INFORMATION PAPER

DHA-IHD
17 December 2019

SUBJECT: Human Papilloma Virus (HPV) and HPV Vaccine

1. Purpose. To describe the disease and the vaccine.

2. Facts.

   a. Microbiology. Human papilloma virus (HPV) is the most common sexually transmitted infection in the United States. HPV is a non-enveloped, double-stranded DNA virus in the family Papillomaviridae. Isolates of HPV are classified as genotypes ("types") or strains, and are assigned numbers based on their genetic sequence. More than 120 HPV types have been identified, including approximately 40 that infect the mucosal epithelium (mouth, throat, and genital area.). Individual types are further classified as “high-risk” and “low-risk” based on their oncogenic ability (potential to cause cancer.) HPV infection is associated with cervical, vulvar, and vaginal cancer in females, penile cancer in males, and anal and oropharyngeal cancer in both genders. HPV can also cause benign or low-grade cervical cell changes, genital warts, and recurrent respiratory papillomatosis. HPV infection occurs in the basal layer of the epithelium. High-risk types affect regulatory genes that control cell proliferation, differentiation, and survival. During an infection, they induce uncontrolled cancer cell proliferation and prevent programmed cell death (apoptosis), leading to cell abnormalities and tumor development. HPV infections are restricted to the epithelium, so are largely shielded from the host immune response: not all infected persons develop detectable antibody. HPV can be diagnosed through virus-like particle (VLP) enzyme immunoassays, but standardized correlates of immunity have not been established. Although the incidence of HPV infections is high, most infections resolve spontaneously. A small percentage of people become persistently infected, which is the most important risk factor for the development of cervical cancer.

   b. Disease. HPV is detected in 99% of cervical cancers. HPV causes squamous cell carcinoma and adenocarcinoma, the most common types of cervical cancer. HPV types 16 and 18 are associated with 70% of these cancers. HPV type 16 is the most likely to persist and progress to cervical cancer with a typical time frame of decades, although rapid progression has been documented. HPV is also believed to be responsible for 91% of anal cancers, 69% of vulvar, vaginal and penile cancers, and 80% of oropharyngeal cancers. HPV types 31, 33, 45, 52, 58 account for an additional 15% of cervical cancers. HPV types 6 and 11 are associated with 90% of genital warts and most cases of

recurrent respiratory papillomatosis. The HPV infection is spread by direct skin-to-skin contact, including sexual intercourse, oral sex, or any other contact involving the genital area, such as hand to genital contact. HPV is very resistant to heat and dryness; nonsexual transmission through fomites can occur, such as during prolonged exposure to shared contaminated clothing. Pregnant women can pass HPV onto their babies during birth, although this is not common. Persons with as few as one lifetime sex partner are at risk for infection, but an increase in the number of recent and lifetime sex partners, sexual behavior of a partner, and immune status are additional risk factors. Most HPV infections are transient and asymptomatic and do not result in clinical disease. There is no way to predict who will clear the virus: 50% of persons with a new HPV infection will clear it within 1 year, and approximately 90% within 2 years. Oral HPV infection is much less common than genital infection, but time to clearance appears to be similar. Persons who are immunocompromised (e.g. HIV), have higher rates of HPV infection and disease progression.

c. Epidemiology. HPV infection occurs worldwide, and humans are the only natural reservoir. It is estimated that 79 million persons are infected in the United States. An estimated 14 million new HPV infections occur every year among persons aged 15–59 years, with 50% of those occurring in persons aged 15-24 years. Additionally, 5-30% of persons infected with HPV have more than one genotype.

d. Vaccine. Gardasil 9™ (9vHPV, Merck) is currently the only HPV vaccine approved for use in the United States. Gardasil 9™ provides protection to nine oncogenic strains: 6, 11, 16, 18, 31, 33, 45, 52 and 58. Of the earlier vaccines, 2vHPV (Cervarix™, GlaxoSmithKline) protected against types 16 and 18 and 4vHPV (Gardasil™, Merck) added types 6 and 11. The estimated protection provided by the HPV vaccine does not differ by race or ethnicity.

e. Immunization. Per the Advisory Committee on Immunization Practices (ACIP):

(1) 9vHPV is recommended for both males and females 9 through 45 years of age per the following:

a. Routinely recommended for all children at 11 or 12 years of age. The vaccination can be started as young as 9 years of age.

b. Catch-up vaccination is recommended for all persons through age 26 who have not completed the series.

c. For adults aged 27 through 45 years, patients and providers

should use shared clinical decision-making to determine if catch-up vaccination is warranted.

d. No pre-vaccination testing (e.g., Pap or HPV testing) is recommended to establish the appropriateness of HPV vaccination.

