

Do Women Have a Prostate-Specific Antigen Level?

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Myth: Because women lack prostate glands, they do not have a prostate-specific antigen (PSA) level that can be assessed with a serum blood sample (see Figure 1).

Answer: PSA is a serine protease expressed in high levels in prostate epithelium, and elevated serum PSA has been a well-established marker for prostate cancer since 1980 (Black & Diamandis, 2000). PSA is a useful laboratory diagnostic tool; as PSA level rises, the risk for prostate cancer increases. In men with cancer, PSA level is used to monitor the effectiveness of cancer therapy and as surveillance for recurrence and advancing disease. However, this column will discuss research that has challenged the belief that PSA is restricted to the prostate gland.

PSA is measured in two forms. The free PSA test measures the percentage that is not bound to proteins in the blood; in men with prostate cancer, the ratio of free to typical PSA is reduced (Hoffman, 2009). The typical PSA test also is known as the total PSA test. In a healthy man, total PSA is 1 ng/ml or less (8.8% risk for prostate cancer); however, the risk rises to 58.2% when the PSA level is higher than 10 ng/ml (Cleveland Clinic Pathology and Medicine Laboratory Institute, 2009). In a healthy woman, serum PSA concentration is less than 0.0004 ng/ml (Black et al., 2000).

Although its physiologic function in women has not been determined, PSA has been found in the periurethral gland, normal and hyperplastic breast tissue, breast tumors and cysts, breast secretions (e.g., nipple aspirate fluid), the milk of lactating women, breast cystic fluid, the placenta, and amniotic fluid. PSA also has been found in cancerous and healthy ovarian, endometrial, adrenal, skin, lung, colon, liver, kidney, and salivary tissue (Black &

Diamandis, 2000; Black et al., 2000; Kocak, Tarcan, Beydilli, Koc, & Haberal, 2004). As in men, PSA in women is affected by hormones; therefore, PSA levels fluctuate during a woman's menstrual cycle (Aksoy, Akcay, Umudum, Yildirim, & Memisogullari, 2002; Galadari, Al-Mazroei, & Alkaabi, 2004). PSA levels peak in the mid- to late-follicular phase of a woman's cycle and are higher in pregnant women than in healthy nonpregnant women (Aksoy et al.). A 2002 study found that the PSA level detected in a woman's saliva equaled serum PSA levels throughout a woman's menstrual cycle (Aksoy et al.). The authors concluded that this cyclic variation should be considered when future research is conducted.

The field of breast cancer has potential uses for measuring PSA in women. Black et al. (2000) measured total and free PSA levels in women with breast cysts, uterine fibroids, and breast cancer before and six months after surgery. Each group had significantly higher total PSA levels versus a control group of healthy women. Women with breast cancer had significantly higher detectable total PSA before surgery than after; serum free PSA was associated with a higher histologic grade of breast cancer. A higher proportion of women with detectable free PSA had tumors classified as grade 3, whereas women with lower or undetectable free PSA levels had tumors that were grade 1 or 2. The researchers theorized that the increase in total PSA was the result of a disrupted hormonal balance that triggered the overexpression of hormone-dependent genes, including PSA. However, free PSA decreased after surgery,

indicating that this form of PSA is produced by the tumor itself. Serum total PSA values were lower in older women than in younger women, but age was not found to be a factor in free PSA values (Black et al.). The high degree of specificity in the detection of breast disease compared to normal tissue suggests that free PSA may be useful alone or in combination with other tumor markers in the clinical setting. PSA may be used as a tool for detection and play a role in monitoring treatment response and surveillance for tumor progression and metastasis.

Black et al.'s (2000) findings were supported by Diamandis's (2000) case study of a woman who was first diagnosed with breast cancer in 1977 and was treated with a radical mastectomy. She was diagnosed with breast cancer in the remaining breast and had a second mastectomy in 1997. She was found to have metastatic disease to the central nervous system; a sample of her spinal fluid contained 10.07 ng/ml total PSA, a level consistent with the diagnosis of prostate cancer in men (Diamandis). Additional research in Poland concluded that the free PSA values of women with benign breast disease were significantly higher than control (Radowicki, Kunicki, & Bandurska-Stankiewicz, 2008).

According to research by Black & Diamandis (2000), PSA values may eventually help clinicians detect breast disease and differentiate higher- and lower-risk cancers. High levels of PSA tend to indicate better outcomes, whereas lower levels are associated with poorer outcomes. However, the opposite is true when using

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