20. VAGINITIS AND SEXUALLY TRANSMITTED DISEASES

Allison L. Diamant, MD, MSPH, and Eve Kerr, MD, MPH

The approach to developing quality indicators for vulvovaginitis and sexually transmitted diseases (STDs) began with reviewing a general text on ambulatory medicine (Barker et al., 1991) and a text of diagnostic strategies for common medical problems (Panzer et al., 1991). Specific treatment recommendations were derived from the Centers for Disease Control (CDC) 1993 Treatment Guidelines for Sexually Transmitted Diseases (CDC, 1993). The guidelines were based on systematic literature reviews by CDC staff and consensus opinions by experts. The literature reviews are summarized, in part, in the April 1995 Supplement to Clinical Infectious Diseases, which was reviewed to add greater detail to treatment controversies. Pertinent articles published since 1993 were also reviewed for additional recommendations regarding screening and treatment of vaginitis and STDs in non-pregnant, non-HIV infected women and non-HIV infected men.

VULVOVAGINITIS

IMPORTANCE

The most common causes of vulvovaginal infections are Gardnerella vaginalis, Candida albicans, and Trichomonas vaginalis. An estimated 75 percent of women will experience at least one episode of vulvovaginal candidiasis in their lifetimes, and 40 to 45 percent will experience two or more episodes (CDC, 1993). There are an estimated 10 million visits to

---

5 This chapter is a revision of one written for an earlier project on quality of care for women and children (Q1). The expert panel for the current project was asked to review all of the indicators, but only rated new or revised indicators.
physicians’ offices each year for vaginitis (Reef et al., 1995). Vulvovaginal candidiasis and bacterial vaginosis (G. vaginalis) are not considered STDs in the heterosexual population, and women who are not sexually active are rarely affected by bacterial vaginosis (CDC, 1993). However, recent nonrandomized studies suggest that vulvovaginal candidiasis and bacterial vaginosis (G. vaginalis) may be transmitted between women who participate in same sex relations (Berger et al., 1995). T. vaginalis is transmitted through sexual activity. Gonococcal and chlamydial infections, although not causative of vulvovaginitis, may sometimes cause women to present with an abnormal discharge. In fact, as many as 25 percent of women with abnormal discharge have cervical infections (Panzer et al., 1991).

Candida vaginitis does not have important medical sequelae but does cause discomfort that may impair the patient’s quality of life. Bacterial vaginosis may be associated with pelvic inflammatory disease (PID) (Joesoef and Schmid, 1995). A recent randomized controlled trial (RCT) found that women with bacterial vaginosis who were treated with metronidazole before abortion had a three-fold decrease in PID after abortion, compared with untreated women (Joesoef and Schmid, 1995).

SCREENING

There is no indication for screening the general population for vaginitis.

DIAGNOSIS

The approach to diagnosis is well summarized by Panzer et al. (1991). The history and physical examination have poor predictive value. For example, approximately 35 percent of symptomatic patients had no evidence of infection, 32 percent of asymptomatic patients had infection, and approximately 15 percent of infected patients had normal pelvic examinations. However, risk factors for STDs -- such as the number and gender of sexual partners in the past month, history of STDs, presence of genitourinary symptoms, and sexual contact with an infected partner -- increase the prior probability of a sexually transmitted cause for vaginal discharge (Indicator 1).
Table 20.1 displays the variability in the operating characteristics of diagnostic tests for vaginitis. For *T. vaginalis*, the wet mount is highly specific (70 to 98 percent) but not particularly sensitive (50 to 75 percent). For *Candida albicans*, the potassium hydroxide preparation is highly specific (90 to 99 percent), but has varied sensitivity (30 to 84 percent) compared with culture. For bacterial vaginosis (*G. vaginalis*), Amsel et al. (1983) developed diagnostic criteria that are widely accepted (Panzer et al., 1991; Joesoef and Schmid, 1995). The diagnosis in a symptomatic patient is based on the presence of at least three of the following four criteria; 1) pH greater than 4.5; 2) positive whiff test; 3) clue cells on wet mount; and 4) thin homogeneous discharge.

Diagnostic strategy in the evaluation of acute vulvovaginitis is often governed by the need to initiate antimicrobial therapy. The first decision lies in determining whether the infection is cervical or vaginal (Indicator 2). An assessment of risk factors for STDs and a careful pelvic examination will help determine this. If the discharge is thought to be vaginal in origin, then a saline wet mount, potassium hydroxide wet mount, and the application of Amsel’s criteria should be used to determine the etiology of the vaginitis (Indicator 3).