(2) 9vHPV vaccine is given in a 2- or 3-dose series depending on the person's age at initial vaccination.

a. Age 9 through 14 years at initial vaccination:

1. 9vHPV is given on a 2-dose schedule (0, 6-12 months). The minimum interval between doses is 5 months: repeat the dose if administered too soon.

b. Age 15 years or older at initial vaccination:

1. 9vHPV is given on a 3-dose schedule (0, 2, 6 months). Minimum intervals are:
   - Dose 1 to dose 2: 4 weeks
   - Dose 2 to dose 3: 12 weeks
   - Dose 1 to dose 3: 5 months (repeat if given too soon)

(3) Special situations:

a. Persons with immunocompromising conditions (including HIV) should complete a 3-dose series.

b. Persons with a history of sexual abuse or assault should begin the series at 9 years of age.

c. Through age 26 for males who are immunocompromised (including those with HIV infection).

(4) If a person has completed a series with any previous vaccine, no additional doses are recommended.

f. Limitations of Use and Effectiveness. Use of HPV vaccine does not eliminate the necessity for recommended cancer screening. HPV vaccination can provide protection against infection with HPV types not already acquired; the vaccine will not have a therapeutic effect on existing HPV infection. Since people can have more than one genotype at a time, vaccination is recommended through the recommended age for males and females regardless of whether they have had an abnormal Pap test or a known HPV infection.

g. Contraindications and Precautions. HPV vaccine is not recommended for the following:

(1) Persons who experienced a severe allergic reaction (e.g., anaphylaxis) to a vaccine component (including yeast) or following a prior dose of HPV vaccine.

(2) Pregnant women: the vaccine has not been causally associated with adverse pregnancy outcomes or with adverse effects on the developing fetus, but data on vaccination during pregnancy are limited. Pregnancy testing before vaccination is not needed. However, if a woman is found to be pregnant after initiation of the vaccination series, the remainder of the series should be delayed until after completion of the pregnancy. No intervention is indicated. Women known to be pregnant should delay initiation of the vaccine series until completion of the pregnancy. Vaccination during pregnancy may be reported to the manufacturer and/or VAERS.

(3) A moderate or severe acute illness is a precaution to vaccination, and vaccination should be deferred until symptoms of the acute illness improve. A minor acute illness (for example diarrhea or mild upper respiratory tract infection, with or without fever) is not a reason to defer vaccination.

h. Adverse Events. No serious adverse events have been associated with HPV vaccines:

(1) The most common adverse reactions reported during clinical trials were local reactions at the site of injection (pain, redness, and swelling) in 20%-90% of recipients. A temperature of 100°F during the 15 days after vaccination was reported in 10%-13% of recipients, although a similar proportion of placebo recipients also reported an elevated temperature.

(2) A variety of systemic adverse reactions were reported during clinical trials, including nausea, dizziness, myalgias and malaise; these occurred with equal frequency among both vaccine and placebo recipients.

(3) Syncope (fainting), sometimes resulting in falling with injury, has been reported among adolescents who receive HPV and other vaccinations recommended for this age group. Recipients should always be seated during vaccine administration, and should be observed by a clinician for 15 minutes afterwards.

(4) Other adverse reactions can include difficulty breathing, hives,

swelling of the face and throat, increased heart rate, and vomiting: these symptoms typically occur a few minutes to a few hours after the vaccination.

i. DoD Policy. HPV vaccination is not mandatory; however, facilities are encouraged to offer the vaccine to Service Members and Beneficiaries who meet ACIP criteria.

1. References.

a. Hamborsky, J., Kroger, A., Wolfe, S. (2015). Epidemiology and Prevention of Vaccine-Preventable Diseases (13th ed.). Washington DC: The Public Health Foundation.

b. Meites E, Kempe A, Markowitz LE. Use of a 2-Dose Schedule for Human Papillomavirus Vaccination — Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2016;65:1405–1408. https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm.

c. Petrosky E, Bocchini J, Hariri S, et al. Use of 9-Valent Human Papillomavirus (HPV) Vaccine: Updated HPV Vaccination Recommendations of the Advisory Committee on Immunization Practices. MMWR 2015:64;300-4.

d. Saraiya, M., Unger, E., Thompson, T., Lynch, C., Hernandez, B., Lyu, C., HPV Typing of Cancers Workgroup. (2015). US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. Journal of the National Cancer Institute, 107(6), djv086. doi:10.1093/jnci/djv086.

e. Multiple resources (e.g., Package inserts and Vaccine Information Statements): http://www.health.mil/HPV.

South Atlantic Region Vaccine Safety Hub
Approved: Deputy Chief, Immunization Healthcare Division
877-438-8222 (DSN 761-4245), option 1