

## INFORMATION PAPER

DHA-IHB  
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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. HPVs are non-enveloped, double-stranded DNA viruses in the family Papillomaviridae. Isolates of HPV are classified as "types" (or strains) and are assigned numbers in the order of their discovery. More than 120 HPV types have been identified, including approximately 40 that infect the genital area. Genital HPV infection is common worldwide. HPV infection is associated with cervical, vulvar, and vaginal cancer in females, penile cancer in males, and anal cancer 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. Oncogenic types manipulate cell cycle regulators, induce chromosomal abnormalities, and block apoptosis. Once infected, normally nondividing differentiating epithelial cells remain in an active cell cycle. A thickened, sometimes exophytic, epithelial lesion can result and as cells exfoliate from the epithelium, the virus is released. HPV infections are largely shielded from the host immune response and not all infected persons develop detectable antibody. HPV can be diagnosed through virus-like particle (VLP) enzyme immunoassays but correlates of immunity have not been established. Most persons infected with HPV resolve the infection. A small percentage of people become persistently infected, which is the most important risk factor for the development of cervical cancers.
  - b. Disease. HPV is believed to responsible for nearly all types of cervical cancer. Worldwide, HPV most commonly causes squamous cell carcinoma, followed by adenocarcinoma, as the most common types of cervical cancer. HPV types 16 and 18 and are associated with 70% of these cancer types. HPV 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 90% of anal cancers, 71% of vulvar vaginal or penile cancers, and 72% of oral pharyngeal cancers. HPV 31, 33, 45, 52, 58 accounts 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. There is a greater risk of becoming infected with HPV if one has multiple sexual partners at any time or if a partner has had multiple sexual partners. HPV is very resistant to heat and dryness; nonsexual transmission through fomites can occur, such as 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 increase in the number of recent and lifetime sex partners, sexual behavior of the partner and immune status are additional risk factors. Most HPV infections are transient and asymptomatic and do not result in clinical disease. Per CDC, 70% of persons with new cervical HPV infection will clear the infection 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. There is no way to predict who will clear the virus. Persons who are immunocompromised (e.g. HIV), have higher rates of HPV infection and disease progression.

- c. Epidemiology. HPV infection occurs worldwide. Humans are the only natural reservoir. It is estimated that 79 million persons are infected in the United States with, and an estimated 14 million new HPV infections occur every year among persons aged 15–59 years. Additionally, 5-30% of persons infected with HPV, have more than one genotype. Approximately half of new infections occur among persons aged 15–24 years.
- d. Vaccine. Gardasil 9 is the only HPV vaccine currently being distributed in the United States. Gardasil 9 provides protection to seven oncogenic strains: 16, 18, 31, 33, 45, 52 and 58 in addition to types 6 and 11 which are most associated with genital warts. Of the earlier vaccines, 2vHPV (Cervarix, GlaxoSmithKline) protected against types 16 and 18 and 4vHPV (Gardasil, Merck) added types 6 and 11.
- e. Immunization. Per the Advisory Committee on Immunization Practices (ACIP):
  - (1) 9vHPV is recommended for both males and females 9 through 26 years of age per the following:
    - a. Routinely given to all children at 11 or 12 years of age. The vaccination can be started as young as 9 years of age.
  - (2) For all females, vaccination may also be given at ages 13 through 26.

- (3) For males, vaccination is recommended:
  - a. for all males ages 13 through 21.
  - b. through age 26 for men who have sex with men (MSM).
  - c. through age 26 for males who are immunocompromised (including those with HIV infection).
- (4) If an individual reaches age 27 before the vaccination series is complete the second or third doses of the series can be administered after age 26 to complete the series.
- (5) Depending on the age of series initiation and patient risk factors, 9vHPV has two different schedules.
  - a. Two dose series 0, 6-12 months:
    1. For adolescents who initiate vaccination series at ages 9 through 14 years 9vHPV is FDA approved on a 2 dose schedule: 0 and 6-12 months. ACIP recommends a 2 dose schedule of HPV vaccine for persons who received the first valid dose before the 15th birthday, except for persons with certain immunocompromising conditions.
    2. The second and final dose should be administered 6-12 calendar months after the first dose. If the second dose has already been administered at least 5 months after the first dose, it can be counted. The four-day grace period can be applied to this 5 month minimum interval. If the second dose is administered at a shorter interval and additional dose should be administered at least 12 weeks after the second dose and at least 6-12 months after the first dose.
    3. Persons who have already received 1 dose of HPV before the 15th birthday and are now 15 years old or older, should be offered the second dose in the series, maintaining a minimum interval of at least 5 months between the 2 doses.
  - b. Three dose series 0, 2, 6 months:

