately, but it attacks in such a way that it disturbs the growth process.

It has been found that the evaluation of the prostate-specific antigen correlates directly with the possibility that the tumor has recurred and further predicts whether that recurrence has occurred locally or through metastases, making this test a more useful tool than a biopsy. For this reason, periodic monitoring of patients after radiation therapy is performed by measuring the PSA.

It is expected that after treatment, PSA levels remain below 0.5 ng/ml. By international standards, to state that a tumor has recurred after radiation therapy there must be three consecutive increases in the PSA above this figure. The variables that determine whether tumor recurrence was local (within the prostate) or distant (metastases) are: the tumor grade (Gleason), the velocity with which the PSA rises, and the time elapsed since the end of radiotherapy until the increase in the PSA. In cases where the PSA rose slowly and there was a long interval between the treatment and this elevation, it can be assumed that the tumor reappeared

locally. If the opposite happens, one can deduce that the tumor growth was at a distance (metastasis).

If the findings suggest there are metastases, hormonal treatment is usually provided. If localized disease is presumed, there are two treatment options: brachytherapy or radical prostatectomy. The first involves the implantation of radioactive seeds in the prostate and has been shown to eradicate tumors in between 30 and 50 % of the patients after 5 years of follow-up. The salvage radical prostatectomy, in turn, represents an option that provides a better prognosis, since results have been reported in which the tumor has been eradicated in 60 % of patients after 10 years of follow-up, though with a high incidence of urinary incontinence and erectile dysfunction.

Combination of Radiotherapy and Hormone Therapy

When the prostate tumor is low risk (described as stage T1–T2a, PSA less than or equal to 10 ng/ml, and with a Gleason score of 6 or less), radiotherapy may be offered with a dose greater than 70 Gy as the sole treatment, with a high chance of success. If the tumors are intermediate risk (described as T2b–T2c stage, PSA between 10 and 20 ng/ml, and with a Gleason score of 7), studies have shown that it's necessary to offer hormone therapy previously, for a period of 2–4 months, in order to induce a state of apoptosis (where cell death is programmed) that makes the tumor more sensitive to radiation. Hormone therapy is the suppression of testosterone to prevent this hormone from stimulating the prostatic carcinoma. It is achieved by taking tablets daily or by taking monthly or quarterly injections.

Finally, when the tumor is high risk (described as stage T3—that is, extending beyond the edge of the prostate but without invading adjacent organs—with PSA greater than 20, or a Gleason greater than 7), it is necessary to take hormone therapy for 2–3 years after completion of the radiotherapy, as this has been shown to improve survival.

Some studies have shown that in patients with intermediate or high risk, it is not enough to irradiate the prostate; the lymph nodes must also be irradiated to reduce the possibility of the tumor progressing later on. However, irradiation of the lymph nodes increases the risk of complications and has not shown benefits in terms of survival. For this reason, it is not a common treatment.

Postoperative external radiotherapy

Recent studies have shown that it is advisable to administer radiation therapy after radical prostatectomy with doses of 64–66 Gy for 7–8 weeks, and on the site where the gland was located when the pathology report indicates positive margins. This reduces the risk of cancer progressing and causing metastasis. Also, radiotherapy is usually offered to those patients who had a radical prostatectomy with an observed rise in PSA above 0.2 ng/ml and in whom there is no suspicion of metastatic disease.

Palliative external radiotherapy

This is offered in cases of prostate tumors that have metastasized.

Indications of metastasis:

1. Bone metastases: When the tumor progresses or when it causes a lot of pain despite hormone therapy, it can be treated with doses of 8–30 Gy of radiation, which benefits 80 % of the patients.
2. Spinal cord compression: When metastasis in the spine compresses the spinal cord there is an imminent risk of paralysis of the lower limbs (paraplegia) and radiotherapy should be offered urgently, at doses of 30–40 Gy.
3. Local tumor progression: When the prostate tumor causes urinary obstruction or bleeding, radiation therapy with doses of 30–40 Gy can be offered. With this a decrease in the size of the gland can be achieved and, therefore, a reduction in the symptoms.

Brachytherapy

This is the placement of radioactive sources within the prostate, which reduces the distance between the tissue being treated and the radiation source (unlike external radiotherapy where radiation is emitted by a linear accelerator located few meters from the patient) to reduce side effects.

This technique was first performed at the beginning of the last century, but due to imprecision in the implantation technique, initial results showed high rates of side effects, for which reason it was abandoned. During the seventies, interest in this technique was renewed in an attempt to offer an alternative to external beam radiation, since the latter also had high rates of complications. With the help of ultrasound, it was possible to refine the accuracy with which the radiation source was implanted, and in recent years the technique has improved with the aid of computers that ensure a more exact and more intense dosage.

There are several types of brachytherapy, according to the dose rate of radiation administered.

