Complete Summary

GUIDELINE TITLE

HPV infection and genital warts. Sexually transmitted diseases treatment guidelines 2006.

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention, Workowski KA, Berman SM. HPV infection and genital warts. Sexually transmitted diseases treatment guidelines 2006. MMWR Morb Mortal Wkly Rep 2006 Aug 4;55(RR-11):62-7. [222 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Centers for Disease Control and Prevention. Human papillomavirus infection. Sexually transmitted diseases treatment guidelines. MMWR Recomm Rep 2002 May 10;51(RR-6):53-7.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Human papillomavirus (HPV) infection
- Genital warts

GUIDELINE CATEGORY

Counseling
Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Preventive Medicine
Urology

INTENDED USERS

Health Care Providers
Managed Care Organizations
Physicians

GUIDELINE OBJECTIVE(S)

- To update the Sexually Transmitted Diseases Treatment Guidelines 2002 (*MMWR 2002;51[No. RR-6]*)
- To assist physicians and other health-care providers in preventing and treating sexually transmitted diseases (STDs)

TARGET POPULATION

Patients with human papillomavirus (HPV) infection and/or genital warts

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis of HPV Infection

1. Human papillomavirus (HPV) nucleic acid levels
2. HPV capsid protein levels
3. Either test above in conjunction with a Papanicolaou test or screening for atypical squamous cells of undetermined significance

Screening for Genital Warts

1. Visual inspection (recommended)
2. Nucleic acid testing (not recommended)
3. Acetic acid application (for flat genital warts; routinely not recommended)

Treatment

External Genital Warts

Patient-Applied

1. Podofilox 0.5% solution or gel
2. Imiquimod 5% cream

Provider-Administered

1. Cryotherapy with liquid nitrogen or cryoprobe
2. Podophyllin resin 10%-25% in a compound tincture of benzoin
3. Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%-90%
4. Surgical removal by tangential scissor excision, tangential shave excision, curettage or electrosurgery
5. Intralesional interferon
6. Laser surgery
7. Combination therapy (not recommended)

Cervical Warts

1. Exclude diagnosis of high-grade squamous intraepithelial lesions (SIL)
2. Consultation with specialist

Vaginal Warts

1. Cryotherapy with liquid nitrogen
2. Trichloroacetic acid or bichloroacetic acid 80%-90%

Urethral Meatus Warts

1. Cryotherapy with liquid nitrogen
2. Podophyllin 10%-25% in compound tincture or benzoin

Anal Warts

1. Cryotherapy with liquid nitrogen
2. Trichloroacetic acid or bichloroacetic acid 80%-90%
3. Surgical removal
4. Specialist consultation for warts on rectal mucosa (use of digital examination or anoscopy)

Special Considerations

1. Removal of warts during pregnancy
2. Treatment of patients with concomitant HIV infection

Management

1. Prevention of transmission of HPV to infants
2. Referral of patients with squamous cell carcinoma in situ
3. Education and counseling, using patient education materials, pamphlets, hotlines, and web sites
4. Follow-up evaluation

5. Counseling of sex partners

MAJOR OUTCOMES CONSIDERED

- Microbiologic cure
- Alleviation of signs and symptoms
- Prevention of sequelae
- Prevention of transmission

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Beginning in 2004, the Centers for Disease Control and Prevention (CDC) personnel and professionals knowledgeable in the field of sexually transmitted diseases (STDs) systematically reviewed evidence (including published abstracts and peer-reviewed journal articles) concerning each of the major STDs, focusing on information that had become available since publication of the *Sexually Transmitted Diseases Treatment Guidelines, 2002*. Background papers were written and tables of evidence constructed summarizing the type of study (e.g., randomized controlled trial or case series), study population and setting, treatments or other interventions, outcome measures assessed, reported findings, and weaknesses and biases in study design and analysis. A draft document was developed on the basis of the reviews.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

