Human Papillomavirus Vaccine Is Crucial for Adolescent and Young Adult Cancer Survivors

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Introduction

ADOLESCENT AND YOUNG ADULT (AYA)-aged cancer survivors comprise a unique group of individuals with specialized healthcare needs.¹ Although efforts are often focused on the many challenging medical and psychosocial needs of these survivors, preventive care measures that are standard for AYAs in the general population may be overlooked amid the complexities of providing AYA cancer survivorship care.²

Human Papillomavirus Infection

The human papillomavirus (HPV) is the most prevalent sexually transmitted infection in the United States. For individuals who are sexually active with a member of the opposite gender, the average lifetime probability of becoming infected with HPV is estimated at 85% for women and 91% for men.³ More than 150 HPV genotypes have been identified to date; a subset of these genotypes have high oncogenic potential and are associated with the development of anogenital cancers.⁴ Although HPV infections can occur at any age, AYAs between 15 and 24 years of age are at particularly high risk for acquiring HPV infection during sexual encounters, with an estimated prevalence of 39% among adolescents of age 15–19 years, and 54% among young adults 20–24 years of age.⁵

Risk of HPV-Related Cancers in AYA Survivors

Some AYA cancer survivors are at increased risk for developing subsequent HPV-associated cancers. In a study of 64,547 cancer survivors diagnosed between 1973 and 2010, female survivors had a 40% relative excess risk of developing HPV-associated cancers compared with the general population, whereas male survivors had a 150% relative excess risk of HPV-associated malignancies.⁶ Individuals who experience prolonged immunosuppression are more likely to develop persistent HPV infection, which is associated with increased risk for HPV-related cancers.⁷ Allogeneic stem cell transplant survivors are at significantly higher risk for developing HPV-related cancers than the general population.⁸

HPV Vaccine

The nonavalent HPV vaccine provides protection against nine types of HPV, including seven oncogenic subtypes (HPV-16, -18, -31, -33, -45, -52, and -58), which together account for ~80% of HPV-related cancers, including ~80% of all cervical cancers and anal cancers and 57%–73% of penile, vulvar, and vaginal cancers in the United States.⁹ Two additional HPV genotypes (HPV-6 and -11), which are associated with anogenital warts, low-grade dysplasia, and respiratory papillomatosis, are also covered by the nonavalent vaccine.¹⁰

The nonavalent HPV vaccine was approved by the Federal Drug Administration (FDA) for use in males and females between 9 and 26 years of age in December 2014. Previously, the quadrivalent form of the vaccine was approved by the FDA in 2006 (for females) and in 2010 (for males). After inception of HPV vaccination in the United States, a significant decline in prevalence of infection with HPV genotypes covered by the vaccine has been observed,¹¹ suggesting that the HPV vaccine is effective in reducing the transmission of the virus. Nevertheless, uptake of the HPV vaccine in AYAs in the United States remains suboptimal.^{12,13}

Infection with oncogenic HPV subtypes is the attributable cause of the majority of anogenital cancers, and the HPV vaccine offers a readily accessible intervention to reduce the risk for development of future HPV-related cancers. AYA cancer survivors are in the age group at highest risk for acquiring HPV infection, and many of these survivors are also at increased risk for developing HPV-related cancers. In addition, the majority of AYA cancer survivors are currently unvaccinated; thus, targeting this population for HPV vaccination is warranted.

Barriers and Opportunities for HPV Vaccination

In the general population, efforts are focused on initiation of the HPV vaccine in pre- or early adolescence to optimize protection against HPV infection before sexual debut. AYA cancer survivors, however, may have had their routine vaccination schedule interrupted while undergoing treatment, and thus may not have received the HPV vaccine on schedule, leaving them vulnerable to remaining unvaccinated. There is a paucity of literature regarding HPV vaccination in AYA cancer survivors. Vaccine uptake has been examined through observational studies in two cohorts of female cancer survivors.^{14–16}

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These studies demonstrate low HPV vaccine initiation rates in female cancer survivors, ranging from 36% to 45% in adolescents^{15,16} to 39% in young adults.¹⁴ Discussion of the vaccine with a healthcare provider and receiving a physician recommendation for the vaccine were identified as consistent predictors of vaccine initiation among AYA female survivors in these studies.^{14–16} To our knowledge, no studies of male survivors or interventions to increase HPV vaccination in cancer survivors have been published to date.

In general, AYA cancer survivors have more frequent interactions with healthcare providers than their peers¹⁷; these interactions can serve as excellent opportunities to increase HPV vaccination. However, cancer survivors are less likely than healthy peers to report a provider recommendation for the HPV vaccine, suggesting that survivorship-focused care interactions may not include a discussion of the HPV vaccine.¹⁴ AYA survivors participate in risky sexual behavior at a similar rate compared with peers,¹⁸ yet they may receive less education from providers regarding sexual health¹⁹; when coupled with their increased risk of HPV-associated cancers, this makes them an especially vulnerable population.

In the general AYA population, parents and healthcare providers have reported hesitation to vaccinate preteens or younger adolescents against HPV, some believing that because the child is not yet sexually active, they should wait until closer to sexual debut to receive the vaccine.²⁰ However, parents often underestimate their child's sexual experience²¹ and most adolescents engage in sexual activity before graduating from high school.²² Another concern raised by parents is that receipt of the HPV vaccine will result in increased sexual activity and risk-taking behavior among adolescents. No consistent indication has been found that receiving the vaccine changes age at sexual debut, number of lifetime sexual partners, or increase in instances of unprotected intercourse among sexually active AYAs.²³ In fact, receipt of the HPV vaccine has been associated with protective sexual behavior, such as reports of using contraception and fewer sexual partners before age 18,²³ suggesting that teens and young adults who have received the HPV vaccine may be more proactive with their sexual health.

Recommendations

The HPV vaccine is recommended by the Advisory Committee on Immunization Practices (ACIP) as part of the routine preadolescent vaccine schedule, to be administered at age 11 or 12 years for both females and males.²⁴ The ACIP also recommends vaccination for females between 13 and 26 years of age and males between the ages of 13–21 years who have not been previously vaccinated, and for higher risk males of age 22–26 years.²⁴ HPV vaccination is endorsed by multiple national organizations, including the American Academy of Pediatrics,²⁵ the American Society of Clinical Oncology,²⁶ and the American Cancer Society.²⁷ AYA survivors who have not received the HPV vaccine should be vaccinated after completion of cancer therapy according to the ACIP immunization catch-up recommendations for children or adults.^{28,29}

Conclusions

There is substantial evidence that most anogenital cancers are attributable to HPV infection, and that the HPV vaccine is an effective intervention to prevent infection with the major

oncogenic genotypes. Since AYA cancer survivors are at high risk for acquisition of HPV, and a subset of these survivors are at increased risk for persistent infection and subsequent development of HPV-related cancers, it is important that healthcare providers caring for AYA cancer survivors encourage their patients to receive the HPV vaccine in a timely manner.

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