Diagnosis and Treatment of Infectious Vaginitis

Case Study and Commentary: *Michael F. Rein, MD*

Series Editor: *Bryan A. Liang, MD, PhD, JD*

DR. LIANG:
Introduction

Infectious vaginitis, which includes the three vaginal infections trichomoniasis, bacterial vaginosis, and candidiasis, is a common disorder in women.[1] Diagnosis of infectious vaginitis is particularly important in pregnant women. Pregnant women diagnosed with bacterial vaginosis, such as the patient reviewed in this case study, have an elevated risk of preterm labor, preterm rupture of membranes, chorioamnionitis, and postpartum endometritis.[2] In addition, reports indicate that effective treatment of high-risk pregnant woman with bacterial vaginosis reduces the rate of preterm delivery,[3,4] although these studies did not assess low-risk pregnant woman and the potential treatment effects on preterm delivery. Generally, this form of infectious vaginitis is associated with a significantly increased risk of pelvic inflammatory disease, postabortion uterine infection, breast abscess, cervical intraepithelial neoplasia, and posthysterectomy cuff infection;[5–8] thus, bacterial vaginosis is an important diagnosis to consider in all women.

A primary care physician must have a high index of suspicion when diagnosing infectious vaginitis in pregnant patients with acute symptoms relating to vaginal discharge. Sensitive chemical parameters, such as the elevated pH of the vaginal discharge noted by the care giver in this case study, are not considered by 95% of health care providers in their diagnostic work-ups.[9] Further, as many as 50% of all patients with bacterial vaginosis present with no symptoms in the lower genetic tract.[9] Available diagnostic techniques should be employed to assess the presence or absence of infectious vaginitis even in the absence of symptoms.

The feasibility of screening pregnant woman for infectious vaginitis in the context of cost constraints in the United State's health care delivery system is a major issue for the primary care physician. No easy, empirically based resolution for this issue exists. For example, in patients such as the woman presented in this case study, infection with bacterial vaginosis yields a greater risk of complications in early pregnancy (ie, second trimester) compared with late pregnancy.[10] However, even a positive diagnosis of bacterial vaginosis in early pregnancy may not be a reliable predictor for development of preterm birth, preterm labor, and premature rupture of membranes.[11] Such findings, in addition to the paucity of literature on low-risk women and pregnancy outcomes after treatment for bacterial vaginosis, have led the Centers for Disease Control and Prevention (CDC) to recommend that only women who are at a high risk for pregnancy complications be screened for bacterial vaginosis; this screening should be performed early in the second trimester.[1] Yet, because of the limited study of low-risk women, such screening recommendations may be underinclusive and miss patients who could benefit from early diagnosis.

Despite CDC recommendations, screening for bacterial vaginosis may also be effective in other circumstances, such as prior to pregnancy termination. A significant incidence of infectious vaginitis has been reported in women screened prior to abortion, with 28% of patients testing positive for bacterial vaginosis, 24% for candidal infection, and 0.75% for trichomoniasis.[12] Approximately 50% of the women who present for pregnancy termination have some form of lower genital tract infection.[12,13] The association between bacterial vaginosis and postabortion upper genital tract infection, which can be effectively mitigated with metronidazole treatment, also emphasizes the need for infectious vaginitis screening in women prior to abortion.[14,15] Providers may wish to consider routine screening for

Dr. Rein is Professor of Medicine, Division of Infectious Diseases, University of Virginia School of Medicine, Charlottesville, VA. Dr. Liang is Dr. Arthur W. Grayson Distinguished Visiting Professor of Law and Medicine, Southern Illinois University School of Law, Carbondale, IL, and a member of the Hospital Physician *Editorial Board.*

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infectious vaginitis of patients who present for abortion. Such screening may be as cost effective as similar programs that screen for chlamydial infection.[12]

Health care providers who work in public health clinics that treat patients with HIV and patients who abuse drugs have a significant role in the assessment of vaginitis. Vaginitis-cervicitis is the most frequently reported gynecologic diagnosis in both HIV-seropositive and HIV-seronegative women undergoing methadone maintenance treatment who present to public health clinics.[16] Pregnancy is also a common presentation in such public health clinics.[16] Further, because women seek care from these public health clinics four times more frequently than men, primary care physicians have significant opportunities to diagnose, treat, and educate women about vaginitis as well as HIV and other sexually transmitted diseases.

Overall, infectious vaginitis is a common disorder that has significant clinical consequences if left untreated. Screening appears to be a reasonable approach to ameliorate these consequences and may be cost effective. However, all physicians must have a high index of suspicion and utilize readily available screening methods to assure that patients with infectious vaginitis are recognized and adequately treated.

CASE PRESENTATION

Initial Presentation

An 18-year-old woman presents to a public health clinic with the complaint of a slightly odorous, nonirritating vaginal discharge of 3 weeks' duration.

