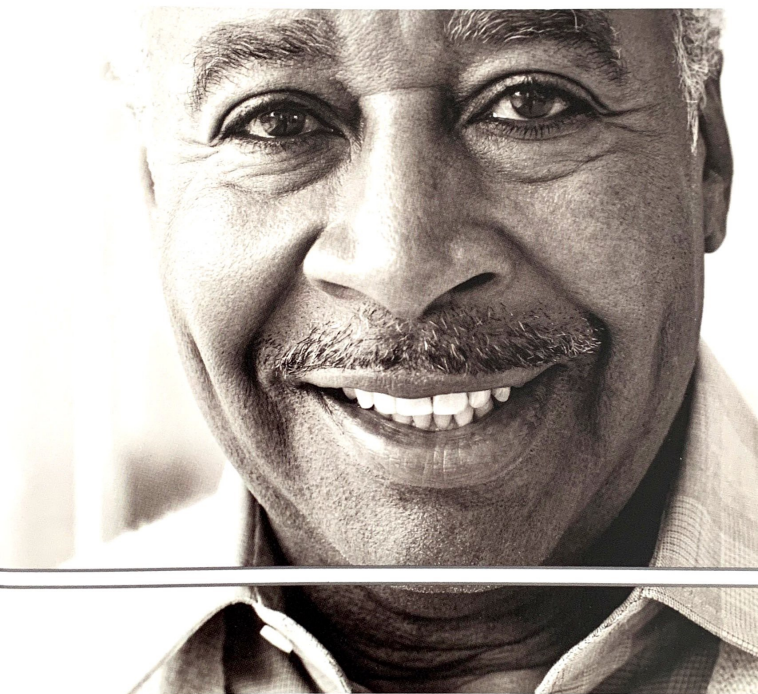




Prostate Cancer

A Visual Reference Guide for Patients



Janssen Biotech, Inc.

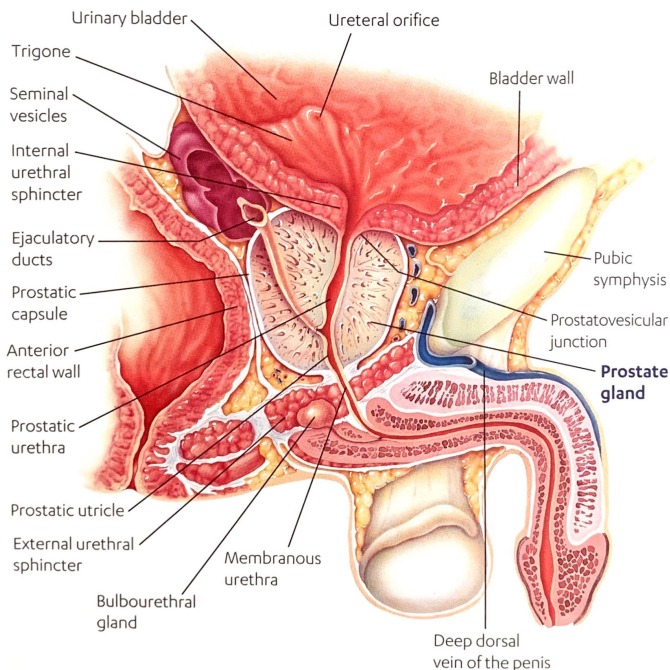




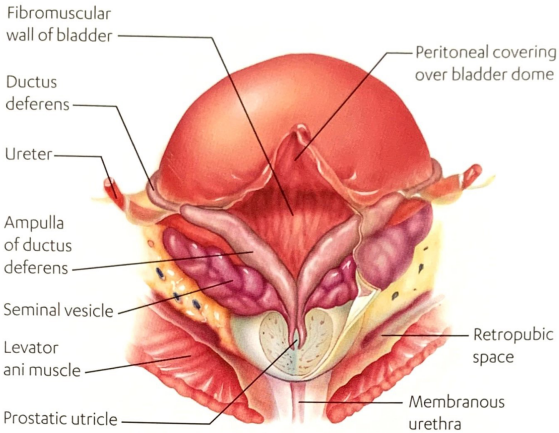
The Prostate

The prostate is a gland consisting of fibrous, muscular and glandular tissue surrounding the urethra below the urinary bladder. Its function is to secrete prostatic fluid as a medium for semen, helping it to reach the female reproductive tract. Within the prostate, the urethra is joined by two ejaculatory ducts. During sexual activity, the prostate acts as a valve between the urinary and reproductive tracts. This enables semen to ejaculate without mixing with urine. Prostatic fluid is delivered by the contraction of muscles around gland tissue. Nerve and hormonal influences control the secretory and muscular functions of the prostate.

