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"From Bench to Bedside"
Research News from Dr. Luis A. Diaz, Jr.

'Pap' test possible for ovarian cancer

By Maggie Fox, NBC News

The Pap test, which has saved tens of thousands of women from cervical cancer, might be able to help fight two other deadly cancers – ovarian cancer and cancer of the uterus, doctors reported Wednesday.

Ovarian cancer is the deadliest women's cancer, killing 15,000 women a year in the United States – in part because it's usually detected too late. Only 46 percent of women diagnosed with ovarian cancer survive for five years or longer.

But the new test could detect little cells dropped by the tumors as they grow in a woman's body. Even better, the test could be done as part of a woman's routine Pap test at her gynecologist's office, the researchers report in the journal Science Translational Medicine.

The findings come as the result of a little serendipity – some water-cooler talk, a decades-long government project to sequence the human genome, and a fundraising effort by volunteers leaping into the Chesapeake Bay.

"The way this really began was with a conversation," says Dr. Luis Diaz, Jr. of Johns Hopkins University, who helped lead the study. His team was already using data from the Human Genome Project to try to detect cancer cells circulating in the blood and other body fluids. They spoke with Dr. Richard Roden, a gynecological pathologist at Hopkins – an expert in examining tumor cells from cervical, endometrial, ovarian and other women's cancers.

"We got to thinking that maybe ovarian cancer shed cells into the female gynecological tract and that these would collect in the cervix," Diaz said. "Likewise, endometrial cancers. And that using very sophisticated technology, we could detect those mutations."

They looked at work from colleagues on sequencing the DNA of ovarian and endometrial tumors. All cancer is caused by mutated DNA, but there are many different mutations in different tumors. They narrowed down the 12 most frequent mutations in each type of tumor.

Diaz and colleagues developed a test and tried it out on 46 women who had been diagnosed with either ovarian or endometrial cancer while getting surgery, and who had been given Pap tests. The new test could simply piggyback onto the the Pap test – which is no longer a smear, but a liquid-based test that also looks for the human papillomavirus or HPV that causes most cases of cervical cancer.

“When we looked to see if cells were shed from these ovarian cancers and endometrial cancers into the cervix, we found we could detect 100 percent of the endometrial cancers and 40 percent of ovarian cancers,” Diaz said.

And many were at stage 1, when they are most easily cured. Better yet, the test did not get any "false positives" when they tested Pap tests from 14 women who did not have cancer.

Endometrial cancer usually causes early symptoms, such as bleeding. More than 90 percent of women diagnosed with early stage endometrial cancer survive to live five years or more. But ovarian cancer is difficult to detect, says Cara Tenenbaum of the Ovarian Cancer National Alliance.

“The symptoms are vague and I think they are easily confused with other diseases. They include bloating, feeling full quickly, frequent urination and the abdominal pain,” she told NBC News.

These are frequent symptoms for a whole lot of other things, including normal menstrual cycles. “There is no early detection test for ovarian cancer. We don’t have anything that’s reliable, especially for the average risk woman,” Tenenbaum said.

A test for a protein called CA-125 has not been very reliable in detecting ovarian cancer, nor have ultrasound tests. A test that could detect ovarian cancer before it begins causing symptoms could save many lives, Tenenbaum said. “This study moves us closer and that is really exciting.”

It will be years before the researchers can even develop a commercial test The next step will be to try it on hundreds of women, not just the dozens tested for the paper, Diaz says. Women with mutations in the BRCA gene, who have an unusually high risk of ovarian as well as breast cancer, would be prime candidates. They'll also try to improve on its ability to detect ovarian cancer.

They’re naming their test after Georgios Papanicolaou, who reported on his “Pap” smear in 1943. The test removes a small number of cells from the cervix, the mouth of the uterus, which can then be examined under a microscope for the changes that commonly develop into cancer.

Women with the precancerous changes can be treated before cervical cancer even develops. Modern tests now also look for HPV, which causes the cells to mutate.

“At that time, he suggested that endocervical sampling could in theory be used to detect not only cervical cancers but also other cancers arising in the female reproductive tract, including endome-

trial carcinomas," Diaz and colleagues wrote.

"In honor of Papanicolaou's pioneering contribution to the field of early cancer detection, we have named the approach described herein as the 'PapGene' test.

Diaz says their new tests costs just $100 and if it were mass produced, it could become much cheaper.

"There are millions of Pap smear tests performed annually in the United States. Could PapGene testing be performed on such a large number of specimens? We believe so, because the entire DNA purification and amplification process can be automated, just as it is for HPV," the team wrote.

Experts are now starting to recommend less-frequent Pap screening for many women. Diaz says it's too soon to say if the new test would need to be performed more frequently, but noted that ovarian and endometrial cancers both take years to develop.

Diaz says the team did its study using money raised by volunteers, including Swim Across America, a charity that raises money for cancer research. The charity, which has been organizing drives since 1987, raised $300,000 for the work, he said. The non-profit Commonwealth Fund also contributed, he said.

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