A small proportion of women have recurrent vulvovaginal candidiasis (i.e., three or more annual episodes of symptomatic vulvovaginal candidiasis). These women should be evaluated for predisposing conditions such as diabetes, immunosuppression, concomitant corticosteroid use, and HIV infection. However, the majority of women with recurrent vulvovaginal candidiasis have no identifiable risk factors (Reef et al., 1995).
<table>
<thead>
<tr>
<th>Infection Type/ Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaginal Infection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Trichomonas vaginalis</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saline wet mount</td>
<td>50-75</td>
<td>70-98</td>
</tr>
<tr>
<td>Direct fluorescent antibody</td>
<td>80-86</td>
<td>98</td>
</tr>
<tr>
<td>Vaginal candidiasis (C. albicans)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium hydroxide preparation</td>
<td>30-84</td>
<td>90-99</td>
</tr>
<tr>
<td>Bacterial vaginosis (G. vaginalis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal pH</td>
<td>81-97</td>
<td></td>
</tr>
<tr>
<td>Clue cells</td>
<td>85-90</td>
<td>80</td>
</tr>
<tr>
<td>“Whiff” test</td>
<td>38-84</td>
<td></td>
</tr>
<tr>
<td>Thin homogeneous discharge</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>Gram stain of vaginal wash</td>
<td>97</td>
<td>79</td>
</tr>
<tr>
<td>Abnormal amines by chromatography</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td><strong>Cervical Infection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Chlamydia trachomatis</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct fluorescent antibody</td>
<td>70-87</td>
<td>97-99</td>
</tr>
<tr>
<td>Enzyme immunoassay</td>
<td>80-85</td>
<td>80-85</td>
</tr>
<tr>
<td>Culture (single cervical swab)</td>
<td>70-80</td>
<td>98</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix Gram stain</td>
<td>50-79</td>
<td>98</td>
</tr>
<tr>
<td>Culture (single cervical swab)</td>
<td>85-90</td>
<td>98</td>
</tr>
<tr>
<td>Herpes Simplex Virus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tzanck smear: vesicular; pustular; crusted</td>
<td>67; 54; 17</td>
<td>85</td>
</tr>
</tbody>
</table>

Source: Panzer et al., 1991
TREATMENT

Bacterial Vaginosis (G. vaginalis)

These recommendations are based, in part, on randomized controlled studies and meta-analyses reviewed by the CDC (Joesoef and Schmid, 1995). According to the CDC review, a seven-day treatment regimen of metronidazole is preferred over a single dose regimen of the same, but all appropriate treatments for non-pregnant women are listed below. The CDC report notes that further evaluation of the topical formulations is required (CDC, 1993) (Indicator 4):

- Metronidazole 500 mg orally twice a day for seven days (95 percent overall cure rate);
- Metronidazole 2 g orally in a single dose (84 percent overall cure rate);
- Clindamycin 300 mg orally twice a day for seven days;
- Clindamycin cream at night for seven days; or
- Metronidazole cream twice a day for five days.

T. vaginalis

For people infected with T. vaginalis, it is necessary to treat both patients and their sex partner(s) with:

- Metronidazole 2 g orally in a single dose; or
- Metronidazole 500 mg twice daily for seven days.

Both regimens have been found to be equally effective in RCTs, with a cure rate of approximately 95 percent (CDC, 1993) (Indicator 5).

Candida albicans

A number of topical formulations in the azole class (e.g., butoconazole, clotrimazole, miconazole, tioconazole, terconazole) provide effective treatment for vulvovaginal candidiasis, with symptom relief and negative cultures after completion of therapy in approximately 90 percent of patients (CDC, 1993). These treatment recommendations are based on clinical trials reviewed by the CDC (Reef et al., 1995) (Indicator 6). In addition, several trials have demonstrated that oral azole drugs (e.g., fluconazole, ketoconazole, and itraconazole) may be as effective as topical
agents. The FDA has approved single-dose fluconazole for the treatment of vulvovaginal candidiasis (Wall Street Journal, July 7, 1994). Practicing physicians report this regimen to be an effective treatment (Inman et al., 1994). Use of fluconazole is contraindicated for treatment of vulvovaginal candidiasis in pregnancy. Optimal treatment for recurrent vulvovaginal candidiasis is not well established, but a role for oral agents is being investigated (Reef et al., 1995).

FOLLOW-UP

Follow up care, including cultures, is unnecessary for women whose symptoms resolve after treatment (CDC, 1993).

DISEASES CHARACTERIZED BY CERVICITIS/URETHRITIS

IMPORTANCE

Mucopurulent cervicitis is most often caused by Neisseria gonorrhoea and C. trachomatis -- two sexually transmitted infections. C. trachomatis is the most common cause of cervical infection, with a prevalence ranging from approximately five to 15 percent in asymptomatic women and 20 to 30 percent in women treated at STD clinics. The incidence of chlamydial infection in 1988 was 215 per 100,000 women (DHHS, 1990). The most common cause of nongonococcal urethritis in men is C. trachomatis (23-55%), although a large number of cases are caused by Ureaplasma urealyticum (20-40%). The prevalence of chlamydia among men tends to decline with age. Approximately 13 percent of women with a chlamydial infection have a concurrent gonococcal infection, and an estimated 30 percent of women with a gonococcal infection have a chlamydial infection (Panzer et al., 1991). Transmission of gonorrhea from infected men to uninfected women occurs in 90 percent of exposures. In 1989, the incidence of gonococcal infection among women aged 15 to 44 was 501 per 100,000 (DHHS, 1990), with approximately one million new infections occurring each year (CDC, 1993).

