Persistent HPV infection raises risk of anal and genital cancers

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Women with a history of severe cervical intraepithelial neoplasia, a precancerous condition of the cervix that arises from infection with the human papillomavirus (HPV), had a long-term increased risk of developing anal, vulvar, and vaginal cancer.

The study is published in *Cancer Epidemiology, Biomarkers & Prevention*, a journal of the American Association for Cancer Research, by Susanne Krüger Kjær, a professor of gynecological cancer epidemiology at The Danish Cancer Society Research Center and Department of Gynecology at the Juliane Marie Centre, Rigshospitalet, Copenhagen University Hospital, Denmark.

Previous research has shown that certain types of HPV cause cervical intraepithelial neoplasia (CIN), a precancerous condition in which abnormal cells are found on the surface of the cervix. CIN is graded on a scale of 1 to 3, depending on how abnormal the cells look under a microscope and how much of the cervical epithelium is affected.

CIN3 is the highest grade, and the most likely to develop into cervical cancer, Kjær explained, adding that while infection with HPV is very common, most cases are cleared by the body within a year or two. Women who develop CIN, particularly a higher grade like CIN2 or CIN3, may be unable to clear the infection, which is one potential explanation for the elevated risk of anogenital cancers.

How the Study Was Conducted: In order to ascertain whether CIN3 was

also associated with anal, vulvar, and vaginal cancer, Kjær and colleagues studied 2.8 million women who were recorded as living in Denmark between 1978 and 2012, following some women for up to 34 years. The researchers identified women through Denmark's system of personal identification numbers, which the researchers linked to the Danish Cancer Registry and the Pathology Data Bank to obtain information on verified cases of CIN2 and CIN3, as well as cancer diagnoses.

Of these women, about 104,000 had CIN3 and about 52,000 had CIN2; the rest of them had no history of these conditions.

Results: The study found that when compared with women with no history of the disease, women with CIN3 were 4.2 times more likely to develop anal cancer, four times more likely to develop vulvar cancer, and 17 times more likely to develop vaginal cancer.

For women with CIN2, a lower-grade infection that is often less persistent than CIN3, the relative risks were lower, but followed a similar pattern, Kjær said. Women with CIN2 were 2.9 times more likely to develop anal cancer, 2.5 times more likely to develop vulvar cancer, and 8.1 times more likely to develop vaginal cancer than women with no history of the disease.

Researchers also evaluated the risk of developing rectal cancer, which is not associated with HPV, and found no excess risk, Kjær said.

Kjær said that while the connection between HPV and cervical cancer is well known, the results of this study add anogenital cancers to the list of potential long-range consequences of HPV infection and could add to support for vaccination against the virus.

"The HPV vaccine is prophylactic, and if we can prevent HPV infection

from occurring in the first place, we can prevent some of these conditions that result from persistent infection," Kjær said.

Kjær said the risk of anal, vulvar, or vaginal cancer was highest in the first year after diagnosis with CIN3. However, the increased risk persisted even when excluding cases that were diagnosed in the first year.

"We had thought that perhaps the women with CIN3 were the ones who were being treated by doctors and, therefore, receiving more examinations and consequently getting diagnosed with other cancers," Kjær explained. "But the risks persist for many years and, therefore, our findings cannot be explained by surveillance bias."

She said a limitation of the study is that some of the early enrollees may have had undiagnosed CIN, leading to underestimation of the risk.

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