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Human Papillomavirus (HPV) Vaccine Recommendations

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Men and women infected with HIV and human papillomavirus (HPV) are at increased risk of cervical and anal dysplasia, as well as various cancers. There are currently two licensed HPV vaccines for the primary prevention of HPV infections: Cervarix®, a bivalent HPV vaccine (HPV2) recombinant manufactured by GlaxoSmithKline, and Gardasil®, a quadrivalent HPV vaccine (HPV4) recombinant manufactured by Merck & Co, Inc. Both vaccines are not live vaccines but rather derived from virus-like particles prepared from recombinant L1 capsid and, therefore, can safely be given to HIV-positive patients. The HPV2 vaccine targets two oncogenic types (HPV 16 and 18), while the HPV4 vaccine also targets HPV 16 and 18 along with two non-oncogenic types (HPV 6 and HPV 11). HPV 6 and HPV 11 account for approximately 90% of genital warts and most cases of recurrent respiratory papillomatosis (benign epithelial tumors of the airway). HPV 16 and HPV 18 account for 70% of cervical cancers. In addition, HPV 16 is a common causative agent of other HPV-associated malignancies such as vulvar, vaginal, anal, oropharynegeal, and oral cavity cancers.

The latest recommendations of the Advisory Committee on Immunization Practices (ACIP) regarding HPV vaccines will be discussed. Full details of the latest ACIP recommendations are accessible at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5920a4.htm and http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5920a5.htm?s_cid=mm5920a5_e. Though the ACIP recommendations for HPV vaccines do not specifically address HIV-infected individuals, they do state that the vaccines can be administered to females who are immunosuppressed from disease or medications. However, they add that the immune response and vaccine efficacy may be less than that in immunocompetent individuals. The latest data on the safety and immunogenicity of the HPV vaccine in HIV-1 infected males as well as in children are also discussed below.

Vaccine Recommendations for HPV2 and HPV4 in Females

- Ideally, administered prior to potential exposure to HPV through sexual contact or for the prevention of:
  - Cervical cancers and precancers (HPV2 or HPV4);
  - Vulvar and vaginal cancers and precancers (HPV4 as there is no sufficient data for HPV2);
  - Genital warts (HPV4).
- Routinely vaccinate females 11 or 12 years of age with 3 doses of either HPV2 or HPV4.
- Can begin at 9 years of age.
- Vaccinate females 13 through 26 years of age who have not received the 3-dose series. Remaining doses can be administered after the age of 26 years if the vaccination series has not been completed.

Vaccine Recommendations for HPV4 in Males

- 3 doses-series of HPV4 may be given to males 9 through 26 years of age to reduce the risk of acquiring genital warts. (FDA approved but not routinely recommended by ACIP)
- When vaccination coverage of females is high (>80%), mathematical models propose that adding males to HPV vaccination programs is not the most cost-effective strategy to reduce HPV-related disease burden.
- Men who have sex with men (MSM) are at increased risk for anal intraepithelial neoplasias, anal cancers, and genital warts.
- A recent study showed that HPV vaccination in MSM is expected to be a cost-effective intervention for the prevention of genital warts and anal cancers.

Special Situations

- Can be administered to females who have abnormalities on their cervical cancer screening or to those with active or past history of genital warts, as the vaccine can protect against infection with HPV vaccine types not already acquired.
- Prevaccination assessments such as Pap testing, screening for high-risk HPV DNA, or serologic testing are not indicated.
- Safe in lactating women.

Precautions and Contraindications

- Most common adverse events include injection-site reaction, headache, fever, fatigue, and myalgia.
- Though safe, not recommended in pregnant women.

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- Defer in those with moderate or severe illness until clinical recovery.
- Syncope can occur; therefore, patient observation is recommended for 15 minutes following vaccination.
- Contraindicated for individuals with a history of immediate hypersensitivity to any vaccine components:
  - In individuals with immediate hypersensitivity to yeast, avoid HPV4 as it is produced in *Saccharomyces cerevisiae* (baker's yeast).
  - In individuals with immediate hypersensitivity to latex, avoid prefilled syringes of HPV2 as it contains latex in the rubber stopper. Single dose vials contain no latex.

HPV Vaccine and HIV-Infected Individuals

- HIV-infected individuals are at increased risk of genital and anal dysplasia and cancers.
- HPV vaccine can be administered to individuals who are immunocompromised as this is not a live vaccine.
- Until recently there was concern that the immune response might be less than that of immunocompetent individuals.
- A recent study demonstrated that the HPV4 was both safe and highly immunogenic in HIV-1 infected men with 95% or greater seroconversion for each of the HPV types contained in the vaccine.
- Another recent study demonstrated that the HPV4 was safe and immunogenic in HIV-infected children ages 7 to 12 years old.
- HPV4 vaccine is shown to prevent 93% of persistent anal infections with vaccine types in young (aged 16-26) HIV-1 uninfected MSM.
- The Infectious Diseases Society of America (IDSA) Primary Care Guidelines for the Management of Persons Infected with Human Immunodeficiency Virus 2009 also recommends HPV4 routine vaccination for females aged 9-26 years, but also state it may be considered for use in other groups.

Future Considerations

- Anal cancer is the result of persistent, high-risk type HPV infections:
  - HPV 16 is responsible for 66% of cases
  - HPV 18 is responsible for 5% of cases
- On December 22, 2010, the U.S. Food and Drug Administration (FDA) approved the HPV4 vaccine for the prevention of anal cancer and associated precancerous lesions due to HPV types 6, 11, 16, and 18 in people ages 9 through 26 years.
- Merck is attempting to obtain an indication for HPV4 vaccine for older women between the ages of 27 and 45.

Summary

- HIV-infected individuals are at increased risk of dysplasia and cancers.
- The HPV vaccine is safe and highly immunogenic when administered to HIV-infected individuals.
- HPV vaccine is indicated for the prevention of cervical cancers and precancers; vulvar and vaginal cancers, and precancers; genital warts; and (with FDA approval) anal cancers.
- HPV vaccine should be considered as a part of routine immunizations in HIV-infected men and women in certain age groups; however, it is not yet a recommendation of the CDC/ACIP.

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