Initially, both gonococcal and chlamydial infections may be asymptomatic in men and women, or may present with a variety of symptoms.
Women may complain of vaginal symptoms (e.g., mucopurulent vaginal discharge, vaginal itching, dyspareunia, dysuria, and vague lower abdominal pain), anorectal symptoms, and pharyngeal symptoms. Both organisms have the potential to cause PID in women, with possible sequelae such as ectopic pregnancy and infertility. Men may notice penile discharge, dysuria, testicular or epididymal pain, or may be asymptomatic. Women and men who engage in fellatio may contract a gonococcal pharyngitis characterized by a white pharyngeal exudate, and pharyngeal discomfort. Anorectal gonococcal disease may occur in men or women who participate in receptive anal intercourse and may present as rectal pain and/or discharge, constipation, and tenesmus.

SCREENING

Screening for both *N. gonorrhea* and *C. trachomatis* should be performed at the annual pelvic examination for all women with multiple male sexual partners (Indicator 7), the presence of other STDs (Barker, 1991), and a history of unprotected sexual intercourse -- and perhaps for all sexually active women 24 years of age or younger (CDC, 1993). There is no currently recommended screening for older women or men of any age.

DIAGNOSIS

The presence of symptoms such as mucopurulent vaginal discharge, vaginal itching, dyspareunia, dysuria, and vague lower abdominal pain in a heterosexual sexually active woman should lead one to suspect cervicitis. The physical examination may reveal a red, edematous, and friable cervix with mucopurulent cervical discharge. For men with a history of penile discharge and/or dysuria, a diagnosis of urethritis due to *C. trachomatis* or *N. gonorrhea* should be considered, although asymptomatic infections are common (CDC, 1993). If a sexually active male patient presents with penile discharge he should be tested for both chlamydia and gonorrhea at the time of presentation (Indicator 9).

*C. trachomatis*

Diagnosis in patients with symptoms of cervicitis or urethritis is confirmed by direct fluorescent antibody testing, which has a 70 to 87
percent sensitivity and a 97 to 99 percent specificity; or by enzyme immunoassay, which has a 80 to 86 percent sensitivity and a 98 percent specificity (Panzer et al., 1991).

**N. gonorrhoea**

Suspected gonococcal infections may be initially confirmed by Gram stain, which has a 50 to 79 percent sensitivity and a 98 percent specificity (Panzer et al., 1991).

**TREATMENT**

In patients with symptoms or physical exam that are inconclusive, one must consider the pre-test probabilities of infection when assessing the need for treatment. In populations with a high prevalence of STDs, in those patients with known or suspected exposures, or in patients who might be unlikely to return for treatment, medical therapy should be provided without waiting for the confirmatory results of cultures. In other cases, according to the CDC, one may wait for the test results to determine the need for treatment (CDC, 1993). Treatment for mucopurulent cervicitis or urethritis should include the following:

- Treatment for gonococcal and chlamydial infections in patient populations with a high prevalence of STDs, such as patients seen at many STD clinics;
- Treatment for chlamydia only, if the prevalence of N. gonorrhoea is low but the likelihood of chlamydia is significant;
- Await test results if the prevalence of both infections is low, and if compliance to return for further treatment if necessary is low (CDC, 1993). Patients should be advised to refer their sexual contacts for evaluation and appropriate treatment.

**C. trachomatis**

Based on the CDC review of RCTs (Weber and Johnson, 1995), either of the following treatment regimens is recommended:

- Doxycycline 100 mg orally twice a day for seven days; or
- Azithromycin 1 g orally in a single dose.
Other effective treatments include: ofloxacin, erythromycin, or sulfisoxazole. The patient’s sexual partner(s) should also be referred for treatment.

**N. gonorrhea**

The treatment for gonorrhea also follows CDC recommendations based on reviews of RCTs (Moran and Levine, 1995). All patients treated for gonorrhea should also be treated for chlamydia (Indicator 8). Any of the following regimens are considered appropriate treatment for gonorrhea:

- Ceftriaxone 125 mg IM in a single dose;
- Cefixime 400 mg orally in a single dose;
- Ciprofloxacin 500 mg orally in a single dose; or
- Ofloxacin 400 mg orally in a single dose.

A clinical trial showed a cure rate of greater than 95 percent for anal and genital infections with one of the above treatment regimens, whereas treatment with either ceftriaxone or ciprofloxacin in the above-listed doses cured 90 percent of pharyngeal infections. Other effective antibiotics are available and may be used, such as spectinomycin, other cephalosporins, and other fluoroquinolones.

**FOLLOW-UP**

Follow-up cultures for chlamydia are not necessary for patients who completed treatment with doxycycline or azithromycin, unless symptoms persist or re-infection is suspected (CDC, 1993). If an alternative antibiotic regimen was selected (e.g., erythromycin, sulfisoxazole, or amoxicillin), re-testing should be performed three weeks after completion of the therapeutic course. Patients treated for gonorrhea who are symptom-free after completion of an appropriate antibiotic regimen do not need follow-up cultures (CDC, 1993).

