

EDITORIAL

The major breakthrough of the 21st century- HPV Vaccine



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Cancer cervix is killing millions of woman worldwide, ½ a million 500,000 develop cancer cervix every year of which 50% die. Of the cancers that develop every year 80% are in developing countries Worldwide, both incidence and mortality from cervical cancer are second only to breast cancer, and in parts of the developing world, cervical cancer is the major cause of death in women of reproductive age. It forms 6% of the genital malignancies. The unfortunate reality of this disease is that in spite of its being completely preventable, we have not yet been able to prevent it.

Of the more than 100 known HPV types, infection with sexually transmitted HPVs is very common in adult populations worldwide. HPV is a double-strand DNA tumor virus that belongs to the papovavirus family (papilloma, polyoma, and simian vacuolating viruses). Of the 100 types of HPV, of which about 25 infect the genital tract. Although a few HPVs, such as types 6 and 11, can cause genital warts, most genital HPV infections come and go without ever causing any symptoms. However, lingering infections with a subset of about 19 “high-risk” HPV types can lead to the development of cervical cancer or other genital/anal cancers, and some forms of HPV, particularly type 16, 18, 31, 33 and 35 are more likely to have cervical intraepithelial neoplasia (CIN) or micro invasive histopathology on biopsy. ¹ Among 16, 18, 31, 33 AND 35HPVs, type 16 (HPV-16) is most commonly linked with cancer, since it is present in 50 percent of cervical cancers and high-grade cervical intraepithelial neoplasias.

There is no effective medical treatment against HPV. Traditional approaches to removing these lesions have centered on destruction of the neoplastic epithelium and careful cytological follow up. This approach has met success in preventing cancer, but has not addressed patients who present with invasive cancer whose pre cancer yet undiscovered. Not only sensitive and specific tests for the detection of HPV DNA in cervical

cells are now available but at Georgetown University Medical Center’s Department of Pathology, after long trail of HPV research, the major breakthrough of the 21st century- vaccine against human papillomavirus (HPV) was developed in the late 1980s by researchers under the leadership of professor Fraser at Georgetown University Medical Center, the University of Rochester, Queensland University in Australia, and the U.S. National Cancer Institute. Manufactured as Gardasil and Cervarix by Merck and co and Glaxo SmithCline. The discovery of vaccine shows great promise for controlling the spread of and the fight against main types of HPV that cause cervical cancer.

HPV vaccines are designed to elicit virus-neutralizing antibody responses that prevent initial infection with the HPV types represented in the vaccine. The vaccines have been shown to offer 100 percent protection against the development of cervical pre-cancers and genital warts caused by the HPV types in the vaccine, with few or no side effects. The protective effects of the vaccine are expected to last a minimum of 4.5 years after the initial vaccination.²

(LPs) The latest generation of preventive HPV vaccines are based on hollow virus-like particles (VLPs) assembled from recombinant HPV coat proteins. The vaccines target the two most common high-risk HPVs, types 16 and 18. Together, these two HPV types currently cause about 70 percent of all cervical cancer. Gardasil also targets HPV types 6 and 11, which together currently cause about 90 percent of all cases of genital warts.³ The immunogenicity of papillomaviruses involves presentation to the immune system of conformational epitopes displayed on viral capsids composed of L1 protein. Empty viral capsids, termed “virus-like particles,” are synthesized with the use of microbial or cellular expression systems. Vaccination with L1 virus-like particles derived from species-specific papillomaviruses neutralizes virus and, in animal models, protects against the development of lesions.

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A three-dose regimen day 1, Month 2, and Month 3, given in a series of three shots over six months. The vaccine protects against four strains of HPV responsible for 70% of cervical cancers and 90% of genital warts cases. With widespread use, HPV vaccination has the potential to lower the occurrence of cervical cancer in future generations.

The HPV vaccine is most effective when administered to girls and women before the onset of sexual activity. While the US Food and Drug Administration has approved the vaccine for girls and women ages 9 to 26, The US Food and Drug Administration (FDA) approved Gardasil on June 8, 2006. The drug is also approved for use in Australia, New Zealand, Canada, Mexico, Croatia, Malaysia, Brazil, Serbia and countries of the European Union.

The federal Advisory Committee on Immunization Practices, The Advisory Committee on Immunization Practice, gave their approval on June 29, 2006 for the vaccination of Gardasil on children as young as nine years old. The ACIP recommend that Gardasil be placed on the childhood immunization schedule at eleven to twelve year old. They also recommend that vaccine be given free of charge to children under eighteen who are uninsured.

The national Cancer Institute, US state “Widespread vaccination has the potential to reduce cervical cancer deaths around the world by as much as two-thirds, if all women were to take vaccine and if protection turns out to be long term.”

American Centre for Disease Control says, getting as many girls vaccinated will reduce cases of cervical cancer among women in 30-40 years and reduce the transmission of this highly communicable disease.

The American College of Obstetricians and Gynecologists (ACOG) recommends that teens first visit an ob-gyn between the ages of 13 and 15. ACOG released clinical recommendations September 2006 for females ages 9 to 26 for the human papillomavirus (HPV) vaccine. Obstetrician-gynecologists should be proactive in educating patients about the vaccine so that as many women as possible are able to take advantage of this medical milestone,” said ACOG President Douglas W. Laube.

Women who previously have had abnormal cervical cytology, genital warts, or precancerous lesions can be vaccinated. Those with suppressed immune systems also can be vaccinated, although the protection may be less than that of patients with normal immune function. The HPV vaccine is not a treatment for current HPV infection or genital warts. Patients undergoing treatment for HPV-related symptoms (cervical cytology abnormalities, genital

warts) should continue with their prescribed medication and therapy.

While the vaccine has not been shown to have a harmful effect on pregnancy, it is not recommended that pregnant women be vaccinated. If a woman discovers she is pregnant during the vaccine schedule, she should delay finishing the series until after she gives birth. Women who are breastfeeding can receive the vaccine.

In early studies, the HPV-16 L1 virus-like-particle vaccines were generally well tolerated and generated high levels of antibodies against HPV-16. FDA and CDC trials have shown that this vaccine is safe and do not have major side effect, except soreness around the injection site. However one unknown property of the vaccine is that whether the vaccine can last its immunogenicity for long or just a few years. Another issue which is of concern is the cost, the three shots each \$120, the total of \$360. Another concern is vaccination could “promote promiscuity” but arguably enough there is no evidence suggesting a connection between a decrease in HPV and an increase in sexual activity.

HPV Vaccine has shown promising results are designed to elicit virus-neutralizing antibody responses that prevent initial infection with the HPV types represented in the vaccine. The vaccines have been shown to offer 100 percent protection against the development of cervical pre-cancers caused by the HPV types in the vaccine, with few or no side effects. The prevention of these cervical precancerous lesions is believed highly likely to result in the prevention of those cancers. It would be very fortunate if our female population in developing countries could take this vaccine, the great discovery of Professor Fraser, the major breakthrough of the 21st century as we know that we are lacking in early detection and effective treatment of this preventable cancer and millions of cervical cancer related deaths are reported every year.

References

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