Low-dose-rate brachytherapy: This consists of the permanent implantation in the prostate of multiple radioactive seeds, the size of a pencil point, composed of iodine or palladium, which are encased in a titanium capsule. Typically between 50 and 100 are implanted, with higher concentration in the peripheral zone of the prostate, where the cancer is more frequently located. Each seed emits a low radiation and the therapeutic effect depends on the three-dimensional interaction among them. The total dose of radiation depends on the type of seed used.

High-dose-rate brachytherapy: In this case a radioactive substance is used that releases a large dose of radiation in a short time, usually iridium 192. The radioactive material is inserted in and removed from different parts of the gland. Each treatment session usually lasts 10–15 min. Although the gland is exposed briefly to the radiation effect, the high intensity thereof and the accuracy with which it is released cause the dose to have a greater or at least equivalent effect in comparison to low-dose brachytherapy.

Technique for administration of brachytherapy

Before any type of brachytherapy, the configuration of the prostate should be studied using computed tomography, magnetic resonance imaging, or ultrasound, to determine the ideal dose the patient will receive and the distribution of the radioactive material.

The size of the gland is important, because those larger than 60 g hinder the action of the radioactive material. When this size is exceeded, the patient may receive hormone treatment during the previous weeks in order to reduce the size before brachytherapy (Fig. 7.34).

Adverse effects and complications of brachytherapy

The radioactive seeds of those patients receiving low-dose brachytherapy continue to emit radiation for several months; for this reason, patients should try to avoid close contact during that time with pregnant women and young children. The emitted dose is very low and cannot affect other groups of people. In the case of high-dose brachytherapy this is not a concern, because after the procedure there is no emission of radioactivity. During the weeks following the brachytherapy, the patient has between 10 and 70 % possibility of developing symptoms of irritation of the urinary and intestinal systems, such as burning, urgency to urinate, increase in the number of bowel movements each day, incontinence, and blood in the urine and the stools. Fortunately, in the majority of cases, these problems resolve spontaneously. However, in 5–10 of every 100 patients, the symptoms continue indefinitely, for which reason a multidisciplinary medical approach frequently is needed, with the participation of an urologist and a colon-rectal surgeon or gastroenterologist.

Due to the inflammation of the prostate caused by the seeds, 4–10 % of the patients can present with urinary obstruction in the days after brachytherapy. In the long term it is possible that a urinary obstruction may occur in 3–8 % of cases, caused by a narrowing of the urethra as consequence of the proximity of the needles inserted and the radioactive material.

