

lesions should be referred to a gynecologist experienced in colposcopy and treatment of these lesions. Treatment of cervical disease involves careful inspection, biopsy, and histopathologic grading to determine the severity and extent of disease. Women with evidence of cervical HPV infection should be referred to a gynecologist familiar with HPV and experienced in colposcopy. Optimal follow-up of these patients includes colposcopic examination of the cervix and vagina on a yearly basis. Guidelines from the American College of Gynecology and Obstetrics are available for the treatment of cervical dysplasia and cancer.

For anal or perianal lesions, cryotherapy or surgical removal is safest and most effective. Anoscopy and/or sigmoidoscopy should be performed when patients have perianal lesions, and suspicious lesions should be biopsied to rule out malignancy.

THERAPEUTIC OPTIONS

Tables 222-1 and 222-2 list the available patient-administered and physician-administered treatments, respectively.

Podophyllotoxin Podophyllotoxin (0.05% solution or gel and 0.15% cream) induces necrosis of genital wart tissue that heals within a few days. It is relatively effective and can be self-administered. Podophyllotoxin is applied twice daily on three consecutive days of the week for a maximum of 4 weeks. Adverse effects are common and include pain, inflammation, erosion, and burning or itching. Podophyllotoxin should not be used to treat vaginal, cervical, or anal lesions. The safety of podophyllotoxin during pregnancy has not been established.

Sinecatechins Sinecatechins (15% ointment) is used to treat genital warts but should not be used to treat vaginal, cervical, or anal lesions. Sinecatechins causes an inflammatory response when applied topically three times a day for up to 4 months. Clearance rates approach 60% in some studies, and recurrence rates are 6–9%. Adverse effects (redness, burning, itching, and pain at the site of application) are generally mild. The safety of sinecatechins during pregnancy is unknown.

Imiquimod Imiquimod (5% or 3.75% cream) is a patient-applied topical immunomodulatory agent thought to activate immune cells by binding to a Toll-like receptor—an event that leads to an inflammatory response. Imiquimod 5% cream is applied to genital warts at bedtime three times per week for up to 16 weeks. Warts are cleared in ~56% of patients, more often in women than in men; recurrence rates approach 13%. Local inflammatory side effects are common. Rates of clearance of genital warts with the 3.75% formulation are not as high, but the duration of treatment is shorter (i.e., daily application for a maximum of 8 weeks), and fewer local and systemic adverse reactions occur. Imiquimod should not be used to treat vaginal, cervical, or anal lesions. The safety of imiquimod during pregnancy has not been established.

Cryotherapy Cryotherapy (liquid nitrogen) for HPV-associated lesions causes cellular death. Genital warts usually disappear after two or three weekly sessions but often recur. Cryotherapy, which

TABLE 222-2 RECOMMENDED TREATMENTS THAT MUST BE ADMINISTERED BY A CLINICIAN FOR GENITAL WARTS AND OTHER HUMAN PAPILLOMAVIRUS-ASSOCIATED LESIONS

Variable	Cryotherapy	Surgical Removal	Laser	Interferon
Effectiveness	Good	Excellent	Excellent	Good
Recurrence	Frequent	Frequent	Frequent	Frequent
Adverse effects	Mild, well tolerated	Mild, well tolerated	Mild to moderate, well tolerated	Frequent, moderately severe
Availability	Good	Good	Fair	Fair
Cost	Inexpensive	Moderately expensive	Very expensive	Very expensive

is nontoxic and is not associated with significant adverse reactions, can also be used for diseased cervical tissue. Local pain occurs frequently.

Surgical Methods Exophytic lesions can be surgically removed after intradermal injection of 1% lidocaine. This treatment is well tolerated but can cause scarring and requires hemostasis. Genital warts can also be destroyed by electrocautery, in which no additional hemostasis is required.

Laser Therapy Laser treatment affords destruction of exophytic lesions and other HPV-infected tissue while preserving normal tissue. Local anesthetics are generally adequate. Efficacy for genital lesions is at least equal to that of other therapies (60–90%), with low recurrence rates (5–10%). Complications include local pain, vaginal discharge, periurethral swelling, and penile or vulvar swelling. Laser therapy has also been used successfully to treat cervical dysplasia and anal disease caused by HPV.

Interferon (IFN) Recombinant IFN- α is used for intralesional treatment of genital warts, including perianal lesions. The recommended dosage is 1.0×10^6 IU of IFN injected into each lesion three times weekly for 3 weeks. IFN therapy causes clearance of infected cells by immune-boosting effects. Adverse events include headache, nausea, vomiting, fatigue, and myalgia. IFN therapy is costly and should be reserved for severe cases that do not respond to cheaper treatments. IFN should not be used to treat vaginal, cervical, or anal lesions.

Other Therapies Both trichloroacetic acid and bichloroacetic acid are caustic agents that destroy warts by coagulation of proteins. Neither of these agents is recommended for treatment.

COUNSELING

Most sexually active adults will be infected with HPV during their lives. For all patients (vaccinated or unvaccinated), certain behavioral interventions can reduce the risk of acquiring HPV. Physicians can provide their patients with measures that can reduce this risk. The only way to avoid acquiring an HPV infection is to abstain from sexual activity, including intimate touching and oral sex. Practicing safe sex (partner reduction, condom use) may lower the likelihood of HPV transmission. Most HPV infections are controlled by the immune system and cause no symptoms or disease. Some infections lead to genital warts and cervical precancers. Genital warts can be treated for cosmetic reasons and to prevent spread of infection to others. Even after resolution of genital warts, latent virus can persist in normal-appearing skin or mucosa and thus theoretically can be transmitted to uninfected partners. Precancerous cervical lesions should be treated to prevent progression to cancer.

TABLE 222-1 RECOMMENDED TREATMENTS THAT CAN BE SELF-ADMINISTERED FOR GENITAL WARTS

Variable	Podophyllotoxin	Sinecatechins	Imiquimod
Effectiveness	Good	Good	Good
Recurrence	Frequent	Frequent	Frequent
Adverse effects	Frequent, can be severe	Frequent, mild	Frequent, mild to moderate
Availability	Good	Fair	Fair
Cost	Inexpensive	Inexpensive	Expensive