

MEditorial June 2012

“PSA Fluctuations: What Goes up May Come Down”

Organized urology is in an uproar. Men and their families are more confused than ever. As referred to in my October 2011 MEditorial (“PSA Redux”), the US Preventive Services Task Force (USPSTF) has now given a final grade of “D” (failing) to PSA as a screening vehicle for prostate cancer. Screening of course implies doing the blood test on men with no prior or current suspicion (e.g., abnormal exam of prostate) of having prostate cancer or even other significant prostate disease. Statistics can be flung all over the place-- but one, from a large screening trial, suggests that over a thousand (perhaps 1400) men may need to be screened for prostate cancer to save one man from dying of the disease. Of these 1400, perhaps 40-50 found to have prostate cancer might not “benefit” in terms of years of life extended by undergoing such aggressive and sometimes harmful (usually but not always curative) treatments as radical prostatectomy and radiation therapy. Furthermore PSA screening creates anxiety over uncertainty—as well as overutilization and the costs of doctor visits; ultrasounds and other radiographic tests; and biopsies which, @ their least, are unpleasant.

What about using PSA results over time as a screening test? It is always a good idea to repeat the PSA and consider the PSA-2 test (free/total ratio) before recommending a biopsy. There are many reasons for PSA fluctuations, some of which are poorly understood. Let’s just say that the PSA going up does not necessarily mean prostate cancer; and it may come down either spontaneously or due to resolution of specific conditions that caused it to elevate in the 1st place.

Prostatitis is an inflammatory condition of the prostate, probably caused by bacteria, but it’s not always evident or identifiable. Inflammation may be present for years or the rest of one’s life, even after all bacteria have been eradicated. In low grade cases of prostatitis, there may be no symptoms at all or perhaps a slight increase in urinary frequency and urge. Tip-offs, besides

symptoms of inflamed urination, might include: a past history of urinary infection or prostatitis; the presence of white blood cells or an enzyme called leukocyte esterase on an office or lab urinalysis; or “bogginess” on prostate exam. I liken the latter to the prostate feeling to me like a round sponge filled with water, not yet “squeezed out”. When we look at the “free percentage” of PSA in the blood, there is an overlap (of especially low, i.e., <10%) percentages both in men with prostatitis and cancer. Significant acute prostatitis, often the symptomatic variety, can cause a rapid increase in PSA: far greater than seen even with a very malignant prostate cancer.

In my practice, I see little harm in giving a course of at least two weeks of an antibiotic, usually so-called fluoroquinolones (Cipro/Levaquin) to those men felt by one or more of the above criteria to have prostatitis as the cause of PSA elevation. Usually the PSA-2 is then repeated one month after finishing antibiotics—I would like to see the PSA be reduced close to the patient’s prior (presumably normal) baseline. Studies are interesting, in that one can expect on average a 25-35% decrease in PSA after treatment for even low grade prostatitis—but a similar % of men with a new PSA elevation NOT treated with antibiotics will fluctuate (downward) in a similar manner! Once down--whether due to prostatitis or not--the PSA may “behave itself” and not rise again.

I would not tend to repeatedly give antibiotics to the man who, once or twice treated with antibiotics, continues to show PSA elevation or worse, PSA “velocity” (steady trending upward over time). This is especially true in the man who has never had symptoms of prostatitis and in whom the only clinical findings are minimal (e.g., an abnormal urinalysis with no bacteria growing on the urine culture). It is conceivable a man might have chronic prostate inflammation concurrent with prostate cancer. Delaying a biopsy too long, in this context, could cause progression of a prostate cancer; also, over-use of antibiotics to treat an asymptomatic or suspected prostatitis may actually increase the risk of a post-biopsy bacterial infection (often with fevers and significant illness), which is increasingly felt caused by fluoroquinolone-resistant bacteria living in the rectum, the pathway by which the prostate biopsy is most commonly done.

What's interesting, but perplexing, is the following: PSA reduction after antibiotics does not necessarily mean that a biopsy will not show cancer. Conversely, failure of PSA to decline with such antibiotic interventions does not mean there is cancer. In addition Dr. William Catalona, an expert out of Northwestern University, has stated that the chance of finding cancer in men with fluctuating ("flu") PSA's is statistically *about the same* as in men with steadily increasing ("si") PSA's. In that study, however, men with fluctuating PSA's had slightly less aggressive pathologies, i.e., tumors which might not act as aggressively as those "si" patients, whose pathology tended to show a worse/more chaotic malignancy.

Given all of the above, a man in good health with a 15+ year life expectancy whose PSA fluctuations continue (and never normalize) despite suspicion of prostatitis and 1-2 rounds of antibiotic therapy should consider having a biopsy. Of course, with all the controversies over whether the discovery and treatment of prostate cancer saves lives, a detailed informed consent should be given by the urologist before scheduling the biopsy.

For the record, some other things, besides prostatitis, that cause PSA fluctuations include variation between different labs and several different lab methodologies of assessing PSA value (consistency in the lab you choose may be important); day-to-day variation in the prostate gland's output of PSA, perhaps by up to 15%; ejaculation or vigorous prostate exam (avoid having PSA checked for 24 hours after these); use of finasteride (low dose=Propecia for balding or high dose=Proscar for prostate enlargement) or its "younger cousin" Avodart (dutasteride); and change of seasons. One French study indicated that summer climate is associated with up to a 25 to 35% increase in PSA versus winter climate. Cause and effect are unclear, but it could be anything from dehydration from the heat (with concentration of the blood from which the PSA sample is taken) or hormonal changes in testosterone (increase), Vitamin D3 (increase) or melatonin (decrease) that directly or indirectly influence genetic production of the PSA molecule by the prostate gland.

With a disease like prostate cancer, which is often slow growing and not necessarily a threat to health or longevity, it is wise to “have perspective” and avoid anxiety over individual PSA results without 1st getting a better overview of the big picture.

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