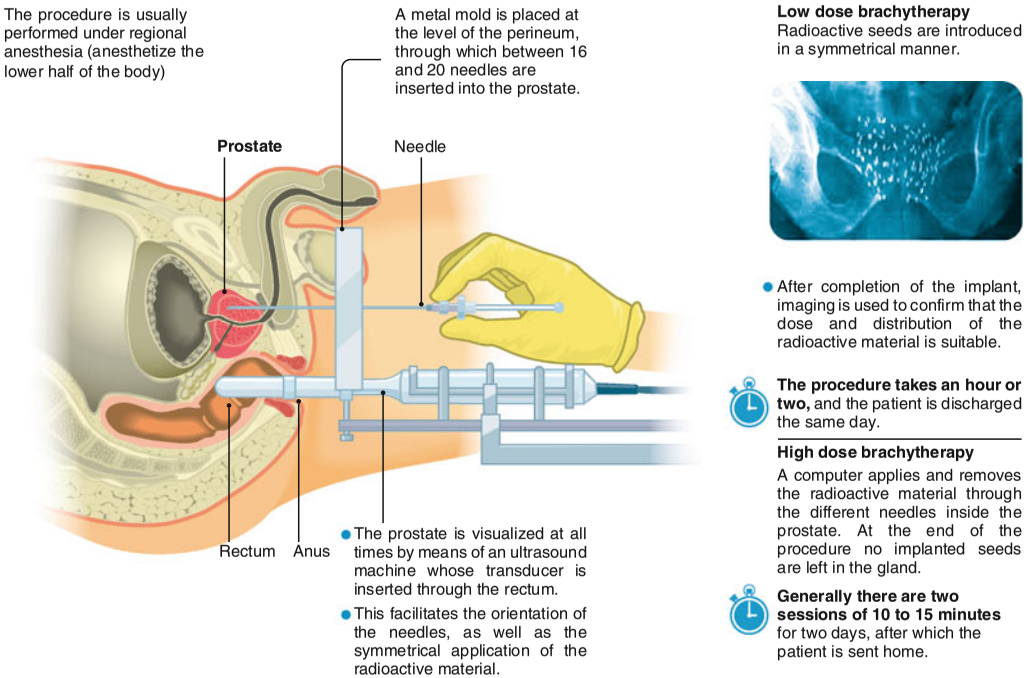


FIGURE 7.34 Brachytherapy

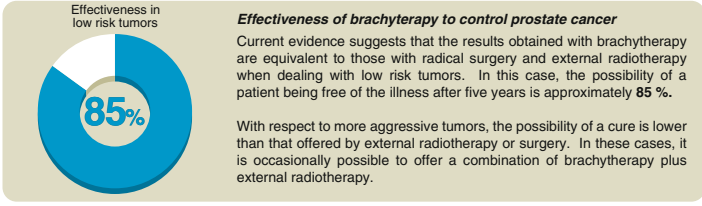


FIGURE 7.35 Effective brachytherapy

Between 30 and 50 % of patients show a progressive reduction of the quality of erections. This happens because the nerves that stimulate the potency of the penis are located very close to the lateral edges of the prostate, so that frequently they are not exempt from receiving the radiation administered to the gland. Studies have been published which compare the adverse effects of high-dose and low-dose brachytherapy, which show that the latter incurs less risk of impotence but with equal probability of generating symptoms of irritation on the urinary and gastrointestinal levels (Fig. 7.35).

Advantages and disadvantages of brachytherapy

The advantages of brachytherapy lie in the ease with which the procedure can be performed and the period of convalescence. It is carried out in a minimally invasive and almost ambulatory way during 1 or 2 days, in contrast to external radiotherapy, which involves daily irradiation for 6 weeks. At the end of the procedure, the patient is left with no wounds of any type and his recovery is rapid. Its limitations are in the adverse affects and in its capacity to cure.

Despite the fact that in theory the direct application of the radioactive charge inside the gland would result in less toxicity for the nearby organs, in practice this has not been proven, and as described, the incidence of urinary and gastrointestinal symptoms, including incontinence and impotence, is significant. On the other hand, the possibility of eradicating the tumor is limited when it shows characteristics of moderate or high aggressiveness, such as a PSA greater than 10, large prostate volume, or a Gleason score greater than 7.

This can be explained by the fact that brachytherapy does not allow all of the prostate to receive a uniform dose of radiation, since the areas near to the implant sites (called *hot sites*) receive a larger dosage than sites far away. If eventually the tumor is localized at a site far from the implant, it might not receive adequate radiation and, therefore, may not be eradicated. Brachytherapy is without doubt a valid option for localized tumors with characteristics suggesting low aggressiveness, especially in cases where the simplicity of the therapeutic technique and a short convalescence are important.

Medical Oncological Treatment

Medical treatment of prostate cancer comprises all therapeutic and pharmacologic interventions that are not related to surgery or radiotherapy. Among these forms of treatment, of special note is the interruption of the production of the male sex hormone called testosterone, either through the use of drugs such as the analogues of the luteinizing hormone-releasing hormone (LHRH) or through definitive surgical castration (surgical removal of both testicles).

Likewise, there are other drugs known as antiandrogens that block the receptors of the androgenic substances. These drugs, in turn, are classified as steroids and non-steroids. Other drugs used in include the inhibitors of the synthesis of adrenal androgens, chemotherapeutic agents, and, more recently, biological therapy, which includes vaccines and therapeutic targets.

There are other drugs that are not directed towards prostate cancer treatment but to some of its more frequent complications, like bone metastasis; these include the biphosphonates (often used in the treatment of osteoporosis) and Denosumab, which is a human monoclonal antibody and which also is highly effective in the management of this painful stage of the illness.

Specialists in medical oncology should handle this arsenal of cancer drugs, since all have certain side effects and the medical oncologist is the person most qualified to handle these adverse events.

Indications

The decision to block the action of testosterone is usually taken when there is a diagnosis of advanced prostate disease, that is, when malignant cells are detected beyond the prostate gland; for example, in the lymph nodes or bones, two places where metastases are frequent.

As already indicated, the hormone blockade decreases and impedes the action of testosterone in the body, so that the tumor cells die due to lack of the hormone. For this reason, it is an excellent therapeutic tool for prostate cancer.

Hormone blockade can also be used when the disease is localized. This can occur in patients who underwent radical prostatectomy, and for whom, once the prostate was removed, risk factors were revealed by pathology tests, for example when the tumor had spread beyond the prostate gland. There are other factors indicating a poor prognosis, such as when lymph nodes are involved or the margins prove positive for cancer cells. In these cases, there is a high risk of disease recurrence, so hormone blockade may be indicated for a specific period, according to the decision of the urologist and medical oncologist. This method is called *adjuvant hormonal treatment*.

Hormone treatment can also be applied in patients who are not candidates for surgery, either because the disease is not localized solely in the prostate or because the individual refuses surgery, or if there are any medical contraindications to it. These cases may also undergo definitive local treatment, such as pelvic radiation therapy.

