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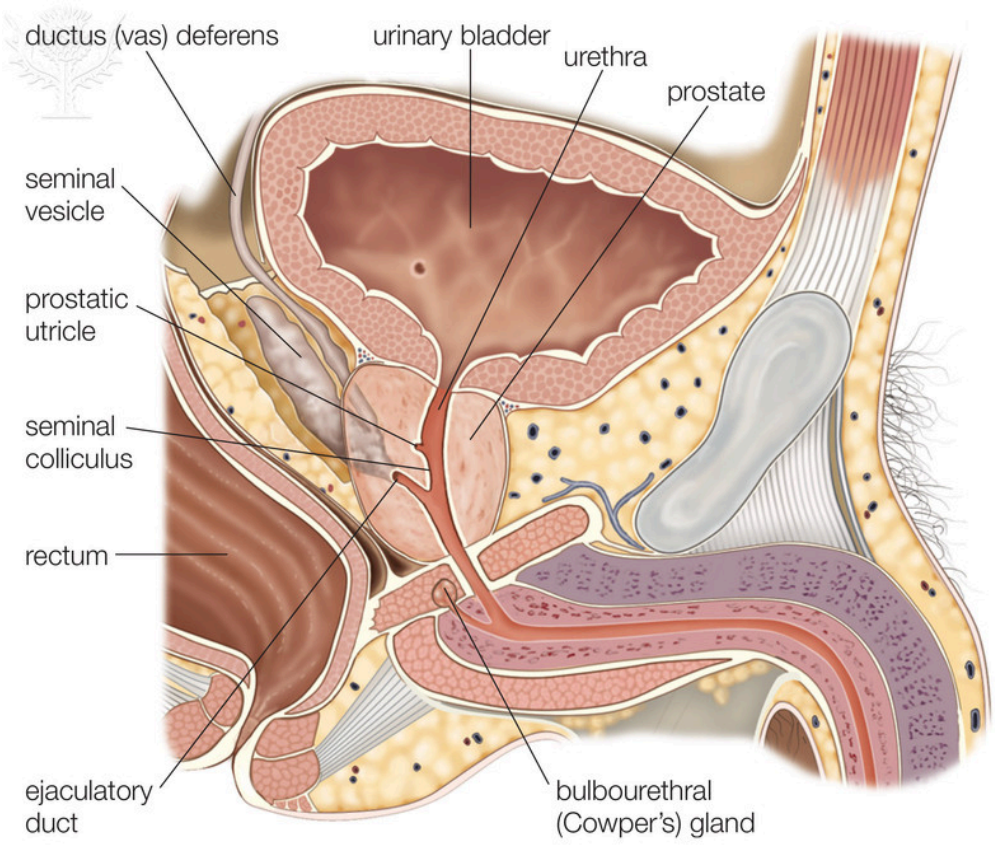
Benign Prostatic Hyperplasia and Prostate Cancer