1. Persons who initiate the series on or after the 15th birthday, and persons with certain immunocompromising conditions should be vaccinated with the 3 dose series.
  2. Persons who should receive 3 doses are those with primary or secondary immunocompromising conditions that might reduce cell mediated or humoral immunity, such as B lymphocyte antibody deficiencies, T-lymphocyte defects, HIV infection, malignant neoplasm, transplantation, autoimmune disease, or immunosuppressive therapy, since immune response to vaccination may be attenuated. The second dose should be administered 2 months after the first dose, and the third dose should be administered 6 months after the first dose (0, 2, 6 month schedule).
- (6) In October 2018, the FDA approved expanding the approved use of the vaccine to include women and men aged 27 through 45 years. To date, ACIP has not recommended routine provision of Gardasil 9 to these additional age groups.
- (7) A schedule begun with 4vHPV (Gardasil 4) or 2vHPV (Cervarix) can be completed with Gardasil 9. There is no ACIP recommendation for routine additional vaccination Gardasil 9 for persons who have completed a 3 dose vaccination series with one of the other HPV vaccines.
- f. Limitations of Use and Effectiveness. HPV vaccination can provide protection against infection with HPV vaccine types not already acquired, therefore vaccination is recommended through the recommended age for females regardless of whether they have had an abnormal Pap test and for females or males regardless of known HPV infection. The vaccine will not have a therapeutic effect on existing HPV infection genital warts or cervical lesions. Pre-vaccination assessments to establish the appropriateness of HPV vaccination are not recommended at any age (e.g. Pap testing or screening for high risk HPV, type specific HPV or HPV antibody).
- g. Precautions.
- (1) HPV vaccine is not recommended for the following:
- a. Women who are pregnant. 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 recipient is found to be pregnant after initiation of the vaccination series, the remainder of the series should be delayed until completion of the pregnancy. No intervention is indicated. Women known to be pregnant should delay initiation of the vaccine series until after delivery. Women vaccinated during pregnancy may be reported to the manufacturer.

- b. Individuals who have had a severe allergic reaction to a dose of HPV vaccine should not get another dose.
- c. Anyone who has a severe allergic reaction to any component of HPV vaccine (including yeast) should not get the vaccine.
- d. 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. The most common adverse events reported during clinical trials were local reactions at the site of injection such as pain redness and swelling in 20-90% of recipients. A temperature of 100°F during the 15 days after vaccination was reported in 10-30% of recipients although a similar proportion of placebo recipients reported an elevated temperature. A variety of systemic adverse reactions were reported by recipients, including nausea, dizziness, myalgia and malaise, however these occur with equal frequency among both vaccine and placebo recipients. Syncope 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 the clinician should observe the recipient for 15 minutes after vaccination. Sitting or lying down for approximately 15 minutes can prevent injuries caused by a fall. Other symptoms can include difficulty breathing, hives, swelling of the face and throat, increased heart rate, dizziness, and weakness. These symptoms typically occur a few minutes to a few hours after the vaccination.
- i. DoD Policy. HPV vaccination is not mandatory for Active Duty or Selected Reserve members; however facilities are encouraged to offer the vaccine to Service Members who meet ACIP criteria.

1. References.

- a. Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases. Hamborsky, J, Kroger A, Wolfe S, eds. 13th ed. Washington D.C. Public Health Foundation, 2015
- b. 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.
- c. Multiple resources (e.g., Package inserts and Vaccine Information Statements): <http://www.health.mil/HPV>.

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