Hormone blockade may also be applied together with radiotherapy and may last for a period ranging from 6 months (short-term hormone blockade) to a maximum of 3 years (prolonged hormone blockade). It is also indicated in patients with **biochemical recurrence** (increase of the PSA to certain levels) after radical surgery or radiotherapy.

Hormone blockade: One of the available treatment strategies for prostate cancer is hormone blockade. It is based on the fact that tumor cells are stimulated to grow by testosterone, and so the suppression of the action of this hormone helps to control its advance (Figs. 7.36 and 7.37).

Hormone blockade can be achieved in two ways

Surgery: by means of a procedure called and orchiectomy, which is the removal of both testicles (testosterone-producing organs)

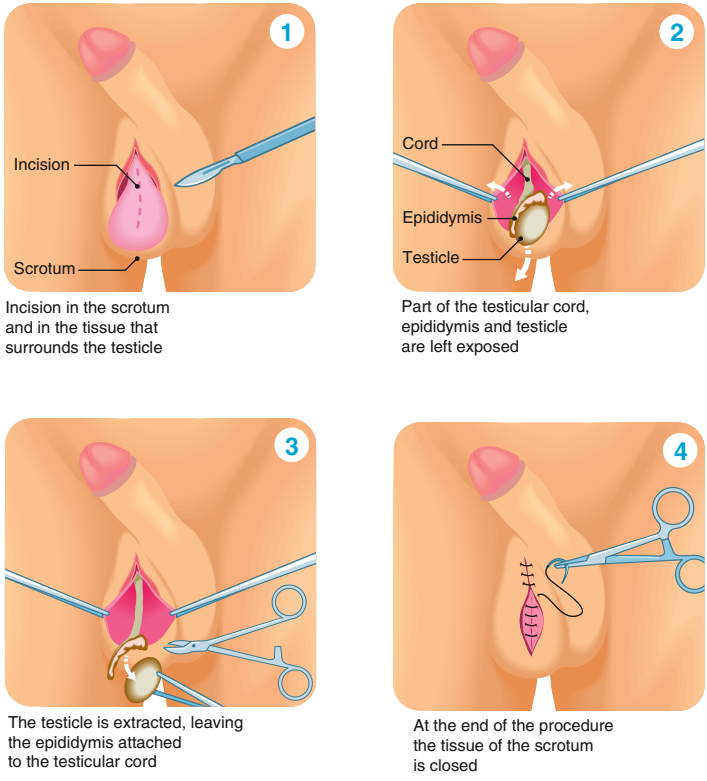
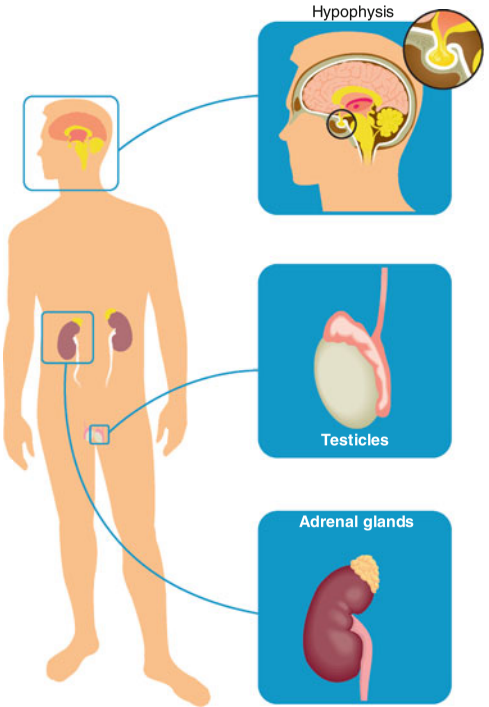


FIGURE 7.36 Orchiectomy

Fact

The term biochemical recurrence is used when levels of prostate-specific antigen exceed 0.2 ng/ml after surgery. In the event that the patient has received radiation therapy, there are two criteria: three consecutive elevations of antigen levels after having reached the nadir (minimum value), or an increase 2 ng (nanograms) above the nadir.



Medications

Luteinizing hormone releasing hormone (LHRH) which acts on the pituitary gland in the neuroendocrine system, it is possible to gradually decrease the stimulation of the testicle, and thereby minimize the production of the hormone.

There are medications that are administered orally, called antiandrogens, which act by blocking the action of testosterone on the androgen receptors and, when combined with LHRH analogues, produce what is known as total hormone blockade.

With this it is possible to achieve, along with a suppression of the synthesis of testosterone, the annulment of the action of any circulating androgen that may come from another part of the body, such as the adrenal glands.