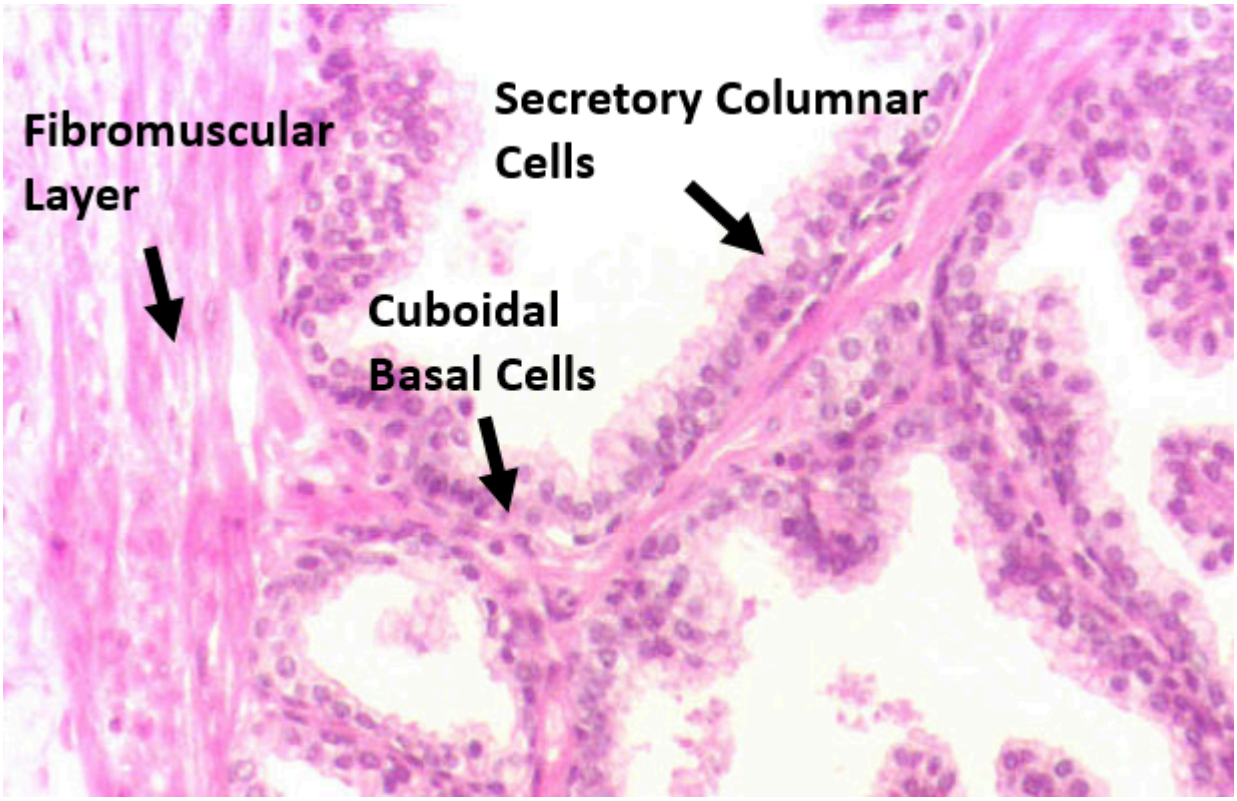


Male Reproductive System. *Illustration. Britannica ImageQuest, Encyclopædia Britannica, 25 May 2016. quest.eb.com/search/309_365517/1/309_365517/cite. Accessed 26 Dec 2019.*

Benign Prostatic Hyperplasia (BPH)

Benign prostatic hyperplasia (BPH) involves an increase in the number of cells of the prostate gland. This condition should not be confused with **hypertrophy**, which is an increase in cell size (not number). These two terms are frequently used interchangeably, even by urologists, but we should remember the formal definitions.

Histologically, the prostate is made up of glands that have 2 layers of epithelial cells. There is a basal layer of flattened cuboidal epithelial cells covered by columnar epithelial cells which are the secretory cells of the gland. The glands are supported by fibromuscular tissue known as the stroma which consists mainly of smooth muscle cells.



Cells layers of the Prostate *Labeled from File:Prostate normal 1.jpg; Alex brollo; https://commons.wikimedia.org/wiki/File:Prostate_normal_1.jpg; This file is licensed under the Creative Commons Attribution-Share Alike 4.0 International licence*