In April 2005, the Centers for Disease Control and Prevention (CDC) staff members and invited consultants assembled in Atlanta, Georgia, for a 3-day meeting to present the key questions regarding sexually transmitted disease (STD) treatment that emerged from the evidence-based reviews and the information available to answer those questions. When relevant, the questions focused on four principal outcomes of STD therapy for each individual disease: 1) microbiologic cure, 2) alleviation of signs and symptoms, 3) prevention of sequelae, and 4) prevention of transmission. Cost-effectiveness and other advantages (e.g., single-dose formulations and directly observed therapy of specific regimens) also were discussed. The consultants then assessed whether the questions identified were relevant, ranked them in order of priority, and attempted to arrive at answers using the available evidence. In addition, the consultants evaluated the quality of evidence supporting the answers on the basis of the number, type, and quality of the studies.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC) and the Centers for Disease Control and Prevention (CDC): When more than one therapeutic regimen is recommended, the sequence is alphabetized unless the choices for therapy are prioritized based on efficacy, convenience, or cost. For sexually transmitted diseases (STDs) with more than one recommended regimen, almost all regimens have similar efficacy and similar rates of intolerance or toxicity unless otherwise specified.

HPV Infection

More than 100 types of human papillomavirus (HPV) exist; more than 30 types can infect the genital area. The majority of HPV infections are asymptomatic, unrecognized, or subclinical. Genital HPV infection is common and usually self-limited. Genital HPV infection occurs more frequently than visible genital warts among both men and women and cervical cell changes among women.

Genital HPV infection can cause genital warts, usually associated with HPV types 6 or 11. Other HPV types that infect the anogenital region (e.g., high-risk HPV types 16, 18, 31, 33, and 35) are strongly associated with cervical neoplasia. Persistent infection with high-risk types of HPV is the most important risk factor for cervical neoplasia.

HPV Tests

A definitive diagnosis of HPV infection is based on detection of viral nucleic acid (i.e., deoxyribonucleic acid [DNA] or ribonucleic acid [RNA]) or capsid protein. Tests that detect several types of HPV DNA in cells scraped from the cervix are available and might be useful in the triage of women with atypical squamous cells of undetermined significance (ASC-US) or in screening women aged ≥30 years in conjunction with the Papanicolaou (Pap) test (see the NGC summary of the CDC guideline Cervical Cancer Screening for Women Who Attend STD Clinics or Have a History of STDs). Women determined to have HPV infection on such testing should be counseled that HPV infection is common, infection is frequently transmitted between partners, and that infection usually goes away on its own. If any Pap test or biopsy abnormalities have been observed, further evaluation is recommended. Screening women or men with the HPV test, outside of the above recommendations for use of the test with cervical cancer screening, is not recommended.

Treatment

In the absence of genital warts or cervical squamous intraepithelial lesions (SIL), treatment is not recommended for subclinical genital HPV infection, whether it is diagnosed by colposcopy, biopsy, acetic acid application, or through the detection of HPV by laboratory tests. Genital HPV infection frequently goes away on its own, and no therapy has been identified that can eradicate infection. In the presence of coexistent SIL, management should be based on histopathologic findings.

Genital Warts

HPV types 6 or 11 are commonly found before, or at the time of, detection of genital warts; however, the use of HPV testing for genital wart diagnosis is not recommended.

Genital warts are usually flat, papular, or pedunculated growths on the genital mucosa. Diagnosis of genital warts is made by visual inspection and may be confirmed by biopsy, although biopsy is needed only under certain circumstances (e.g., if the diagnosis is uncertain; the lesions do not respond to standard therapy; the disease worsens during therapy; the patient is immunocompromised;

or warts are pigmented, indurated, fixed, bleeding, or ulcerated). No data support the use of HPV nucleic acid tests in the routine diagnosis or management of visible genital warts.

The application of 3%-5% acetic acid usually turns HPV-infected genital mucosal tissue to a whitish color. However, acetic acid application is not a specific test for HPV infection, and the specificity and sensitivity of this procedure for screening have not been defined. Therefore, the routine use of this procedure for screening to detect HPV infection is not recommended. However, some clinicians, who are experienced in the management of genital warts, have determined that this test is useful for identifying flat genital warts.