FIGURE 7.37 Medications and mechanism of action

In these situations the patient should receive what is called a *rescue* or *salvage treatment*. When a local recurrence of the disease is suspected, that is to say at the surgical site, the patient should be offered *salvage radiotherapy*, ideally with the value of the antigen as low as possible, preferably below 0.5 ng. In the case of systemic progression, metastasis, or doubling of the PSA levels in a short period of 3–6 months, the use of hormone treatment should be considered.

If the patient receives radiation therapy as his initial treatment and there is biochemical recurrence, the doctor will consider alternatives such as *salvage surgery* (radical prostatectomy) in those cases where there are few associated health problems and a life expectancy of at least 10 years, the tumor was classified as T1–T2, the Gleason score was less than 7, and the PSA before surgery was less than 10 ng/ml. Otherwise, hormonal salvage therapy or other local therapies should be considered as options.

Medicines for hormone blockade

One of the pharmacological options is to suppress the synthesis of testosterone with LHRH drug analogues. The main drugs available on the market are: Goreselin (Zoladex®), Leuprolide (Lupron Depot®), and Triptorelin (Decapeptyl®). These drugs play a role similar to orchiectomy (surgical removal of the testes), because they inhibit the production of testosterone by the testicles through their mechanism of action at the level of the hypothalamic-pituitary-testicular axis. They are generally administered subcutaneously or intramuscularly on a monthly or quarterly basis, and the duration of the treatment will depend on the stage of the patient's illness (Fig. 7.38).

Another possibility is the use of antiandrogen medications, which will block the action of circulating testosterone at the level of the androgen receptors. The product most commonly used is Bicalutamide (50 mg tablets) whose dosage is once a day. Another is Flutamide (250 mg tablets), which is indicated three times a day. The addition of an antiandrogen to medical or surgical castration is what is called *total androgen blockade*.

LHRH analogues

Commercial name	Composition	Presentation	Administration	Frequency
Zoladex	Goserelin	Amp. 3.6mg	Subcutaneous (SC)	Every 28 días
		Amp.10.8mg	SC	Every 84 días
Lupron Depot	Leuprolide	Amp. 3.75mg	Intramuscular /SC	Every 28 días
		Amp.11.25mg	Intramuscular / SC	Every 84 días
Decapeptyl	Triptorelina	Amp. 3.75mg	Intramuscular	Every 28 días

FIGURE 7.38 LHRH analogues

Fact

Recently, LHRH antagonist drugs have been introduced in Europe and North America. The pharmacological name of the LHRH antagonist drug is Degarelix, approved by the Food and Drug Administration (FDA) in 2008. The advantage of this product is that it can produce testosterone levels close to castration more rapidly than LHRH agonists and apparently with minimal toxicity.

Intermittent hormone blockade

Because of the undesirable effects produced by the prolonged administration of hormone therapy, the idea of intermittent hormone blockade was developed. The intention is to improve the quality of life of the patients, preventing the accumulation of the adverse effects of continuous treatment without compromising the efficacy.

Intermittent hormone blockade is the interrupted administration of LHRH analogues and antiandrogens. The period in which they will be administered is determined by the doctor, and is usually a period of 6–9 months, after which the hormone treatment is suspended, so long as PSA levels are brought down to their lowest value and there are no disease-related symptoms. The ideal scenario for the application of this therapeutic maneuver is in a patient with an advanced disease that requires ongoing and indefinite treatment.

After this, measurements of PSA and testosterone levels are made every 12 weeks. Once the patient has reached the PSA values determined by the doctor, the hormone therapy must be started again.

Fact

What is the value used to re-start hormone therapy? In daily practice there is no standard value that determines it. There are two possibilities: one takes as a measure that the prostate-specific antigen reaches 50 % of its initial value before the start of the first blockade. Example: If a patient begins hormone blockade with a PSA of 20 ng/ml and this reaches a value of 0 (zero), the blockade is restarted when the PSA reaches 10 ng/ml, which is 50 %. The other possibility accepts as a standard measure an increase of PSA between 5 and 10 ng/ml, independent of the initial value.

The ideal condition for the implementation of intermittent hormone therapy is when testosterone levels rise before prostate antigen values. Once the patient reaches the predetermined PSA value indicated by the doctor, the treatment is restarted for a period of 6–9 months or until it achieves the maximum decrease in PSA, and in this way the process will continue. Usually the rest periods of intermittent hormone blockage diminish over time. That is, the first time hormone therapy is suspended, the rest period is generally longer, and as more and more intermittent blockade cycles occur, the rest periods tend to become shorter. Intermittent therapy is considered to be a valid option in patients with advanced disease, low tumor volume, and proven hormone-sensitive disease. The effectiveness of intermittent hormone blockade is also seen in the recurrent biochemical disease after the failure of local treatment.

Hormone resistance

In certain stages of the disease, patients with prostate cancer who are undergoing hormone blockade may not respond to the treatment. This happens frequently in those patients who during several months, or even years, take an analogous drug to LHRH and an antiandrogen drug.