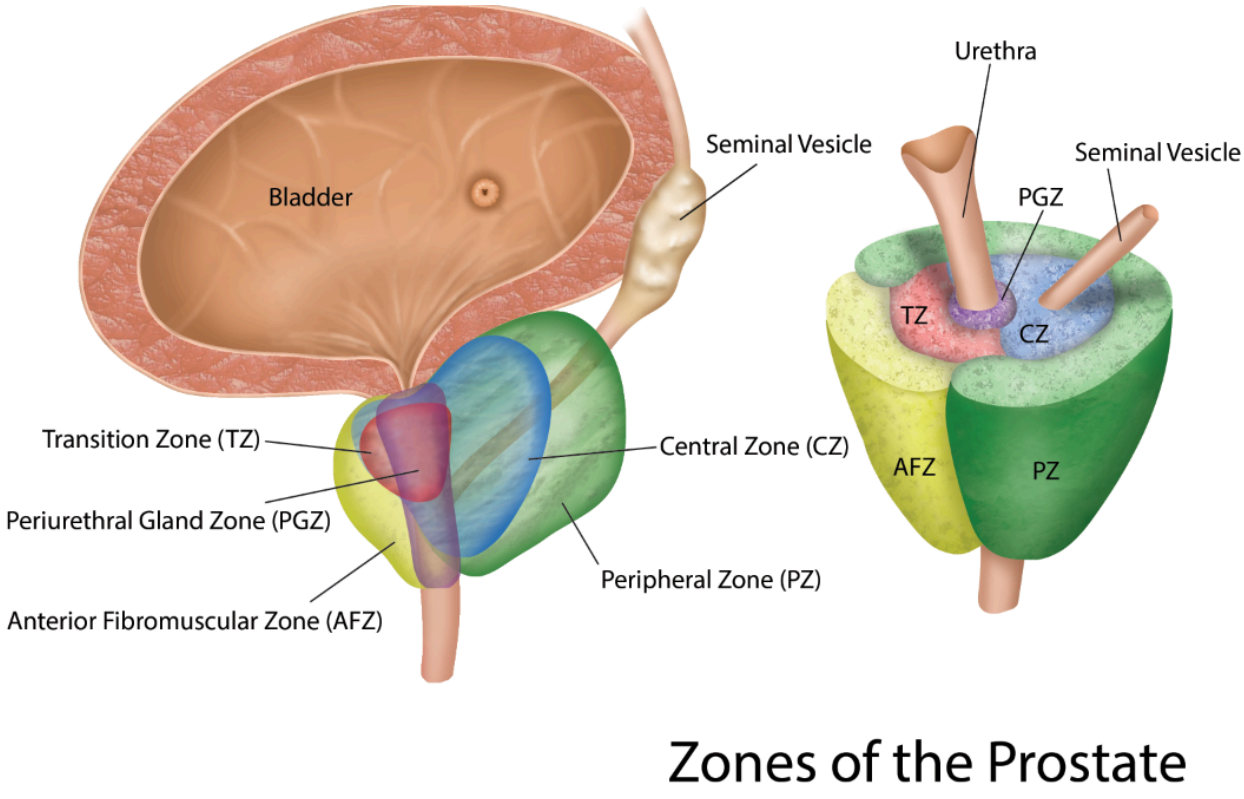


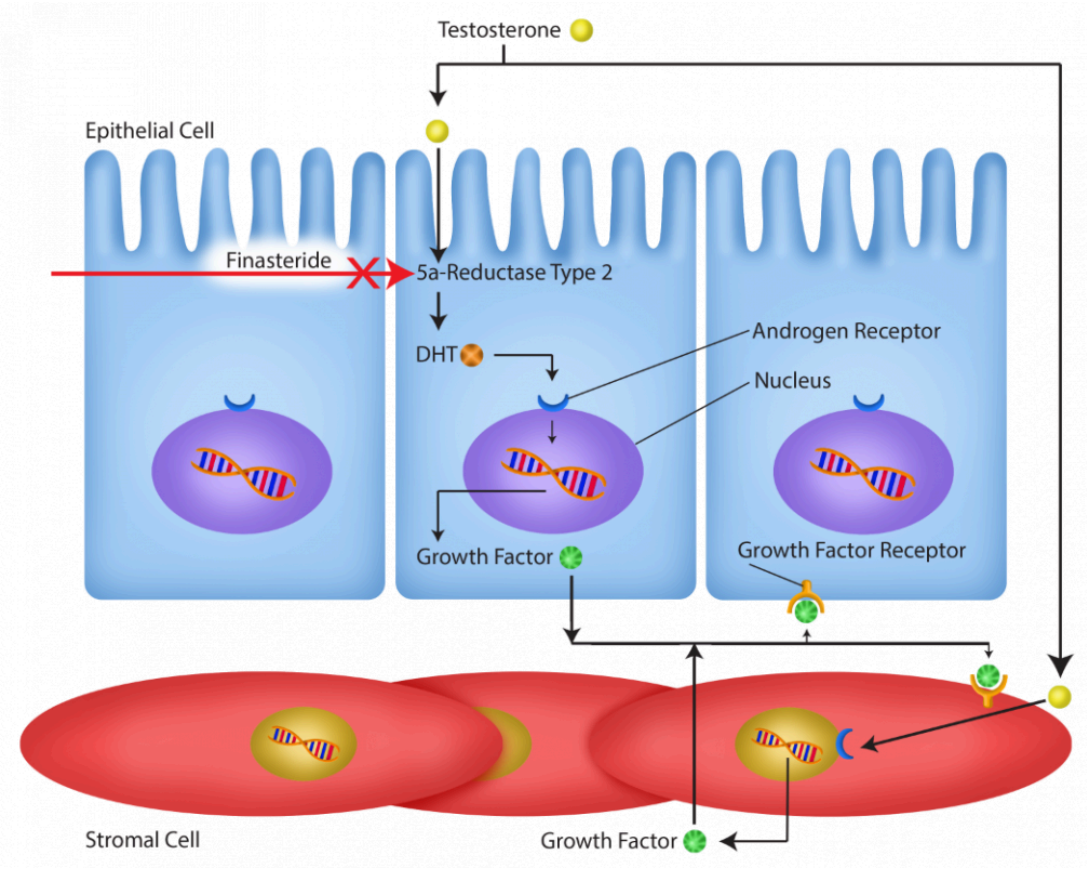
Image by Becky T. BYU-Idaho W20

BPH mostly affects the zone of the prostate located next to the urethra called the periurethral zone. In contrast, most prostate carcinomas affect the outside regions of the prostate known as the peripheral zone. Nodules that form in the periurethral zone in men with BPH compress on the urethra and obstruct urine flow. Individuals with BPH experience symptoms such as poor urinary stream, increased urinary frequency, nocturia, difficulty with stopping and starting urination, and even painful micturition (dysuria). As BPH progresses, patients can also experience bladder distention, hydroureter, hydronephrosis, and possibly renal failure if the compression of the prostatic urethra prevents the bladder from fully emptying.

Aging is by far the predominant contributor to developing BPH. While only about 10% of men have symptoms of BPH before 40 years old, by 50 years old, 50% of men have symptoms. By the time a man reaches 90-100 years old, the incidence of BPH symptoms is close to 100%.

The **androgen** called **dihydrotestosterone (DHT)** is related to BPH. DHT is produced mainly by the stromal cells which make it from testosterone with an enzyme called **5-alpha reductase type 2**. DHT binds to a **nuclear androgen receptor** in the stromal and epithelial cells and leads to upregulated expression of growth factors and their receptors. The growth factors cause the stromal cells to proliferate and decrease epithelial cell death. Type 1, 5-alpha reductase is expressed in cells of the liver and skin which also produce circulating DHT that increases growth of the prostate in an endocrine fashion.

