



C-Gyn 18

Guidelines for HPV vaccine

Cervical cancer is one of the leading causes of cancer morbidity and mortality in women throughout the world. Persistent infection with oncogenic Human Papilloma Virus (HPV) is associated with the development of cervical cancer. Infection with oncogenic HPV types is also implicated in the development of other cancers, including neoplasms of the vulva, vagina, anus and penis. Of the oncogenic HPVs, types 16 and 18 account for some 70% of cervical cancers. Non-oncogenic HPV types cause genital warts. HPV infection is common with an estimated 70% of sexually active women becoming infected.[1-3] Vaccination to prevent infection with oncogenic HPV types has the potential to reduce the incidence of precursor lesions and cervical cancer.[4]

Two products for vaccinations are available in Australia and New Zealand, Gardasil and Cervarix*.

Recommendations

Vaccination of Girls, Adolescents and Young Women

- The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) recommends the vaccination of females aged 9–26 years against HPV, with the initial vaccination target of females aged 11 or 12 years.
- Both Australia and New Zealand have initiated National HPV Vaccination Programs, which are endorsed by the RANZCOG.
- The Australian program funded free HPV vaccination for all women aged 12 to 26 years. The catch-up program for schoolgirls concluded at the end of 2008 and the program for young women concludes at the end of 2009. On an on-going basis, 12 year old Australian girls will receive free HPV vaccination in the first year of high school. (Insert Ref below: <http://www.health.gov.au/cervicalcancer>)
- In New Zealand, the vaccine is available free to girls and young women born after 1 January 1990. From 1 September 2008, young women born in 1990 or 1991 have been able to get the vaccine from their doctor, practice nurse or health clinic. Young women born in 1990 or 1991 have until 31 December 2011 to start the immunisation programme. From 2009, most girls and young women attending year 8 and upwards at school (approximately 12 to 18) will be offered the vaccine at school. (Insert Ref below: <http://www.cervicalcancervaccine.govt.nz/>)

Vaccination of Sexually Active Women

- Sexually active women can receive the HPV vaccine.
- Women with a history of previous HPV infection will most likely benefit from protection against disease caused by the other HPV vaccine genotypes with which they have not been infected.

- The need for continued cervical cytology screening according to recommended national policies should be emphasised.

These patients should be counselled that the vaccine may be less effective in women who have been exposed to HPV before vaccination than in women with no prior HPV exposure at the time of vaccination.[5]

Cervical Cytology Screening

- Current cervical cytology screening recommendations remain unchanged and should be followed regardless of vaccination status.[7]
- The vaccine is a preventive tool and is not a substitute for cancer screening. Both vaccines protect against future acquisition of HPV genotypes that account for approximately 70% of HPV-related cervical cancer worldwide and screening should be continued to cover the remaining oncogenic types. [1-3]

Human Papillomavirus Testing

- There is no practical or reliable method for screening for HPV susceptibility prior to consideration of vaccination.
- Testing for HPV is currently not recommended before vaccination.
- Testing for HPV DNA is not usually type specific and would not identify past HPV infections, only current HPV infections.
- Serologic assays for HPV are unreliable and currently not commercially available. Requiring any type of screening test would raise the cost of vaccination programs dramatically and reduce the cost-effectiveness of vaccination.
- There is currently no public health benefit in recommending screening for HPV prior to HPV vaccination.

Vaccination of Women with Previous Cervical Intraepithelial Neoplasia

- Women with previous abnormal cervical cytology or genital warts also can receive the HPV vaccine. There is no practical method for determining the specific HPV type associated with these lesions.
- There is concern that provision of the vaccination to women with previous cervical intraepithelial neoplasia may create a false sense of protection, potentially deterring patients from continuing their regular screening and management.
- The vaccine can be given to patients with previous cervical intraepithelial neoplasia, but practitioners need to emphasize that the benefits will be limited to future HPV exposure. Cervical cytology screening and corresponding management based on RANZCOG [7] recommendations must continue.

