American Academy of Pediatrics
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Maryland Chapter

The HPV Series: Human Papillomavirus Lifecycle and the Demographics of Infection
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Through financial support from The Department of Health and Mental Health (DHMH) it is our pleasure to share with you a series dedicated to the HPV vaccine in the pediatric setting. Each issue will present a literature review for the provider with questions and answers on key issues for parents and caretakers. The AAP and CDC both recommended vaccination starting at eleven to twelve years of age for both boys and girls; however, the vaccine still remains poorly utilized.[1]

The last issue focused on the current acceptance of vaccination and the differing strains of human papillomavirus. This issue focuses on the HPV virus life cycle and demographics of infection.

All HPV strains are double stranded DNA viruses that infect epithelial tissue. The life cycle begins when HPV gains access to the basal layer where it infects progenitor cells. The exact access route is highly variable. Mechanisms for access include minor trauma, chemical disruption, invasion of hair follicles, and infection of the single layer of columnar epithelial cells of the developing cervix. For example, the common plantar wart typically uses abrasives surfaces in pools or public showers for transmission, whereas the HPV strains that cause cervical cancer and genital warts rely on direct exposure to existing lesions or body fluids. Once the virus is in contact with the cells of the basement membrane internalization is a slow process that may take several hours. (1)

After being taken up by the cell, 'early' or 'E' proteins E6 and E7 derange the cell cycle resulting in cells that divide quickly but fail to mature into epithelial cells. This results in a hyperproliferative progenitor cell line that can persist to perpetually create more virus. The life cycle is completed when the particle is repackaged with 'late' or 'L' proteins to make the outer virus capsid. (1) The lifecycle of the virus poses unique opportunities for protection with a vaccination. Normal serum antibodies are not found outside the basal membrane; however, for HPV microtrauma is an important part of the lifecycle which releases antibodies that can inactivate the virus during the extended time taken for internalization. The vaccine is created by making synthetic copies of the late protein 'L1' which spontaneously assemble into a particle that is similar to the final structure or HPV and provides a repetitive target for antibodies. This copy does not contain the early proteins or the genetic material of the virus. (2)

HPV is highly contagious. Large studies have found that the virus is highly prevalent and infects a majority of the population at some time during the human lifetime. The most robust study was completed in 2011 and found that 42% of females age 14-59 years old at any given time were infected with HPV. This leads to an estimated 39.5 million individuals in the US population who have active infections. In the same study, a statistically significant increase was observed between women who are 14-19 years old who had a prevalence of 32.9% and women who are 20-24 years old who had a prevalence of 53.8%.

A major risk factor for infection is a person's lifetime number of sexual partners. For those with >6 partners THE prevalence of HPV was found to be as high as 55.5%. Interestingly though, in those who reported only one lifetime partner, HPV was still found in 18% of cervical swabs and in those who reported zero sexual partners, HPV was could even be found in 15% of cervical swabs. (3) This may represent under-reporting sexual partners, the easy spread of HPV with non-penetrative sexual contact, or both. These statistics emphasize the need for early vaccination.

Several studies have attempted to monitor the changes in HPV prevalence with vaccination and have shown a decrease in HPV 16 and 18 infections in those who have received the vaccine in comparison to those who have not. (4) Post-vaccination epidemiology and expanding the types included in vaccination will continue to be an important subject of research. (5)

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[1] The Author: Theodore Wilson MD is working with the Maryland AAP chapter. He has no financial conflicts of interest or investments in any products discussed. Reproduction is permitted.

This can be printed as a hand-out for parents to answer their questions.

<u>The HPV Series:</u> Family questions about HPV and Cervical Cancer

How common is Human Papillomavirus (HPV)?

A large study in 2011 showed that almost a third (32%) of young females 14 to 19 years old and half (53%) of young females age 20 to 24 are infected with HPV.

How common is Human Papillomavirus in individuals who don't have sex?

The same study also asked young women about their number of lifetime sexual partners. They found:

- With only **<u>one</u>** lifetime sexual partner **<u>18% still had HPV</u>**
- With **<u>zero</u>** lifetime partners **<u>15% still had HPV</u>**

these infections were likely acquired from close physical contact.

Who should <u>not</u> receive the HPV vaccination?

The HPV vaccine is expected to be safe during pregnancy though has not been approved for that use. You should let your doctor know if you may be pregnant or become pregnant while receiving the series. Patients who have had an allergic reaction to an earlier HPV vaccine, to a previous vaccine or a previous vaccine component should also not receive the HPV vaccine.

What are the key ingredients of the vaccine?

A single surface protein from the HPV germ is the major ingredient of the HPV vaccine. The vaccine contains a tiny amount of yeast, which is used to create this protein. In addition, the vaccine contains other ingredients, used safely in many vaccines, that help the HPV vaccine successfully reach its target. The vaccine does NOT contain human cells, antibiotics, mercury, or preservatives.

References:

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3) Hariri, Susan "Prevalence of Genital Human Papillomavirus Among Females in the United States, the National Health and Nutrition Examination Survey 2003-2006" The Journal of Infectious Disease 2011:204 (15 August) http://jid.oxfordjournals.org/content/204/4/566.full.pdf+html

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6) Merck "Full prescribing information" revised 03/2014 http://www.merck.com/product/usa/pi_circulars/g/gardasil/gardasil_pi.pdf