Estrogen also plays a role in BPH and prostate cancer. Both **estrogen receptors (ER)** are expressed in prostate tissue: ER-alpha and ER-beta. These receptors play a role in regulating prostate tissue proliferation. Prostate tissue also expresses **aromatase** which catalyzes the production of estrogen from androgen precursors. Estrogen is also produced by many non-endocrine tissues including adipose (which increases with aging), liver, skin, and the brain. With age, testosterone decreases while estrogen increases. Processes that we don't understand about male aging along with this imbalance of estrogen and testosterone appears to affect prostate tissue in a way that it expresses more nuclear androgen receptors. DHT has a 10 fold higher affinity for androgen receptors compared to other androgens. The fact that prostate cells have more androgen receptors with age means that the production of DHT by the prostate (or other tissues) has a significantly greater effect on prostate growth.



Growth Factor Production Due to the Conversion of Testosterone into DHT *Image by Becky T. BYU-I W20*

It is important to distinguish BPH from more serious diseases like prostatic cancer. A digital rectal exam, urinalysis, and blood tests for serum creatinine (to test kidney function) and prostate-specific antigen (PSA) may be useful in the diagnosis of BPH. PSA is discussed in detail in the next section, but understand that it can be elevated in those with BPH. Ultrasound and a prostate MRI can also be used to confirm the diagnosis. Early diagnosis is helpful to have positive treatment outcomes.

