

PROSTATE SPECIFIC ANTIGEN

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Prostate specific antigen (PSA) is a protein secreted by the acinar cells of the prostate, and is highly specific for the prostate. Serum PSA levels are useful for determining the extent of prostate cancer, and assessing the response to therapy. However, it is NOT prostate cancer specific, and other conditions such as benign prostatic hyperplasia (BPH) or prostatitis can affect PSA levels. PSA is commonly used as a tool to detect prostate cancer, but its role in screening programmes is widely debated and controversial.

Clinical utility:

PSA has a half-life of 2.2 days. Where levels are increased by different benign conditions, the time to return to baseline levels is variable. The common causes of an elevated PSA are:

A) Perineal Trauma:

- Mechanical manipulation of the prostate during biopsy or transurethral resection of the prostate (TURP) can significantly affect PSA. In a study of 101 men who underwent one of these procedures, it was determined that PSA levels should not be measured for at least 6 weeks thereafter². In the same study, the median change in PSA level was of a lesser magnitude following cystoscopy.
- Digital rectal examination (DRE) has minimal effect on PSA levels (leading to transient elevations of 0.26 – 0.4 ng/ml).
- Sexual activity can also elevate PSA levels by approximately 0.4 - 0.5 ng/ml.

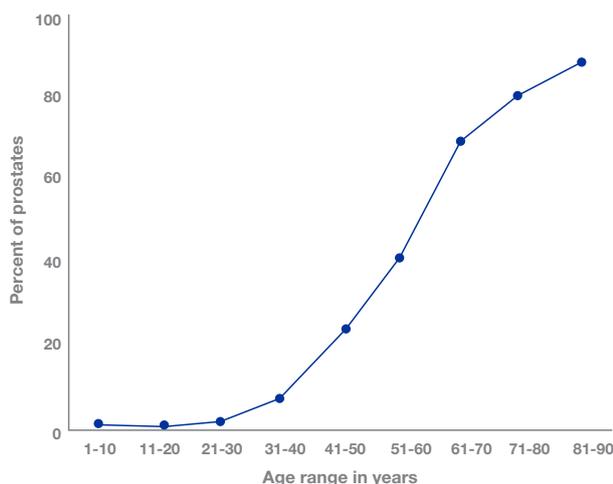
B) Infection and inflammation:

Prostatitis, with or without active infection, is an important cause of an elevated PSA. Levels as high as 75 ng/ml have been reported. Many physicians will make a presumed diagnosis of infection, initially treating a patient with an isolated increase in PSA with antibiotics and repeating the PSA measurement afterwards. A reduction in PSA levels can be expected if prostatitis with infection was solely responsible for the elevation. However, prostatitis can often exist without active infection, in which case the PSA will not normalise after treatment with antibiotics. Serum PSA should only be repeated about 2 - 4 weeks after completion of treatment for reassessment.

C) Benign Prostatic Hyperplasia

There is a high prevalence of this condition in men older than 50 years of age, and serum PSA levels in patients with BPH overlap considerably with those obtained from men who have prostate cancer.

Prevalence of benign prostatic hyperplasia pathology with age⁷:



In a study of pre-operative PSA levels of 187 men with BPH and 198 men with organ-confined prostate cancer, the median PSA concentrations were 3.9 (range 0.2 – 55) and 5.9 (range 0.4 – 58) ng/ml, respectively¹. Although this was a statistically significant difference, the distribution of PSA values in both groups overlapped significantly with the majority of PSA values below 10 ng/ml in both groups.

D) Prostate Cancer

Prostate cancer is the second most common cancer in men worldwide.

Clinically, the tumour can range from a microscopic, well differentiated tumour that may never be clinically significant to an aggressive, high grade cancer that causes metastases, morbidity and death.

The widespread availability of PSA testing has led to major shifts in the epidemiology of the condition. These shifts have manifested in an increasing number of cases, as well as a younger age and earlier clinical stage at diagnosis.

The laboratory aspects of prostate cancer will be discussed in a follow-up newsletter.

Key Points on Screening for Prostate Cancer:

- The prevalence of undiagnosed prostate cancer at autopsy is high and increases with age (from > 40% among men aged 40 – 49 years to > 70% among men aged 70 – 79 years).
- Only a small proportion of men with prostate cancer have symptoms, or die from the disease. Most prostate cancers are slowly progressive and not life threatening.
- Screening with the PSA test may lead to a small reduction in prostate cancer mortality, but not a reduction in all-cause mortality.
- Thresholds for PSA of 2.5 to 4.0 ng/ml are commonly used for screening. Lower thresholds increase the probability of false positive results, but no threshold completely excludes cancer.
- *Serum free and bound PSA*: In men with a normal prostate, the majority of free PSA in the serum reflects the mature protein that has been inactivated by proteolytic cleavage. In contrast, the cleaved fraction is relatively decreased in men with prostate cancer. Thus, the percentage of free PSA (f/t PSA) is **lower** in the serum of men with prostate cancer, compared to those that have a normal prostate or BPH.
- The f/t PSA measurement has been used to improve the sensitivity of cancer detection when the total PSA is in the normal range (< 4 ng/ml), and to increase the specificity when total PSA is in the grey zone (4.1 – 10 ng/ml). In this latter group, the lower the value of f/t PSA, the greater the likelihood that an elevated PSA represents cancer, and not BPH. As with total PSA, there is no absolute f/t PSA cut-off that completely discriminates between cancer and BPH.
- Harmful side-effects associated with PSA screening (e.g. bleeding, infection, urinary incontinence) are common.
- The PSA test should be used for screening only after a detailed discussion with the patient, ideally with the use of decision aids to facilitate comprehension of the pros and cons of screening for prostate cancer. The American College of Physicians (ACP) recommends screening using PSA only in those patients who express a clear preference for the test or in patients identified as high risk after clinical evaluation¹³.

References:

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