In addition to the external genitalia (i.e., penis, vulva, scrotum, perineum, and perianal skin), genital warts can occur on the uterine cervix and in the vagina, urethra, anus, and mouth. Intra-anal warts are observed predominantly in patients who have had receptive anal intercourse; these warts are distinct from perianal warts, which can occur in men and women who do not have a history of anal sex. In addition to the genital area, HPV types 6 and 11 have been associated with conjunctival, nasal, oral, and laryngeal warts. Genital warts are usually asymptomatic, but depending on the size and anatomic location, genital warts can be painful, friable, or pruritic.

HPV types 16, 18, 31, 33, and 35 are found occasionally in visible genital warts and have been associated with external genital (i.e., vulvar, penile, and anal) squamous intraepithelial neoplasia (i.e., squamous cell carcinoma in situ, bowenoid papulosis, Erythroplasia of Queyrat, or Bowen's disease of the genitalia). These HPV types also have been associated with vaginal, anal, and CIN and anogenital and some head and neck squamous cell carcinomas. Patients who have visible genital warts are frequently infected simultaneously with multiple HPV types.

Treatment

The primary goal of treating visible genital warts is the removal of the warts. In the majority of patients, treatment can induce wart-free periods. If left untreated, visible genital warts might resolve on their own, remain unchanged, or increase in size or number. Treatment possibly reduces, but does not eliminate, HPV infection. Existing data indicate that currently available therapies for genital warts might reduce, but probably do not eradicate, HPV infectivity. Whether the reduction in HPV viral DNA, resulting from treatment, impacts future transmission remains unclear. No evidence indicates that the presence of genital warts or their treatment is associated with the development of cervical cancer.

Regimens

Treatment of genital warts should be guided by the preference of the patient, the available resources, and the experience of the health-care provider. No definitive evidence suggests that any of the available treatments are superior to any other and no single treatment is ideal for all patients or all warts. The use of locally developed and monitored treatment algorithms has been associated with improved clinical outcomes and should be encouraged. Because of uncertainty regarding the effect of treatment on future transmission of HPV and the possibility

of spontaneous resolution, an acceptable alternative for some persons is to forego treatment and wait for spontaneous resolution.

The majority of patients have <10 genital warts, with a total wart area of 0.5-1.0 cm^2. These warts respond to various treatment modalities. Factors that might influence selection of treatment include wart size, wart number, anatomic site of wart, wart morphology, patient preference, cost of treatment, convenience, adverse effects, and provider experience. Factors that might affect response to therapy include the presence of immunosuppression and compliance with therapy. The majority of patients require a course of therapy rather than a single treatment. In general, warts located on moist surfaces or in intertriginous areas respond better to topical treatment than do warts on drier surfaces.

The treatment modality should be changed if a patient has not improved substantially. The majority of genital warts respond within 3 months of therapy. The response to treatment and its side effects should be evaluated throughout the course of therapy.

Complications occur rarely if treatments for warts are employed properly. Patients should be warned that persistent hypopigmentation or hyperpigmentation occurs commonly with ablative modalities. Depressed or hypertrophic scars are uncommon but can occur, especially if the patient has had insufficient time to heal between treatments. Rarely, treatment can result in disabling chronic pain syndromes (e.g., vulvodynia or analdynia, and hyperesthesia of the treatment site) or, in the case of rectal warts, painful defecation or fistulas. A limited number of case reports of severe systemic effects from podophyllin resin and interferon have been documented.

Treatment regimens are classified into patient-applied and provider-applied modalities. Patient-applied modalities are preferred by some patients because they can be administered in the privacy of the patient's home. To use patient-applied modalities effectively, compliance with the treatment regimen is important along with the ability to identify and reach all genital warts.

Recommended Regimens for External Genital Warts

Patient-Applied:

- **Podofilox** 0.5% solution or gel. Patients should apply podofilox solution with a cotton swab, or podofilox gel with a finger, to visible genital warts twice a day for 3 days, followed by 4 days of no therapy. This cycle may be repeated, as necessary, for up to four cycles. The total wart area treated should not exceed 10 cm^2, and the total volume of podofilox should be limited to 0.5 mL per day. If possible, the health-care provider should apply the initial treatment to demonstrate the proper application technique and identify which warts should be treated. The safety of podofilox during pregnancy has not been established.

  OR

- **Imiquimod 5% cream** Patients should apply imiquimod cream once daily at bedtime, three times a week for up to 16 weeks. The treatment area should be washed with soap and water 6-10 hours after the application. The safety of imiquimod during pregnancy has not been established.

