CHANGING THE LANDSCAPE IN WOMEN'S HEALTH

ROCHE'S COBAS® HPV DNA TEST FOR CERVICAL CANCER SCREENING CAN TRANSFORM HOW THE DISEASE IS DETECTED AND TREATED BY PHYSICIANS AROUND THE WORLD.

Personalized medicine, which has its roots in molecular oncology, is traditionally described as the right treatment for the right patient at the right time.

"I think that still holds true, but its role is now expanding," says Alan Wright, M.D., MPH, chief medical officer for Roche Diagnostics, noting that personalized medicine is now venturing into the preventive-care arena.

Roche is one of the leaders in personalizing medicine. In the mid-'90s the company developed the first personalized pharmaceutical, Herceptin for breast cancer, and has continued its tradition of innovation in the realms of both pharmaceuticals and diagnostics.

"We can leverage both of our core competencies to lead the way in personalized diagnostics for personalized medicine," says Whitney Green, senior vice president of molecular diagnostics at Roche.

Molecular diagnostics, which identify genetic characteristics based on specific mutations, play a key role in developing increasingly effective screening tests.

One of those tests changing the global landscape in women's health is the Roche cobas® HPV DNA Test for cervical cancer screening.

"There are about 4,000 fatalities per year in the U.S. alone from cervical cancer," Green says. "The goal of Roche is to reduce the number of women suffering from this disease by developing better diagnostics."

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MAKING HISTORY

In the mid-1940s, Dr. George Papanicolaou introduced the Pap test to screen for cervical cancer. After its adoption in the 1960s, the incidence of cervical cancer and deaths due to the disease decreased by more than 60 percent. It's no wonder the Pap has been the standard of care for cervical cancer screening for the past 50 years.

As the Pap test technology evolved, it became possible to pinpoint pre-cancerous cells and then diagnose three stages of cervical pre-cancer.

However, since a pathologist interprets the results, there's the potential for human error. And the test doesn't catch all incidents of the disease.

"The way to correct for that was to test more often, so we would be more likely to capture those true 'abnormals,'" says Mark Gentry, M.D., a specialist in obstetrics and gynecology with Hendricks Regional Health Medical Group.

But the introduction of HPV DNA testing signaled a new approach that's changing the paradigm in cervical cancer screening. Instead of focusing on whether cancer is already present, Roche's cobas HPV Test detects the presence of human papillomavirus, the virus responsible for virtually all cases of cervical cancer.

The cobas HPV DNA Test specifically

detects HPV 16, HPV 18, and 12 additional HPV genotypes that put women at a higher risk for developing cervical cancer. HPV 16 and HPV 18 are responsible for 70 percent of all cervical cancers.

"The unique aspect of the Roche test is that we have the ability with one sample and one test to differentiate among those different genotypes," Green says.

That has huge value for physicians, researchers, and, ultimately, patients.

"Knowing if a patient has a high-risk genotype has much more meaning for me," says Dr. Beth Meyerson, co-director of the Rural Center for AIDS/STD Prevention at Indiana University School of Public Health–Bloomington. "It will transform how we reach women who are underscreened for cervical cancer."

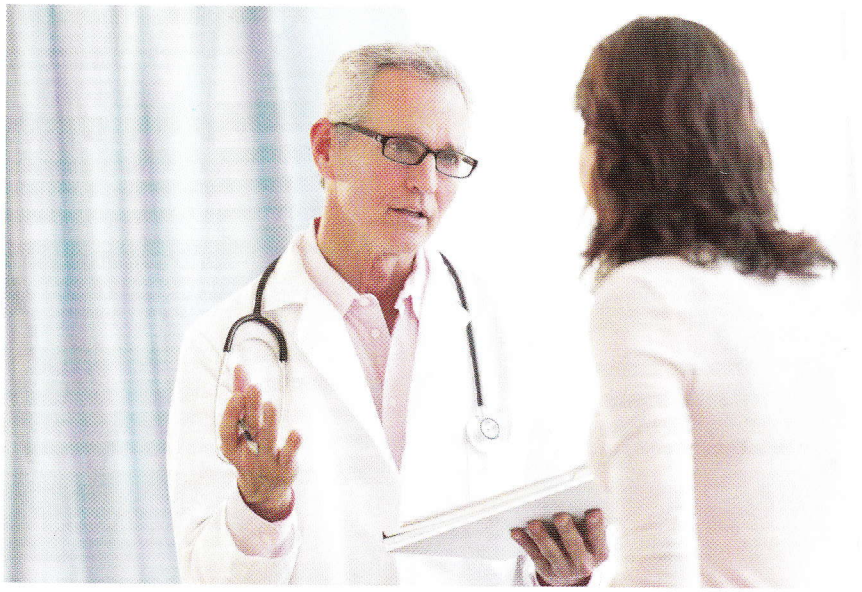
Compared to the Pap, the Roche cobas HPV Test is a more objective and sensitive tool that can be used to assess a woman's risk and monitor at-risk patients closely, so that if cancer or pre-cancerous disease does develop, it can be treated early.