Patients treated for gonorrhea should undergo screening for syphilis at the time of diagnosis.
PELVIC INFLAMMATORY DISEASE

IMPORTANCE

PID represents a spectrum of upper genital tract inflammatory disorders, including endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis. In the U.S., more than one million cases of PID are diagnosed and treated annually (DHHS, 1990). PID and its associated complications of ectopic pregnancy and infertility are estimated to cost more than $2.7 billion per year, with the total as high as $4.2 billion when all direct and indirect costs are included (Walker et al., 1993). The most common etiologic agents are \textit{C. trachomatis} and \textit{N. gonorrhea}.

DIAGNOSIS

The diagnosis of PID is usually made on the basis of clinical findings, including both speculum and bi-manual examinations (Indicator 10). In some cases, women may have an atypical presentation with abnormal bleeding, dyspareunia, or vaginal discharge. In the absence of an established cause other than PID (such as ectopic pregnancy or acute appendicitis) the CDC (1993) suggests that empiric treatment for PID should be initiated when all of the following clinical criteria for pelvic inflammation are present (Indicator 11):

- Lower abdominal tenderness;
- Adnexal tenderness; and
- Cervical motion tenderness.

The specificity of the diagnosis is increased if the following signs are also present (CDC, 1993):

- Oral temperature greater than 38.3°C;
- Abnormal cervical or vaginal discharge;
- Elevated erythrocyte sedimentation rate;
- Elevated C-reactive protein; and
- Laboratory documentation of cervical infection with \textit{N. gonorrhea} or \textit{C. trachomatis}. 

332
Algorithms based only on clinical criteria fail to identify some women with PID, and may misclassify others. Assessment by endometrial biopsy and laparoscopy, either separately or in combination, is more specific but less sensitive (Walker et al., 1993)

TREATMENT

Primarily on the basis of expert opinion, the CDC (1993) recommends hospitalization for parenteral antibiotic therapy under any of the following circumstances (Indicator 12):

- The diagnosis is uncertain and potential surgical emergencies such as acute appendicitis and ectopic pregnancy cannot be excluded;
- A pelvic abscess is suspected;
- The patient is pregnant;
- The patient is an adolescent;
- The patient is seropositive for HIV;
- There is severe illness or intractable nausea and vomiting that preclude outpatient management; or
- Clinical follow-up within 72 hours of initiating antibiotic therapy cannot be arranged.

Based on RCTs and extensive study of inpatient antimicrobial treatment for PID, the CDC recommends therapy with two antibiotics in either of the following regimens (Indicator 13):

**Regimen 1:**
- Cefoxitin 2 g IV every 6 hours or Cefotetan 2 g IV every 12 hours (for at least 48 hours); and
- Doxycycline 100 mg IV or orally every 12 hours (for 14 days).

**Regimen 2:**
- Clindamycin 900 mg IV every 8 hours; and
- Gentamicin.
- This regimen should be continued for at least 48 hours, followed by oral doxycycline or clindamycin.

No specific comparisons of inpatient and outpatient treatment have been performed, and there is limited information from clinical trials.
regarding outpatient management for PID (Walker et al., 1993). Patients who do not respond to outpatient therapy within 72 hours should be hospitalized, because it is expected that they would be afebrile and improved in terms of subjective complaints by that time (Peterson et al., 1990). For patients who do not respond to outpatient treatment, either of the following regimens is appropriate:

**Regimen 1:**
- Cefoxitin 2 g IM plus probenecid, 1 g orally in a single dose concurrently, or ceftriaxone 250 mg IM or any other parenteral third-generation cephalosporin; and
- Doxycycline 100 mg orally twice a day for 14 days.

**Regimen 2:**
- Ofloxacin 400 mg orally twice a day for 14 days; and
- Either clindamycin 450 mg orally 4 times a day OR metronidazole 500 mg twice a day for 14 days.

**FOLLOW-UP**

Patients who receive outpatient therapy should be followed up within 72 hours to assess clinical improvement (Indicator 14), and should also undergo microbiologic re-examination seven to ten days after completing antibiotic therapy.

Patients who require hospitalization for antimicrobial therapy should also have repeat cultures performed, seven to ten days after completion of the course of treatment to determine cure. Some patients may warrant further microbiologic re-examination after four to six weeks (CDC, 1991a). The male sexual partners of all patients should be empirically treated for *C. trachomatis* and *N. gonorrhoea* (CDC, 1993).

**DISEASES CHARACTERIZED BY GENITAL ULCERS**

**IMPORTANCE**

The majority of persons with genital ulcers in the U.S. have genital herpes simplex virus (HSV), syphilis, or chancroid, with genital herpes
being the most common. Three to ten percent of patients with genital ulcers may have more than one infection present. All of these infections are associated with an increased risk for HIV infection (CDC, 1993).

GENITAL HERPES SIMPLEX VIRUS

Screening

The literature does not suggest a useful role for screening for genital HSV infection.

