May 2007

Human Papillomavirus (HPV)

Clinician Fact Sheet

This Fact Sheet is intended for use by Ontario clinicians. Every effort has been made to ensure the accuracy of this information which is summarized from the current body of rapidly evolving evidence.

Summary

- HPV is usually transmitted by sexual activity, but occurs rarely through other means, e.g., intrapartum acquisition or non-sexual means such as transmission from fingers or clothing.
- There are oncogenic (high-risk) and non-oncogenic (low-risk) types of HPV.
- Oncogenic HPV infection is a necessary but not a sufficient cause of invasive cervical cancer.
- Most infections caused by oncogenic HPV resolve spontaneously without producing disease manifestations.
- Persistent infections may progress to pre-cancerous lesions.
- Oncogenic HPV has been implicated in cancers other than cervix.

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ontario cervical screening program
a cancer care ontario program

programme ontarien de dépistage du cancer du col de l’utérus
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Biology of HPV

- Over 40 different types of HPV infect the epithelial lining of the ano-genital tract.
- Types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59 have been shown to be associated with cervical cancer, i.e., oncogenic.
- Types 26, 53, 66, 68, 73 and 82 are probably oncogenic.
- Types 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81 and CP6108 are associated with genital warts; they rarely, if ever, cause cervical cancer.
- Types 16 and 18 account for 70% of cervical cancers and more than 30-40% of cancers of the vulva, penis and oropharynx.
- HPV is associated with squamous cell carcinoma (primarily HPV 16), adenocarcinoma (primarily HPV 18) and other types of cervical cancer.
- The vast majority of squamous dysplasia occurs in the cervical transformation zone (the area where columnar cells change into squamous cells).
- Types 6 and 11 are the cause of almost all ano-genital warts, recurrent respiratory papillomatosis and rare verrucous cancers.

Prevalence of HPV Infection

- Genital infection with HPV is the most common sexually transmitted infection among women.
- Oncogenic HPV types are detected more frequently than non-oncogenic types.
- HPV prevalence varies from 2%–44% among women with no manifestations of disease. The variability in prevalence depends on age, sampling method and country of residence.
- Over 50% of women will be exposed to one or more HPV types in their lifetime.
- The peak incidence of HPV infection is in women aged 18-25.
- Among men, the prevalence varies from 4-45% for all types of HPV and 2-35% for oncogenic HPV, depending on method of sample collection and country of residence.
- Genital warts occur in up to 4% of adults (based on United Kingdom reports).
- Genital warts are seldom indicative of a cancer-causing type of HPV; however, co-infection with oncogenic HPV has been noted in 20-50% of genital lesions.

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Burden of Cervical Cancer and Link to HPV

- Worldwide, it is the second most common cancer in women.
- In developing countries, it accounts for 15% of female cancers and is the leading cause of cancer deaths in women.
- In developed countries, cervical cancer accounts for 3.6% of all female cancers.
- In 2007, approximately 1,350 new cases and 390 deaths will occur in Canada due to the disease.
- In Ontario, cervical cancer is the tenth most common cancer diagnosed in women but is the second most common in women under 50 years.
- Ontario incidence and mortality rates have decreased by more than 60% in the last 30 years, due to widespread availability of the Papanicolaou (Pap) test.
- Aboriginal women and newcomers to Canada have higher rates of cervical cancer.
- Oncogenic HPV-DNA is present in 99.7% of cases of cervical cancer.
- Oncogenic HPV is implicated in cancer sites other than the cervix, but much less frequently.
- Other sites include the vulva, vagina, anus and penis, as well as non-genital sites like the oral cavity, pharynx and larynx.
- Epidermodysplasia verruciformis-HPV types, which are rarely encountered types that infect the skin and are not sexually-transmitted, may be co-carcinogens with ultraviolet radiation or immunosuppression in the development of non-melanoma skin cancer.