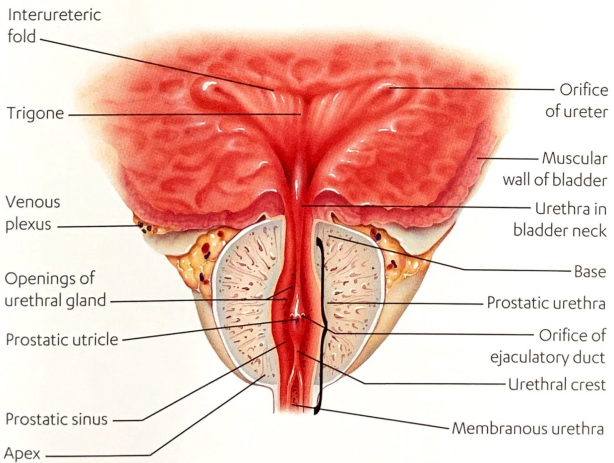
Normal Prostate



Posterior View



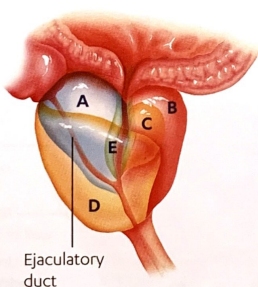
Anterior View with Exposed Prostatic Urethra



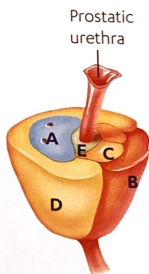
What is Prostate Cancer?

Prostate cancer, a malignant growth of cells in the prostate gland, is the most common cancer in U.S. men. Of all newly diagnosed cases of cancer in U.S. men, it is estimated that approximately 26% will be prostate cancer. Mortality rates due to prostate cancer have declined since 1991. This decrease in death rate suggests greater public awareness is leading to earlier detection and treatment of prostate cancer. Although early or local prostate cancer may be asymptomatic, lumps are detectable upon physical examination. With disease progression, symptoms occur, including urinary problems such as painful episodes and the presence of blood. Metastasis, most commonly to the lymph nodes, lungs and bones in the hip region, is characteristic of advanced prostate cancer.

Zones of the Prostate



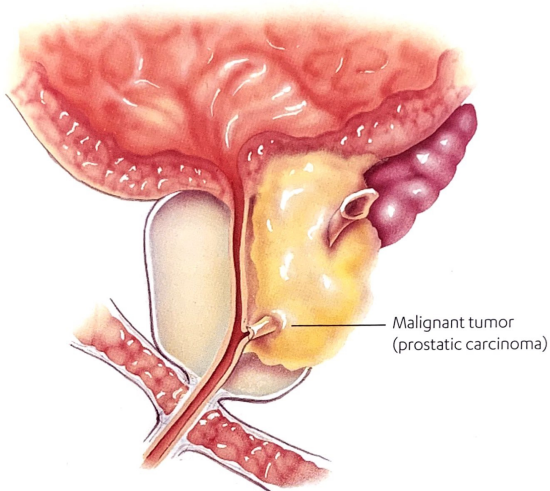
- A** Central zone
- B** Fibromuscular zone
- C** Transitional zone



- D** Peripheral zone
- E** Periurethral gland region

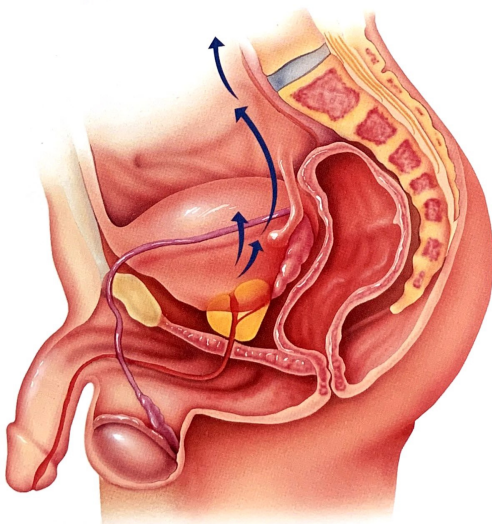
Prostatic Carcinoma (Malignant Tumor)

Prostatic carcinoma is the most common malignant tumor in men. Unlike Benign Prostatic Hyperplasia (BPH), prostate cancer enlarges the prostate and also metastasizes (spreads) to other parts of the body through lymphatic and venous channels.