Diagnosis

Based on serologic studies, the prevalence of genital HSV infection in the U.S. is 30 million people (CDC, 1993). The diagnosis is most often made on the basis of the history and physical examination, and is confirmed by HSV culture or antigen test. The sensitivity of the culture decreases with the duration – that is, with the age of the lesion(s). The sensitivities for vesicular, pustular, and crusted lesions are 70 percent, 67 percent, and 17 percent, respectively (Panzer et al., 1991). Specimens from primary and cutaneous lesions are most likely to grow HSV in culture.

Treatment

RCTs have demonstrated the effectiveness of acyclovir in decreasing the symptoms and signs of HSV during the initial and subsequent episodes, as well as when used for suppressive daily therapy (CDC, 1993; Stone and Whittington, 1990). The CDC does not generally recommend treatment with acyclovir for recurrent episodes of HSV infection because early therapy can rarely be initiated. The CDC does recommend that after one year of continuous suppressive therapy, acyclovir should be discontinued to allow re-assessment of the patient’s recurrence of disease. If the recurrence rate for HSV is low, suppressive therapy may be discontinued either permanently or temporarily.

Other Management Issues

Patient education is very important in preventing the transmission of HSV. Patients should be advised to abstain from sexual activity while lesions are present, and to use condoms during all sexual exposures.
(Indicator 15). All patients with genital ulcers should undergo serologic testing for syphilis, and HIV testing should be offered for those patients with known or suspected HSV (Indicator 16).

CHANCROID

Screening

Screening for chancroid is not indicated.

Diagnosis

The causative agent of chancroid is the bacterium *Haemophilus ducreyi*. As many as ten percent of patients with chancroid may be co-infected with *Treponema pallidum* or HSV (CDC, 1993). Because of the lack of a readily available method of testing for *H. ducreyi*, the diagnosis is made primarily on clinical grounds. The CDC supports the probable diagnosis of chancroid based on the following: 1) The presence of one or more painful genital ulcers; 2) The absence of evidence of *T. pallidum* infection on dark field exam or via a serologic test for syphilis performed at least seven days after the onset of the ulcers; and 3) The clinical presentation of the ulcer(s) is not typical of HSV and/or the HSV test results are negative.

Treatment

The CDC recommendations for treatment include single-dose azithromycin or IM ceftriaxone, or a seven-day course of erythromycin (Indicator 17). Patients with chancroid should be tested for HIV and syphilis, and if the initial test results are negative, they should be advised to undergo re-testing in three months (CDC, 1993). All persons with whom the patient had sexual contact within ten days before the onset of symptoms should be examined and treated.

Follow-Up

Patients should be re-examined within 10 days after initiation of antimicrobial treatment to assess clinical response (Indicator 18).
PRIMARY AND SECONDARY SYPHILIS

Syphilis is a systemic disease caused by *T. pallidum*. The incidence of primary and secondary syphilis in the U.S. has been rising steadily, with 118 cases per 100,000 population reported in 1989 (USDHHS, 1990). There appears to be an association between genital ulcer disease and the spread of HIV via sexual contact.

**Screening**

Screening of the general population is not indicated, except in the pregnant population. Those populations at risk for infection with *T. pallidum* (i.e., those with other STDs) should be screened using a non-treponemal test (CDC, 1993).

**Diagnosis**

Primary syphilis should be diagnosed based on the presence of a usually nonpainful genital ulcer (or recurrent history of a genital ulcer), and a positive laboratory test for syphilis. Twenty percent of patients will have a negative nontreponemal test (VDRL or RPR) at the time of presentation, but direct examination of the chancre via dark-field microscopy or direct fluorescence antibody will be positive (Panzer et al., 1991).

Secondary syphilis is a systemic illness characterized by a prominent rash which develops six weeks to several months after the initial exposure. According to the CDC recommendations, persons sexually exposed to individuals with any stage of syphilis should be evaluated clinically and serologically.

**Treatment**

Treatment of primary and secondary syphilis should be initiated with Benzathine penicillin G (2.4 million units IM in a single dose), in the absence of a penicillin allergy (Indicator 19). The decision to treat should not rely on waiting for the test results, but on the history, physical examination, and index of suspicion (Indicator 20).
Follow-up

Treatment failures occur in approximately five percent of patients treated with penicillin-based regimens, and more frequently in other regimens (Rotls, 1995). The CDC recommendations for follow-up include re-examination clinically and serologically at three and six months for assessment of successful response to therapy (CDC, 1993) (Indicator 21).

DISEASES CHARACTERIZED BY GENITAL WARTS (HUMAN PAPILLOMA VIRUS)

IMPORTANCE

The prevalence of infection with human papilloma virus (HPV) is increasing, with over one million new cases each year (Mayeaux, 1995). Although over 60 different types of HPV have been identified, only a relative few have a moderate risk (types 33, 35, 39, 40, 43, 45 and 51) or high risk (types 16 and 18) of oncogenic potential (Mayeaux, 1995; CDC, 1993). There is usually a very long latency period between infection with the virus and any manifestation of cervical cancer. Individuals of all ages may contract HPV through sexual contact, although sexually active young adults have the highest prevalence and incidence of infection. HPV infection occurs at mucosal surfaces where micro-abrasions have caused epithelial disruption. Individuals, not knowing that they are infected with HPV, may transmit the virus to their sexual partners. Various viral strains of HPV have been strongly associated with the development of cervical cancer in women. The risk for contracting HPV increases with a woman’s number of lifetime male sexual partners.

