HPV vaccine for primary prevention of cervical cancer in developing countries: The missing links

Almost half a century of sustained public health programme for cervical cancer screening with cytology and effective treatment of early pre-cancers and cancers has resulted in a major reduction in mortality from cervical cancer in western countries. This disease however continues to kill a quarter of a million women every year globally. Since 80% of the global incidence of half a million cervical cancers is in low and middle income countries, any scientific or technological advancements with a potential for primary or secondary prevention of this cancer need to be evaluated from the public health perspective of these countries.

Human Papilloma Virus (HPV) infection of the genital tract is the most common sexually transmitted infection and is usually transient. Persistent infection with a high-risk oncogenic variant of HPV (type 16, 18 and a few other types) could however result in a precancerous cervical lesion, which if left untreated may progress to become invasive cervical cancer over the next few decades. Translating findings from laboratory and epidemiological research confirming the causative role of HPV in cervical cancer to clinical development of a vaccine to prevent HPV infections and high risk cervical precancerous lesions can be considered as a benchmark in translational cancer research. We are at the crossroads where we need to understand and overcome obstacles in translating this scientific breakthrough into a public health success, especially in low and middle-income countries, which ironically bear the brunt of this disease. Until we have effective therapeutic vaccines to clear established HPV infections, the currently available vaccines would be useful if girls were to be immunized against the prevalent oncogenic HPV types before or at the time of their sexual debut. The challenges are therefore not limited to scientific issues of refining and improving vaccines and demonstrating their long-term efficacy and safety, but also to integrate them in the public health programmes of countries with stark differences in resource availability, socio-cultural attitudes and practices. For the HPV vaccine to achieve its full potential as a public health tool against cervical cancer, the community of biomedical researchers, social scientists and policy makers in the field of cancer need to enter uncharted territories such as female adolescent health and sexual behavior; cultural diversities and sensitivities; programmatic challenges in universal immunization; and cost-effectiveness.

The World Cancer Declaration 2008 made during the recent Geneva World Cancer Congress has not only advocated affordable screening programs but also makes a plea to "undertake actions to ensure that vaccines and other strategies that are shown to prevent cancer causing infection are made more widely available". While the last century has witnessed a spectacular success of vaccines in the primary prevention of a wide range of infectious diseases, the rate at which such success was achieved, or is likely to be achieved, shows marked geographical variation. Despite decades of concerted and well-funded global efforts, many developing countries are yet to realize the expected dividends of their long running national programs for immunization against crippling or fatal common childhood infections. Against this background it may seem unrealistic to expect public health success from immunization of adolescent female population to prevent cervical cancer, a relatively less common disease which may affect them after a few decades and about which these teenage girls and their families have very little or no knowledge. Worse still, ill conceived attempts may prove to be counterproductive if they divert significant resources from nascent cancer control programs; instill a false sense of security; or alienate communities by communicating risks of sexually transmitted infection in adolescent girls in a culturally insensitive manner. Faced with such realities shall we concede that available HPV vaccines cannot be strategically integrated in the public health program for cancer in low-income countries? Or should we unravel the missing
links to bring about synergy between global partners, biotechnologists, industry and governments in order to capitalize on this scientific breakthrough for the benefit of women in low-income countries who are at the highest risk for dying from this common cancer?

In anticipation of two HPV vaccines becoming available in 2006 – 2007, the World Health Organization and UNFPA in 2006 under technical consultation on HPV vaccines and sexual and reproductive health programmes published “Policy and programme guidance for countries - Preparing for the introduction of HPV vaccines”. This document discusses the opportunities, challenges and possible approaches towards integrating HPV vaccines in cancer control programmes in low and middle income countries, emphasizing the potential to build synergy between immunization, cancer control and sexual and reproductive health programmes. Regarding advocacy and communication strategies for HPV vaccines, this WHO guidance has a cautionary note “to ensure that complementary messages about delay of sexual debut, condom use, HIV risk reduction, and cervical cancer screening and treatment are clearly articulated and evaluated during the introduction process”.

Presently the market cost for vaccinating a girl with the recommended 3 doses of HPV vaccine is $360. In a review of cost-effectiveness of the HPV vaccine at the Geneva Congress, it was estimated that the HPV vaccine could be cost effective even in the poorest countries of the Asia-Pacific region, which has over half of the world’s cervical cancers, by bringing down the cost per vaccinated girl to the range of $10 – 25. The WHO guidance document acknowledges that the cost of HPV vaccine would be an obstacle and discusses various avenues including differential pricing between high and low income countries; international financing through Global Alliance for Vaccines and Immunization (GAVI) or UNICEF; and private-public partnership. Nodal government agencies responsible for health, biotechnology and science in India and some other developing countries have initiated a broad range of biomedical research to develop and evaluate vaccines which would either be more suitable for the oncogenic HPV types prevalent in their region or potentially more cost effective.

We need continued research to develop more effective or therapeutic vaccines and at a much lower price; programmatic evaluation of pragmatic delivery and communication strategies; twinning of immunization with screening and reproductive health; and finally establishing long term safety and efficacy data. It would be very difficult to predict how long it may take for this biomedical breakthrough to succeed in the public health domain in countries with the maximum burden of disease. However, if policy makers, governments and communities across the world become true advocates and partners, we can dare to attempt elimination of this cancer in the first half of the 21st century. Science and society would rejoice if vaccines could do for cervical cancer what they have done for many other infectious diseases.