What is Prostate Cancer?

Pathways for Prostate Cancer Spread



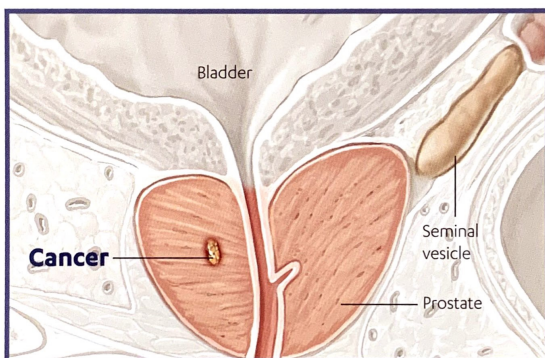


Prostate Cancer Stages

In order to plan treatment, the physician must understand the extent (stage) of the disease. The stage is based on the size and spread of the tumor; the higher the stage, the more advanced the cancer. To determine if the cancer has spread, imaging tests such as a bone scan, CT scan or MRI may be performed. Recurrent cancer is cancer that has come back after a period of being undetectable.

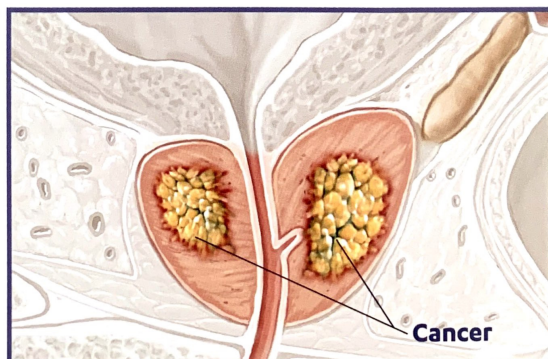
Stage 1

The cancer is not found during a digital rectal exam, but found when doing a biopsy for increased prostate-specific antigen (PSA) or surgery for another reason. The cancer is located only in the prostate.



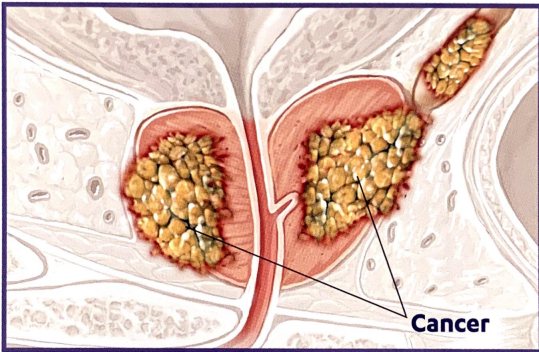
Stage 2

The cancer can be felt on digital rectal exam but has not yet spread outside the prostate.



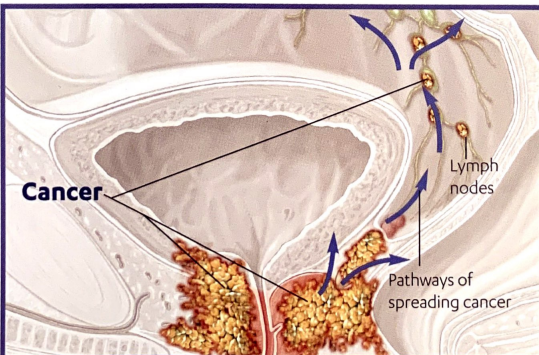
Stage 3

The cancer has spread outside the prostate, perhaps to the seminal vesicles, but not to the lymph nodes.



Stage 4

The cancer may have spread to nearby muscles, organs, lymph nodes or other parts of the body.

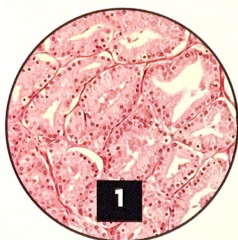




Gleason Pathologic Scoring System

If cancer is not found, medicine to reduce the symptoms caused by an enlarged prostate may be suggested. If cancer is found, the tumor(s) will be graded on the aggressiveness of the disease – how fast the cancer will grow and spread. One system of grading is the Gleason Pathologic Scoring System, which ranges from 1 to 5. The two most common histological patterns are added together to get a Gleason score between 2 and 10. A lower score indicates a less aggressive cancer, and a higher score indicates a more aggressive cancer.

