HPV vaccination

Dear Editor

I would like to clarify two important points raised in the article 'HPV vaccination: a paradigm shift in public health' (*AFP* March 2007) which could be open to misinterpretation.

The statement that vaccination is 'indicated for males 9–15 years' could be misinterpreted to mean that HPV vaccine is recommended for use in this group. The 'indication' refers to the approval indications as registered with the Therapeutic Good Administration. This registration is based on safety and immunogenicity (ie. antibody response) data only. There are no clinical efficacy data to support its use in males at this time, but such data should become available in 2008. Unfortunately efficacy in males cannot necessarily be assumed, despite high antibody titres, because there are clearly significant differences in the structure of the male and female genital tracts and there is precedent of clinical efficacy of a genital herpes simplex type 2 vaccine only being demonstrated in females.[1] If patients request vaccination of males, GPs should explain the lack of efficacy data during tinformed consent.

Although the results cited for prophylactic efficacy of HPV vaccines are impressive, great care needs to be taken in extrapolating clinical trial results in HPV unexposed women to populations of sexually active women. Even among the total trial populations, who had no history of Pap abnormalities and <4–5 sexual partners, overall vaccine efficacy against cervical intraepithelial neoplasia (CIN) was limited – intention to treat analysis showed only a 12.2% reduction in any CIN2/3.[2] This was due to the presence of pre-existing HPV infections and the multiple HPV types that cause cervical dysplasia. So although the vaccine has been funded for women in Australia on the basis of acceptable cost effectiveness for the population overall, women who are sexually active before vaccination must be made aware that they may still experience Pap abnormalities and disease in the future. Otherwise we will see a generation of disappointed GPs and upset women who believe that the vaccine has failed them. This will be a particular problem given the lack of availability or existing clinical indications for type specific HPV DNA testing of diagnosed lesions. For this reason, type specific HPV surveillance and monitoring of linked HPV vaccine register and Pap test register data will be of great importance in the future in assessing the true impact of HPV vaccination.

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References

1. Stanberry LR, Spruance SL, Cunningham AL, et al. Glycoprotein-D-adjuvant vaccine to prevent genital herpes. N Eng J Med 2002;347:1652–61.
2. Centers for Disease Control and Prevention. Quadrivalent human papillomavirus vaccine. Recommendations of the Advisory Committee on Immunisation Practices (ACIP). MMWR 2007;56:1–24.

Reply

Dear Editor

The indication statement in the Gardasil Product Information clearly states that bridging immunogenicity studies have been conducted to link efficacy in females aged 16–26 years, to the younger male and female populations. This point was also made in *AFP* article. There is currently no efficacy data for the younger cohorts, 9–15 years, in the product information, and in addition, the company has clearly communicated that there are ongoing efficacy studies in males aged over 16 years.

My observation as a GP is that the success of the vaccination program will be hugely boosted if clinical efficacy data does support its use in boys and immunisation occurs for both boys and girls such as has occurred in rubella vaccination.

The issue about efficacy in sexually active women is a pertinent one. General practitioners need to ensure women understand the vaccine is not therapeutic. If a woman has been exposed to one of the vaccine HPV types before vaccination, the vaccine will not prevent infection or disease due to that type, but will confer protection against the types to which she is naive. Vaccinated women will continue to require cervical screening as the vaccine protects against cervical cancer due to HPV types 16 and 18. These types account for ~70% of cervical cancer cases.

The efficacy results quoted for the vaccine were in the per-protocol population, where the women were naïve to the relevant HPV types before vaccination. It is important to note that vaccination does not affect infection and/or disease present before immunisation. Over a longer duration of follow up, the magnitude of impact observed with the vaccine compared with placebo is expected to increase.

HPV vaccination is a first step toward a preventive approach to cervical cancer. Surveillance of both vaccinated and nonvaccinated women will be crucial in assessing the impact of vaccination on reducing the burden of both cervical cancer and precancerous abnormalities.

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