Programmatic issues in the implementation of an HPV vaccination program to prevent cervical cancer

Kevin Ault a,*, Keith Reisinger b

a Department of Gynecology and Obstetrics, Emory University School of Medicine, Atlanta, GA, USA
b Primary Physicians Research, Inc., Pittsburgh, PA, USA

KEYWORDS
Cervical cancer; Human papillomavirus; Screening; Vaccination; Cervical screening

Summary
Background: Cervical cancer remains an important health problem even in countries with effective cervical screening programs. HPV vaccines offer great potential for primary prevention of cervical cancer and other HPV-related diseases.

Perspectives: Eventual implementation of an HPV vaccination program raises several key issues, including universal vs. targeted vaccinations, the age and gender of vaccine recipients, the acceptability of this vaccine to health care providers, adolescents, and parents, and the effect of this vaccine on cervical cancer screening. These issues were explored among symposium attendees during an interactive question-and-answer session using computerized voting pads.

Conclusions: Preventative HPV vaccination programs should ideally be executed universally in both women and men with an emphasis on children and adolescents prior to their first sexual experience. Parent education on HPV disease and vaccine efficacy and safety will be critical to the acceptability of HPV vaccination for their children. HPV vaccination will not eliminate the need for Pap screening. Further research will be needed to develop rational and cost-effective cervical surveillance programs for women protected by HPV vaccines.

© 2007 International Society for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

Introduction
Late-phase clinical trials have generated a plethora of promising clinical data relating to the efficacy of human papillomavirus (HPV) vaccines to prevent cervical dysplasia and other HPV-related diseases (reviewed by Professors Frazer and Villa in this supplement). However, several key issues remain concerning the eventual implementation of an HPV vaccination program, including universal vs. targeted vaccinations, the age and gender of vaccine recipients, the acceptability of this vaccine to health care providers, adolescents, and parents, and the effect of this vaccine on cervical cancer screening. The purpose of this article is to explore these topics and briefly summarize feedback obtained from symposium attendees during an interactive question-and-answer session using computerized voting pads.

Universal vs. targeted vaccination
HPV infection is widespread with a lifetime risk of HPV infection for sexually active men and women estimated to
be more than 50%. As a result, it is impossible to identify an at-risk group to target for vaccination. Routine universal vaccination aims at reaching most potential carriers of any virus and, thus, is more likely to produce substantial reductions in HPV disease burden over the long term.

The hepatitis B immunization experience provides an interesting example of the benefit of universal vs. targeted vaccination (Figure 1). The Centers for Disease Control in the USA found that universal immunization of infants combined with "catch-up" immunization of adolescents for a limited number of years achieve the most rapid reduction of hepatitis B incidence. The hepatitis B immunization experience provides an interesting example of the benefit of universal vs. targeted vaccination (Figure 1). The Centers for Disease Control in the USA found that universal immunization of infants combined with "catch-up" immunization of adolescents for a limited number of years achieve the most rapid reduction of hepatitis B incidence.

Polling of the audience attending this symposium indicated that most (78.5%) agreed that preventive HPV vaccination should be performed on a broad age-range cohort, including all 9–10 year olds and 11–26 year olds as well as older individuals who could still benefit from vaccination. This view is consistent with the highest risk of HPV infection occurring in adolescents 15–19 years of age and the risk of HPV infection acquisition continuing throughout life. In a cohort of HPV-negative Colombian women 15–85 years of age, the highest five-year cumulative risk (42.5%) occurred among women 15–19 years of age, but risk in women 45 years of age and older was still high (12.4%).

Vaccinating both genders vs. females only

The greatest pathologic burden of HPV infection unquestionably occurs in women, but men serve as vectors for HPV transmission to women and develop a variety of HPV-related diseases such as genital warts and anal cancer. Since gender-specific vaccination programs, such as the rubella vaccination program that focused on vaccinating girls only were not effective, the clinical development program for the quadrivalent HPV vaccine also includes studies on the immunogenicity, efficacy, and tolerability in males. The audience overwhelmingly supported (78.9%) the contention that HPV vaccination should be administered routinely to both females and males.

