

Concerned About HPV-Related Cancer Rise, Researchers Advocate Boosting HPV Vaccination Rates

Anna Azvolinsky

Deaths from the major cancers—lung, colorectal, breast, and prostate—continue to decline, a trend that started in the early 1990s. Cancer incidence is also declining, if slightly, for both sexes. That's the good news from the annual *Report to the Nation on the Status of Cancer*, a joint research effort by the American Cancer Society, the Centers for Disease Control and Prevention, the National Cancer Institute, and the North American Association of Central Cancer Registries (*J Natl. Cancer Inst.* 2013;105:175–201).

But the study also shows an uptick in rates of anal and oropharyngeal cancer, a type of head and neck cancer related to infection with the human papillomavirus (HPV), in the 10-year period ending in 2009. Cancer of the oropharynx increased among white men and women (3.9% and 1.7%, respectively). Anal cancer also increased in both sexes, with the greatest increase among black men (5.6%) and white women (3.7%). Rates of vulvar cancer, another HPV-related cancer, also increased among women despite continued lower rates of cervical cancer.

Researchers attribute this rise in HPV-related cancers to more HPV infections. “We think that increases in oral–genital sexual practices and increasing number of sexual partners that occurred some 30 years ago as part of the sexual revolution may be implicated in part of the increase in cancer rates we are seeing today,” said Edgar P. Simard, Ph.D., M.P.H., senior epidemiologist of surveillance research. Although rates of HPV infection from three decades ago were not available in the joint report, a trend exists of men and women now in their 50s and 60s having the highest rates of both oropharyngeal and anal cancers.

To directly relate HPV infection with cancer development later in life, epidemiologists are attempting to understand how HPV, the most common sexually transmitted infection in the U.S., is spread and which populations are most at risk. HPV infection of the cervix increases with number of sexual partners and younger age of first sexual experience. Studies now show similar trends for oral HPV infection rates, which can lead to oropharyngeal cancer.

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More than 100 strains of the virus are passed through skin contact. Most cause benign warts on the genitals, hands, or face, but about 15 strains can cause cancer of the cervix, vagina, vulva, penis, anus, and oropharynx (tonsils, back of the throat, and base of the tongue). Most people with HPV clear the infection, but those with persistent infection for many years or decades are at risk for these cancers, depending on the site of viral infection.

Screening for Noncervical HPV-Related Cancers

The Pap smear screening test has drastically reduced both cervical cancer incidence rates and deaths. Screening methods for other HPV-related cancers are not so straightforward. “Right now, it is just cervical cancer screening and some anal cancer screening that is done for certain individuals who are high risk,” said Simard. HPV causes an

estimated 90% of anal cancers. Anal cancer screenings are offered to HIV-positive men who have sex with men, but not enough research has yet occurred to adapt this type of screening for other cancer sites.

HPV infection causes approximately 60% of oropharyngeal cancers, but screen-

ing remains problematic. “We have a serious problem trying to screen for oropharyngeal cancer because we have not clearly identified a pre-malignant lesions that can be used for screening,” said Douglas R. Lowy, M.D., chief of the



Edgar P. Simard, Ph.D., M.P.H.

NCI Laboratory of Cellular Oncology, who works on HPV. This type of cancer has been studied for a relatively short time, and more research is needed to fully understand whether premalignant lesions caused by HPV could be identified early.

Oropharyngeal Cancer–HPV Link

Oropharyngeal cancers were seen predominantly in older men who had comorbidities and who tended to have a history of drinking or smoking. “What we see now is still more men than women, but these men are younger, in their 40s and 50s, and they don't have the comorbidities from smoking and drinking and in general are more healthy,” said Everett E. Vokes, M.D., head and neck expert at the University of Chicago.

Researchers now distinguish two types of oropharyngeal cancers—those related to HPV infection, which generally have a better prognosis, and those related to tobacco

and alcohol use. At the molecular level, HPV-related cancers are not only positive for HPV DNA but also express the human p16 gene, induced by the virus's oncoproteins. Most HPV-positive patients also have detectable antibodies against HPV.

