

## Tests may better detect prostate cancer

Prostate cancer is common in men as they age, with roughly 180,000 men in the United States receiving the diagnosis every year. If detected early enough, however, the disease is curable with surgery and radiation treatments. Unfortunately, a prostate tumor can grow silently until it spreads and becomes incurable.

Two novel tests may help physicians catch many more cases of prostate cancer early on. The tests may also produce fewer false alarms and be less invasive of men's bodies than current screening and follow-up tests are.

Measurement of prostate-specific antigen, or PSA, a protein made in the prostate and found in the blood, currently serves as the best predictor of prostate cancer. A concentration higher than 10 nanograms of PSA per milliliter of blood provides a strong indication of cancer. Physicians regard a test showing PSA at more than 4 ng/ml of blood as a sign that a biopsy of the walnut-size gland should be performed. That biopsy is expensive and uncomfortable.

Among men with 4 to 10 ng/ml PSA concentrations, only 20 to 25 percent have cancer, says Peter H. Gann of Northwestern University Medical School in Chicago. For up to 80 percent of the men who receive a positive result from current PSA tests, the biopsy turns out to be negative. Most of these men instead have benign enlargement of the prostate.

Gann and his colleagues decided to differentiate the cancer risks among men in the "gray zone" where the PSA test results don't give a firm diagnosis. Most of the total PSA measured in such tests is bound to another molecule in the blood. Ten years ago, European researchers found that some PSA floats freely in the body. Subsequent studies have found that, on average, men with prostate cancer have less of their total PSA in this free, unbound form than healthy men do, Gann says.

"This became a strategy people could look at to discriminate between men with and without cancer," Gann says.

The researchers analyzed frozen blood samples taken in the early 1980s—before PSA testing was used for diagnosis—from 430 men who developed prostate cancer over the next decade. They also studied blood taken at the same time from 1,642 men who didn't have cancer during the 12 years after the samples were obtained. The researchers found men in both groups with total-PSA blood concentrations of 4 to 10 ng/ml.

Information about free-PSA can make the standard PSA test a better indicator of cancer, Gann and his colleagues determined. They calculate that the free-PSA measurement could eliminate the need for a biopsy in up to 40 percent of men who fall into the gray zone.

Had physicians in the early 1980s been able to use both measurements on these groups, they could have correctly detected about 80 percent of all the prostate cancers that arose over the next 4 years, the researchers assert. Gann also calculates that the combined test would yield fewer false positive results.

Currently, "the economic and psychological costs [of false positives] are huge," Gann says. He reported the findings at the 91st Annual Meeting of the American Association for Cancer Research in San Francisco this week.

The large number of false-positive diagnoses have made the total-PSA tests controversial, says Ronald Morton of Baylor College of Medicine in Houston. With the free-PSA test, physicians can catch cancer earlier and correctly identify patients who require intervention, he says.

Meanwhile, researchers at the Johns Hopkins Medical Institutions in Baltimore and the Fox Chase Cancer Center in Philadelphia are pursuing a prostate cancer test that is even less invasive than PSA blood tests. It analyzes urine.

Because the prostate supplies a portion of a man's semen and secretes this fluid into the

urethra, the researchers reasoned that urine might contain cells with some of the telltale genetic aberrations of prostate cancer.

The question has been which aberration to build a test around, says Paul Cairns of Fox Chase. "The ideal [genetic] target would be something that is cancer-specific and is altered early and frequently," says Cairns. The researchers settled on a defect in the *GSTP1* gene. Genetic tests have found this abnormality in most prostate tumors but not in other cells.

The researchers identified 22 prostate cancer patients who had the *GSTP1* defect in their tumor cells. Urine tests turned up the same defect in six of the men.

While that's not quite one-third of the sample, Cairns says, "this is the first time somebody has demonstrated that molecular detection of curable prostate cancer is feasible in urine."

A urine test based on such a genetic alteration could prove to be a major advance in prostate cancer diagnosis, says William G. Nelson of Johns Hopkins. "The [traditional] PSA test is like a smoke alarm. Having elevated PSA doesn't mean you have cancer—that's why you need a biopsy. This kind of abnormal DNA in prostate cancer cells seen in urine is not a smoke alarm anymore. It's like seeing the flame itself," he says.

—N. Seppa