

Cancer Association of South Africa (CANSA)

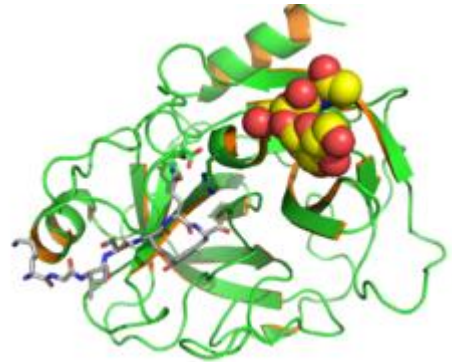


Fact Sheet on Prostate Specific Antigen (PSA)

Introduction

Prostate-specific antigen (PSA), a substance that is also known as gamma-seminoprotein or kallikrein-3 (KLK3), is a glycoprotein enzyme encoded in humans by the *KLK3* gene. PSA is a member of the kallikrein-related peptidase family and is secreted exclusively by the epithelial cells of the prostate gland.

[Picture Credit: KLK3]



PSA is produced for the ejaculate (semen that has been ejected from the body), where it liquefies semen in the seminal coagulum and allows sperm to swim freely. It is also believed to be instrumental in dissolving cervical mucus, allowing the entry of sperm into the uterus. PSA is present in small quantities in the serum of men with healthy prostates. Serum is an amber-coloured, protein-rich liquid which separates out when blood coagulates. PSA is produced by cancerous as well as non-cancerous prostate tissues.

Healthy men have low amounts of PSA in their blood. The amount of PSA in the blood normally increases as a man's prostate enlarges with age. PSA may increase because of inflammation of the prostate gland (prostatitis) or prostate cancer. An injury, a digital rectal examination (DRE), or sexual activity (ejaculation) may also raise PSA levels.

(Wikipedia; Prostate Cancer Research Foundation, Rotterdam; WebMD; Mayo Clinic; MedicineNet).

The Prostate Specific Antigen (PSA) Blood Test

The PSA test is a blood test that measures the amount of prostate specific antigen (PSA) in one's blood. PSA is a protein produced by normal cells in the prostate and also by prostate cancer cells. It is normal to have a small amount of PSA in one's blood, and the amount rises as one gets older and one's prostate gets bigger. A raised PSA level may suggest one has a problem with one's prostate, but not necessarily cancer.

One can have a PSA test at one's general practitioner's (GPs) surgery. One will need to discuss it with one's GP first.

(Prostate Cancer UK).

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Symptoms that Suggest One should have a PSA Test

Symptoms to look out for include:

- Urinating more frequently - especially at night
- Difficulty in starting or stopping urination
- Straining or taking a long time to urinate
- Weak flow of urine
- Feeling that one's bladder has not completely emptied
- Urgency – occasionally leaking urine before one gets to the toilet
- Dribbling urine
- Pain when passing urine
- Pain when ejaculating
- Problems getting or keeping an erection
- Blood in urine or semen

Please be aware that having one or more of these symptoms does not necessarily indicate one has prostate cancer.

(Prostate Cancer Research Foundation, Rotterdam).

What to Consider Before Having a PSA Test

The following should be considered before having a PSA test done:

- A PSA test goes hand-in-hand with a digital rectal examination (DRE)
- PSA screening in men under age 40 is not recommended
- Men of 40 years and older who have a high risk of prostate cancer should have an annual PSA test - this represents men with a close relative (e.g. father, brother) who was diagnosed with prostate cancer
- Men of 40 years and older who have a close relative (e.g. mother, sister) who was diagnosed with breast cancer should have an annual PSA test
- Every man should have an annual PSA test as from age 50
- The PSA test may help to find prostate cancer at an early stage even before there are any symptoms
- However, many small prostate cancers detected by PSA would never develop enough to cause any symptoms
- A low test result can be very reassuring
- Even if one's PSA level is raised, this could be for reasons other than prostate cancer and one may have unnecessary stress while this is checked out
- With a high PSA level one may need further tests such as a biopsy, which can be painful and lead to blood in urine, semen or stools
- Occasionally having a biopsy can lead to infection of the prostate gland, which can be difficult to treat
- In a small number of men, a biopsy may not always detect a significant cancer even when it is present

(WebMD; Prostate Cancer Research Foundation, Rotterdam).