HPV Vaccine Reaching Broader Population

Current HPV vaccination rates will at least partly influence the cancer statistics that will emerge in 20–30 years as a result of current HPV infection rates. Over time, “prevention is the key, and prevention is either abstinence or vaccination,” said Vokes.

The HPV vaccine can reduce the risk of HPV-related cancers that in 10–30 years could affect people who are now teenagers. The vaccine, a series of three shots, is recommended for girls aged 11 or 12 years (with catch-up until age 26 years) and boys aged 11 or 12 years (with catch-up until age 21 years), to protect against HPV infection and HPV-related diseases, including cancer. Researchers initially developed the vaccine to protect against cervical cancer and genital warts, and the U.S. Food and Drug Administration has now approved it to protect against anal, vaginal, and vulvar cancers. In principle, the vaccine should also protect against HPV-positive oropharyngeal cancer because as many as 90% of cases are attributed to the two HPV strains that the vaccine targets.

“A critical aspect of the HPV vaccine is that it should reduce the risk of all cancers caused by the HPV types targeted by the

vaccine, not just cervical cancer, for which we don't have another public-health intervention,” said Lowy.

Yet uptake of the vaccine in the U.S. remains low: Only 35% of girls aged 13–17 years were fully vaccinated as of 2011, compared with 18% in 2008—considerably short of the 80% goal of the Healthy People 2020 program.

Studies indicate that physician recommendation is a main determinant of whether a teen will receive the vaccine. Susan T. Vadaparampil, Ph.D., associate member of the Health Outcomes and Behavior Program at the Moffitt Cancer Center in Tampa, Fla., who studies trends in HPV vaccination, said that pediatricians are more likely than family physicians to offer the vaccine (*Cancer* 2013;119:621–8). Her study also showed that physicians who care primarily for minority groups are more likely to administer the vaccine to these patients. Cost is not necessarily a deterrent because children from families who cannot pay can receive the vaccine free through Medicaid or the Vaccines for Children program.

These findings are consistent with results of a national survey that Vadaparampil conducted to compare rates of physicians' HPV vaccine recommendations for girls aged 11–12 years from 2010 and 2011. Recommendation rates increased little, and another study focusing on low-income families showed that despite free programs and recommendations, vaccination rates for girls remained low.

“There has been very poor and slow uptake compared with the meningococcal

and Tdap [combined tetanus–diphtheria–pertussis] vaccines given to teens,” said Robert M. Jacobson, M.D., a pediatrician at the Mayo Clinic. Jacobson recently found that the number of parents who opt out of vaccinating their teens against HPV is increasing nationally despite recommendations (*Pediatrics* 2013;131:645–51). “The most alarming finding, frankly more disturbing than the poor uptake, is the increasing concern of parents regarding safety issues and the decreasing number of parents who say they will vaccinate their daughters,” said Jacobson.

To better understand how to improve physician–parent communication, Jacobson and colleagues will, as part of a large national study, go directly to physicians' offices to analyze the conversations physicians are having with parents and teens. “We need to find out what is being said and, perhaps more important, what is not being said.”

CDC and other organizations are leading campaigns to increase HPV vaccination rates. According to Simard, the campaigns underscore the vaccine's anticancer function. As for the scientifically unfounded safety concerns, “we need to continue to communicate the scientific rationale for HPV vaccines to the public and underscore that all of the data support the conclusions that the vaccines are safe and efficacious,” said Simard. “We are confident in that, but we do need additional ways to combat people's misperceptions about the HPV vaccine.”

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Shaking Tobacco's Residual Grip: Endgame Strategies Emerge

By Susan Jenks

In 1984, humorist and radio personality Garrison Keillor penned a satire about the last smokers in America for the *New Yorker*, describing them as a beleaguered group of three women and two men, puffing their “little smoke puffs.”

The group had lost contact with “the only other band of smokers they knew of—five writers holed up in an Oakland apartment,” Keillor wrote, as law enforcement closed in on them inside a box canyon south of California's Donner Pass. Ultimately, handcuffed and

returned to their families, the hapless smokers were tried and convicted of violating the “28th Amendment” and sentenced to write 20,000 words on personal integrity.

Keillor's portrait of the country's final smokers in “The End of the Trail” seemed