

S18. HPV vaccination and other approaches to prevent cervical cancer

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The establishment of sexually transmitted human papillomavirus (HPV) infections as the central cause of cervical cancer provides an exceptional opportunity for cancer prevention by preventing oncogenic HPV infections. Prophylactic HPV vaccines are based primarily on induction of virion neutralizing antibodies by non-infectious virus-like particles (VLPs) composed of assemblages of the L1 major capsid protein. In clinical trials, Merck- and GSK-produced VLP vaccines have consistently induced high titers of neutralizing antibodies with minimal side effects and induced complete, or nearly complete, protection from incident type-specific persistent infection and cervical dysplasia by HPV16 and HPV18, the major oncogenic types. The Merck vaccine is also highly effective at preventing genital warts. However, vaccination of women with prevalent infections did not increase the rate of clearance. The Merck vaccine was recently approved by regulatory agencies in over 80 countries and GSK vaccine was recently approved in the

EU and Australia. Important questions remaining include duration of protect and degree of cross-protection against other related genital HPV types. The high cost of VLP vaccine production and distribution will be impediments of particular concern for vaccine implementation in developing countries, where 80% of cervical cancer occurs. Second-generation vaccines to address these limitations are under preclinical development, including live L1 recombinant *Salmonella* Ty21a, and *E. coli* produced L2 vaccines that induce broadly cross-neutralizing antibodies. To evaluate other measures to prevent genital HPV infections, we have developed the first murine cervicovaginal challenge model for HPV, based on HPV pseudovirions transducing a marker gene plasmid. In this model, nonoxynol-9, the active ingredient in most over-the-counter spermicides, greatly potentiated HPV infection. However, HPV infection was prevented by carrageenan, a gelling polysaccharide used in some sexual lubricants, even in the presence of nonoxynol-9.