The condition is manifested by an increase in the prostate-specific antigen after it has already been controlled, with levels near zero. If the value of the marker rises three times consecutively, with a lapse of a single month between

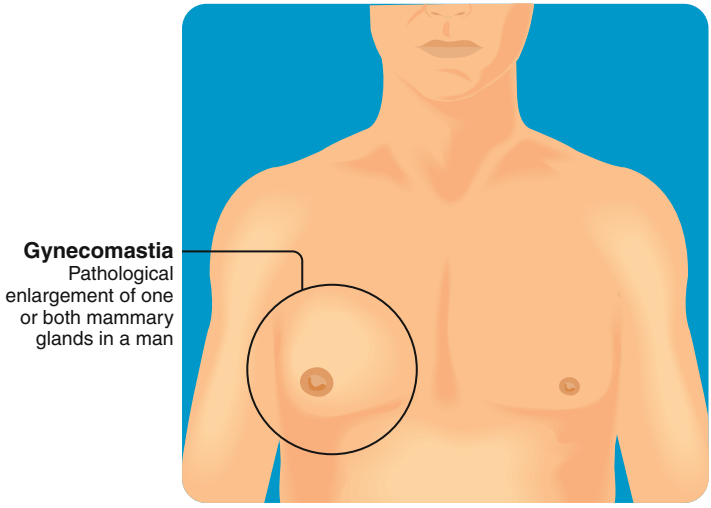


FIGURE 7.39 Gynecomastia

measurements, this is considered a failure of the hormonal treatment and the oncologist is obliged to seek therapeutic alternatives for the patient. Hormone resistance is considered when there is an illness that is clinically progressing while under hormone treatment.

In order for doctors to confirm the condition "hormone resistance," they must be sure that the patient is taking his oral medication and that the analogue of LHRH is being administered correctly. The doctor can easily prove this by determining the levels of testosterone in the blood.

Adverse effects of hormone blockade: While hormone therapy can control the cancer, it can also cause unpleasant side effects, among which are: hot flashes, anemia, depression, lethargy, osteoporosis, swelling, tenderness and breast enlargement (gynecomastia), erectile dysfunction, and metabolic syndrome. For this reason, the medical oncologist is the one who should direct the hormone treatment, identifying and managing these complications when they arise (Fig. 7.39).

Fact
The metabolic syndrome or plurimetabolic syndrome is also known as insulin resistance syndrome. It is characterized by insulin resistance and hyperinsulinism, high blood-pressure levels, lipid abnormalities (elevated triglycerides; decreased good cholesterol, known as HDL; increased bad cholesterol, known as LDL; increased free fatty acids; and postprandial lipemia), and obesity, all of which increase the risk of atherosclerosis and cardiovascular morbidity.

Chemotherapy
Chemotherapy for prostate cancer is indicated only in patients with advanced prostate cancers that are hormone resistant; that is, when hormone therapy and other similar strategies have failed. It involves the administration of drugs intravenously or orally. These drugs enter the bloodstream and reach the whole body, so that this treatment is potentially effective in cases where there has been metastasis.

Among the drugs used for chemotherapy, according to guidelines from the Food and Drug Administration (FDA) is Docetaxel, one of the main drugs available today. In mid 2010, the drug Cabazitaxel was approved as a second-line treatment. Finally, there is a third drug, Mitoxantrone, whose use is recommended to improve the quality of life of patients, as it has been seen to relieve the pain resulting from bone metastases in cases of advanced hormone-resistant prostate cancer.

Newer studies are evaluating the effectiveness of chemotherapy in early stages of the disease, as cases of high-risk localized disease or previous surgery situations (this is known as neoadjuvant chemotherapy). The results are not available yet, so the application must be individualized and applied so far only in centers of excellence in research.

Secondary effects of chemotherapy
These depend upon the type of drug used, the dose, and the duration of the treatment. Temporary side effects include nausea and vomiting, anorexia, hair loss, and mouth sores

(mucositis). Because chemotherapy affects blood production in the bone marrow, blood cell counts may be low. Due to the reduction of white blood cells, the likelihood of infections increases; because of the decrease in platelets, there may be significant bleeding even with minor injuries; and from the decreased red blood cells, fatigue. Most of these effects disappear when the treatment is stopped. There are medications to calm these temporary side effects such as antiemetics and drugs that stimulate the production of blood cells, for both white blood cells and for hemoglobin.

