

## Evaluation of Elevated PSA Levels

PSA is the abbreviation for **prostate specific antigen**, a protein made by certain cells in the prostate gland. Normally, a small amount of PSA is present in the blood stream and is detectable by a blood test. Certain abnormal conditions will result in elevated levels of PSA. Most of these conditions are benign and easily treated, but prostate cancer will also cause PSA elevation, and for this reason, it is important to evaluate all cases of elevated PSA to determine the cause of the elevation.

A “normal” PSA is generally considered to be between 0 and 4.0, although the upper limit may be higher in older patients and patients with very large prostate glands. Some clinicians use ranges of normal varying from 0 to 2.5 in men in their 40s to as high as 10 for men in their 80s. Some laboratories accept 0 to 4.0 as normal. Prostatic enlargement is often accompanied by symptoms of urinary obstruction – urinary frequency, getting up at night to urinate, slow stream, difficulty initiating urination, dribbling. If you have such symptoms, be sure you discuss these with the urologist.

Infection of the prostate or inflammation of prostatic tissues can also produce PSA elevation. Often a mild prostatic infection may be present without producing much in the way of symptoms. Such infections can still produce abnormal levels of PSA, and many clinicians will treat patients with a course of antibiotics as a first step in evaluating the elevated PSA. If the PSA responds to antibiotic treatment, a follow-up PSA 3 to 6 months later is usually scheduled.

If the PSA is dramatically elevated (to more than 15 or 20), or if it does not return to normal with antibiotic treatment– usually done in the office – the urologist anesthetizes the nerves that supply the prostate with lidocaine much as the nerves supplying the jaw, are anesthetized prior to a dental procedure .Using ultrasound to visualize the prostate, the urologist obtains about 12 small pieces(cores) of prostate tissue using a very small caliber needle guided by the ultrasound. On occasion, a more extensive biopsy – sometimes referred to as a “saturation biopsy” -- may be suggested, and such a biopsy may be done with anesthesia in the hospital or one-day-surgery unit. If the rectal examination is abnormal – demonstrating nodularity or firmness, a biopsy may be indicated even in the face of a normal PSA level.

If the biopsy shows that cancer cells are present, the urologist will meet with you to discuss appropriate further treatment. If the biopsy is negative, the urologist will arrange appointments to monitor the PSA, usually by suggesting a repeat PSA test and rectal exam after 3 to 6 months. If PSA levels remain elevated over time, a repeat biopsy may be suggested. In some cases where a repeat biopsy is suggested, a “saturation biopsy” as described above, is indicated.

While PSA is one of the most valuable tumor markers used in medicine, there are constant efforts to develop new markers that can be used in conjunction with PSA to improve accuracy. No other blood test markers are currently in routine use. PCA 3 is a urine test that can be used to improve the diagnostic accuracy of the PSA blood test

## **PSA Testing after 75**

A recent announcement from the American Task Force for Prevention of Disease which advised against PSA testing among men greater than 75 years of age was received with a significant amount of controversy and strong objections.

The position and sentiments of a large cohort of men aged 75 and older who rightfully consider themselves productive members of society and who are fit enough to anticipate many future golden years enjoying the fruits of their labor, their children and grandchildren is that they should avail themselves of PSA testing. In their lifetime they have witnessed medical advances which have extended life expectancy and they have been the grateful beneficiaries. To hear that a recommendation to avoid a simple blood test that could provide early identification of the most dreaded of diseases, cancer, seems totally illogical, counterproductive and at odds with the mantra “take good care of yourself by taking greater control of your health”. When the concept of population and societal risks and benefits are brought to the table in a discussion about PSA testing in the aging male, patients listen with interest but the burning issue, nevertheless, distills to the concern “what about me?”. For a 75 year old, who is vigorous and healthy, who is attentive to his health issues, who is blessed with familial longevity, and who desires to know his PSA status, strong advice against testing seems unreasonable and counter to the physician / patient relationship.

I am reminded of an experience I had several years ago in following a very healthy and well educated 80 year old gentleman with a PSA of 7. We had the discussion about the high likelihood of his prostate containing cancer cells because of his age and the likelihood that he was at very low risk for problems. He was satisfied with the explanation. The following year his PSA was 13, and he was quite alarmed and I no longer had the assurance that everything was in control. A biopsy was performed and both he and I were disheartened with the Gleason 4+5 readings from multiple cores. I could see his confidence evaporate and he sought opinion and received treatment. Several years later, when one of the Swedish trials was published that supported watchful waiting, he responded with a letter to the editor in our paper warning men against this strategy and citing his own case of aggressive cancer allowed to proliferate as he watched and waited. I have experienced similar encounters with other patients and I am sure every urologist has as well. (also see <http://www.evms.edu/vpc/docs/prostate-cancer-perspective.pdf>)

Such anecdotes are not evidence-based medicine, but they can not be disregarded.

However, when a PSA is done for a 75-year-old male, it cannot be the first of a number of reflex reactions. PSA testing needs to be placed in context before a decision to obtain is made and before proceeding to any biopsy. Positive biopsy results need to be placed in context before processing to any recommendations for therapy. As urologists we wish to follow the admonition to first do no harm. To accomplish this for the 75 year old presenting for PSA test requires individual assessment, thoughtful discussion, and recognition of competing mortality as illustrated in the table – and we, as physicians must strive to reduce the numbers in each of the columns.

At age 75, men are much more likely to die of heart disease and other conditions than prostate cancer. How many of 1,000 men will die in the next decade from:

	Heart disease	Stroke	Lung cancer	Prostate cancer	Pneumonia
Never smoked	137	32	8	<b>19</b>	12
Smoker	140	39	109	<b>15</b>	16

Source: *Journal of the National Cancer Institute*

The challenge which thus far has not been solved by the PSA test or through multiple PSA derivatives (PSA velocity, PSA doubling time, % free PSA, pro-PSA, etc), rests in the discovery of a reproducible marker panel which both identifies prostate cancer when it is present (with very few false positive readings) and more critically distinguish cancers non-concern for disability and death, and this will be the majority, from those that threaten life and well being.