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Popular, successful Pap test faces challenge

Studies show that testing for HPV may be superior

By Rita Rubin
USA TODAY

A growing body of research suggests the Pap test has passed its prime.

No question, the Pap test, which detects abnormal cells in the cervix, has been the biggest success story in the history of cancer screening. U.S. cervical cancer death rates have been cut in half since widespread use of the test began in the early 1970s, according to the American College of Obstetricians and Gynecologists.

But study after study — three of them published in the past month — has shown that testing for the presence of the human papillomavirus, or HPV — certain types of which are found in virtually all cervical cancers — is a superior screening tool for most women.

"The original Pap test was developed in 1928 and was used as a screening test (beginning) in the 1940s," says epidemiologist Jack Cuzick, a leading HPV researcher at Cancer Centre UK in London. "It's kind of a dinosaur now. The evidence for moving forward is overwhelming."

A Canadian study published last month in The New England Journal of Medicine found that the Pap test picked up only 55% of "high-grade" precancerous cells; the HPV test picked up 96%. In other words, says Eduardo Franco, the McGill University scientist who was the report's senior author, women screened with the Pap test alone might as well toss a coin to figure out whether they're on their way to developing cervical cancer.

"The data are already there: The Pap does not perform as well as HPV in terms of detecting disease," says Thomas Wright, director of obstetrical and gynecological pathology at Columbia University's College of Physicians & Surgeons.

With the HPV test, says National Cancer Institute physician/ scientist Mark Schiffman, "if it's negative, it's incredibly powerful. If it's negative, the chance of having cancer there that day is extremely low." (For his HPV work, Schiffman last week received the American Cancer Society's Medal of Honor for Clinical Research, the same medal awarded to George Papanicoloau, developer of the Pap test, a half-century earlier.)

By Stephanie E. Keith for USA TODAY

Detecting disease: "The Pap does not perform as well" as HPV testing, says Thomas Wright of Columbia University's College of Physicians & Surgeons.

60 million Pap tests a year

So why is the Pap test still No. 1 for cervical cancer screening?

Approximately 60 million Pap tests are performed each year in the USA; switching to screening with only an HPV test would represent a sea change in women's health care.

For now, the most obvious roadblock is the fact that only one HPV test, made by Digene, is sold in the USA, and it is approved for use only when a Pap test is inconclusive or as a "co-test" with a Pap. It is not approved as a stand-alone primary screening test, but it can be performed on the same specimen collected for a "liquid-based" Pap test such as ThinPrep.

But the explanation for the Pap test's continued reign is more complicated than that. On top of the regulatory issues are doctor and patient attitudes, malpractice concerns and aggressive marketing of Pap tests, researchers say.

"There's a lot of money here," Cuzick says. "It's not purely academic."

In response to Franco's study, Jasmine Fielding, a publicist for ThinPrep, which accounts for the bulk of the U.S. Pap test

market, told reporters the Canadian findings weren't relevant to U.S. women. The reason, according to Fielding: The Canadian study compared the HPV test with the conventional Pap smear, not a liquid-based Pap test, which, she said, is superior.

But the main difference between the conventional Pap smear and the more expensive ThinPrep is how cells are prepared for evaluation, not how sensitive the tests are in identifying serious precancers or cancers. "We have yet to see any documented evidence that ThinPrep or any of its (liquid-based) competitors catch more high-grade" abnormalities, says Cindy Pearson, director of the National Women's Health Network.

In the hands of doctors or nurses who are experienced at collecting cervical specimens, the conventional Pap smear and ThinPrep appear to be comparable, says Debbie Saslow, director of breast and gynecologic cancer at the American Cancer Society. It's probably easier for an inexperienced person to get a good sample of cells for evaluation, though, says Saslow, noting that "sampling errors are a major source of false-negative Paps."

A big challenge for HPV test

Many doctors and patients are reluctant to give up on a test with the Pap's track record, especially considering that a clinical trial to prove that screening with the HPV test actually saves lives might be prohibitively costly and time-consuming.

At a 2000 FDA advisory panel meeting convened to discuss HPV and Pap co-testing, says Kaiser Permanente's Walter Kinney, one cytologist — someone who studies cells, including those on a Pap test slide — suggested that the only way to prove that HPV screening reduces cervical cancer deaths would be to conduct a trial following at least 200,000 women for 20 years.

But no company would ever pay for such a trial, says Kinney, a specialist in women's cancers at Kaiser Permanente's Northern California region, and no researcher would want to wait that long to publish in a scientific journal.

A more reasonable trial would follow a smaller number of women for five years to see whether the HPV test reduces the likelihood of developing the most serious precancers, Wright says. That approach led to FDA approval of the HPV vaccine, he says.

Even if HPV testing were approved as a stand-alone primary screening tool, though, convincing doctors and patients of its merit will be a challenge, Kinney says. "Actually changing people's perceptions and educating them ... that's really hard."

Cervical cancer screening 101

1. Vaccination does not replace screening.
Even if you've been immunized against the human papillomavirus, or HPV, you still need to be screened for cervical cancer beginning three years after you start having vaginal intercourse or when you're 21, whichever is earlier. The vaccine does not protect against all cancer-causing HPV types, nor does it clear up pre-existing HPV infections.

2. If you're under 30, you should be screened with a Pap test, not the HPV test.
Women under 30 are more likely to have transient HPV infections that clear up on their own, so screening with the HPV test could lead to a lot of unnecessary follow-up testing. The American College of Obstetricians and Gynecologists says women under 30 should get a Pap test every year; the American Cancer Society says women that age could be screened every other year if a "liquid-based" Pap test is used. The main reason for the longer screening interval, says the cancer society's Debbie Saslow, is the higher cost of liquid-based tests.

3. If you're 30 or older, you probably don't need to be screened every year.
Cervical cancer grows slowly, and it is long-lasting HPV infection that leads to the disease. If you're 30 or over and you're sceened with a Pap test, you can be screened every two or three years once you've had three negative annual tests in a row. If you're screened with both the Pap and HPV tests, and they're negative, you shouldn't be screened more than once every three years. If one of the tests is positive, you will need more frequent screening.

4. Although not as sensitive as the HPV test, a Pap test is better than no screening.
Most of the 11,150 U.S. women who will be diagnosed with cervical cancer this year either have never been screened or haven't been screened in at least five years.

Sources: American College of Obstetricians and Gynecologists, American Cancer Society and USA TODAY research