Routine vaccination against human papillomavirus

Publication on January 22 of guidance from the European Centre for Disease Prevention and Control (ECDC) on the introduction of human papillomavirus (HPV) vaccines in EU countries follows similar recommendations in June, 2006, from the US Advisory Committee on Immunization Practices. The reason for vaccinating against HPV infection is to prevent cervical cancer, the primary cause of which is persistent infection of the genital tract by so-called high-risk HPV types. The virus is transmitted during sexual contact. The authors of the ECDC report are firmly of the opinion that vaccination against HPV is an effective preventive strategy against cervical cancer. That high-risk HPV types are also associated with other anogenital cancers and head and neck cancers in men and women provides another spur for vaccination. What is the evidence behind the latest recommendations, and what concerns remain over routine vaccination against HPV?

Since we last wrote on the topic in January, 2006, results of phase III trials of the quadrivalent Gardasil (Sanofi Pasteur MSD) and bivalent Cervarix (GlaxoSmithKline) vaccines have been reported. Gardasil has been licensed in the USA and both vaccines are licensed in Europe. The recommended immunisation schedule for both vaccines is three intramuscular doses over 6 months. The evidence of efficacy is compelling. In young women aged 16–24 years who received at least one dose of Gardasil or placebo, vaccine efficacy was 95% for prevention of high-grade cervical precancers related to HPV 16 or 18 after an average follow-up of 3 years. Among young women aged 15–25 years who received at least one dose of Cervarix or placebo, vaccine efficacy was 90% for the same efficacy endpoints as Gardasil after mean follow-up of 14·8 months.

Because the vaccines prevent new infections with high-risk HPV types, girls aged under 15 years who are not yet sexually active would be the prime target group for routine vaccination. Therefore vaccine trials have been done in such girls, the endpoints of which have been immunological because cervical smear testing would be unethical. Trials among girls (and a group of boys) aged 9–15 years given Gardasil found that there was an excellent immune response, with at least 91% seropositive for the vaccine HPV types at 18 months of follow-up.

Cost-effectiveness of a routine HPV vaccination strategy is a crucial issue. Estimates of cost-effectiveness vary considerably depending upon the assumptions made in the model and the characteristics of national health systems. The ECDC report sets the bar for cost-effectiveness of a health intervention at below €40 000 per quality-adjusted life year saved. On this basis, the report concludes—after reviewing the available data—that a strategy of vaccinating adolescent girls plus continuing cervical screening has a cost-effectiveness at least as good as that of "other preventative or therapeutic interventions commonly applied". Additionally, the report concludes that, given available data, routine vaccination of boys would not ultimately prove cost effective.

Safety of the vaccines will be an important consideration for parents thinking about having their children immunised against HPV. The WHO advisory committee that reviewed safety data from trials and post-licensure surveillance for both HPV vaccines found no cause for concern. Pain, redness, and swelling at the injection site occurred in about 80% of study participants, and were significantly more common in the vaccine group than the placebo. Some mass sociogenic illnesses such as post-vaccination dizziness and syncope have been reported during adolescent vaccination campaigns in the USA; however, the WHO committee stated that these events were prevented by post-vaccination observation and encouraging good hydration. By the end of June, 2007, four deaths had been reported in the USA among girls who received Gardasil, but the Centers for Disease Control and Prevention concluded than none were caused by the vaccine. Data on the safety and efficacy of giving HPV vaccination at the same time as other immunisations are lacking, so it is wise not to do this until more research has been done.

Some parents will be concerned that vaccinating teenagers in some way condones sexual activity. This concern must be balanced against the fact that most sexually active people become HPV positive, whether or not they are virgins at the time of marriage.

We believe that there is solid evidence in favour of routine vaccination of adolescent girls against HPV, and that this policy should be supported by responsible governments. Because such a policy will take many years to have a public-health impact, cervical screening programmes must be continued for the foreseeable future. ■ *The Lancet Infectious Diseases*

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For more information on the **ECDC's guidance on HPV vaccination** see http://www.ecdc.europa.eu/pdf/HPV_report.pdf