Ideal age for vaccination

The choice of ideal age to vaccinate against HPV is influenced by the impact of age on the magnitude of the immune response to HPV vaccination and by the age of sexual debut of adolescents. As reviewed by Professor Frazer (this supplement), a robust immune response to a quadrivalent HPV vaccine occurs in children aged 9 through young adults aged 26. Immunogenicity bridging studies indicate that the greatest anti-HPV levels occur in prepubertal children (9 to 12 years). Since HPV infection often occurs within months after sexual debut, which can be less than 13 years of age for many adolescents throughout the world, it follows that maximum protection from an HPV vaccine would be expected to occur when children and adolescents are vaccinated prior to their first sexual experience. Vaccinating against HPV at this age would be compatible with the current adolescent immunization schedules for tetanus, diphtheria, polio, measles, mumps, and rubella in some countries, including the USA, UK, Germany, Spain, and France; however, variations from country to country do exist.

Approximately one third (32%) of symposium participants believed that the ideal age of the primary cohort for routine vaccination against HPV should be 9 to 10 years old. An additional third (32%) thought that the ideal age for vaccination should be 9 to 13 years old and a further 20% indicated that vaccination should take place across young people of all ages (9 to 26 years).

Importance of parent education on acceptability of HPV vaccination in young adolescents

While many consumers are not familiar with HPV and often confuse it with human immunodeficiency virus, parents nevertheless have high levels of interest in an HPV vaccine for their children. Understanding the key issues in parental acceptance of HPV vaccination of adolescents will be critical to the development and implementation of effective HPV immunization programs. According to studies conducted in the US, UK, and Mexico, parents are willing to vaccinate their children once they are properly informed about HPV; if they believe their children will likely be exposed to HPV; and if the benefits outweigh risks.

Several factors are important for parental acceptability of an HPV vaccine, including disease severity, vaccine efficacy, physician recommendation, and the parents' personal history of the disease. Not surprisingly, physicians' acceptance and communication about the vaccine appear to have the greatest influence in motivating parents to have their children vaccinated. Audience polling indicated that approximately 84% of attendees consid-
HPV vaccination complementary to a cervical screening program

Detection of early cervical cytological abnormalities using the subjective Papanicolaou (Pap) test is an effective tool in reducing (but not eliminating) the burden of cervical cancer. However, the Pap test has a number of technical limitations, including high false positive and false negative rates due to errors in interpretation, poor sample collection and poor slide preparation. In addition, even in countries with well organized Pap cytological screening programs, cervical cancer is still unacceptably high.

The development of HPV vaccines promises effective primary prevention of cervical cancer and has created a dilemma for healthcare policy makers about the future scope of cervical cancer screening. Two factors are relevant to screening programs. The first is that current HPV vaccines do not cover all the HPV types capable of causing cervical cancer. The second is that only vaccinees will be protected; thus, the full impact of HPV vaccination on cervical cancer will take many decades to evolve. While HPV vaccination may result in fewer referrals, fewer colposcopy procedures, and fewer clinic visits by preventing the low-level cervical dysplasia that would have been caused by the HPV strains in the vaccine. A majority of the audience concurred with this assertion, with 48% of attendees believing that cervical cancer screening will not change as a result of HPV vaccination.

Acknowledgements

Writing assistance for this paper was provided by Jan S. Redfern, PhD, Goshen, NY, and funding was provided by Merck & Co., Inc., Whitehouse Station, NJ 08889.

Conflict of Interest statement

Kevin Ault has done prior clinical research with Merck and GlaxoSmithKline concerning their HPV vaccines. He also has a current clinical trial with Merck. He has served on an advisory board with Merck.

Dr. Reisinger has been a speaker on behalf of Merck & Co., Inc.

References