

# POLICY STATEMENT\*

## HUMAN PAPILLOMAVIRUS INFECTIONS: GUIDELINES FOR INVESTIGATION AND MANAGEMENT

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*These guidelines have been prepared by the SOGC/GOC/SCC Policy and Practice Guideline Committee and were approved by Council.*

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Human Papillomavirus (HPV) infection of the genital tract is a sexually transmitted disease (STD). Different HPV sub-types can lead to the development of morphologically dissimilar lesions. For instance, low-risk types (HPV-DNA 6-11 etc.) can cause such benign lesions as condyloma acuminata and low grade intra-epithelial lesions (LGSIL). Conversely, the high risk types

(HPV-DNA 16-18 etc.) are responsible for cancer and high-grade intra-epithelial lesions (HGSIL). In these guidelines, we are focusing mainly on benign HPV infections.

Genital tract HPV infections present in three forms: clinically evident condyloma acuminata (CA) or exophytic warts, the subclinical infection that is evidenced only after the application of acetic acid and the use of magnification, and latent infection, identified by molecular biology (HPV-DNA) tests.

### I. CONDYLOMA ACUMINATA

These lesions can be found on the vulva, vagina, cervix, and peri-anal area. They are generally asymptomatic unless a superimposed infection is present. When the vulva is affected by the typical exophytic lesions, the diagnosis is not in doubt. However, if the lesion is not characteristic, it can be confused with physiologic changes<sup>1</sup> (vestibular papillomatosis, Fordyce glands), other STDs (molluscum contagiosum, condyloma lata) or benign tumours (verruca vulgaris). When they are rather flat and/or pigmented, one should exclude vulvar intra-epithelial neoplasia (VIN) by a biopsy. Condyloma

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acuminata of the vulva, vagina, and cervix can also mimic exophytic invasive cancer, and must be distinguished from the more serious disease by biopsy specimens, when they are not typical. Every patient with newly diagnosed condyloma of the vulva should be screened for other STDs (chlamydia) and should undergo a Pap. test in order to rule out the presence of subclinical cervical and/or vaginal lesions. Colposcopy is not routinely indicated.

Vulvar warts are treated best by local application of podophyllotoxin (Podofilox™) or 85 percent trichloroacetic acid (TCA). Podophyllotoxin is applied by the patient herself twice daily for three days. The treatment can be repeated for three or four cycles. It should neither be used during pregnancy nor in the vagina because of the medication's toxicity. Trichloroacetic acid is applied by the physician or the nurse directly on the wart with a cotton tip applicator. It can be used on the vulva or in the vagina when limited numbers of exophytic lesions are present. The treatment is repeated once weekly so it necessitates multiple clinic or office visits. The applications cause temporary pain and local necrosis. Cryotherapy is a good alternative when there are few warts. But with extensive condylomata, it is much too time consuming. Laser vaporization is usually reserved for recurrent condylomata, because it necessitates local and sometimes general anaesthesia. Because multiple painful injections are necessary, interferon is also reserved for recurrent condyloma. An interferon inducer, Imiquimod (Aldara™) has shown very good results in clinical studies<sup>2</sup> both as first-line treatment and in recurrences. Table 1 shows the success and recurrence rates for different modes of therapy.

Formerly, electrocautery or electrodesiccation was used in the case of persistent or recurring vulvar condylomata, but these methods caused scarring. At present,

cryotherapy, laser vaporization or diathermy loop excision are the treatments of choice for CA that is not responsive to local therapy. Interferon use has been disappointing for recurrent condyloma.

With widespread vaginal condylomata, the treatment of choice is 5-Fluorouracil (Efudex™) cream.<sup>3</sup> Because this preparation can cause burning, the vulvar area should be protected by petroleum jelly, and a vaginal tampon be inserted before rising in the morning to prevent escape of the medication. 5-Fluorouracil can also induce vaginal adenosis, causing vaginal discharge and contact bleeding. For cervical condyloma acuminata, excision by punch biopsy or by diathermy loop is the treatment of choice.

## II. SUBCLINICAL HPV INFECTIONS

Between three to five percent of Papanicolaou smears show cytologic signs of HPV infection (koilocytosis and dyskeratosis). When HPV changes are discovered in cervico-vaginal smears, the patient is usually referred to a clinic where colposcopically-directed biopsies are taken, to rule out intra-epithelial neoplasia (SIL). It has been shown that around 20 percent of such patients will be found to have cervical HGSIL.<sup>4</sup> Because the risk of invasive cancer is very low in patients showing only koilocytotic atypia, the National Workshop on Screening for Cancer of the Cervix recommended that a patient with benign HPV changes on the Pap. smear should have a repeat smear in six months, and referral for colposcopy should be reserved for patients with Pap. smears showing CIN-II (high grade) or more.<sup>5</sup> However, this recommendation is to be followed only where effective provincial screening programmes are organized (central information system, quality control etc.). At this time, only British Columbia, Nova Scotia, and Prince Edward Island have such a programme.

Management of benign HPV infection of the cervix (LGSIL) is controversial. The arguments in favour of treating LGSIL are to suppress an STD and to avoid progression to HGSIL or cancer. The arguments against are that the virus is not destroyed by local therapy and that the majority of lesions will disappear spontaneously in three to five years. The evidence to support either side is rather weak. In laboratories where viral typing is performed, treatments could be offered to patients when oncogenic types (16-18) are found.<sup>6</sup> The progression rate

Therapy	% Efficiency	% Recurrence
Podophyllotoxin	45-48	33-60
Trichloroacetic acid	20-70	40-70
Cryotherapy	68	38
CO <sub>2</sub> laser	27-82	7-72
Interferon	32-60	65
Imiquimod 5%	50-71	10

\* Modified from reference no. 2



of LGSIL positive for HPV-DNA 16-18 is around 80 percent in five years, against 20 to 30 percent when positive for HPV-DNA 6-11 (non-oncogenic types).<sup>7</sup>

### III. LATENT INFECTIONS

With the development of more sophisticated molecular biology tests, HPV-DNA can be detected easily in samples taken from the cervix and/or vagina (smears, swabs, tissue etc.). Screening with HPV-DNA tests has been shown to enhance the efficiency of Pap. smears. For example, a woman who has a negative smear but positive HPV-DNA has between 24 to 55 times the risk of presenting with an SIL in the next two years. However, the cost effectiveness of HPV-DNA testing has not been studied. Therefore, for the time being, another recommendation of the National Workshop on Screening for Cancer of the Cervix not to use HPV-DNA tests for screening should be followed.<sup>5</sup>

### PREGNANCY

Condylomata acuminata can grow faster during pregnancy and they usually need treatment. Currently, 85 percent TCA or cryotherapy is the preferred treatment in pregnancy. Podophylline is contra-indicated. Laser vaporization can be used for refractory or extensive lesions but can produce excessive bleeding. Caesarean section has not been shown to prevent the transmission of HPV to the infant or to lower the risk of the development of laryngeal papilloma. Thus, Caesarean section should only be performed for obstetrical indications.

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