PUTTING IT IN PERSPECTIVE

Initial results from the ATHENA study, a landmark three-year clinical trial that evaluated the performance of the Roche cobas HPV Test compared to the Pap test, were released in 2011. More than 47,000 women in the U.S. participated in this study, with an age representation that closely mirrored the demographics of the U.S. population.

Findings confirmed that the Pap test alone missed a significant amount of disease. One in 10 women who had a negative Pap test result but were positive for HPV 16, for example, already had cervical precancer. Another study showed that approximately one-third of women who had a normal Pap result were found to have cervical cancer precursors or cancer.

From Gentry's perspective as an OB/GYN, the most important finding is that patients who test negative for the Roche test are twice as likely to be free from cervical cancer after three years than women who receive a negative (normal) Pap test.



With longer time between cervical cancer screening tests, patients can use their annual well-woman exam to discuss with their doctor other important issues.

The cobas HPV Test was initially approved by the U.S. Food and Drug Administration in April 2011 as a screening test for cervical cancer to be used in conjunction with a Pap test, known as co-testing.

Later that year, the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology updated their guidelines for cervical cancer screening to indicate that Pap/HPV DNA co-testing was now preferred to Pap testing alone for women ages 30 to 65. If a Pap test result (with no HPV co-test) comes back negative, the guidelines recommend that women be re-tested every three years; if both co-testing results come back negative, the re-testing interval is five years. It's a case of "watch and wait" with follow-up testing for women who have a normal Pap test and a positive HPV DNA test.

SHIFTING ROLES

Results from the ATHENA study have some wondering if the lead role in cervical cancer screening should be given to the cobas test instead of the Pap.

This April, Roche's cobas HPV Test received an expanded approval by the FDA for primary screening of cervical cancer—the only test to receive this status since the Pap.

"The FDA found that, in fact, HPV testing first is comparable, if not superior, to cytology testing first," Wright says.

Roche is increasing awareness about the importance of HPV-based screening by working with patient-advocacy groups and other organizations that influence the development of guidelines for medical practice. Roche cleared one hurdle when the test received FDA approval. The next obstacle is gaining acceptance in physicians' offices, but the process of incorporating new science into longstanding medical practices is traditionally a slow one.

"We've also invested in a dedicated professional sales team to talk to practicing OB/GYNs and educate them on cobas HPV screening and HPV 16 and 18 genotyping," Green says.

WHAT IT MEANS FOR WOMEN & HEALTHCARE PROVIDERS

Longer time between tests and a reluctance to give up the familiarity of the Pap will likely be the main concern for women.

"I tell my patients, we're not taking something away," Gentry says. "The technology has changed, and you're actually getting a better negative predictive value for greater reassurance that you won't have the disease."

Since a specimen won't need to be gathered at every annual well-woman visit, that time can now be used for women and their providers to discuss other issues.

"HPV primary testing would signifi-

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cantly simplify the process," Gentry says.

The act of gathering the specimen in a physician's office is the same for both tests. However, the HPV DNA specimen is conducive to self-sampling via vaginal swabs, and, in the future, that could have huge implications for women worldwide.

"For me, I think of the opportunities for outreach screening in venues where you can't do a Pap," says Meyerson, who envisions kits being made available in public restrooms, walk-in clinics, and other venues. "You can start to see how technology can bring the system closer to women and girls who don't have access to healthcare."