Vaccination is Not Treatment

- The HPV vaccine is not therapeutic and is not intended to treat patients with cervical cytologic abnormalities or genital warts.
- Patients with these conditions should undergo the appropriate evaluation and treatment. It is important to note that many early cytologic abnormalities can be detected and managed

conservatively given the significant rate of regression. This is especially true in adolescents and young women.

Vaccination of Pregnant and Lactating Women

- Gardasil® and Cervarix® have been classified as pregnancy category B2. The vaccine is not recommended for use in pregnancy. There is no evidence to suggest that administration of Gardasil® or Cervarix® adversely affects fertility, pregnancy or infant outcomes.[5, 6]
- Women who become pregnant during the course of vaccination should defer the subsequent doses until the completion of pregnancy, regardless of timing. Vaccination should resume at the appropriate dose interval. There is no need to recommence the complete vaccination program. For example, women who have received one or two doses should receive the second and/or third dose at the completion of the pregnancy.

Vaccination of Immunosuppressed Patients

- The presence of immunosuppression, either medically or in patients with HIV infection, is not a contraindication for Gardasil® or Cervarix®. However, the immune response may be smaller in the immunocompromised patient than in immunocompetent patients.[5, 6]

Vaccination of Women Older Than 26 Years

- Although the peak incidence of genital HPV infection is within the first five years after commencement of sexual activity, new HPV infections do occur throughout a woman's life, particularly in the context of new sexual partners and changing sexual behaviour.
- While it is impossible to give women older than 26 years an exact assessment of their individual potential for benefit, women can be provided with information to make a balanced decision about the costs and benefits of vaccination. [9] It should be emphasised however that vaccination is about prevention of future HPV infections, whilst continuation of cervical screening is vital to detect pre-neoplastic changes related to past infections.

Vaccination of Males

- Gardasil® is approved for use in males aged 9 to 15 years. This approval is based on the demonstration of safety and HPV antibody responses in males. Preliminary data from phase three clinical trials regarding the benefits of vaccination of males older than 15 years have demonstrated reduction of infection and disease but registration of the vaccine in this setting has not yet been given.
- Available data indicate that the vaccine is safe in this population but are insufficient to make recommendations regarding efficacy in this population.

*** Available Vaccines**

Two prophylactic HPV vaccines are currently available in Australia and New Zealand.

- Gardasil® - licensed for use in females aged 9 to 45 years to be given in a three dose schedule at 0, 2 and 6 months. It provides protection against persistent infection and cervical/genital disease due to HPV types 16 and 18 and HPV types 6 and 11, the latter two which cause 90% of genital warts. Gardasil® has also been registered for the prevention of vulvar and vaginal cancer, and their precancerous or dysplastic lesions. Gardasil® is also approved for use in males aged 9 to 15 years for the prevention of HPV infections.[1, 5]

- Cervarix[®] - licensed for use in females from 10 to 45 years of age for the prevention of cervical cancer and its precursor lesions due to HPV types 16 and 18.[6] It is given at 0, 1 and 6 months.

Both vaccines have been shown to demonstrate limited cross-protection against other non-vaccine types, although the clinical significance of this remains to be demonstrated.

References

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4. Frazer, I., *Prevention of cervical cancer through papillomavirus vaccination*. *Nature Reviews Immunol*, 2004. 4: p. 46-54.
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7. RANZCOG, *College Statement C-Gyn 5: Screening for the prevention of cervical cancer*. July 2006.
8. Munoz et al, Safety, immunogenicity and efficacy of quadrivalent HPV (types 6, 11, 16 , 18) recombinant vaccine in women aged 24-45 years. *Lancet* 373:19491957,2009.
9. Skinner SR et al, Human papillomavirus vaccination for the prevention of cervical neoplasia: is it appropriate to vaccinate women older than 26? *MJA* 2008; 188 (4): 238-242.

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