History

The patient is 4 months pregnant. She has had unprotected sexual contact with her regular partner for the past 6 months, and her most recent episode of coitus occurred 7 days prior to presentation. Approximately 4 weeks before presentation, she had a single episode of unprotected vaginal intercourse with a former partner. Both men are, as far as she knows, asymptomatic. The patient has not taken antimicrobial agents and has not douched since becoming pregnant. She has not received prenatal care. She has no history of vaginitis or sexually transmitted diseases (STDs). The discharge was heavy enough to leave a small stain on the patient's underwear. The patient attempted self-treatment with vaginal miconazole cream, a commonly used nonprescription preparation, and experienced partial relief of symptoms throughout the 7-day course. The odorous discharge returned within 48 hours of completion of therapy. She has no history of dysuria or abdominal pain.

Physical Examination

On physical examination, the patient's labia are uninflamed. The vagina contains an excessive, homogeneous discharge with small bubbles. The cervix is erythematous, and cervical discharge is heavy but mucoid. The uterus is enlarged, consistent with the date of gestation, and no adnexal tenderness is evident.

QUESTION

- **What conditions are suggested by the history and physical examination findings?**

DISCUSSION

Differential Diagnosis

The consistency of the patient's discharge suggests an infectious vaginitis. Three infections predominate among women with symptoms of vaginitis: bacterial vaginosis, vulvovaginal candidiasis, and trichomoniasis. Diagnostic features are listed in **Table 1**. The fact that the patient is pregnant is a major risk factor for vulvovaginal candidiasis. Vulvovaginal candidiasis is reported to occur in 10% of women during the first trimester of pregnancy and in one-third to one-half of women in their third trimesters.[17] In addition, the patient is at increased risk for bacterial vaginosis and trichomoniasis because she has had unprotected sexual contact with multiple partners.[18,19] However, trichomoniasis has become far less common than other forms of vaginitis,[20] possibly because of the frequent use of metronidazole in sexually active populations.

The presence of cervical erythema raises the question of a coincident cervicitis. None of the organisms that cause vaginitis is capable of producing an endocervicitis, and its presence should raise suspicion of coincident infection with *Chlamydia trachomatis,* herpes simplex virus, or *Neisseria gonorrhoeae.*[21]

Although not a factor in this case, women sometimes seek medical attention in response to a normal physiologic discharge. A discharge consisting of cervical mucus and desquamated vaginal epithelial cells or cervical mucus that results from changes in hormonal levels may alarm the patient. Cervical mucus increases at the time of ovulation, in pregnancy, and in response to the use of gestational hormones. Thus, a woman who begins to use oral or implantable contraceptives and assumes a sexual relationship without barrier prophylaxis may observe a coincidental increase in vaginal discharge, fear that she has contracted an STD, and seek medical attention. Although usually not irritating, such physiologic vaginal discharge may be odorous. However, because odor can be the only symptom of

Table 1. Typical Features of Common Infectious Vaginitides

	Bacterial Vaginosis	Vulvovaginal Candidiasis	Physiologic Trichomoniasis	Discharge
Symptoms				
Vulvar irritation	±	++	++	–
Dysuria	–	+	20% of patients	–
Odor	++	–	±	–
Signs				
Labial erythema	–	±	±	–
Satellite lesions	–	+	–	–
Discharge				
Consistency	Homogeneous, ± frothy	± Curdy	Frothy (25% of patients)	Floccular
Color	Gray, white	White	Yellow-green (25% of patients)	White
Adherence to vaginal walls	+	+	–	–
Positive whiff test	70%–90% of patients	–	60%–90% of patients	–
pH	≥ 4.7 (90% of patients)	≤ 4.5	≥ 4.7 (70%–90% of patients)	≤ 4.5
Microscopy				
Epithelial cells	Clue cells (90%)	Normal	Normal	Normal
PMNs/epithelial cell	≤ 1	Variable	≥ 1	≤ 1
Bacteria	Gram-variable coccobacilli	Gram-positive rods	Gram-positive rods	Gram-positive rods
Pathogens	Coccobacilli and motile rods	Yeasts and pseudohyphae (50% of patients)	Trichomonads (70% of patients)	–
Bimanual examination				
Vaginal tenderness	–	+	+	–
Rugal hypertrophy	–	±	+	–
Adnexal tenderness	–	–	±	–

++ = usually present and may be severe; + = usually present; ± = variably present; – = not usually present and presence should raise concern for other diagnosis; PMNs = polymorphonuclear leukocytes.

bacterial vaginosis, the patient who presents with complaints of vaginal odor without other symptoms must not be dismissed.