Provider-Administered:

- **Cryotherapy** with liquid nitrogen or cryoprobe. Repeat applications every 1-2 weeks.

  OR

- **Podophyllin resin** 10%-25% in a compound tincture of benzoin. A small amount should be applied to each wart and allowed to air dry. The treatment can be repeated weekly, if necessary. To avoid the possibility of complications associated with systemic absorption and toxicity, two important guidelines should be followed: 1) application should be limited to <0.5 mL of podophyllin or an area of <10 cm^2 of warts per session, and 2) no open lesions or wounds should exist in the area to which treatment is administered. Some specialists suggest that the preparation should be thoroughly washed off 1-4 hours after application to reduce local irritation. The safety of podophyllin during pregnancy has not been established.

  OR

- **Trichloroacetic acid (TCA) or bichloroacetic acid (BCA)** 80%-90%. A small amount should be applied only to the warts and allowed to dry, at which time a white "frosting" develops. If an excess amount of acid is applied, the treated area should be powdered with talc, sodium bicarbonate (i.e., baking soda), or liquid soap preparations to remove unreacted acid. This treatment can be repeated weekly, if necessary.

  OR

- **Surgical removal** either by tangential scissor excision, tangential shave excision, curettage, or electrosurgery

Alternative Regimens

- **Intralesional interferon**

  OR

- **Laser surgery**

Podofilox 0.5% solution or gel, an antimitotic drug that destroys warts, is relatively inexpensive, easy to use, safe, and self-applied by patients. The

majority of patients experience mild-to-moderate pain or local irritation after treatment. Imiquimod is a topically active immune enhancer that stimulates production of interferon and other cytokines. Local inflammatory reactions are common with the use of imiquimod; these reactions include redness and irritation and are usually mild to moderate. Traditionally, follow-up visits are not required for patients using self-administered therapy. However, follow-up might be useful several weeks into therapy to determine the appropriateness of medication use and the response to treatment.

Cryotherapy destroys warts by thermal-induced cytolysis. Health-care providers must be trained on the proper use of this therapy because over- and undertreatment might result in complications or low efficacy. Pain after application of the liquid nitrogen, followed by necrosis and sometimes blistering, is common. Local anesthesia (topical or injected) might facilitate therapy if warts are present in many areas or if the area of warts is large.

Podophyllin resin, which contains several compounds, including antimitotic podophyllin lignans, is another treatment option. The resin is most frequently compounded at 10%-25% in a tincture of benzoin. However, podophyllin resin preparations differ in the concentration of active components and contaminants. The shelf life and stability of podophyllin preparations are unknown. A thin layer of podophyllin resin must be applied to the warts and allowed to air dry before the treated area comes into contact with clothing; overapplication or failure to air dry can result in local irritation caused by spread of the compound to adjacent areas.

Both TCA and BCA are caustic agents that destroy warts by chemical coagulation of proteins. Although these preparations are widely used, they have not been investigated thoroughly. TCA solutions have a low viscosity comparable with that of water and can spread rapidly if applied excessively; therefore, they can damage adjacent tissues. Both TCA and BCA should be applied sparingly and allowed to dry before the patient sits or stands. If pain is intense, the acid can be neutralized with soap or sodium bicarbonate.

Surgical therapy has the advantage of usually eliminating warts at a single visit. However, such therapy requires substantial clinical training, additional equipment, and a longer office visit. After local anesthesia is applied, the visible genital warts can be physically destroyed by electrocautery, in which case no additional hemostasis is required. Care must be taken to control the depth of electrocautery to prevent scarring. Alternatively, the warts can be removed either by tangential excision with a pair of fine scissors or a scalpel or by curettage. Because the majority of warts are exophytic, this procedure can be accomplished with a resulting wound that only extends into the upper dermis. Hemostasis can be achieved with an electrocautery unit or a chemical styptic (e.g., an aluminum chloride solution). Suturing is neither required nor indicated in the majority of cases if surgical removal is performed properly. Surgical therapy is most beneficial for patients who have a large number or area of genital warts. Carbon dioxide laser and surgery might be useful in the management of extensive warts or intraurethral warts, particularly for those patients who have not responded to other treatments.