THE ROLE OF VACCINES

Vaccinations for HPV are recommended for girls and boys 11 or 12 years of age, but they haven't been universally adopted.

"Testing will be necessary until every young woman and man has been vaccinated," Meyerson says. "We have not uniformly normalized HPV vaccination as part of our preventive-care immunization regimen in the U.S. That means at least for now, we'll always have to test."

Another concern is how long the vaccines will last.

"How long will they provide protection for a young woman—particularly women who are vaccinated in their early teens who are most likely to be sexually active for a number of years afterward?" Gentry says. "The answer is, we don't know yet."

LOOKING TO THE FUTURE

"I think we're at the beginning of the journey," Roche's Green says. "Personalized healthcare can be a factor for improving outcomes, reducing adverse effects, and reducing overall costs in the future. And molecular diagnostics are going to be a critical component of that."

Developing diagnostics that improve breast cancer treatments continues to be an emphasis for Roche. Other prominent projects include establishing tests to target treatment for lung and colon cancer, osteoporosis, and heart disease.

"Roche is a company that emphasizes innovation," Wright says. "We're always developing new tests in anticipation of what patients will need next."

BY SHARI HELD

PHOTOS COURTESY KIRK FORBES

THE KRISTEN FORBES EVE FOUNDATION

One family channels its grief into educating people about HPV, with the ultimate goal of eradicating cervical cancer.

Kristen Forbes

In 2007 at age 22, Kristen Forbes had everything going for her. She'd just graduated from IUPUI and had landed a job in Walgreens' management program. She was young, beautiful, and full of life.

But four weeks into her new job, she noticed swelling in her right ankle. Within three weeks, she received a diagnosis of stage III cervical cancer.

Her Pap test had been normal just 18 months earlier. Kristen put up a fight, but succumbed to the disease 12 months later.

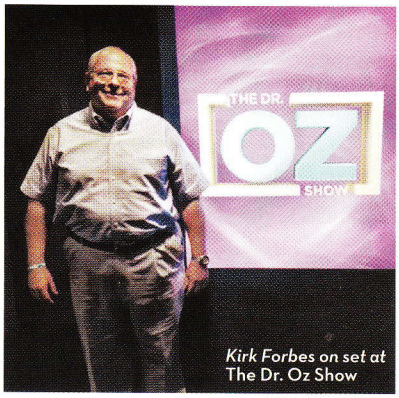
"At that point, every friend Brenda and I talked to knew nothing about HPV," says Kirk Forbes, Kristen's father. "They'd never heard of it."

In 2010, Kirk and his wife, Brenda, created the Kristen Forbes EVE (Educate, Vaccinate, Eradicate) Foundation to teach the public about HPV, its vaccine, and the test, and to encourage women to use these life-saving tools.

"Between the Roche cobas® HPV Test and the vaccine, there's no excuse why we can't eradicate these HPV-caused cancers," Forbes says.

Forbes has shared Kristen's story on *The Dr. Oz Show* and regularly makes speeches at Indiana colleges. He and Brenda presented to the Women in Government Foundation, a group of female state legislators based in Washington, D.C.

The EVE Foundation receives support from Merck and Glaxo SmithKline, the makers of the HPV vaccine, and Roche Diagnostics, the developer of the cobas HPV DNA Test.



Kirk Forbes on set at The Dr. Oz Show

Collaboration with Roche has proved mutually beneficial. Roche provides the Forbeses with up-to-date information and education and speaking opportunities. A film of the Forbeses talking about the effects of cancer on a family helps Roche put a personal face on the disease and shows employees what their research and products really mean.

"We can never say thank you enough to everyone at Roche for their support of our efforts," Kirk says. "It's been priceless."

The Forbeses are excited that Kristen's story, and those of four other young women, are featured in *Someone You Love: The HPV Epidemic*, which has appeared in several international film festivals, including the Heartland Film Festival.

"Our final goal is to raise our glasses in a toast when the CDC announces that cervical cancer and other HPV-caused cancers are eradicated," Kirk says.

–SHARI HELD