Treatment for BPH depends on the severity of the symptoms and can range from no treatment to medications and surgery. The drug classes known as 5-alpha reductase inhibitors (e.g., finasteride and dutasteride) and alpha-1 antagonists (e.g., terazosin, prazosin) are useful in the treatment of BPH. 5-alpha reductase inhibitors help by inhibiting the production of DHT. As DHT levels decrease, there is less stimulation of the prostate tissue to grow. The ureters and urethra have alpha-1 receptors on them which cause smooth muscle contraction. Alpha-1 antagonists allow the ureters and urethra to relax and open to a greater diameter so urine flow can occur more easily. A surgical procedure known as **transurethral resection of the prostate (TURP)** is another treatment option for BPH. This procedure involves the insertion of a scope through the tip of the penis until it reaches the prostate tissue. The inserted scope is fitted with a tool that can then trim away excess prostate tissue.

Prostate Cancer

Prostate cancer (or prostate adenocarcinoma) is a malignant tumor that forms from glandular structures in the peripheral zone of the prostate gland. The incidence of prostate cancer is second only to skin cancer among men. Men of African descent have the highest risk of prostate cancer while Asian men have the lowest risk of prostate cancer. Common risk factors for developing prostate cancer are advancing age and a family history of the disease. While dietary factors like saturated fats, cholesterol, and red meat have often been associated with prostate cancer, the research is controversial and it is difficult to blame any particular dietary factor for increased incidence of prostate cancer. A mutation in the tumor suppressor gene known as **BRCA 2** imparts a 20-fold increase in the risk for the

development of prostate cancer. Case studies have also shown that those with many sexual partners over a lifetime and those that start sexual activity early in life have an increased risk for developing prostate cancer as well.

If prostate cancer is discovered before it has metastasized to other parts of the body, the 5 year survival rate is close to 100%. When it is discovered after it has spread to other parts of the body, the 5 year survival rate is about 30%. Prostate cancer cells generally proliferate slowly making symptoms less noticeable until the disease has progressed to a more advanced state. This is why routine check-ups are recommended in older men.

Treating prostate cancer involves surgery, radiation, and chemotherapy. It is quite common for these treatments to result in serious complications that include impotence and incontinence. Since prostate cancer progresses slowly, it is often not the main cause of death in older men. Many older men are expected to die from other health problems before prostate cancer becomes a lethal concern. As a result, some men choose not to receive radiation or chemotherapy treatment. However, there are aggressive forms of prostate cancer that can metastasize to the blood and lymph nodes. This results in the spread of cancer cells to the bones, brain, liver, lungs, and possibly other areas.

Prostate-specific antigen (PSA) (also known as gamma-seminoprotein or kallikrein-3) is a part of the ejaculate that functions to help liquefy the semen coagulate so sperm can swim freely. It is possible to measure a small amount of PSA in blood serum. Conditions that cause serum PSA levels to rise include BPH, prostatitis, prostate cancer, and age. PSA levels have often been measured to assess the possibility of prostate cancer; however, this test is highly controversial. There is natural variation in the male population for how much PSA is in the serum, and even if PSA levels are high, the suspicion of cancer requires a biopsy to confirm. This fact can create a lot of anxiety for a man trying to decide if he should ignore a high PSA level or if he should undergo a painful surgery to get a biopsy. Elevated PSA levels may actually indicate a slow progressing prostate cancer; however, the decision to treat the patient may end up being worse for the patient than leaving the patient untreated. While PSA tests are not strong predictors for prostate health outcomes, PSA screening is estimated to help some men avoid death by undiscovered prostate cancer. PSA tests are especially useful when an individual's PSA levels are well documented. Sudden and radical increases in PSA can suggest an unexpected change in the prostate such as the reemergence of cancer in a patient previously treated for cancer.

Prostate brachytherapy is a treatment for prostate cancer that involves surgically implanting tiny particles about the size of a grain of rice known as radioactive "seeds" into the prostate gland between the scrotum and the anus. The particles emit radiation that kills the cancerous prostate cells (along with other non-cancerous cells in proximity). This treatment has become a well-accepted option for patients with early, localized prostatic cancer.