

Counseling about the HPV Vaccine: Desexualize, Educate, and Advocate

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A B S T R A C T

Information is provided for clinicians who treat adolescents and adult women to use when counseling patients about human papillomavirus (HPV) vaccine. A literature search was done to determine: (1) reasons for refusal of the vaccine, including cost and concerns that immunization against HPV will lead to promiscuity; (2) potential for non-sexual transmission of HPV; (3) non-genital locations of HPV; (4) non-genital cancers associated with HPV.

Vaccines for Children Program and the Affordable Care Act eliminate many costs. Neither biological nor behavioral evidence supports the idea that sexual behavior changes after immunization. HPV is transmitted from person to person by non-sexual routes including mother to child at birth and apparently by touch after birth. HPV is persistent in the environment, including medical environments. It has been found on apparently sterilized instruments used in vaginal exams. Pathogenic HPV has been recovered from breast tissue, sinonasal areas, and nipples as well as from hair follicles on arms, legs, scalps, eyebrows, and pubic hair. Pathogenic HPV was found in 6.5% of the oral cavities of a random sample of Americans. HPV is known to cause anal and oral cancers. It has also been associated with skin cancers, breast tumors, and prostate cancers. It is not known if the vaccine is protective against these cancers, but it is useful to educate about these other routes of transmission and non-genital HPV linked cancers so that patients/parents do not just focus on the sexual nature of the human papillomavirus.

Key Word: HPV vaccine

Introduction

In June of 2006, the Federal Drug Administration approved a quadrivalent vaccine that protects against 4 strains of the human papillomavirus (HPV) for use among women and girls between the ages of 9 and 26. This vaccine offers protection against HPV types 6 and 11, which cause genital warts, as well as types 16 and 18, which are known to be oncogenic. The vaccine trials proved that this new immunization was highly effective in preventing infection with the 2 HPV strains known to cause approximately 70% of cervical cancers.¹ In 2009, a bivalent vaccine for types 16 and 18 was approved and the quadrivalent vaccine was approved for use among males. Release of these vaccines sparked hope that there would be rapid uptake and that a gradual decline in the number women with cervical cancer would ensue. To be most effective in preventing infection, the immunization series should be initiated prior to sexual debut. Therefore, the Advisory Committee on Immunization Practices (ACIP) recommends the routine vaccination of all females with 3 doses of the vaccine starting at age 11 or 12. Given that, in the United States, nearly 33% of 9th graders have already had sex, and almost 9% had first intercourse before the age of 13, this recommendation seemed more than reasonable.² There was also a recommendation that older girls and women aged 13-26 should be immunized. This means that counseling patients about the utility of the vaccine becomes the

province of pediatricians, gynecologists, and other physicians who see young female patients. Despite initial enthusiasm, the actual use of the vaccine in the United States has been less than ideal. The Centers for Disease Control and Prevention (CDC) estimated that by 2010 only 48.7% of females aged 13-17 have received ≥ 1 dose of HPV and 32% have received the necessary 3 doses.³ A study of Kaiser Permanente women over 17 years of age showed that they are only about half as likely to receive the vaccine as younger adolescent females while a national survey of women ages 18-24 indicated that only 9% had received 1 injection of the vaccine.^{4,5} Uptake among male patients has also been low.

This poor response to the vaccine represents a major lost opportunity to reduce the prevalence of pathogenic HPV strains, as well as to decrease the chance of benefiting from herd immunity.⁶ The potential impact of herd immunity arising from the vaccine can be seen by a study from Australia where a school based immunization program resulted in 72% of 14-15-year-old and 66% of 16-17-year-old girls being immunized by 2009.⁷ The study showed that among patients under 21 who appeared at the major sexually transmitted disease clinic in Melbourne, the rate of genital warts declined in women from 18.6% to 1.9% and from 22.9% to 2.9% among heterosexual men.⁸

