# Just the Berries

## Prostate-specific antigen testing

### *Should we recommend it?*

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The role of prostate-specific antigen (PSA) in screening men for cancer of the prostate is controversial and confusing, even though a large study in Finland showed that the test does detect cancer.[1]

To try to sort out this thorny problem, I searched MEDLINE from January 1999 to December 2001 using the key word PSA (prostate-specific antigen). I also visited the Bandolier website and reviewed the article, "Prostate-specific antigen testing for early diagnosis of prostate cancer."[2]

**Controversies and complications**

The controversy over PSA is due, in part, to the lack of randomized controlled trials showing that early detection of prostate cancer and aggressive treatment of early cancers reduce mortality. In fact, studies show that many more men are diagnosed with cancer of the prostate than die of it (although, as life expectancy increases, prostate cancer will become a more important clinical problem). Moreover, treating early cancer sometimes leads to serious complications, such as impotence and urinary incontinence.

To complicate things further, negative test results do not guarantee freedom from disease, nor do positive test results necessarily indicate true cancer. Prostate-specific antigen levels can be raised by benign prostatic hyperplasia, biopsy of the prostate, transurethral prostatectomy, acute urinary retention, acute prostatitis, and ejaculation.[3] Digital rectal examination appears to have no clinically important effect on PSA levels. To further muddy the waters, there are several PSA testing kits available, and results can vary from kit to kit, although there is movement toward standardizing the commercially available tests.[4]

Traditionally, a PSA level of 4.0 ng/mL has been used as the upper limit of normal, although two studies of men with PSA levels between 2.5 ng/mL and 4 ng/mL, who had had biopsies, reported finding cancer in 12% to 23% of cases.[5,6] When PSA levels are found to be mildly elevated, the test should be repeated, perhaps with a recommendation of sexual abstinence for 48 hours before the test to ensure that results are consistent. Levels above 4 ng/mL or abnormal results of digital rectal examination warrant further evaluation with transrectal ultrasound-guided biopsy. Some researchers have even questioned the accuracy of this criterion standard investigation[7,8] because it results in a residual probability of cancer of at least 10%.

Because 75% of men with PSA levels between 4 ng/mL and 10 ng/mL have negative results of biopsy, there is interest in

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improving the specificity of the test. Several suggestions have been made, but none seems ideal. Using age-specific reference ranges, with a lower threshold for biopsy in younger men, can be helpful in deciding whom to investigate. The recommended reference range for serum PSA testing (95th percentile) for men aged 40 to 49 years is 0.0 to 2.5 ng/mL; for those aged 50 to 59 years, 0.0 to 3.5 ng/mL; for those aged 60 to 69 years, 0.0 to 4.5 ng/mL; and for those aged 70 to 79 years, 0.0 to 6.5 ng/mL.[9] Monitoring the rate of change in PSA level (a change of >0.75 ng/mL per year is more suggestive of prostate cancer than of benign prostatic hyperplasia) requires annual testing for at least 3 years.

Prostate-specific antigen is found in the blood both as free PSA and as PSA complexes. For some unknown reason, patients with cancer of the prostate have lower levels of free PSA than patients with benign prostatic hypertrophy do, and this fact can be used to help improve diagnosis of cancer.[10,11] Some have postulated that patients with a ratio of free PSA to total PSA of >25:1 do not require biopsy. Using this cutoff, however, would miss approxmately 8% of cancers.

The interval between testing is also in question; many men are now tested annually. Recent analysis suggests that testing every 2 years is adequate, although testing might begin at a younger age and stop at age 75, or even age 65 in men with persistently low levels of PSA (0.5 to 1.0 ng/mL).[12]

## How should we advise our patients?

The best option seems to be to have a full discussion with each patient and explain that the test can have false-positive or false-negative results, and that there is no good evidence that early detection reduces mortality. We should also explain that treatments for early cancer of the prostate sometimes have serious side effects, such as impotence and incontinence. We should indicate that some groups of men are at higher risk of cancer (black men and men with a positive family history, especially among their younger relatives). It also appears that a ratio of free PSA to total PSA of >25 to 30:1 increases the chance that the elevation is due to cancer.

In the end there appears to be no right answer. Physicians and patients will make decisions based on how they feel after examining all the available information. In my experience, most men who inquire about PSA testing want to have it done.

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