SCREENING

There is no indication for general population screening for HPV in either men or women, and no widely accepted screening tests exist.

DIAGNOSIS

HPV may be diagnosed in the presence of genital warts, condyloma acuminate, which have a hypertrophic appearance. Application of five-
percent acetic acid to small flat lesions suspicious for condyloma acumminata produces characteristic acetowhite changes. The differential diagnosis of HPV includes other sexually transmitted diseases condyloma latum (syphilis), HSV, and molluscum contagiosum, as well as common benign skin lesions, and dermatologic neoplasms. (Mayeaux, 1995). Lesions may be found in many genito-anal locations on both men and women. Single or multiple lesions may exist, as well as sub-clinical infection that is not apparent without the application of acetic acid. HPV lesions are rarely found on other non-genital mucosal surfaces such as the oral mucosa, larynx, and trachea (Mayeaux, 1995). Mucosal changes indicative of HPV infection may be noted on Pap smears (Indicator 22), although viral typing using recombinant DNA techniques is not routinely performed.

**TREATMENT**

It is not possible to eradicate HPV with the currently available treatment regimens. Therefore, the goal of treatment is to reduce the symptoms and signs of infection. Treatment of external genital warts is not likely to influence the development of cervical cancer (CDC, 1993). The results of many RCTs and other treatment studies have shown a wide range of 22 to 94 percent in the effectiveness of available therapies for clearing exophytic genital warts, and a very high recurrence rate of 25 percent at three months (CDC, 1993). The recurrence of genital warts is believed to be most commonly due to activation of sub-clinical infection rather than re-infection. Genital warts due to HPV may resolve, remain unchanged, or grow if they are left untreated. Providers should inform patients of the necessity of practicing safe sexual habits such as the use of condoms, abstinence, or monogamy in order to reduce the spread of HPV.

A number of treatments for genital warts due to HPV exist, and RCTs have been conducted to assess the various treatment modalities (CDC, 1993). Some of the treatments are site-specific and include cryotherapy with liquid nitrogen or cryoprobe, Podofillox, Podophyllin, Trichloroacetic acid, and electrodesiccation or electrocautery.
FOLLOW-UP

Regularly scheduled follow-up is not necessary after the warts have responded to therapy. Annual cytologic screening is recommended for women with a history of genital warts. Recommendations for cervical cancer screening are covered in Volume II of this series, which covers ocologic conditions and HIV (see Chapter 3: Cervical Cancer Screening).
REFERENCES


RECOMMENDED QUALITY INDICATORS FOR VAGINITIS AND SEXUALLY TRANSMITTED DISEASES

The following indicators apply to men and women age 18 and older. Only the indicators in bold type were rated by this panel; the remaining indicators were endorsed by a prior panel.

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Quality of Evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaginitis - Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 1. A sexual history should be obtained at the time of presentation from all women with a chief complaint of vaginal discharge. The history should include:  
  a. Number of male partners in the previous 6 months;  
  b. Absence or presence of symptoms in partners;  
  c. Prior history of sexually transmitted diseases. | III | Panzer et al, 1991; CDC, 1993 | Decrease discharge, itching, and dysuria. Decrease PID and abdominal pain. Decrease infertility. Decrease mortality from ectopic pregnancy. | In patients with one or more risk factors, there is an increased prior probability of an STD (i.e., chlamydia or gonorrhea) as a cause of discharge, and a culture for the causative organisms may be appropriate. This is important because cervicitis has more significant long-term consequences than vaginitis, such as PID, infertility, and ectopic pregnancy. |
| 2. In women presenting with a chief complaint of vaginal discharge, the practitioner should perform a speculum exam at the time of the initial presentation to determine if the source of the discharge is vaginal or cervical. | III | Panzer et al, 1991 | Decrease discharge, itching, and dysuria. | Since implications of and treatment for cervicitis and vaginitis differ substantially, physical exam must be performed. |
| 3. If three of the following four criteria are met, a diagnosis of bacterial vaginosis, or gardnerella vaginitis should be made:  
  • pH greater than 4.5;  
  • positive whiff test;  
  • clue cells on wet mount; and  
  • thin homogeneous discharge. | III | Panzer et al, 1991 | Decrease discharge, itching, and dysuria. | pH determination is also sensitive, but its specificity is unknown. Therefore, at a minimum, the two wet mounts should be performed. |
<p>| <strong>Vaginitis - Treatment</strong> | | | | |
| 4. Treatment for bacterial vaginosis should be with metronidazole (orally or vaginally) or clindamycin (orally or vaginally) at the time of diagnosis. | I | CDC, 1993 | Decrease discharge, itching, and dysuria. | These are the only proven effective regimens; RCTs reviewed by the CDC show that the evidence for efficacy of oral treatment is better than that for topical treatment. |</p>
<table>
<thead>
<tr>
<th>Indicator</th>
<th>Quality of Evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. Treatment for T. vaginalis should be with oral metronidazole, if the patient does not have an allergy to metronidazole or is not in first trimester of pregnancy at the time of diagnosis.</td>
<td>I</td>
<td>CDC, 1993</td>
<td>Decrease discharge, itching, and dysuria.</td>
<td>Based on RCTs reviewed by the CDC this is the only known effective treatment.</td>
</tr>
<tr>
<td>6. Treatment for non-recurrent (&lt; 3 episodes in the previous year) yeast vaginitis should be with topical 'azole' preparations (e.g. clotrimazole, butoconazole, etc.) or fluconazole at the time of diagnosis.</td>
<td>I</td>
<td>CDC, 1993</td>
<td>Decrease discharge, itching, and dysuria.</td>
<td>Based on RCTs reviewed by the CDC. These regimens are approved by the FDA.</td>
</tr>
</tbody>
</table>