Reasons for Poor Uptake

A number of reasons have been offered to explain the poor uptake of receiving the vaccine. The vaccine is costly; an estimated \$350-500 for the 3 shot series.⁹ An example of the impact of cost on uptake was demonstrated in a study that

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found girls with some form of health insurance were 3 times more likely to receive the vaccine.¹⁰ However, cost should not be an issue for the pediatric population because the vaccine is covered by the Vaccines for Children Program, which provides vaccines at no cost to children that are uninsured or underinsured through age 18.¹¹ While this may be a problem for those over 18, this concern should be less of a problem as the Affordable Care Act (also known as Obamacare) is implemented. Under its provisions, the HPV vaccine will be covered at no cost for insured women beginning in 2013.¹²

Failure to achieve high rates of immunization has also been associated with physician knowledge and behaviors. A 2006 paper found that only 46% of the pediatricians surveyed would recommend giving the HPV vaccine to their female patients ages 10 to 12.¹³ This is consistent with a 2009 survey of 287 pediatricians which found that only 47% of pediatricians reported that they always recommended the HPV vaccine to their 11 and 12-year-old patients. The same survey showed that family practitioners and obstetrician/gynecologists recommended it to this age only 34% and 36% of their patients. Overall the 3 specialty groups recommended the vaccine in all age groups \leq 53% of their patients.¹⁴ This may be due to lack of physician knowledge about the vaccine. In a 2009 survey on HPV knowledge of 1300 obstetrician/gynecologists, over 95% of whom said that they provided care to adolescent females, the respondents were asked to answer 3 questions about the HPV vaccine. These were “Gardasil protects against ___ forms of HPV that cause ___% of cervical cancer and ___% of genital warts.” Less than 30% of the respondents got all 3 questions correct and less than 50% correctly answered either of the last 2 questions.¹⁵ (The correct answers were 4 types, 70% of cervical cancers, and 90% of genital warts).

Acceptability and Concerns

One barrier to HPV immunization may be parental concerns about the vaccine, for both their sons and their daughters. There is limited information about the acceptability of the vaccine for boys. Two small convenience sample studies found that mothers are as likely to immunize their sons as they are their daughters.^{16,17} In contrast there are a large number of studies of the reasons for and against taking the vaccine in adolescent females. In most cases, the decision to vaccinate adolescents is made by mothers. This decision to approve HPV immunization has been shown to be connected to the mother's attitudes and behaviors. Sadigh et al¹⁸ found that women who had more lifetime male sexual partners were over 3 times more likely have their daughters immunized. There were also attitudinal enablers and barriers to mothers having their daughters immunized. Low levels of religiosity and a mother's acceptance of premarital sex among 18-year-olds were correlated with their daughters being immunized.¹⁹ Several studies have revealed that some parents are concerned that their daughters will become promiscuous if they receive the vaccine.^{19–21} This fear seems to be linked to religiosity; parents with frequent attendance at religious services were 3 times more likely than parents who do not attend services to have decided against vaccination.²² In

Calgary, Canada, the archbishop of the Catholic diocese has forbidden requiring the vaccine in Catholic schools because of this concern. While elsewhere in Canada, 70%–75% of teen girls are immunized, only 18.9% of Catholic school girls in Calgary have received the vaccine.²³ In addition some mothers are concerned that having their daughters immunized will be interpreted as giving their daughters permission to have sex or to practice unsafe sex.^{24,25} In some ways, this opposition is understandable in that most of the professional and public discussion of the need for the vaccine has been based on its protection against sexually transmitted diseases and on making certain that children receive the vaccine before sexual debut.^{26,27}

The studies on the impact of attitudes and behaviors of unimmunized individuals as they reach adulthood show that they have a number of concerns. In 1 study of 244 women between 18 and 24 years of age found that unimmunized women cited concerns about cost of the vaccine (27% of the sample), vaccine safety (22%), not needing the vaccine because they were not sexually active (19%), uncertainty about the effectiveness of the vaccine (16%), and my doctor does not think that it is needed (7%). Interestingly, 87% of the women said that they would take the vaccine if their doctor recommended it.⁵ This suggests an important educational and advocacy role for gynecologists as young women transition from pediatric care to adult care and become the decision makers about their own care.