Interferons, both natural or recombinant, have been used for the treatment of genital warts. They have been administered systemically (i.e., subcutaneously at

a distant site or intramuscularly [IM]) and intralesionally (i.e., injected into the warts). Systemic interferon is not effective. The efficacy and recurrence rates of intralesional interferon are comparable to other treatment modalities. Administration of intralesional interferon is associated with stinging, burning, and pain at the injection site. Interferon is probably effective because of its antiviral and/or immunostimulating effects. Interferon therapy is not recommended as a primary modality because of inconvenient routes of administration, frequent office visits, and the association between its use and a high frequency of systemic adverse effects.

Because of the shortcomings associated with all available treatments, some clinics employ combination therapy (i.e., the simultaneous use of two or more modalities on the same wart at the same time). No data support the use of more than one therapy at a time to improve efficacy of treatment, and some specialists believe that combining modalities might increase complications.

Recommended Regimens for Cervical Warts

- For women who have exophytic cervical warts, high-grade SIL must be excluded before treatment is initiated. Management of exophytic cervical warts should include consultation with a specialist.

Recommended Regimens for Vaginal Warts

- **Cryotherapy** with liquid nitrogen. The use of a cryoprobe in the vagina is not recommended because of the risk for vaginal perforation and fistula formation.

  OR

- **TCA or BCA** 80%-90% applied to warts. A small amount should be applied only to warts and allowed to dry, at which time a white "frosting" develops. If an excess amount of acid is applied, the treated area should be powdered with talc, sodium bicarbonate, or liquid soap preparations to remove unreacted acid. This treatment can be repeated weekly, if necessary.

Recommended Regimens for Urethral Meatus Warts

- **Cryotherapy** with liquid nitrogen

  OR

- **Podophyllin** 10%-25% in compound tincture of benzoin. The treatment area must be dry before contact with normal mucosa. This treatment can be repeated weekly, if necessary. The safety of podophyllin during pregnancy has not been established.

Although data evaluating the use of podofilox and imiquimod for the treatment of distal meatal warts are limited, some specialists recommend their use in some patients.

Recommended Regimens for Anal Warts

- **Cryotherapy** with liquid nitrogen

  OR

- **TCA or BCA** 80%-90% applied to warts. A small amount should be applied only to warts and allowed to dry, at which time a white "frosting" develops. If an excess amount of acid is applied, the treated area should be powdered with talc, sodium bicarbonate, or liquid soap preparations to remove unreacted acid. This treatment can be repeated weekly, if necessary.

  OR

- **Surgical removal**

Warts on the rectal mucosa should be managed in consultation with a specialist. Many persons with warts on the anal mucosa also have warts on the rectal mucosa, so persons with anal warts can benefit from an inspection of the rectal mucosa by digital examination or anoscopy.

Counseling

Genital HPV Infection

Education and counseling are vital aspects of managing patients with genital warts. Patients can be educated through patient education materials, including pamphlets, hotlines, and websites (http://www.ashastd.org> or http://www.cdc.gov/std/hpv).

Attempts should be made to convey the following key messages:

- Genital HPV infection is common among sexually active adults. The majority of sexually active adults will have it at some point in their lives, although the majority of them will never know because the infection usually has no symptoms and clears on its own.
- Genital HPV infection is usually sexually transmitted. The incubation period (i.e., the interval between initial exposure and established infection or disease) is variable, and determining the timing and source of infection is frequently difficult. Within ongoing sexual relationships, sex partners usually are infected by the time of the patient's diagnosis, although they might have no symptoms or signs of infection.
- No recommended uses of the HPV test to diagnose HPV infection in sex partners have been established. HPV infection is commonly transmitted to partners but usually goes away on its own.