Histological Patterns



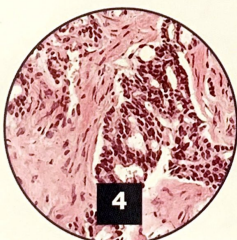
1



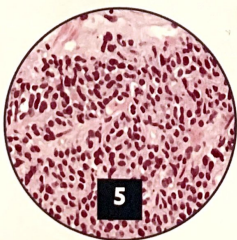
2



3



4



5

Well
Differentiated



Poorly
Differentiated

Tests

Diagnostic Tests

Depending on the results of the screening test(s), the physician will perform additional diagnostic tests, which may include:

- **Transrectal ultrasound** – A probe is inserted into a man's rectum to check for abnormal areas.
- **Transrectal biopsy** – After a needle is inserted through the rectum to the prostate, tissue is removed to look for cancer cells.

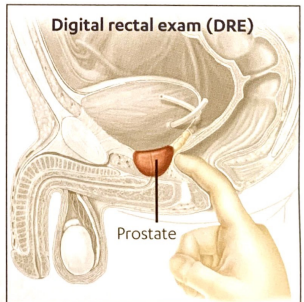
Screening Tests

Screening refers to testing to find a disease such as cancer in people who do not have symptoms of that disease. For some types of cancer, screening can help find cancers in an early stage when they are more easily cured. Prostate cancer can often be found early by testing the amount of prostate-specific antigen (PSA) in the blood. Another way to find prostate cancer is the digital rectal exam (DRE).

- **Blood test for Prostate Specific Antigen (PSA) –**

Prostate-specific antigen (PSA) is a substance made by cells in the prostate gland (it is made by normal cells and cancer cells). Although PSA is mostly found in semen, a small amount is also found in the blood. Most healthy men have levels under 4 nanograms per milliliter (ng/mL) of blood. The chance of having prostate cancer goes up as the PSA level goes up. When prostate cancer develops, the PSA level usually goes above 4. Still, a level below 4 does not mean that cancer isn't present -- about 15% of men with a PSA below 4 will have prostate cancer on biopsy. Men with a PSA level in the borderline range between 4 and 10 have about a 25% chance of having prostate cancer. If the PSA is more than 10, the chance of having prostate cancer is over 50%.

- **Digital rectal exam (DRE)** – For a digital rectal exam (DRE), a doctor inserts a finger into the rectum to feel for any bumps or hard areas on the prostate that might be cancer. The prostate gland is found just in front of the rectum, and most cancers begin in the back part of the gland, which can be felt during a rectal exam. This exam is uncomfortable, but it isn't painful and only takes a short time.





Treatments

There are several ways to treat prostate cancer, and a combination of treatments may be recommended by the physician. Treatment depends on a number of factors, such as the prostate-specific antigen (PSA) level, the Gleason score which indicates how aggressive the cancer is, the spread (stage) of the cancer, and the age, the symptoms and the general health of the patient.

Treatment options include active surveillance, surgery, radiation therapy, hormone therapy, and chemotherapy.

For patients with early or localized prostate cancer, active surveillance, surgery or radiotherapy is the treatment of choice, depending on risk of recurrence and expected survival.

- **Active surveillance (also called “watchful waiting”)** – Prostate cancer can progress slowly in some cases, and the risks or possible side effects of the treatment options may outweigh the benefits. Hence, the physician may recommend close monitoring of the health of the patient rather than initiate treatment. If the cancer progresses or symptoms occur, then the above treatment options may be considered.
- **Surgery** – Procedures can include the removal of all of the prostate gland or part of it. Cryotherapy is minimally invasive and uses controlled freeze and thaw cycles to destroy cancer cells.
- **Radiation therapy** – Radiation therapy can be delivered externally, using high-energy rays from a machine directed at the target area of the body to kill cancer cells, or internally, from small seeds implanted inside the prostate tissue. The latter facilitates the use of a higher total dose of radiation to treat a smaller area over a shorter duration of time than is possible with external beam radiation therapy.
- **Hormone therapy** – Hormone therapy either inhibits the action or blocks the production of male sex hormones that can stimulate the growth of cancer cells. Hormonal control can be achieved by surgical castration or by medical castration, using hormonal drug therapy.