The sexualization of the vaccine has created difficulties for providers in convincing their patients and their patients' parents of the need to be immunized. In addition there is evidence that vaccine messages that only target sexual transmission of HPV reduce the probability that sexually inexperienced, college age women will take the vaccine.²⁸ The continual emphasis on the sexual transmissibility of HPV has led to ignoring other potential routes of transmission. The genital focus of HPV dismisses the evidence that HPV is found elsewhere in the body and in the environment. The emphasis on the vaccine in prevention of cervical cancer overlooks evidence of other HPV-related malignancies. Furthermore, providers have had to deal with parental concerns about the safety of the vaccine. This paper will discuss the scientific evidence related to each of these issues.

Educating Patients and Parents

In counseling patients and their parents it is necessary to desexualize the vaccine. Parents may raise the issue of: “If I give my son/daughter the vaccine he/she will think it is o.k. to have sex.” There are no data to support the notion that vaccinated teens are more likely to have sex. Contrarily, since the introduction of the vaccine in 2006, the number of teens reporting that they have ever had sex and the number stating that they have had 4 or more sexual partners has remained constant.²⁹ In a national probability sample of 1243 women ages 15–24, it was found that those who had been given the HPV vaccine were not more likely to be sexually active or to have more sex partners.¹⁰ However, sexually active women who received the vaccine were 3 times more likely to always use a condom.⁹ Another study

showed that most adolescent females who received the vaccine did not perceive that they could cease practicing safe sex.³⁰ Most recently, a study of over 1300 girls found that the girls who received the vaccine at ages 11 to 12 were not more likely to have sexual activity-related medical conditions. During a 3-year follow-up period, the girls in this study who received the HPV vaccine were no more likely to have infections with chlamydia, or a positive pregnancy test.³¹ Women in their late teens or early twenties may also say that they are not having sex so that they do not need the vaccine. It should be pointed out to these women that it is the ideal time to be immunized before they have the chance to become infected and that their current level of sexual activity is not likely to last for the rest of their lives.

Parents may also raise the concern; “Why should I give my child a vaccine to protect against a sexually transmitted infection?” Patients in their late teens and early twenties may raise the same question about themselves. Clinicians must educate parents and patients that while HPV infection can be sexually transmitted there are other ways that it can be transmitted. Many studies have shown that HPV is transmitted vertically, from mother to child. A meta-analysis of 9 studies involving 2113 mother infant pairs showed a pooled risk of an HPV infected mother having an infected infant was 24.3%. Two of the 9 studies in the meta-analysis looked for only HPV types 16 and 18 and these studies revealed that 2.8% of infants born to mothers who tested negative for HPV were found to be positive for HPV types 16 or 18.³² Whether the transmission occurs in utero or at the time of birth is not clear. A study from Brazil showed that there was concordance between HPV types found in cord blood or the placenta and the serotype that was found in the infant after delivery.³³ The previously mentioned meta-analysis showed that infants who were vaginally delivered were 1.8 times more likely to be infected. Apparently, transmission may take place either before or during birth.³² There is also evidence that infants who are HPV negative at birth are found to be positive at older ages³⁴ with 1 study showing that 136 and 116 infants acquired oral and genital HPV respectively after having previously tested negative.³⁵ The route of transmission for this is not clear but is presumably from touch of the mother, although HPV type 16 has also been found in breast milk,³⁶ on nipples,³⁷ and in breast tissue.^{38,39} Whether HPV infections persist in children is not clear. A study of children who acquired HPV at birth or infancy showed that it did persist for 26 months in over 10% of the infected children.³⁵ However, HPV was only sought in the oral cavity and with genital swabs. So, it is possible there could be other locations where the virus is present or there could be a reservoir for these viruses elsewhere in the body. Further evidence of persistence of HPV in children is found in a Swedish study of 1031 children aged 0 to 13 years in Stockholm. HPV seroprevalence among these children was 3.0% for HPV16, 0.6% for HPV18, and 2.7% for HPV33 (another oncogenic subtype).⁴⁰ However, these children may have cleared the virus but been re-infected through contact with their parents.