Genital Warts

- Genital warts are caused by specific types of HPV infection. The types that cause genital warts are different from the types that cause cervical and other anogenital cancers.
- Persons can possibly have infection with the types of HPV that cause genital warts but never develop symptoms. Why some persons with genital HPV infection develop warts and others do not is unclear. Immunity probably plays a key role.
- The natural history of genital warts is usually benign, but recurrence of genital warts within the first several months after treatment is common. Treatment for genital warts can reduce HPV infection, but whether the treatment results in a reduction in risk for transmission of HPV to sex partners is unclear. The duration of infectivity after wart treatment is unknown.
- Condoms might reduce the risk for HPV-associated diseases (e.g., genital warts and cervical cancer). Consistent condom use also may reduce the risk for genital HPV. HPV infection can occur in areas that are not covered or protected by a condom (e.g., scrotum, vulva, or perianus).
- The presence of genital warts is not an indication for HPV testing, a change in the frequency of Pap tests, or cervical colposcopy.
- HPV testing is not indicated for partners of persons with genital warts.

Follow-Up

After visible genital warts have cleared, a follow-up evaluation might be helpful. Patients should be cautioned to watch for recurrences, which occur most frequently during the first 3 months. External genital warts can be difficult to identify, so it might be useful for patients to have a follow-up evaluation 3 months after treatment. Earlier follow-up visits also might be useful for some patients to document the absence of warts, to monitor for or treat complications of therapy, and to provide an additional opportunity for patient education and counseling. Women should be counseled to undergo regular Pap screening as recommended for women without genital warts.

Management of Sex Partners

Examination of sex partners is not necessary for the management of genital warts because no data indicate that reinfection plays a role in recurrences. In addition, providing treatment for genital warts solely for the purpose of preventing future transmission cannot be recommended because the value of treatment in reducing infectivity is unknown. However, sex partners of patients who have genital warts might benefit from counseling and examination to assess the presence of genital warts and other STDs. The counseling of sex partners provides an opportunity for these partners to 1) learn that HPV infection is common and probably shared between partners and 2) receive STD evaluation and screening and Pap screening if they are female. Female sex partners of patients who have genital warts should be reminded that cytologic screening for cervical cancer is recommended for all sexually active women.

Special Considerations

Pregnancy

Imiquimod, podophyllin, and podofilox should not be used during pregnancy. However, because genital warts can proliferate and become friable during pregnancy, many specialists advocate their removal during pregnancy. HPV types 6 and 11 can cause respiratory papillomatosis in infants and children. The route of transmission (i.e., transplacental, perinatal, or postnatal) is not completely understood. Whether cesarean section prevents respiratory papillomatosis in infants and children is unclear; therefore, cesarean delivery should not be performed solely to prevent transmission of HPV infection to the newborn. Cesarean delivery might be indicated for women with genital warts if the pelvic outlet is obstructed or if vaginal delivery would result in excessive bleeding. Pregnant women with genital warts should be counseled concerning the low risk for warts on the larynx (recurrent respiratory papillomatosis) in their infants or children. No controlled studies have suggested that cesarean section prevents this condition.

HIV Infection

No data suggest that treatment modalities for external genital warts should be different in the setting of HIV-infection. However, persons who are immunosuppressed because of HIV or other reasons might have larger or more numerous warts, might not respond as well as immunocompetent persons to therapy for genital warts, and might have more frequent recurrences after treatment. Squamous cell carcinomas arising in or resembling genital warts might occur more frequently among immunosuppressed persons, therefore, requiring biopsy for confirmation of diagnosis. Because of the increased incidence of anal cancer in HIV-infected homosexual men, screening for anal SIL by cytology in this population is recommended by some specialists. However, evidence is limited concerning the natural history of anal intraepithelial neoplasias, the reliability of screening methods, the safety and response to treatments, and the programmatic considerations that would support this screening approach. Until additional data are generated on screening for anal SIL, this screening approach cannot be recommended.

Squamous Cell Carcinoma in Situ

Patients in whom squamous cell carcinoma in situ of the genitalia is diagnosed should be referred to a specialist for treatment. Ablative modalities usually are effective, but careful follow-up is essential. The risk for these lesions leading to invasive squamous cell carcinoma of the external genitalia in immunocompetent patients is unknown but is probably low. Female partners of male patients who have squamous cell carcinoma in situ are at high risk for cervical abnormalities.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

Throughout the 2006 guideline document, the evidence used as the basis for specific recommendations is discussed briefly. More comprehensive, annotated discussions of such evidence will appear in background papers that will be published in a supplement issue of the journal *Clinical Infectious Diseases*.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis, treatment, and management of patients with human papillomavirus (HPV) infection, including external genital warts, vaginal warts, urethral meatus warts, anal warts, oral warts, and subclinical genital HPV infection without exophytic warts.

