Several new screens improve upon PSA mainstay

Promising Prostate-Cancer Tests Proliferate

By Todd Neff

For nearly two decades, the prostate-specific antigen (PSA) test has been the workhorse in screening for prostate cancer. Approved by the U.S. Food and Drug Administration in 1994, the test remains a screening pillar. But a raft of new prostate-cancer tests has arrived, with more on the way, and they are already changing the lives of patients at University of Colorado Hospital.

One of those men we’ll call Tim, a 46-year-old metro-Denver businessman. Last fall, Tim felt ill; his PSA test came back at 13.4. A normal level for someone his age is less than one; scores above 10 represent a two-thirds chance of having prostate cancer. His urologist performed a 12 core biopsy of his prostate that came back negative. He took antibiotics, after which his symptoms subsided, and a follow-up PSA score fell to nine. The urologist and an infectious-disease specialist wondered whether the problem might have been inflammation triggered by an autoimmune disorder or infection. Tim felt he was out of the woods.

“I’m done — this is good news. I’m out of here,” Tim recalled thinking.

Just to make sure, however, he scheduled an appointment with E. David Crawford, MD, head of the Urologic Oncology section at the University of Colorado School of Medicine. On February 25, they met. Crawford sent the outside biopsy for review by CU Associate Professor Francisco G. La Rosa, MD, a specialist in prostate pathology, who agreed it was clear. Crawford ordered another PSA test, which came back at six. Not long ago, that might have been the final test.

“We might have watched him. We might have tried to talk him into more antibiotics. We might have had another biopsy and not found anything,” Crawford said.

But the PSA test was no longer the end of the line.

One-two punch. Crawford had Tim take a urine test called Progensa PCA3, which the FDA approved in February 2012 for men with previously clean biopsies but in whom prostate cancer is suspected. It looks for the expression of a messenger RNA called PCA3. Unlike a lot of messenger RNA, PCA codes no proteins. But prostate-cancer cells crank it out in volumes about 66 times higher than healthy cells. Because 95 percent of prostate-cancer cells create PCA3, there’s enough of it be detected in urine. Crawford is familiar with the PCA3 test — he was lead author of the November 2012 Journal of Urology paper that established the

ConfirmMDx detects an epigenetic “halo” around a cancer lesion, which can appear despite having a normal appearance under the microscope and low PSA scores.
test’s effectiveness based on more than 1,900 men at 50 U.S. urology practices, including UCH, which has been at the forefront in evaluating this new marker, Crawford said.

Like the PSA test, the PCA3 test boils down to a score. Tim’s was 53. Anything above 25 warns of cancer.

So Crawford ordered a second test, ConfirmMDx. Released in May 2012, this test teases out telltale genetic slicing of genes from the “halo” of healthy tissue near prostate-cancer cells – in effect, rooting out false negatives, a problem that has plagued diagnosis of prostate cancer.

Perhaps 75 percent of the roughly 1 million prostate biopsies done each year in the United States come back negative. But because a typical grid of 10 or 12 needles captures less than 1 percent of prostate tissue, the procedure is hit-or-miss. As a result, roughly one-third of apparently clear biopsies are simply missing the cancer cells. Crawford sent MDxHealth, the test’s developer, Tim’s old biopsy samples.

“Three of them came back showing a hot area in his prostate very near to where those biopsies were taken,” Crawford said.

He sent Tim for an MRI scan, which came back with three suspicious areas in Tim’s prostate. A week ago, Tim underwent a second biopsy targeting those areas. They were cancerous.

Tim said he hadn’t been aware of the new tests, and was surprised when Crawford sent the negative biopsy off for screening. He had, after all, felt like he was in the clear.

“In reality, it’s actually better news now, because I know what I have and we can correct at the earliest stages, and not have to worry about it 10 years from now,” he said.

More on the way. The Confirm MDx and Progensa PCA3 tests are two of a dozen new prostate-cancer screens either recently arrived or coming soon (for a rundown, check out the recent New York Times article on the topic). The tests sniff out different genetic markers, proteins and other chemicals associated with prostate cancers. Some seek to determine whether a biopsied cancer is aggressive or benign.

The tests aren’t cheap: $440 for Progensa PCA3 and $2,500 for ConfirmMDX. But prostate-cancer treatment rises with the severity of the disease, and Crawford and others have estimated the average cost at about $60,000 during the first two years after diagnosis. In ConfirmMDX’s case, a negative result also adds confidence to the initial biopsy reading, which means possibly avoiding follow-on biopsies (Crawford said one of his patients recently had four negative biopsies before his prostate cancer was confirmed).

While these tests appear to be important tools in the diagnostic arsenal, they will be no silver bullet. That’s because detecting prostate cancer is only part of the story of dealing with it.

“We have to remember that prostate cancer is just different than other cancers – most men develop it with advanced age and the real issue is not who has it, but who has a lethal form of prostate cancer,” said CU genitourinary medical oncologist Thomas Flaig, MD, in an email. “The focus of ongoing work in this area should be on tests that will tell us who is at greatest risk from prostate cancer, and then we will be able to tailor treatment recommendations based on this information. Validating any new test properly will be the big issue moving forward in this area.”

Even with more targeted testing, prostate cancer differs from injured knees and clogged arteries, where the relative risks and benefits of undergoing treatment are more straightforward. Some prostate cancers stay relatively quiescent; others spread aggressively. Michael Glodé, MD, the CU Genitourinary Oncology Program’s medical director, said that about one-third of diagnosed men will never be bothered by their prostate cancer. The possible side effects of prostate removal, or prostatectomy, give pause: incontinence and impotence. The calculus is different for a young patient like Tim than for a man in his seventies.
“These tests hold promise for the possibility of finding the patients who truly need to be found and leaving alone those you don’t want to find,” Glodé said.

The ultimate success of the new tests will depend on what happens after diagnosis, Glodé adds. Some patients could rack up hundreds or thousands of dollars in new tests to establish a 5 percent threat of future metastatic prostate cancer — and go ahead with extensive treatment anyway. Other men might choose to wave off therapy if their chances of an aggressive type are 10 percent or even higher. It will come down to each man’s individual decision regarding risk/benefit of treatment, Glodé said.

“So the cynical view is that this is going to add costs of medical care,” he said.

Regardless of that debate, for some patients the decision about how to treat their conditions will be much clearer because of the tests. Crawford said that while Tim’s cancer is low-grade, a prostatectomy is the prudent course, given his age. They’ll talk through the options when they meet again later this month.

Tim agreed.

“With the results, in my mind, this is a very clear-cut decision,” he said. “I want to get this out of me.”