The ability of either adults or children to clear the body of HPV is not known. The research in this area is confounded

by whether prevalence is measured by examination of cells recovered from various body locations, by actual recovery of the virus itself or by the presence of antibodies. Recovery of skin cells depends on the technique that is used, how extensive the swabbing used in the cell recovery is and which body sites are examined. Seroprevalence of antibodies may reflect infections that occurred recently or long before. This is very useful in determining incidence but is not necessarily a good measure of persistence of the virus. A meta-analysis of persistence in cervical lesions from studies of over 100,000 women showed that most women who had normal cytology at baseline but developed abnormal cytology subsequently managed to clear their cervical HPV infections within a year or so with median time of 12.4 months for HPV 16 and 9.8 months for HPV 18. Follow up periods in the reviewed studies were relatively short so it is not clear whether some HPV strains persist in some women for extended periods of time or whether what appears to be persistence merely reflects reinfection.⁴¹

A study of persistence of HPV in Danish male soldiers used penile swabs on a periodic basis to examine persistence. It was found that 31 of 73 HPV infected men cleared their HPV infections of the penis by 6 months after infection. However, most of these men were sexually active so the failure to clear may also indicate re-infection.⁴² A study of 1110 men from the United States, Mexico and Brazil used polymerase chain reaction and genotypic testing for HPV in the anus at baseline and 6 months later. Among men who have sex with men (MSM), 41.7% were infected with at least 1 oncogenic HPV type during the course of the study. Men who had sex with women (MSW) had a period prevalence rate of 9.0%. Sixteen percent of MSM had at least 1 oncogenic type at the anal canal that was persistent from baseline to the 6-month visit. This was only 1.6% for MSW.⁴³ However, it needs to be recognized that some of what appear to be persistent cases may actually be reinfections.

So, it is possible that HPV does persist in adults although these studies only examined genital areas. What appears to be clearance in these subjects may only reflect the disappearance in the sampled sites. The potential for a reservoir was found in a study that discovered that high risk HPV types could be found in the vas deferens of men who underwent vasectomies even though HPV could not be found in semen sera.⁴⁴

In study of 290 Finnish women who were followed for 36 months after their first post partum visit showed that there was little decay in HPV 6, 11, 16, and 18 antibodies. Seroprevalence of HPV 6, 11, 16, and 18 was 53.3, 21.5, 34.9, and 21.5% at baseline and antibody decay was observed in only 2.3, 4.0, 5.3, and 4.5% respectively in these women. Decay time varied from 27.2 to 35.8 months. This may be due to the persistence of the infection or due to the fact that they were being constantly infected by their sexual partners. The latter may be a more likely explanation in that HPV seroconversion rates during the period were 26.7% for HPV 6, 13.9% for HPV 11, 17.0% for HPV 16, and 16.8% for HPV 18.⁴⁵

