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Review

Comprehensive Control of Human Papillomavirus Infections and Related Diseases

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ABSTRACT

Infection with human papillomavirus (HPV) is recognized as one of the major causes of infection-related cancer worldwide, as well as the causal factor in other diseases. Strong evidence for a causal etiology with HPV has been stated by the International Agency for Research on Cancer for cancers of the cervix uteri, penis, vulva, vagina, anus and oropharynx (including base of the tongue and tonsils). Of the estimated 12.7 million new cancers occurring in 2008 worldwide, 4.8% were attributable to HPV infection, with substantially higher incidence and mortality rates seen in developing versus developed countries. In recent

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Vulvar cancer
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years, we have gained tremendous knowledge about HPVs and their interactions with host cells, tissues and the immune system; have validated and implemented strategies for safe and efficacious prophylactic vaccination against HPV infections; have developed increasingly sensitive and specific molecular diagnostic tools for HPV detection for use in cervical cancer screening; and have substantially increased global awareness of HPV and its many associated diseases in women, men, and children. While these achievements exemplify the success of biomedical research in generating important public health interventions, they also generate new and daunting challenges: costs of HPV prevention and medical care, the implementation of what is technically possible, socio-political resistance to prevention opportunities, and the very wide ranges of national economic capabilities and health care systems. Gains and challenges faced in the quest for comprehensive control of HPV infection and HPV-related cancers and other disease are summarized in this review. The information presented may be viewed in terms of a reframed paradigm of prevention of cervical cancer and other HPV-related diseases that will include strategic combinations of at least four major components: 1) routine introduction of HPV vaccines to women in all countries, 2) extension and simplification of existing screening programs using HPV-based technology, 3) extension of adapted screening programs to developing populations, and 4) consideration of the broader spectrum of cancers and other diseases preventable by HPV vaccination in women, as well as in men. Despite the huge advances already achieved, there must be ongoing efforts including international advocacy to achieve widespread—optimally universal—implementation of HPV prevention strategies in both developed and developing countries.
This article summarizes information from the chapters presented in a special ICO Monograph '*Comprehensive Control of HPV Infections and Related Diseases*' Vaccine Volume 30, Supplement 5, 2012. Additional details on each subtopic and full information regarding the supporting literature references may be found in the original chapters.

1. Global prevention and management of HPV related diseases: the pressing challenges and the compelling opportunities [1]

1.1. Introduction

The scientific community has gained tremendous knowledge about human papillomaviruses (HPVs) and their interactions with host cells, tissues and immune systems; has validated and implemented strategies for prophylactic vaccination against HPV infections; has developed increasingly sensitive and specific molecular diagnostic tools; and has substantially increased global awareness of HPV and the many associated diseases of women, men, and children. In so doing, we have come up against new and daunting challenges: costs of HPV prevention and medical care, the implementation of what is technically possible, the diverse societal standards around the globe concerning reproductive health, and the very wide ranges of national economic capabilities and health care systems. HPV is one of the few agents causing disease and cancer where the emerging opportunities for prevention have encountered some socio-political resistance, the nature of which depends on country and culture. In addition, there has been a resistance for policy makers, funding agencies and corporate stakeholders to discount the need for significant new developments, particularly in the arenas of therapeutics and affordable interventions. An expanded repertoire of health care options is urgently needed to bring HPV under short-term management and long-term elimination. Thus, we are at crossroads that will require thoughtful discussions, compassionate decisions and concerted actions.

1.2. Appreciation of disease causality and need for management

There is inadequate recognition of the social impact of the successive stages of HPV infections: the infants who acquire low-risk HPV types 6 and 11 and develop recurrent respiratory papillomatosis (RRP); the adolescents with benign but highly contagious infections; the middle aged with consequences on reproductive capabilities and well being of the mother; the older persons with an increasing risk of cancer. Of the major cancers of women, cervical cancer tragically results in the most years of life expectancy lost (estimated at 29 years), considerably more than for women succumbing to breast cancer. This places an exceptional—and avoidable—burden on young families, and to a very serious degree on children who lose their mother. Yet these facts have not moved sufficiently into the public discourse. There is also a troubling disjunction between the popular culture, celebrities, and the media, entertainment and fashion industries, which popularize sexuality and beauty versus the need for candid and frank discussion about sexual health and the impact of sexually transmitted infections. The biological reality is that early age exposure to and frequent reinfection with mucosotropic HPV types can have serious long-term outcomes in the form of future cervical, penile, vulvar, vaginal and anal cancer, RRP and certain head and neck afflictions.

1.3. The success and promise of prophylactic vaccines

The quadrivalent and bivalent HPV vaccines have proven to be very safe, with long-term durability of protection against primary infection with vaccine types and a moderate degree of cross-protection against some non-vaccine types. Next-generation vaccines targeting additional oncogenic genotypes are completing clinical trials.

Childhood vaccination programs are nearly universal. However, there are few effective strategies for vaccinating pre-adolescents, the currently recommended age for HPV vaccination. A good case can be made for clinical trials to evaluate vaccination at younger ages, within the schedules of pediatric vaccination against other common viral infections to improve coverage and to eliminate the negative rhetoric about the vaccines possibly altering sexual behavior. The significantly stronger immune response to the HPV vaccines at younger ages, compared to adolescents, combined with the durability of protection from infection that is becoming demonstrable, and the small but real risk of HPV infection of children as a result of abuse, together suggest that early vaccination of toddlers could become good public health policy.

1.4. A range of diagnostic methods

Diagnostic screening for HPV lesions is generally available in the developed world but scarce everywhere else for lack of public health policy, professional and general education, media awareness, clinical settings, financial resources and, most crucially,