Expanding the benefits of HPV vaccination to boys and men

We emphatically endorse the important arguments proffered by Kathleen Schmeler and Erich Sturgis (April 30, p 1798) regarding human papillomavirus (HPV) vaccination in men and boys. Two further points could have been made.

First, there is a growing number of patients who are susceptible to serious HPV-related morbidity, including cancer, because of acquired immunosuppression resulting from other diseases and their therapy. These patients include transplant recipients, patients with cancer, those with chronic inflammatory disorders treated with conventional and biological immunomodulatory drugs, and individuals with HIV (in whom, for example, the increased risk of oro-ano-genital cancer is well recognised). An opportunity is being lost to mitigate the prospective impact of HPV disease in these future patients by not currently vaccinating prepubescent boys.

Second, there is an unexploited scope for post-exposure prophylactic HPV vaccination in men and boys (as well as women and girls) in several populations, including those already mentioned. Our own interest is in men with HPV-driven penile pre-cancer and cancer, in whom we have been routinely recommending quadrivalent vaccination for years, based on a compelling rationale, indirect evidence from other groups (eg, women with cervical disease), and the safety and low cost of the vaccination. Clearly, direct evidence from randomised clinical trials would be the gold standard, but the rarity of HPV disease (in whom, for example, the increased risk of oro-ano-genital cancer is well recognised). An opportunity is being lost to mitigate the prospective impact of HPV disease in these future patients by not currently vaccinating prepubescent boys.

Defective interfering genomes and Ebola virus persistence

Michael Jacobs and colleagues (July 30, p 498) provide clinical and virological evidence of a relapse of Ebola virus disease (EVD) presenting as acute meningo-encephalitis 9 months after recovery from an acute infection. However exceptional, this case adds to an increasing number of reports suggesting that Ebola virus can persist for months in immune-privileged anatomical sites, such as semen, ocular tissues, breastmilk, and the central nervous system. In such cases, unknown immunological dysfunctions certainly play a part in delaying the clearance of Ebola-infected cells. However, immune tolerance itself does not explain how the virus can persist without causing cytopathic effects. Many, if not all non-segmented negative strand RNA viruses (such as measles virus and Ebola virus) can generate copy-back defective-interfering genomes (cbDIs) in cell culture infections. cbDIs interfere by competing with the replication of their non-defective (wild-type) helper genome, presumably because they contain the stronger trailer replication promoter on both their genomes and anti-genomes. This competition attenuates a cytopathic wild-type virus infection and promotes persistence. The most prominent example of cbDI involvement in natural persistent infections is that of measles virus in the brain cells of patients with subacute sclerosing panencephalitis. In-situ hybridisation of brain slices found that the trailer region of the measles virus genome was strongly over-represented relative to the leader region, which is characteristic of the presence of cbDIs. Using a PCR-based amplification specific for cbDIs, abundant, discrete cDNAs of cbDIs were generated from the brain of each patient with subacute sclerosing panencephalitis.

We declare no competing interests.

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References