Finally it can be pointed out to parents that their child has already been vaccinated against another virus that is often sexually transmitted – hepatitis B. The hepatitis B vaccine is given usually at birth and at 2 and 6 months of

age. It was first made available for children in 1984; however it did not become a routine part of the vaccine schedule in the US until 1991. So, almost all pre-adolescents have already been immunized against a virus that is sexually transmitted. Since 1991, rates of new hepatitis B infections have declined 82% in the United States. The decline has been greatest among children born since 1991, when routine vaccination of children was first recommended.⁴⁶ Chronic hepatitis B infection is the cause of about 80% of liver cancer worldwide with 1 study suggesting that Hepatitis B surface Antigen (HBsAg) carriers have a 273-fold higher risk of developing hepatocellular carcinoma.⁴⁷ In children, HBsAg is present in 100% of liver cancers. Taiwan implemented routine HBV vaccination in 1984, and within ten years child HBsAg carrier-rates declined from 10% to less than 1%.⁴⁸ Since vaccination of the infants has become the standard, rates of hepatocellular cancer have declined 75% in Taiwanese children 6–9 years old.⁴⁹ Parents may also say that; “My child is not having sex, why isn’t it o.k. to delay vaccination until he/she is old enough to have intercourse?” Parents may also argue that their daughters may never be a risk for cervical cancer because they may not engage in sexual activity until their marriage. Post-teen age women may make the same argument. The educational demand in this case is to point out that the vast majority of women are not virgins at the time of their marriage. In addition, it is highly unlikely that the person that they marry will be a virgin and that perfect marital fidelity is an ideal but not always a reality. This was illustrated by a study of 244 college women, all of whom were virgins at entry to the study. After they began having sex with their first male partner, 28.5% were HPV infected within a year and 50% were infected within 3 years. The risk for HPV infection increased if their partner had more lifetime partners.⁵⁰

In educating patients and parents about HPV transmission, clinicians need to dispel the myth that pathogenic HPV is only found on the genitals and in the anuses of men and women who have had penetrating sex. There is abundant evidence that HPV can be found elsewhere on the body. A recent study that collected specimens from a representative sample of Americans between the ages of 14 and 69 showed that HPV could be found in oral cavities of 6.9% of the sample.⁵¹ A study of 128 female university students demonstrated that HPV could be found on the fingertips of nearly 30% of these women during a study period that averaged 8 months.⁵² Another study found that 12 of 22 patients with genital warts also had similar HPV subtypes on their fingertips.⁵³ Pathogenic HPV has also been found in eyebrow hairs,⁵⁴ hair follicle samples taken from arms, legs, scalps, and eyebrows,⁵⁵ pubic hair,⁵⁶ breast tissue,⁵⁷ sinus areas,⁵⁸ and nipples.³⁷ Given that HPV is known to be transmitted by skin to skin contact, non sexual transmission is not only possible but quite likely. This is reinforced by an Italian study which found genital warts in 88 women with intact hymens who denied ever having sex.⁵⁹

There is also the potential of transmission from objects in the environment. Pathogenic strains of HPV have been recovered from surfaces in a genitourinary medicine clinic including examination lamps, treatment beds, and colposcope handles, cryoguns, and bed control switches.⁶⁰ These

strains have likewise been recovered from light switches and toilet seats in this clinic.⁶¹ HPV has also been recovered from the underwear of HPV infected women.⁶² Furthermore, there is the potential of nosocomial infections resulting from improperly decontaminated medical instruments including specula⁶³ and ultrasound probes.⁶⁴ HPV has a remarkable facility for surviving outside of the body and being resistant to decontamination procedures. Studies have shown that HPV can be recovered from surfaces as long as 7 days after being planted there.^{65,66} Attempts to eradicate HPV with heat to 56°C for 1 hour or use of ethylenediaminetetraacetic acid did not eliminate HPV in all samples.⁶⁶ Another study showed that cleaning with a “general purpose neutral liquid detergent” and water, or with a disinfecting detergent in 70% methylated spirits did not eliminate the virus from all contaminated surfaces.⁶¹ Another study attempting to eradicate HPV samples from ultrasound probes using “standard disinfection” was also unable to eliminate HPV in all cases.⁶⁶

A final area of education that needs to be done is to make certain that genital cancers are not the only cancer that is linked to HPV infection. It is true that HPV is associated with approximately 11,500 cervical cancers, 500 vaginal, 1600 vulvar, and 400 penile cancers each year. However, HPV is also strongly linked to approximately 4500 anal cancers with about 2900 of them in women.⁶⁷ Women who report having had anal sex are more likely to get anal HPV infections but HPV infection is also found in the anal canal of women who deny ever having anal sex. The latter may acquire the infection due to contact with the scrotum during vaginal sex⁶⁸ as the scrotum is a common site for infection with HPV.⁶⁹ As a result, the HPV vaccine is now approved for prevention of anal cancer and that fact can be emphasized in educating patients and parents.