Normal Urinary Habits

Men often notice a slight change in their urinary habits around the age of 50. This can be quite normal and may simply be a sign of getting a little older. On average one should pass

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urine about four to seven times a day depending on how much one drinks. One should be aware when one's bladder is full, but still have enough time to reach a toilet. Every time one passes urine one's bladder should empty completely and one should not experience leaking.

At night, most people will be able to sleep for six to eight hours without having to pass urine. As we get older we produce more urine overnight and middle aged and older men often find they have to get up once in the night. Changes in one's urinary habits may be a sign that one has a problem. This might be a problem of one's prostate or another health condition such as diabetes. If one notices a change, one should consult one's doctor. (Prostate Cancer Research Foundation, Rotterdam).

How to Prepare Before a PSA Test

Before one has a prostate-specific antigen (PSA) test, tell the doctor whether any of the following has occurred or was done:

- A test to look inside the bladder (cystoscopy) in the past several weeks
- Prostate needle biopsy or prostate surgery in the past several weeks
- Digital rectal examination in the past several weeks
- Prostate infection (prostatitis) that has not gone away
- An urinary tract infection (UTI) that has not gone away
- Tube (catheter) inserted into the bladder recently to drain urine

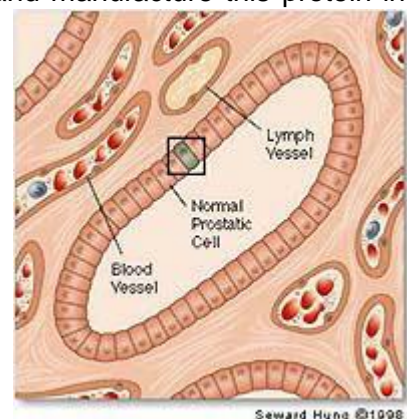
One should not ejaculate for at least 24 hours before a PSA blood test, either during sex or masturbation as this may artificially increase the PSA test result. (WebMD)

Where PSA can be Found in the Body

PSA is found primarily in prostate epithelial cells and in the seminal fluid. The exact mechanism by which PSA gains access to the serum is unknown, although a possible mechanism has been suggested. PSA is the enzyme responsible for liquification of semen a few minutes after it has clotted. Cells inside the prostate gland manufacture this protein in large quantities.

[Picture Credit: Cross Section of Prostate Gland Tubule]

Imagine looking at a single normal prostate gland tubule cut in cross section. The cells lining the centre, or lumen, manufacture prostate secretions including PSA. There is also a circle around the cells, called the basement membrane, which stops PSA and other secretions from entering the blood stream. All of one's glands, one's intestines, and one's urinary tract are organised the same way: a secreting or absorbing layer of cells with a basement membrane to keep a tight separation between what is inside and what is outside. That is how the prostate makes a lot of PSA but only a tiny amount normally leaks into the blood. This is what is measured with the PSA test.



The lumen of the prostate gland contains the highest concentration of PSA in the body. A number of barriers exist between the glandular lumen and the capillaries, including the

basement membrane of the glands, the prostatic stroma, and the capillary endothelial cell. Diseases such as infection, inflammation, and cancer may produce a breakdown in these barriers, allowing more PSA to enter the circulation.

PSA levels can rise dramatically with a prostate infection, but they return to the reference range after the infection has healed. A vigorous prostate massage also can produce an elevation of the PSA level.

Low concentrations of PSA have been identified in urethral glands, endometrium, normal breast tissue, breast milk, salivary gland tissue, and the urine of males and females. PSA also is found in the serum of women with breast, lung, or uterine cancer and in some patients with renal cancer.
(Male Care; Medscape).

Reliability of a PSA Test

A question on the mind of many is: "How reliable is the prostate-specific antigen (PSA) test when it comes to detecting prostate cancer?"