Secondary hormonal therapy

As mentioned earlier, at some point, PSA levels begin to rise despite hormonal treatment. This indicates that hormonal therapy is no longer working to reduce testosterone levels in the body. When this happens, doctors may decide to make changes to the hormonal therapy. This is called secondary hormone therapy or hormonal manipulation. It can be done in several ways. For instance, if you have had surgery to remove your testicles, your doctor may suggest that you start taking an antiandrogen. If you have been using combination therapy that involves an antiandrogen and LHRH analogs, your doctor may stop the use of the antiandrogen. Another option is to change the type of hormone drug. However, the use of an LHRH drug must be continued to maintain the testosterone at castrate level.

Abiraterone acetate (Zytiga®): This is a new antiandrogen medication. It works by decreasing the production of the testosterone, which promotes tumor growth. It is indicated for use in advanced prostate cancer in combination with prednisone after progression of prostate cancer while receiving docetaxel. It is also used upon progression after completion of a docetaxel chemotherapy regimen. The overall survival was increased by 3.9 months according to a recent clinical study (14.8 months for abiraterone versus 10.9 months for placebo); it was approved by the FDA in April 2011.

Ketoconazole: As an antifungal agent, this inhibits adrenal and testicular synthesis of testosterone when used at high doses. Response rates in a second-line setting are 20–40 % with significant side effects. The drug can cause adrenal insufficiency. Hydrocortisone is given simultaneously with this drug to prevent this significant side effect.

Diethylstilbestrol (DES): This inhibits testicular synthesis of testosterone. It is rarely used today because of its serious side effects.

Enzalutamide: formerly known as MDV3100, is a new androgen receptor antagonist drug. In August of 2012, the U.S. Food and Drug Administration approved enzalutamide for the treatment of castration-resistant prostate cancer.

New oncological agents to treat advanced prostate cancer:

Provenge® (sipuleucel-T)

This is a "vaccine" for advanced prostate cancer that helps prolong survival. According to a recent clinical trial, it has extended survival by a median of 4.1 months. It is an immune therapy created by harvesting immune cells from a patient, genetically engineering them, and then infusing them back into the patient. It's approved only for treatment of patients with few or no prostate cancer symptoms whose cancer has spread outside the prostate and is no longer responsive to hormone therapy.

The treatment first involves removal of a quantity of white blood cells, primarily antigen-presenting cells (APCs), also called dendritic cells, from a patient's blood. Dendritic cells show pieces of tumor to immune cells, priming them to attack cells that carry those pieces. The patient's doctor ships the cells to Provenge's® manufacturer. They are exposed to the vaccine and become active. The activated blood products are then shipped back to the doctor who infuses them back into the patient. This is done three times in 1 month. The first infusion primes the immune system. The second and third doses spur an anticancer immune response.

The most common side effect is chills, which occurs in more than half of the men that receive Provenge®. Other common side effects include fatigue, fever, back pain, and nausea. These adverse events usually occur within the first few days of treatment. In addition, clinical trials suggest that this treatment might be linked to a slightly increased risk of cardiovascular events.

Management of bone metastases: As mentioned above, there are two classes of drugs for symptomatic management of bone disease. The first one is zoledronic acid (Zometa®). This drug is administered intravenously every 28 days and its function is to relieve the symptoms of pain caused by bone metastases and reduce the number of adverse events such as bone fractures, the use of palliative radiotherapy in the bones, the amount of analgesics, etc.

The other drug, recently approved by the FDA, is Denosumab (Xgeva®). This medication is a human monoclonal antibody; it is also administered subcutaneously every 28 days, and is slightly superior to zoledronic acid, though also much more expensive.

Chapter 8
How to Get a Second Opinion

René Sotelo and Rafael Andrés Clavijo Rodríguez

Reasons for seeking a second opinion
Find our for yourself—search the internet
Family and friends
Primary care physician or family doctor
Another doctor
Who is right? Whom should we believe?

Reasons for Seeking a Second Opinion

It is normal when we receive unpleasant or unexpected news that we feel it must be confirmed by other means, perhaps in hope of more agreeable news. We also seek to share the news with our loved ones so they can know the situation we are

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facing and to hear the experiences of those who have already lived through something similar. That is when we seek what is understood as a *second opinion*.

Find Out for Yourself—Search the Internet

Today it is easier for all of us to get a second opinion thanks to the internet. You can research your conditions and the treatments available, and widespread access to the internet has become the primary tool for this. It is critical that you are well-informed about matters related to your illness and its likely treatment. However, you should also be aware that to date there is no regulation about creating web pages and validating their content, so you run the risk of consulting pages that do not contain the appropriate information; rather than guide, some internet pages may confuse and worry the patient.

In the case of queries related to health issues, it's best to search websites of universities, well-known hospitals, national libraries, or certain other institutions that are outstanding for their scientific research and academic activities they carry out. Having the backing of these organizations, the pages will surely receive the support of professionals with experience and provide access to information about the recognition they have achieved and their credentials. Such web pages include information that adheres to scientific reality and offers useful and reliable guidance to make decisions.