HPV Transmission and Acquisition

- HPV infection is mostly acquired via unprotected sexual activity or intercourse (vaginal and anal) with infected partners.
- It is not known how long HPV can persist in humans.
- Most HPV infections regress without any evidence of tissue alternation. Of the minority that become precancerous lesions, most of these are low grade and a majority of them also regress.
- HPV infections are typically not detectable beyond 1-2 years.
- Pre-cancerous lesions are not associated with symptoms or clinically visible signs (except when colposcopy is performed).
- Younger women (especially less than 30 years) are more likely to clear infection than older women.
- The risk of developing precancerous lesions (dysplasia, intraepithelial lesions) increases with long-term HPV infection and viral load.
- Low-grade lesions will regress spontaneously at a higher rate than high-grade lesions.
- Risk of dysplasia increases with long-term infections and viral load.
- Approximately 2% of women have a persistent HPV infection and are at higher risk for dysplasia and cervical cancer.
- More than 20-30% of women with cervical infections have multiple HPV types.
- Estimated progression from HPV infection to high grade lesions typically takes 7–10 years. In some instances, the disease can progress more rapidly.
- Genital warts typically associated with non-oncogenic HPV types are highly contagious: about two-thirds of people who have intimate contact with a partner with genital warts will develop warts (usually within 3 months).
- Condom use may provide some protection against HPV transmission and may promote regression of cervical neoplasia and penile lesions, or clearance of HPV infection in both sexes.
- Condoms also effectively help prevent transmission of other sexually transmitted infections (STIs) which may act as cofactors for HPV infection and cervical cancer.
- HPV can be transmitted via contact with unprotected genital areas.
- Preliminary evidence suggests that male circumcision may reduce the risk of HPV transmission.

Risk/Co-Factors for HPV Infection and Cervical Cancer

- HPV infection is a necessary but not a sufficient cause of cervical cancer; other co-factors which suppress the host immune system are also involved.
- Risk factors for acquiring HPV infection include:
  - High number of intimate partners
  - Early age at sexual début
  - Acquiring a new sexual partner
  - Male sexual partners with a higher lifetime number of partners
  - Sexual partners who are HPV carriers.
- Co-factors associated with neoplastic transformation of an HPV infection include:
  - Smoking tobacco and exposure to second-hand smoke
  - Long-term (>5 years) use of oral contraceptives
  - More than 5 full-term pregnancies
  - Other STIs, i.e., *Chlamydia trachomatis*, HSV-2, HIV
  - Poor diet (especially low antioxidant intake)
  - Immunosuppression, e.g., HIV, organ transplant, immuno-suppressive drug therapy or chemotherapy
- Genetic susceptibility-polymorphisms in certain cell regulatory genes (p53) and immunity-associated molecules (HLA-2) may potentiate the progression of HPV infection, but evidence is inconclusive.

Cancer of the cervix is almost entirely preventable with regular Pap tests.

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Preventive HPV Vaccines

- In July 2006, Health Canada approved a quadrivalent preventive HPV vaccine for 2 oncogenic types (16 and 18) and 2 non-oncogenic types (6 and 11) for females between 9 and 26 years of age.
- HPV vaccine does not preclude the need for regular screening with Pap tests.
- Both the quadrivalent (approved) and the bivalent (not yet approved) prophylactic vaccines contain virus-like particles.
- Thereapeutic vaccines (targeting viral oncoproteins E6 and E7) have shown limited efficacy so far.

HPV-DNA Testing

- Ontario Cervical Screening Program (OCSP) Guidelines recommend HPV testing (Hybrid Capture II) as a triage mechanism for screening women over 30 years with ASCUS Pap tests. In some jurisdictions, HPV testing is used as a primary screening tool.
- Testing can be useful for follow-up of women after treatment for squamous intraepithelial lesions, but guidelines are not yet in place.
- HPV testing is not recommended for men, or to check the HPV status of individuals (or their partners) with genital warts or other STIs.

Resources

More detail is available in the 2007 publication "Frequently Asked Questions on Cervical Dysplasia and Human Papillomavirus: A Reference Guide for Clinicians" which can be ordered from the Ontario Cervical Screening Program (OCSP). See also *Vaccine 24S3* monograph (Supplement 3, 2006) "HPV Vaccines and Screening in the Prevention of Cervical Cancer" and *Cervical Cancer: From Etiology to Prevention* by TE Rohan and KV Shah. Kluwer Academic Publishers, 2004.

HPV vaccine does not preclude the need for regular screening with Pap tests.

Additional information about HPV, cancer of the cervix and screening is available on the OCSP website at:
http://www.cancercare.on.ca/index_cervicalScreening.htm

Current Ontario Cervical Screening Practice Guidelines are available at:
http://www.cancercare.on.ca/documents/CervicalScreeningGuidelines.pdf

The National Advisory Committee on Immunization (NACI)'s *Statement on human papillomavirus vaccine* can be found at:
http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07vol33/acs-02/index_e.html

A Patient Fact Sheet (Form # 271881(E)) is also available for the general public. Copies of these and other materials can be ordered by calling the Canadian Cancer Society at 1 888 939-3333.

Distributed with the help of the

Canadian Cancer Society Société canadienne du cancer

271883

Revised May 2007
Revised September 2005
Original version: November 2004