

## Vaccination for Human Papillomavirus, Part 1: Why We Need It

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**H**uman papillomavirus (HPV) is an ubiquitous DNA virus that infects basal keratinocytes. More than 200 types of HPV have been identified, and approximately 20 types infect humans frequently.<sup>1</sup> HPV has been an important public health issue in the past 30 years because it is the primary cause of many precancerous and cancerous conditions in healthy individuals, including cervical intraepithelial neoplasia, cervical cancer, Bowen disease, and verrucous carcinoma of the penis. In immunocompromised patients, including those with transplants, HPV may cause squamous cell carcinoma of the head and neck. In children, HPV also is a cause of juvenile-onset recurrent respiratory papillomatosis (JORRP), a vertically transmitted infection manifested by papillomas of the respiratory passageway, resulting in respiratory distress.

The incidence of genital HPV in the United States is astoundingly high, with an estimated 10% of the population being infected. It is thought that more than half of sexually active individuals will become infected with HPV in their lifetime. Approximately 9710 new cases of cervical cancer are diagnosed each year and are the cause of 3700 deaths annually in the United States. Cervical cancer is the second most common type of cancer worldwide, with 470,000 new cases and 233,000 new deaths annually.<sup>2</sup>

The high numbers of patients with genital HPV are only surpassed by the cost of treatment of genital HPV-related diseases. A study looking at the cost of JORRP based on a database of cases in Maryland stated:

The annual cost for a single case of JORRP is \$57,996 (range, \$32,407–\$94,114). The annual cost of JORRP in the United States is between \$40 million and \$123 million

depending on the prevalence. Cesarean section for women with condyloma has been suggested as a potential strategy to prevent JORRP, but its efficacy remains to be determined. Our results suggest that if only 1% of the cesarean sections actually prevented JORRP, this strategy would be a cost-effective means to prevent JORRP.<sup>3</sup>

Intervention for abnormal Papanicolaou tests is less costly but still expensive; just pursuing enforced follow-up for those at high risk due to irregular Papanicolaou tests can cost \$681 to \$959 per patient.<sup>4</sup> Approximately 6.2 million Americans are infected with JORRP annually.

Vaccination against genital HPV has recently become a reality. Physicians may expect to successfully vaccinate patients, as 90% of cases of genital warts are caused by HPV-6 and HPV-11, and 70% of cases of cervical cancer are caused by HPV-16 and HPV-18.<sup>2</sup> HPV infects basal keratinocytes of the skin and mucous membranes through small breaks. Infection of the stem cells may result in warts, papillomas, or condylomas. Infection of resting cells may result in latent infection. The HPV virus has 72 pentamers; each pentamer is referred to as a viruslike particle. Viruslike particles are highly immunogenic<sup>1</sup> and vaccination with them, by many routes, has been shown to induce good anti-HPV antibodies.<sup>5</sup>

The first HPV vaccine (HPV quadrivalent [types 6, 11, 16, and 18] recombinant vaccine) was approved by the US Food and Drug Administration in 2006 in females aged 9 to 26 years.<sup>2</sup> A phase 2 study of the vaccine in 277 women (mean age, 20.2 years) who received doses of the vaccine at 0, 2, and 6 months demonstrated a 90% decrease in combined incidence of persistent infection or disease with HPV (types 6, 11, 16, and 18).<sup>6</sup>

Follow-up of a 2004 bivalent HPV-16 and HPV-18 (with ASO4 adjuvant absorbed) trial showed maintenance of seropositivity in more than 98% of patients (n=393 for the ASO4 vaccine group).<sup>5</sup> This vaccine

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has been approved in Australia and the Philippines, with recent submission to the US Food and Drug Administration of a Biologics License Application (March 29, 2007). Furthermore, incident infection prevention was more than 96% and 100% effective against cervical intraepithelial neoplasia, caused by HPV-16 and HPV-18, respectively. Related subtypes HPV-31 and HPV-45 also have been prevented, an outcome which had not been predicted in early vaccination literature.<sup>5</sup> These results are serendipitous indeed!

HPV vaccination is an important public health prevention strategy, and as dermatologists, we need to encourage our patients to obtain HPV vaccines for their long-term health.

*This editorial is the first of a 2-part series. The second part on public health aspects and strategies for HPV vaccination in the United States will appear in a future issue of Cutis®.*

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