**Cervicitis - Diagnosis**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Quality of Evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. Routine testing for gonorrhea (culture) and chlamydia trachomatis (antigen detection), should be performed with the routine pelvic exam for women with multiple male sexual partners (more than 1 during the previous 6 months).</td>
<td>III</td>
<td>CDC, 1993; ACOG, 1993 (The Obstetrician Gynecologist Primary Preventive Healthcare)</td>
<td>Alleviate pain. Alleviate fever. Decrease infertility. Decrease mortality from ectopic pregnancy.</td>
<td>This recommendation is based on epidemiologic studies of transmission and prevalence, as summarized by the CDC. Women with multiple sexual partners are at higher risk for STDs, and these may be asymptomatic.</td>
</tr>
</tbody>
</table>

**Cervicitis - Treatment**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Quality of Evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>8. Women treated for gonorrhea should also be treated for chlamydia at the time of presentation.</td>
<td>II-2; III</td>
<td>CDC, 1993</td>
<td>Prevent PID. Decrease infertility. Decrease mortality from ectopic pregnancy.</td>
<td>Women with gonorrhea are likely to be coinfected with chlamydia. Since the sensitivity of chlamydia assays are variable, concurrent treatment is recommended.</td>
</tr>
</tbody>
</table>

**Urethritis - Diagnosis**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Quality of Evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. If a sexually active male patient presents with penile discharge he should be tested for both chlamydia and gonorrhea at the time of presentation.</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Decrease infertility. Provide accurate diagnosis and treatment.</td>
<td>This is based on epidemiologic studies of transmission and prevalence, as summarized by the CDC.</td>
</tr>
</tbody>
</table>
### Pelvic Inflammatory Disease (PID) - Diagnosis

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Quality of Evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>10. Patients with the diagnosis of PID should receive all of the following at the time of diagnosis:</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Alleviate pain. Alleviate fever. Decrease infertility. Decrease mortality from ectopic pregnancy.</td>
<td>The diagnosis of PID is based primarily on physical exam. In addition, one should obtain cervical specimens for culture. Therefore, a physical exam is mandatory before treatment can be initiated.</td>
</tr>
<tr>
<td>a. Speculum exam;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Bi-manual exam.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. If a patient is given the diagnosis of PID, at least 2 of the following signs should be present on physical exam:</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Alleviate pain. Alleviate fever. Decrease infertility. Decrease mortality from ectopic pregnancy.</td>
<td>It is important to correctly identify PID since symptoms may mimic appendicitis and ovarian torsion. The CDC states that all 3 signs should be present. We have stated that at least 2 must be present and documented.</td>
</tr>
<tr>
<td>• lower abdominal tenderness;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• adnexal tenderness; and</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• cervical motion tenderness.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Pelvic Inflammatory Disease - Treatment

