Virtual Mentor
American Medical Association Journal of Ethics
December 2007, Volume 9, Number 12: 823-826.

POLICY FORUM
Should Human Papillomavirus Vaccination Be Mandatory?
Raphael P. Viscidi, MD, and Keerti V. Shah, MD, DrPH

The recognition that invasive carcinoma of the uterine cervix is the end result of some genital tract human papillomavirus (HPV) infections and the development of prophylactic vaccines to prevent these infections are major recent achievements of public health medicine.

The quadrivalent Gardasil HPV vaccine from Merck & Co., Inc., was licensed by the Food and Drug Administration (FDA) in June 2006 and was subsequently recommended by the Advisory Council on Immunization Practices (ACIP) for vaccination of adolescent girls and young women. Gardasil is designed to protect against infections with four of about 40 genital tract HPVs, types 16, 18, 6, and 11. HPV 16 and HPV 18 are responsible for about 70 percent of invasive cervical cancers and for a larger majority of the HPV-related cancers at other sites [1, 2]. Worldwide, about 500,000 cervical cancers annually and about 100,000 cancers at other sites, including vulva and vagina, anus, penis, and oropharynx, are attributable to genital tract HPV [1].

HPV 6 and HPV 11 account for over 90 percent of genital warts, which are very common, with millions of cases annually worldwide, and for nearly 100 percent of a rare disease, recurrent respiratory papillomatosis of juvenile or adult onset. A second HPV vaccine, Cervarix, is expected to be available in the U.S. in the near future. Cervarix, from GlaxoSmithKline, is a bivalent vaccine designed to prevent infections with the oncogenic HPV types 16 and 18 [3].

Both vaccines have been shown to be well tolerated, safe, and highly immunogenic in clinical trials [1-3]. Over a 4- to 5-year period of observation, they have been nearly 100 percent effective in preventing incident persistent infections and cervical intra-epithelial neoplasia by HPV types in the vaccine. Gardasil was also nearly 100 percent effective in preventing genital warts associated with HPV 6 and HPV 11. It is not yet known whether the vaccine will provide decades-long protection over the sexual life of a woman immunized when young, or a girl immunized in her preteen years.

It is anticipated that vaccinated women will have significantly fewer Pap smear abnormalities and therefore less need for treatment of cervical precursor lesions. Pap smear screening will still be required, but at lengthier intervals.

Because HPV is sexually transmitted, the vaccine is recommended for use in early adolescents prior to the initiation of sexual activity. The effort by several state legislators and aggressive lobbying by Merck to make the Gardasil vaccine mandatory for school attendance produced a backlash. The controversy has been comprehensively described in a recent issue of *CQ Researcher* [4].

Mandating vaccination as a public health policy measure has a long history in the U.S., dating back to the middle of the 19th century, and it invariably creates tension between public health policy and individual rights [3]. In the past 30 years, every state in the union has mandated vaccines for school-aged children. The most compelling case for doing so can be made when the vaccine prevents a serious infectious disease that is spread by casual contact in the age group for which it is mandated, and when that disease can be effectively controlled only by vaccination of a high proportion of the population. Examples of vaccines in this category are those that protect against polio, measles, mumps, rubella, diphtheria, and pertussis. Exemptions are available, but, if widely used, exemptions result in a lowering of what is called "herd immunity" and a resulting increase in disease incidence [4].

HPV vaccine does not meet the high threshold for mandating. HPV is spread by intimate sexual contact and therefore is not an epidemic infectious disease among school-aged children. Most infections are harmless, and screening methods (Pap smear and HPV testing) are available to identify individuals who are at risk of cervical cancer, which occurs 10 to 20 years following initial infection. Treatment of precursor lesions by minor surgical procedures is completely effective in preventing cervical cancer. Thus, there is no compelling public health rationale for mandating HPV vaccine in school-aged children.

Because vaccines are an economical and effective way to prevent many infectious diseases, mandates have sometimes been used more broadly, as in the instances of tetanus and hepatitis B. While a case for mandating HPV vaccine can be made on grounds of good medical and public health practice, the arguments against its use also have merit. The autonomy of the individual to make his or her own decisions about medical care can be disregarded only when the public health is threatened. While this might be the case during an influenza epidemic, for example, it is certainly not the case for HPV. Moreover, when the public health is not threatened, vaccine safety is of paramount importance.

Despite the promising results from clinical trials, the number of vaccinated individuals is still too small to exclude rare serious adverse effects, and more experience with the HPV vaccine is advisable before its mandatory use comes up for consideration. The availability of alternative strategies for detection and control of cervical cancer, discussed above, must also be factored in to the recommendation for the HPV vaccine. But these strategies are less economical than vaccination, potentially less effective, and medically and psychologically more burdensome for women.

The controversy surrounding the HPV vaccine has also raised questions about the appropriate procedures for making vaccination against a given illness or disease mandatory and about possibly restricting lobbying on the part of the manufacturer. While laws mandating vaccine use have to be passed by legislatures, and while manufacturers should be free to make the case for their product, recommendations are best made by state health departments after soliciting input from diverse sources.

The high cost of Gardasil is a deterrent for its use for many families. It has been suggested that Merck would profit substantially even if it cut the cost of Gardasil by 90 percent [5]. In any case, economic considerations should not drive the decision. Many existing government programs provide needed vaccines to children at low cost or no cost. Vaccines that are either mandated or "officially recommended" are covered by the federally funded Vaccines for Children program in the United States.

HPV vaccine provides us an opportunity to reduce the cancer burden for women in all parts of the world, however. We think the widespread use of the vaccine by men and women and availability of the vaccine in the developing world will be the best use of this resource.

References

1. Parkin DM, Bray F. Chapter 2: the burden of HPV-related cancers. *Vaccine*. 2006;24(Suppl 3):S11-S25.
2. Future II Study Group. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. *N Engl J Med*. 2007;356(19):1915-1927.
3. Paavonen J, Jenkins D, Bosch FX, et al. Efficacy of a prophylactic adjuvanted bivalent L1 virus-like-particle vaccine against infection with human papillomavirus types 16 and 18 in young women: an interim analysis of a phase III double-blind, randomised controlled trial. *Lancet*. 2007;369(9580):2161-2170.
4. Bristol N. HPV vaccine: should it be mandatory for school girls? *CQ Researcher*. 2007;17(18):409-432.
5. Malone KM, Hinman AR. Vaccination mandates: the public health imperative and individual rights. In: Goodman RA, Rothstein MA, Hoffman RE, et al, eds. *Law in Public Health Practice*. New York, NY: Oxford University Press; 2003: 262-284.
6. Offitt PA. Fatal exemption. *Wall Street Journal*. January 20, 2007:A10.
7. McGee G. How much should Gardasil cost? *Scientist*. 2007;21(8):26.

Disclosure

Keerti V. Shah, MD, DrPH, served in a scientific capacity on expert committees for GlaxoSmithKline and Merck that met one time each.

Raphael P. Viscidi, MD, is a professor of pediatrics in the Johns Hopkins University School of Medicine in Baltimore. He is an infectious diseases specialist with a primary research interest in human papillomavirus infections.

Keerti V. Shah, MD, DrPH, is a professor of microbiology and immunology in the Johns Hopkins University Bloomberg School of Public Health in Baltimore. He is a virologist with a primary research interest in human papillomavirus and polyomavirus infections.

Related in VM
Development of the Human Papillomavirus Vaccine and Guidelines for Its Use
January 2007