Luteinizing hormone-releasing hormone (LHRH) agonists prevent the testicles from producing testosterone, thereby causing chemical castration. An LHRH agonist may be combined with an antiandrogen in order to further block the androgen receptor.
- **Chemotherapy** – Chemotherapy is a general term for treatments that use chemical agents (drugs) to kill cancer cells. Many different kinds of drugs are used, either alone or in combination to treat different cancers, depending on the type and extent of the cancer.
- **Immunotherapy** – Immunotherapy is a form of biologic therapy or biotherapy. The treatment uses certain parts of the immune system. This is accomplished by either stimulating your own immune system to work harder or smarter, or by giving your immune system components, such as man-made immune system proteins.

bladder (blad'ěr)

A stretchable musculomembranous organ that holds fluid (gallbladder, urinary bladder).

carcinoma of the prostate (kahr'si-nō'mă pros'tāt)

Prostatic adenocarcinoma (PA) is the most commonly occurring visceral cancer in men, and it ranks second only to lung cancer as a cause of cancer deaths in men. It is both more common and more aggressive in African-American men. PA must be differentiated diagnostically from benign prostatic hyperplasia, which is not a premalignant lesion.

At the time of diagnosis, more than 40% of patients have disease that has spread beyond the gland. Bones of the axial skeleton are the usual sites of distant metastasis. The liver, lungs, and brain are other common sites. Early disease is asymptomatic; the diagnosis is most often made by screening of apparently healthy men with digital rectal examination, assay of prostate-specific antigen (PSA), or both. PA is graded by the Gleason scoring method, which reflects the degree of histologic differentiation in the two most prominent malignant foci.

In elderly men and those with concurrent life-threatening illness, benign neglect may be the treatment of choice. Radical prostatectomy (removal of the entire gland along with the seminal vesicles) is generally reserved for patients with early or limited disease and a life expectancy of at least 10 years. This treatment is associated with a substantial risk of urinary incontinence and impotence. Some authorities oppose digital rectal examination and PSA screening of asymptomatic men with life expectancies of less than 10 years, on the grounds that the risks of false-negative results and of adverse consequences of aggressive treatment outweigh any possible benefit in survival or quality of life.

chemotherapy (kē'mō-thār'ă-pē)

Treatment of disease by means of chemical substances or drugs; usually used in reference to cancer.

complexed prostate-specific antigen (PSA) test

(kom'plekst pros'tāt spē-sif'ik an'ti-jěn test)

Laboratory serum test to detect PSA complexed to α1-antichymotrypsin; cPSA appears to be more specific for detection of prostate cancer at low total levels of PSA than measurement of total PSA and free:total PSA ratios.

digital rectal examination (DRE) (dij'í-tăl rek'tăl eg-zam'í-nā'shŭn)

Manual inspection using the physician's gloved finger to check anatomic structures in the pelvis and lower abdomen.

prostate (pros'tāt)

A chestnut-shaped body, surrounding the beginning of the urethra in the male, which consists of two lateral lobes connected anteriorly by an isthmus and posteriorly by a middle lobe lying above and between the ejaculatory ducts. The secretion of the glands is a milky fluid that is discharged by excretory ducts into the prostatic urethra at the time of the emission of semen. Usage note: Often mispronounced as prostrate, and so misspelled.

prostate-specific antigen (PSA) (pros'tāt-spě-sif'ik an'ti-jen)

A single-chain, 31-kD glycoprotein with 240 amino acid residues and 4 carbohydrate side-chains; a kallikrein protease produced by prostatic epithelial cells and normally found in seminal fluid and circulating blood. Elevations of serum PSA are highly organ-specific but occur in both cancer (e.g., adenocarcinoma) and benign disease (e.g., benign prostatic hyperplasia, prostatitis). A significant number of patients with organ-confined cancer have normal PSA values.

prostatic fluid (pros-tat'ik flū'id)

Also called succus prostaticus. A whitish secretion that is one of the constituents of semen.

prostatic sinus (pros-tat'ik sī'nŭs)

The groove on either side of the urethral crest in the prostatic part of the urethra into which the prostatic ducts open.

prostatic utricle (pros-tat'ik yū'tri-kěl)

A very small pouch in the prostate that opens on the summit of the seminal colliculus.

prostatism
(pros'tă-tizm)

A clinical syndrome, occurring mostly in older men, usually caused by enlargement of the prostate gland and manifested by irritative symptoms (waking at night to urinate, frequency, sensory urgency, and urgent incontinence) and obstructive symptoms (hesitancy, decreased stream, terminal dribbling, double voiding, and urinary retention).

semen
(sē'měn)

The penile ejaculate; a thick, yellowish-white, viscid fluid containing sperm; a mixture produced by secretions of the testes, seminal glands, prostate, and bulbourethral glands.

urinary bladder
(yūr'i-nar-ē blad'ěr)

A musculomembranous elastic bag serving as a storage place for the urine.