HPV is also linked to 7400 cases of oropharyngeal cancer each year.⁶⁷ HPV has been found in squamous cell skin cancers at other locations on the body.⁷⁰ The rate of detection of various types of HPV in cutaneous squamous cell cancers in immunocompetent patients has ranged from 27% to 70%.⁷¹ Other studies have shown a much higher rate of oncogenic HPV types in skin tumors of individuals who are immunosuppressed from HIV or post-transplant medications, suggesting a role for HPV in the etiology of these tumors.^{72,73,74} These cancers have been found in the ungual and periungual areas,⁷⁵ toes,⁷⁶ oral cancers,⁷⁷ and the prostate.^{78,79} HPV has also been found in breast cancer tumors. A review of 20 studies from 19 different countries showed rates of HPV being found in breast cancer tumors that ranged from 0% to 86%.⁸⁰ It is not clear whether the presence of HPV is causative in any of these cancers but it is intriguing that the virus is found so often in these tumors.

Another parental and patient concern is about the safety of the vaccine. This concern may be linked to internet based warnings about not taking the vaccine.⁸¹ However, these warnings are not based on scientific data. The Center for Disease Control and Prevention Vaccine Safety Datalinks’s active surveillance looked at specific adverse events following more than 600,000 doses of Gardasil. These events were Guillain-Barré syndrome, stroke, venous thromboembolism, appendicitis, seizures, syncope, allergic

reactions, and anaphylaxis. No statistically significant increased risk for any of these adverse events was detected after vaccination. The CDC further reported that “Post-licensure safety monitoring from June 2006 through March 2012 continues to show no new HPV vaccine safety concerns.”⁸² A review of 5 clinical studies compared 11,778 subjects who received at least 1 dose of the HPV vaccine to 9686 persons who received placebo injections. Serious adverse events that occurred within 6 months of the injections were found in 0.9% of those receiving the vaccine vs 1.1% in the placebo group. In addition, it was found that other medical conditions were more likely to occur in the placebo group.⁸³ So, concerns about the safety of the vaccine seem to be related to the cult beliefs about the dangers of vaccines in general.

Advocacy

Obtaining parental and patient acquiescence to receipt of the vaccine can have a significant benefit to the patient and is strongly impacted by the attending physician. One study demonstrated that, if their physician strongly recommended the HPV vaccine, 19–26-year-old women were 3 times more likely to receive the vaccine than if the physician’s recommendation was lukewarm.⁸⁴ Pediatricians need to pre-empt and allay parental concerns about the vaccine being an inducement to promiscuity and about the safety of the vaccine when they advocate the vaccine. Clinicians who are counseling their patients and the parents of their patients about the importance of receiving the HPV vaccine not only have to talk about the sexual nature of HPV transmission but also have to emphasize the potential for transmission from other forms of skin to skin contact and from fomites. The discussion can also point out that there are approximately as many non-genital cancers linked to HPV as those associated with the cervix. In counseling patients, the vaccine should be described as a protection against skin and mucous membrane cancers and not just as protection against a sexually transmitted infection because there are more than sufficient data to believe that the infection can be transmitted by non-sexual means. It is crucial that parents and patients understand that this vaccine is more than a preventer of sexually transmitted disease. For, until the acceptance rate of the HPV vaccine becomes high enough to reach a level where we achieve herd immunity, we will never see the extraordinary reduction in transmitted HPV infections that has been achieved by the Australians.

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