Subgroups Most Likely to Benefit

Patients who are also pregnant, immunodeficient, or have squamous cell carcinoma in situ

POTENTIAL HARMS

- Complications rarely occur if treatments for warts are employed properly. Patients should be warned that persistent hypopigmentation or hyperpigmentation are common with ablative modalities. Depressed or hypertrophic scars are uncommon but can occur, especially if the patient has had insufficient time to heal between treatments. Rarely, treatment can result in disabling chronic pain syndromes (e.g., vulvodynia or hyperesthesia of the treatment site) or, in the case of rectal warts, painful defecation or fistulas. A limited number of case reports of severe systemic effects from podophyllin resin and interferon have been documented.
- The majority of patients using podofilox 0.5% solution or gel experience mild to moderate pain or local irritation after treatment.
- Local inflammatory reactions are common with imiquimod; these reactions include redness and irritation and are usually mild to moderate.
- With cryotherapy, pain after application of the liquid nitrogen, followed by necrosis and sometimes blistering, is common.
- Over-application or failure to air-dry podophyllin resin can result in local irritation caused by spread of the compound to adjacent areas.
- Trichloroacetic acid (TCA) and bichloroacetic acid (BCA) solutions have low viscosity comparable with that of water and can spread rapidly if applied excessively; thus, they can damage adjacent tissue.
- Administration of intralesional interferon is associated with stinging, burning, and pain at the injection site. Interferon therapy is not recommended as a primary modality because of inconvenient routes of administration, frequent office visits, and the association between its use and a high frequency of systemic adverse effects.

CONTRAINDICATIONS

CONTRAINDICATIONS

Imiquimod, podophyllin, and podofilox should not be used during pregnancy.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These recommendations were developed in consultation with public- and private-sector professionals knowledgeable in the treatment of patients with sexually transmitted diseases (STDs). The recommendations are applicable to various patient-care settings, including family planning clinics, private physicians' offices, managed care organizations, and other primary-care facilities.
- These recommendations are meant to serve as a source of clinical guidance: health-care providers should always consider the individual clinical circumstances of each person in the context of local disease prevalence These guidelines focus on the treatment and counseling of individual patients and do not address other community services and interventions that are important in sexually transmitted disease/human immunodeficiency virus (STD/HIV) prevention.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention, Workowski KA, Berman SM. HPV infection and genital warts. Sexually transmitted diseases treatment guidelines 2006. MMWR Morb Mortal Wkly Rep 2006 Aug 4;55(RR-11):62-7. [222 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1993 (revised 2006 Aug 4)

GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

GUIDELINE DEVELOPER COMMENT

These guidelines for the treatment of persons who have sexually transmitted diseases (STDs) were developed by CDC after consultation with a group of professionals knowledgeable in the field of STDs who met in Atlanta, Georgia, during April 19–21, 2005.

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Chairpersons: David Atkins, MD, Agency for Healthcare Research and Quality, Rockville, Maryland; Kimberly A. Workowski, MD, National Center for HIV, STD, and TB Prevention, CDC, and Emory University, Atlanta, GA

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Centers for Disease Control and Prevention. Human papillomavirus infection. Sexually transmitted diseases treatment guidelines. MMWR Recomm Rep 2002 May 10;51(RR-6):53-7.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Centers for Disease Control and Prevention (CDC) Web site:

- HTML Format
- Portable Document Format (PDF)

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Workowski KA, Levine WC, Wasserheit JN. U.S. Centers for Disease Control and Prevention guidelines for the treatment of sexually transmitted diseases: an opportunity to unify clinical and public health practice. Ann Intern Med. 2002 Aug 20;137(4):255-62. Electronic copies: Available through Annals of Internal Medicine Online.
- The CDC Sexually Transmitted Diseases Treatment Guidelines 2004 for PDA or Palm OS. Available from the CDC National Prevention Information Network (NPIN) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on September 5, 2002. This summary was updated by ECRI on October 13, 2006.

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Date Modified: 10/13/2008