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The HPV Vaccine Controversy

Karlie A. Intlekofer, PhD, Michael J. Cunningham, MS, and Arthur L. Caplan, PhD

The development of the human papillomavirus (HPV) vaccine provides an opportunity to prevent the majority of HPV infections that cause genital warts and cervical cancer. Although the vaccine is largely recognized as a medical breakthrough, its acceptance by the public is lagging for several reasons. Contributing factors include underestimation of HPV risk, the challenge of completing a three-shot regimen, concerns about cost, and parental barriers to acceptance. There is also some public concern about vaccine safety in general, although HPV vaccines have excellent safety records. Attempts to publicize the vaccine's safety have been undermined by recent erroneous claims linking the vaccine to mental retardation by political figure Michele Bachmann. These inflammatory and irresponsible remarks mislead the public about the safety and efficacy of the vaccine. We examine the facts concerning the HPV vaccine, its utility, and appropriate responses medical professionals can make to false claims.

Introduction

Among the most recent controversial vaccines are those developed to target HPV, a large category of at least 120 double-stranded DNA viruses. HPV is primarily known for causing *Condyloma acuminata* (genital warts) and is the most common sexually transmitted infection in the United States and worldwide [1, 2]. The prevalence of genital HPV infection is more than 10 percent among 15-49-year-olds in the United States [3]; however, most infections are cleared within 1 year [4, 5]. Although clearance yields natural immunity, individuals remain susceptible to other strains, and more than 40 of the 120 catalogued HPV types are implicated in the development of genital warts [6]. Approximately 90 percent of genital warts infections are caused by HPV types 6 and 11 [6-8].

More than 20 HPV types cause genital warts and also cause cervical intraepithelial neoplasia, a condition of abnormal growth that can progress to cervical cancer [9]. These high-oncogenic-risk types cause virtually all cervical cancers and most anal cancers [10], and some vulvar [11, 12], vaginal [13], and head and neck cancers [14]. Compared to the clearance rates of types 6 and 11, the oncogenic HPV types show delayed clearance [15-18], and together, oncogenic types 16 and 18 account for more than 70 percent of cervical cancers [19, 20]. Given the role of types 6 and 11 in genital warts and types 16 and 18 in cervical cancer, vaccination against these specific HPV types has been recommended [21] and in a few instances mandated [22].

Vaccine Safety

Cervical cancer ranks as the second most common cancer and the fifth leading cause of death of women worldwide [23]. In response to this serious health issue, more than 20 years of incremental research culminated in the development of HPV vaccines that elicit strong immunogenic reactions without the risk of causing infection [24-26]. Researchers achieved this through the recombinant expression of an HPV capsid protein that spontaneously self-assembles into virus-like particles [27]. These particles form into capsomeres that resemble HPV virions [28] but lack viral DNA; the capsomeres are combined with an adjuvant to elicit robust antibody responses, creating long-term immunity [27, 29, 30].

Vaccines are administered via three intramuscular injections spaced over 6 months. Results of several clinical trials show that vaccinated women remain free of HPV types targeted by the vaccine through the entire duration of the trial [25, 31, 32]. Importantly, the vaccine affords a high degree of protection against HPV infection that extends to protection from associated cervical lesions [33]. Ongoing studies are assessing the duration of protection.

Based on these findings, the FDA approved Gardasil, a quadrivalent vaccine against HPV types 6, 11, 16, and 18 licensed by Merck, in 2006 and Cervarix, a bivalent vaccine for types 16 and 18 made by GlaxoSmithKline, in 2009. Both have been approved and are in use in many nations [34, 35] In fact, the FDA reports that more than 65 million doses of Gardasil have been distributed worldwide [36].

Both HPV vaccines have strong safety records. The most commonly reported adverse events are pain and swelling at injection site [37, 38]. There has been no evidence that Gardasil or Cervarix administration increases rates of death, blood clots, or cognitive impairment. Even though these vaccines continue to generate excellent safety records, low coverage rates in the United States still leave many susceptible to the threat of cervical cancer and genital warts [39].

Maximizing Vaccine Efficacy

HPV vaccination only protects against HPV types to which the individual has never been exposed. Routes of exposure include skin-to-skin and sexual contact [40-42]. It follows that vaccination efficacy is maximized in individuals who are not yet sexually active and thus likely to be HPV-negative. Indeed, clinical studies fail to demonstrate any benefit to women previously exposed to HPV types covered by the vaccine [31, 43]. Acknowledging these facts, the FDA approved Gardasil and Cervarix for females aged 9-26 and 10-25, respectively, and the general consensus among health organizations in the United States and worldwide is for vaccination of girls aged 11-12 [21, 41-47].

Although most research addresses the vaccination impact on female health outcomes, optimizing HPV vaccine efficacy also requires immunizing males. The value of including both sexes in HPV vaccination programs is indirect, in reducing transmission rates to females [48], and direct through the individual protective

effects afforded by HPV vaccination. Males deserve access to a vaccine that can prevent the majority of cases of genital warts, especially considering that males often suffer longer duration of genital warts and incur greater treatment costs than females [49]. Furthermore, HPV is responsible for a wide range of cancers including 70-100 percent of penile intraepithelial neoplasia and 40-50 percent of all invasive penile cancers [50]. In recognition of these factors, the FDA approved Gardasil for the prevention of genital warts [51], anal cancer, and associated precancerous lesions in males in 2010 [36]. The prophylactic prevention of HPV infection is clearly warranted regardless of sex, and the vaccination of males is regarded as a cost-effective approach to reduce rates of HPV infection [52].

