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FAST TRACK

Only estradiol had a direct effect on sexual function, but relationships and prior sexual function were more important

Q Do androgen levels help diagnose low libido?

A No. Clinical measures of circulating androgens are not useful in the diagnosis of low libido and other forms of female sexual dysfunction.

EXPERT COMMENTARY

In women, androgen insufficiency is generally defined as a cluster of symptoms and signs—diminished well-being, unexplained fatigue, decreased sexual desire, and thinning pubic hair—in the presence of decreased bioavailable testosterone and normal estrogen. However, we lack evidence that this syndrome can be diagnosed by measuring circulating androgens.

Davis and colleagues explored the question by randomly recruiting 1,423 women aged 18 to 75 from the electoral rolls of Victoria, Australia. Voting is mandatory in Australia, where every adult is on the rolls; thus, the study population represented a cross-section of the general female adult population in that country.

After exclusions, Davis et al measured circulating androgens and sexual function (by a self-reported scale) in 1,021 women. The objective: to determine whether women who reported "low sexual well-being" were more likely to have low serum androgen levels than women who did not.

No correlation between testosterone and libido

Davis and colleagues found no evidence that total or free testosterone levels help determine which women have low sexual function. Although significant associations were noted between low levels of dehydroepiandrosterone sulfate (DHEAS) and sexual dysfunction, Davis et al found no diagnostically useful reason to measure DHEAS. Most women with low DHEAS reported no sexual dysfunction, and most women with sexual dysfunction lacked low DHEAS.

The likelihood of a clinically useful association between women with low sexual function and a low androgen level was greatest when the proportion of women with low sexual function was small (less than the fifth percentile) and the normal range for the serum androgen level was relatively large, such as the DHEAS level among young women.[1]

Still no correlation in women at midlife

In the second study, Dennerstein et al used data collected over 8 years from the Melbourne Women's Midlife Health Project, a prospective, longitudinal, population-based study of Australian women aged 45 to 55. They chose this age group because hormonal changes during the menopausal transition "do not occur in a vacuum." Rather, the midlife years coincide with other transitions as children leave home and parents age. In addition, some women may lose or change sexual partners, some of whom have their own problems with sexual function. The authors wanted to determine whether women's sexual function is more dependent on psychosocial and relationship factors than on actual hormone levels.

CONTINUED

The study involved annual measurements of both sexual function (by questionnaire) and hormone levels. Data were available from 336 women.

The findings: Only estradiol levels had a direct effect on sexual function, and then only on sexual response and dyspareunia. However, estradiol levels were less important than prior levels of sexual function, a change in partners, or feelings for the partner. Testosterone and DHEAS levels did not correlate with sexual function.

So how do we diagnose low libido?

Although a correlation may exist between low levels of circulating androgens and sexual dysfunction,[2] there is no consensus on the clinical utility of measuring androgens to diagnose it. These studies are consistent with others that have failed to find serum testosterone levels useful in diagnosing androgen insufficiency.[3]

One possibility may be that commercial assays for testosterone lack sufficient sensitivity and reliability to accurately measure the low levels of testosterone found in women, although the authors of both studies used reliable and reproducible methods.

Thus, for the time being, at least, androgen insufficiency syndrome remains a clinical diagnosis.

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Q Is there a blood test for ovarian cancer?

A Not yet, but 4 serum protein markers may hold the key and solve the problem of finding a "needle in a haystack."

Mor G, Visintin I, Lai Y, et al. Serum protein markers for early detection of ovarian cancer. Proc Natl Acad Sci U S A. 2005;102:7677–7682.

EXPERT COMMENTARY

Ovarian cancer will strike 22,000 American women this year and ultimately kill 16,000.[1] This cancer tends to exhibit few early symptoms, present at an advanced stage, and have low survival rates. As Mor and colleagues note, "Despite being one tenth as common as breast cancer, epithelial ovarian cancer is 3 times more lethal." Although modest but significant gains have been achieved through advances in surgical and medical therapy, the holy grail of ovarian cancer investigation is an effective method of early detection.

Unlike breast or prostate cancer, ovarian cancer has a very low prevalence in the general population (50/100,000). Looking for a "needle in a haystack" requires a screening tool of exceptional sensitivity and specificity. The problem: Even a screening test with 99% specificity and 100% sensitivity would yield only 1 in 21 women with a positive screen who actually has the disease.[2] Ultimately, confirming the validity of a positive screen requires surgery.

How technology is spurring progress

Recent developments in molecular biology have led to an explosion of new biomarkers. Microarray technology allows the rapid screening of proteins differentially expressed in cancer versus normal cells. Each of these proteins has the potential to be used for cancer screening.

With this new technology, Mor and colleagues at Yale University identified 4 markers that, when used together, achieved a sensitivity, specificity, and positive predictive value of 95%, with a negative predictive value of 94%. The markers are leptin, prolactin, osteopontin, and insulin-like growth factor-II. They successfully detected 23 of 24 patients with stage I and II disease. When compared with screening strategies based on proteomic patterns generated by mass spectroscopy, these markers are far less complex and expensive.[3]

Ovarian cancer screening strategies pursued over the past 20 years include the use of serum tumor markers such as CA 125, imaging modalities such as transvaginal sonography, or both. To date, no single test or combination of tests has achieved the high standards required for screening, even among high-risk populations. However, this may soon change.

The bottom line

Unfortunately, these markers do not yet meet the stringent requirements for population-based screening. To do so, they must be validated in a much larger population of patients and must have sensitivity and specificity well above current levels. When compared to CA 125 alone, however, they represent a remarkable improvement.

In the future, the authors predict the markers should "improve our ability to accurately detect premalignant change or early stage ovarian cancer in asymptomatic women at increased risk." ■

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FAST TRACK

Together, the 4 markers detected stage I or II disease in 23 of 24 women

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