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Quality of Evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>12. Women with PID and any of the following conditions should receive parenteral antibiotics at the time of diagnosis:</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Alleviate pain. Alleviate fever. Prevent sepsis. Decrease infertility. Decrease mortality from ectopic pregnancy.</td>
<td>Although other reasons for hospitalization may exist (i.e., cannot rule out appendicitis), these conditions have been recommended by the CDC and should be discernible by chart review. The purpose of hospitalization is to ensure effective treatment in persons at risk of complications (e.g., HIV infection) or poor follow-up (e.g., adolescents).</td>
</tr>
<tr>
<td>a. Pelvic abscess is present or suspected;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Pregnancy;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. HIV infection;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Uncontrolled nausea and vomiting;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Lack of clinical improvement within 72 hours of beginning therapy.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Duration of total antibiotic therapy for PID should be no less than 10 days (inpatient, if applicable, plus outpatient).</td>
<td>III</td>
<td>CDC, 1993; Peterson et al, 1991</td>
<td>Alleviate pain. Alleviate fever. Prevent sepsis. Decrease infertility. Decrease mortality from ectopic pregnancy.</td>
<td>The standard of care is 10-14 days, although RCTs have not specifically addressed duration of treatment. Shorter treatment periods may result in lower cure rates.</td>
</tr>
<tr>
<td>Indicator</td>
<td>Quality of Evidence</td>
<td>Literature</td>
<td>Benefits</td>
<td>Comments</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------</td>
<td>------------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td><strong>Pelvic Inflammatory Disease - Follow-Up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Genital Ulcers - Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. All patients with genital herpes should be counseled on reducing the risk of transmission to a sexual partner.</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Prevent spread of genital herpes.</td>
<td>Genital herpes is can be transmitted even in the absence of current outbreak. Unlike most other STDs, there is not an effective cure for herpes. Therefore, prevention of transmission is of primary importance.</td>
</tr>
<tr>
<td>16. If a patient presents with the new onset of genital ulcers then all of the following should be offered at the time of presentation: a. Cultures for HSV b. Blood test for HIV c. Blood test for syphilis.</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Prevention of complications of untreated syphilis and HIV. Limit transmission of genital herpes.</td>
<td>There has been an increase in the prevalence of genital herpes in association with HIV. Effective treatment for syphilis is available with a single IM injection of penicillin. There is no effective cure for herpes; therefore preventing transmission of the virus is of prime importance.</td>
</tr>
<tr>
<td><strong>Genital Ulcers - Chancroid - Treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Patients with chancroid should be treated with azithromycin, ceftriaxone, or erythromycin (in the absence of allergy to these medications).</td>
<td>I</td>
<td>CDC, 1993</td>
<td>Decrease pain. Heal ulcer. Limit transmission of chancroid.</td>
<td>These have been shown to be effective in RCTs reviewed by the CDC.</td>
</tr>
<tr>
<td><strong>Genital Ulcers - Chancroid - Follow-up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18. Patients receiving treatment for chancroid should be re-examined within 10 days of treatment initiation to assess clinical improvement.</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Prevent complications of untreated syphilis. Prevent transmission of chancroid, syphilis, and herpes.</td>
<td>Most patients will have improved by 7 days.</td>
</tr>
<tr>
<td>Indicator</td>
<td>Quality of Evidence</td>
<td>Literature</td>
<td>Benefits</td>
<td>Comments</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------</td>
<td>------------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td><strong>Genital Ulcers - Syphilis - Treatment</strong></td>
<td>19. Patients with primary and secondary syphilis who do not have a penicillin allergy should be treated with IM-administered benzathine penicillin G.</td>
<td>I</td>
<td>CDC, 1993</td>
<td>Prevent late complications of syphilis.</td>
</tr>
<tr>
<td>20.</td>
<td>If a patient has a primary ulcer consistent with syphilis, treatment for syphilis should be initiated before laboratory test results are available.</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Prevent late complications of syphilis.</td>
</tr>
<tr>
<td><strong>Genital Ulcers - Syphilis - Follow-up</strong></td>
<td>21. Patients with primary or secondary syphilis should be re-examined clinically and serologically within 6 months after treatment.</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Prevent complications of untreated syphilis.</td>
</tr>
<tr>
<td><strong>Genital Warts - Diagnosis</strong></td>
<td>22. Women with an initial diagnosis of HPV should have a speculum examination and a pap smear (if not performed during the preceding year).</td>
<td>III</td>
<td>CDC, 1993; CDC, 1997</td>
<td>Identify cervical dysplasia and exophytic warts.</td>
</tr>
<tr>
<td><strong>STDs (General) - Diagnosis</strong></td>
<td>STDs include herpes, syphilis, genital warts, gonorrhea, chlamydia, trichomoniasis, HPV, and chancroid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23. If a patient presents with an initial infection of any STD, HIV testing should be discussed and offered at the time of presentation.</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Prevent progression and reduce transmission of HIV.</td>
<td>Persons with one STD are at high risk for another. Treatment to slow the disease course of HIV and prophylaxis against opportunistic infections are available.</td>
</tr>
<tr>
<td>24. If a patient presents with any STD, a non-treponemal test (VDRL or RPR) for syphilis should be performed at the time of presentation</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Prevent late complications of syphilis.</td>
<td>Persons with one STD are at high risk for another. Since there is effective treatment to prevent late complications of syphilis, testing is recommended.</td>
</tr>
<tr>
<td>Indicator</td>
<td>Quality of Evidence</td>
<td>Literature</td>
<td>Benefits</td>
<td>Comments</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------</td>
<td>------------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>STDs (General) - Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25. Sexual partners of patients with new diagnoses of gonorrhea, chlamydia, chancroid, and primary or secondary syphilis should be referred for treatment as soon as possible.</td>
<td>III</td>
<td>CDC, 1993</td>
<td>Prevent complications from PID and syphilis.</td>
<td>Persons with one STD are at high risk for another. Since there is effective treatment to prevent late complications of syphilis, testing is recommended. Women with untreated gonococcal and chlamydial infections are at increased risk for PID and ectopic pregnancy.</td>
</tr>
</tbody>
</table>

Quality of Evidence Codes

I RCT
II-1 Nonrandomized controlled trials
II-2 Cohort or case analysis
II-3 Multiple time series
III Opinions or descriptive studies