Finally, research indicates that nonsexual modes of HPV transmission include perinatal transmission from an infected mother [53]. Vertical transmission of the virus occurs primarily during vaginal delivery [54], but HPV can also infect infants delivered by caesarean section [55] and can be transmitted transplacentally to the fetus [56]. Newborns who acquire genital HPV infection may incur higher risks for genital dysplasia and cancer in addition to genital warts. The virus is just as likely to infect the oral mucosa of the newborn as the genitals [57], posing an additional risk of respiratory tract papillomas, which are the most common benign tumors of the larynx in infants and children [58]. Given the diverse manifestations of HPV infection, widespread vaccination coverage holds the potential to benefit a broad range of people.

Sexual Politics and Corporate Suspicions

Although the medical and scientific establishment has embraced the vaccine [59], HPV vaccination rates are inadequate in the United States [39]. Vaccine coverage is hindered by public perceptions regarding HPV's status as a sexually transmitted infection and dissent over the recommended age of vaccination [60]. Social conservatives have countered vaccine mandates with the argument that they infringe upon parental rights to discuss the topic of sex on their own terms [61]. Pro-abstinence activists raise similar concerns that HPV vaccination may increase teenage promiscuity [62], though there is no evidence for this claim [63]. Another suspicion is that HPV vaccine manufacturers have obtained FDA approval through corporate influence in lieu of proper safety testing [64-66]. Finally, several studies have shown that parents fail to vaccinate due to misperceptions about the risk of HPV infection [47].

Inflammatory False Claims

On September 12th, 2011, controversy over the HPV vaccine was reignited by the remarks of Republican presidential candidate Michele Bachmann during a debate. After denouncing an opponent's role in mandating HPV vaccination in Texas, Bachmann made unsubstantiated claims that the HPV vaccine was hazardous. During an interview with Fox News she told this anecdote:

There's a woman who came up crying to me tonight after the debate. She said her daughter was given that vaccine. She told me her

daughter suffered mental retardation as a result of that vaccine. There are very dangerous consequences [67].

Bachmann repeated this dramatic encounter during an interview on NBC's *Today* show [68]. These remarks were met with outrage by members of the scientific community, with multiple health and medical organizations denouncing their validity within days [69-71]. In jockeying for political gain, Bachmann disseminated false information to the detriment of public health. She made no attempt to apologize for her remarks or correct them. In fact, she reasserted her claims about the danger of the vaccine as recently as November 2011 [72]. As a public figure with access to an enormous audience, her promoting misconceptions that lead to higher risk for women, men, and babies is inexcusable.

Such events are likely to increase public distrust of vaccines and confusion, but the ultimate repercussions of Bachmann's charged rhetoric are not yet clear. Although few would argue that spreading blatant misinformation should be a punishable offense, false claims about vaccine risk can have deadly consequences when they discourage vaccination [73, 74], so they should not be ignored. To counter the effects of invalid statements, the public health sector must work even harder to educate the public in order to reach vaccination coverage. Whatever one's views on mandates or the cost of the vaccine, its excellent safety record and capacity to benefit human health make protecting the reputation of the HPV vaccine from damaging false claims worthwhile.

Studies show that the influence of accurate information about vaccines is maximized when conveyed from physician to parent or patient [75]. In prioritizing this approach over general health advertisement campaigns, physicians retain their position as patient advocates rather than agents of the government who must enforce policy. Research suggests that physicians are the most influential source of information about vaccines, including the HPV vaccine [76-78], for parents [79, 80]. In fact, some research shows that physicians' attitudes have a larger impact on immunization rates than the media coverage [81]. Ultimately, the decision to vaccinate a child must be based on an informative discussion between a parent and a physician, not on the erroneous claims of political candidates. When public figures imperil the safety of the public with irresponsible claims and fear mongering, it is imperative that both organized medicine and individual physicians speak up.

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Karlie A. Intlekofer, PhD, is a postdoctoral fellow at the Institute for Memory Impairments and Neurological Disorders at the University of California at Irvine. She researches the boosting effect of physical exercise on hippocampal neural plasticity and the therapeutic potential of exercise interventions on neurodegenerative disease and in normal aging.

Michael J. Cunningham, MS, is a first-year medical student at the University of Vermont College of Medicine in Burlington. He holds a bachelor of science degree and a master of science degree in neuroscience and behavior from the University of Massachusetts Amherst.

Arthur L. Caplan, PhD, is the director of the Center for Bioethics and the Sydney D. Caplan Professor of Bioethics at the University of Pennsylvania in Philadelphia. He co-directs the Center for Vaccine Ethics and Policy, which is a collaboration among

the Wistar Institute, the Children's Hospital of Philadelphia, and the Center for Bioethics.

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