Although PSA testing can help catch prostate cancer at an early stage, having an elevated PSA (generally considered to be more than 4 nanogram/mL) does not necessarily mean that a man has cancer. Noncancerous conditions, including benign prostatic hyperplasia (BPH), or an enlarged prostate, and prostatitis, can raise PSA levels. In fact, studies have shown that about 70% to 80% of men with an elevated PSA who have a biopsy do not have cancer. For many men a decision to undergo an ultrasound and prostate biopsy to be certain, may be a good one.

Conversely, the PSA test does not detect all cancers. About 20% of men who have cancer also have a normal PSA (less than 4 nanogram/mL), so the test may give some men a false sense of security. For this reason, some experts take a man's age into account when considering a PSA level. Most doctors observe how a man's PSA level changes over time, a measure called PSA velocity which is the rate of change in PSA levels, rather than using it as a one-time indicator. PSA scores tend to rise more rapidly in men with cancer than in those with benign prostatic hyperplasia (BPH), for example.

[Picture Credit: PSA Blood Test]

Some doctors also measure the level of free PSA. The PSA protein circulates in the blood in two forms: bound to other proteins or unbound (free). Several studies suggest that men with elevated PSA levels and a very low percentage of free PSA are more likely to have prostate cancer than a benign condition. Knowing one's free PSA level will not give one a definitive answer about cancer, but it may be useful when considering whether a biopsy is an appropriate next step.



Researchers are developing new screening tests for prostate cancer. Like the PSA test, they rely on biomarkers, such as antigens or proteins, which are elevated or may only be present in men who have prostate cancer. The hope is that these tests will better detect existing cancers without raising the alarm for cancer when it is not there.

(Kevin R. Loughlin; National Cancer Institute).

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Pharmacokinetics of PSA

The half-life and metabolic clearance rate of PSA have been determined from studies of patients undergoing radical prostatectomy. Researchers found the half-life to be approximately 2.2 ± 0.8 days. Because of the relatively long half-life of PSA, a minimum of 2 to 3 weeks is required for the serum PSA to reach its nadir (lowest level).

It is, therefore, advised that one should make allowance for a period of at least three (3) weeks to pass before having a PSA test in the event of any occurrence that could possibly have caused an increase in the PSA blood levels. (Medscape).

Conditions which may Cause Elevated Prostate Specific Antigen (PSA) Levels

One's "normal" PSA depends on one's age, but even if one's PSA level is elevated between 4 and 10 nanogram/mL, one only has about a 25 percent chance to be diagnosed with prostate cancer.

[Picture Credit: Elevated PSA Levels]

Here are some causes, besides prostate cancer, that may cause one's PSA level to be above normal (in no particular order):

- Acute urinary retention
- Benign prostatic hyperplasia (enlarged prostate)
- Increased age
- Prostatitis
- Transurethral resection of the prostate
- Urinary catheterisation
- Riding a bicycle
- Ejaculation (from sexual intercourse or masturbation)
- Prostate massage
- Digital Rectal Examination
- Heavy exercise in the last 48 hours

(Everyday Health; NHS Choices).



Age-specific Reference Ranges for PSA Values

Prostate Specific Antigen (PSA) cut-off values:

<u>Age</u>	<u>PSA Cut-off</u>
40 – 49	2.0 nanogram/mL or higher
50 – 59	3.0 nanogram/mL or higher
60 – 69	4.0 nanogram/mL or higher
70 or older	5.0 nanogram/mL or higher

There are no age-specific reference limits for men older than 80 years of age. (Patient.info).

Prostate Cancer Risk at Low PSA Levels

<u>PSA (ng/mL)</u>	<u>Prevalence of Prostate Cancer</u>
0.5 or less	6.6%
0.6–1.0	10.1%
1.1–2.0	17%
2.1–3.0	23.9%
3.1–4.0	26.9%

Source: Thompson, *et al.* *New England Journal of Medicine*, 2004, Vol. 350, pp. 2239–2246. (Harvard Medical School).

Medical Disclaimer

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PSA Blood Test

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