Family and Friends

There are times when those close to us worry about our situation as much or more than we do. For them and for us it is important to know and consult about our state of health and the options we have with professionals so as to not let unnecessary worry interfere with the facts. Rather than asking them for a second opinion, it is necessary to share and hear experiences similar to our own.

It is not pleasant to receive the prognosis of cancer, but some reassurance is provided by sharing the news and realizing that all around there are people close to us who have already had to deal with cancer—and have overcome it. Just like when we decide to buy a car and the day we get it we realize the same car is almost everywhere, by sharing our experience we realize that we are not alone in this situation. We find out about all the friends who have gone through it. Sharing opinions nurtures us emotionally; advice turns out to be invaluable and helps us face the situation in a better way.

Most of the time, this type of opinion lacks scientific foundation and is based only on the experiences accumulated in the circle of persons close to us. Each case is different and the evolution and the outcome depends on many factors, such as the age of the patients, the type and location of the cancer, as well as the characteristics of the treatment and the expertise of the attending physician.

Primary Care Physician or Family Doctor

This situation is not rare. Most families have a family doctor who often focuses on some conditions, though they are not those of his or her particular specialty. Such opinions may be most appropriate because while the doctor has the interest, affection, and confidence to help, he or she also has scientific knowledge and information on the performance of the best specialists, so is able to provide good opinions and excellent recommendations.

Another Doctor

Today, all patients demand more detailed information on our diseases and know we have the right to receive an additional opinion from another professional. The fact of finding another doctor to whom we present our case does not mean that we are disqualifying the doctor who gave us the first

news. Instead, we are inquiring what is best for our health and what will translate into our greater well-being. It's simply a responsible thing to do.

To begin, we need a specialist that is dedicated almost exclusively to the disease that afflicts us, with a successful, verifiable, medical career, and who belongs to the medical societies and scientific associations that govern the professional practice of his or her specialty.

For this, we can take into account the experiences and views of those close to us. Of course, we can also find information in specialized medical directories or on the internet in order to get to know the curriculum and expertise of the doctor we have decided to consult.

Once we request a consultation, it is necessary to develop a list of the questions that we will ask, in order of importance, ensuring that they include the questions we have about the variety of treatments available for our disease, with their risks and benefits. It is always good to ask what might happen if we decide not to receive one or another treatment.

We should take to this consultation the prescriptions or names of the drugs we have received and the treatments that have been indicated, also, all of the tests that have been performed, so that the specialist can give a truthful and complete opinion.

You can request printed or audiovisual materials to help you better understand your case and can even ask to participate in a support group with other patients. All this is for the purpose of making informed decisions about our health. This second opinion is probably the most important and most beneficial to us.

Who Is Right? Whom Should We Believe?

Definitely, the most reliable opinion is that which is supported by current scientific knowledge, while at the same time clearing up all doubts, and that meets our personal and family expectations, the opinion which facilitates the

improvement of the condition, takes into account our current health status, and shows concern that the process always maintain a goal to maintain a dignified quality of life, without sacrificing physiological, employment, and social activities. If you choose a good second opinion, there is hardly need for a third.

Recommended Resources

http://www.urologyhealth.org/. Official website of the Foundation of the American Urological Association, with information about various urological diseases, causes, methods of prevention, diagnosis, and treatment, among others.

http://www.uroweb.org. The website of the European Association of Urology. English-language page with access to clinical guidelines for diagnosis and treatment of common diseases in urology. Offers access to sites of interest to expand your knowledge about diseases in urology.

http://www.ttmed.com/urology/latam/. Page of free access to articles of scientific journals that are about the most prevalent urologic diseases. Allows entry to conferences, video surgeries, interviews, and case studies, among other services.

Resources for Second Opinions

http://www.nci.nih.gov/. Provides timely and accurate scientific information from the National Cancer Institute, United States.

http://www.cancer.org. Official site of the American Cancer Society, where you will find information about benefits, risks, and side effects of chemotherapy and radiotherapy for different cancers.

http://www.kidney.niddk.nih.gov. Page of the Information Center for Kidney and Urologic Diseases. It offers the most relevant information on nephrology and urologic diseases, including urinary incontinence, sexual dysfunction, and renal failure, among others.

http://nlm.nih.gov/medlineplus/healthtopics.html. Website of the National Library of Medicine. Provides information about

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general health topics, a medical dictionary, and an encyclopedia of health and drug information, among other things.

http://www.nccn.org. This is the official website of nineteen international centers specializing in cancer. Provides detailed information for patients and updated guidelines for diagnosis and treatment for health care staff.

http://www.prostatecancerfoundation.org. This is the largest philanthropic organization in the world dedicated to research in prostate cancer. Information about new findings for the diagnosis and treatment of disease and the information necessary to make donations for research into the disease.

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