QUESTION

- **What further evaluations can assist in making a definitive diagnosis of bacterial vaginosis?**

DISCUSSION

Diagnostic Tests

Vaginal pH determination. In the healthy adult female, each mL of vaginal fluid contains more than 10^5 lactobacilli, principally *Lactobacillus crispatus* and *Lactobacillus jensenii*.[22] Strictly anaerobic bacteria such as *Bacteroides* and *Prevotella* species are recovered in similar numbers from only approximately one-sixth of women.[22] Normal lactobacillary flora is considered an important host defense. These organisms elaborate hydrogen peroxide, which limits the growth of anaerobic bacteria and other pathogens.[23] Such lactobacilli also maintain the normal acidity of the vagina at a pH of around 4 to 4.5. The lactobacillary flora, and hence a normal pH, is maintained in patients with vulvovaginal candidiasis, but the flora is altered and the pH elevated in 90% of women with bacterial vaginosis and in 60% to 90% of women with trichomoniasis. Thus, a normal vaginal pH in a symptomatic woman suggests a diagnosis of vulvovaginal candidiasis, whereas an elevated pH

supports a diagnosis of bacterial vaginosis or trichomoniasis. The pH can be determined with a suitable indicator paper applied to the lateral third of the vaginal wall during speculum examination or by testing the vaginal discharge pooled in the speculum.

The lactobacillary vaginal flora, and hence the vaginal pH, are unaffected by pregnancy.[24] Certain antimicrobials can reduce the flora and elevate the pH. Vaginal pH may be artifactually elevated by recent unprotected coitus because the pH of semen is more neutral than that of vaginal discharge. Also, cervical discharge has a relatively elevated pH; contamination of the vaginal pool with this cervical discharge can result in an erroneous finding.

Amine liberation (whiff) test. Anaerobic bacteria, such as members of the genera *Prevotella*, *Bacteroides*, *Mobiluncus*, and *Peptococcus*, are present in large numbers in the vaginas of women with bacterial vaginosis.[17,24] Some of these organisms elaborate amines, including triethylamine, putrescine, and cadaverine, which are responsible for the odor noticed by affected patients.[24] When alkalinized, these compounds become more volatile and are easily smelled. Adding 10% potassium hydroxide to vaginal material liberates these amines, producing a pungent, fishy odor. A positive whiff test has been used as part of the case definition of bacterial vaginosis in some studies, yielding an artificially high apparent sensitivity, but the whiff test has been described in approximately 70% of cases in other series. The whiff test is negative in patients whose lactobacillary flora has been reduced by antimicrobials but positive in a poorly defined fraction of patients with trichomoniasis. The whiff test is negative in patients with vaginal candidiasis. Enhanced odor with alkalinization explains why some women with bacterial vaginosis note an increase in vaginal odor following coitus—semen elevates the pH of vaginal contents.

Microscopy. Differentiation between bacterial vaginosis and trichomoniasis depends on microscopic evaluation of material recovered from the vagina. The most useful approach to evaluation in the clinical setting is the wet mount. Material from the vagina is collected on a swab, which is then agitated in approximately 1 mL of saline in a test tube. A drop of the suspension is transferred to a microscope slide, a coverslip is applied, and the preparation is viewed at ×400 magnification with the substage condenser racked down and the substage diaphragm closed. The presence of relatively few polymorphonuclear leukocytes (PMNs) (no more than 1 per epithelial cell) and the presence of epithelial cells studded with coccobacilli (clue cells) support a diagnosis of bacterial vaginosis. Clue cells are observed in 90% of patients with bacterial vaginosis. The presence of large numbers of PMNs supports the diagnosis of trichomoniasis. The diagnosis of trichomoniasis is confirmed by observing the motile protozoa; however, the sensitivity of the wet mount for trichomonads is only approximately 60%.[25] Thus, it is appropriate to consider a diagnosis of trichomoniasis in a woman who has an elevated vaginal pH and a wet mount revealing excess PMNs, whether or not protozoa are actually observed. Motile trichomonads and clue cells often coexist in the same patient. In this circumstance the patient should be treated for bacterial vaginosis with metronidazole because the regimen is effective for both conditions.

The wet mount can be treated with 10% potassium hydroxide and examined for fungal elements. A diagnosis of vaginal candidiasis is suggested in the symptomatic woman who maintains a flora of rods. The wet mount has a sensitivity of only approximately 50% to 70% for yeasts,[26] so a patient with appropriate clinical features (Table 1) and a flora of rods should never be denied treatment for vaginal candidiasis on the basis of a wet mount that fails to reveal the organism.

Bacterial vaginosis can also be diagnosed on the basis of a Gram stain of vaginal discharge. In bacterial vaginosis, the normal lactobacillary flora, which manifests as gram-positive rods, is supplanted by large numbers of gram-variable coccobacilli *(Gardnerella vaginalis)*, which may be seen adhering to the epithelial cells (clue cells) or in clumps in the vaginal material.[27] However, Gram stain cannot be used effectively to diagnose trichomoniasis, and the Clinical Laboratory Improvement Act does not permit the use of Gram stain in most physicians' offices. If a microscope is unavailable, however, a slide of vaginal material can be heat-fixed and sent to a central laboratory for Gram stain interpretation.

Vaginal Culture

The presence of *Trichomonas vaginalis* on culture or microscopic evaluation (including cervical cytology) is an indication for treatment. *Candida albicans*, in contrast, is carried by 15% to 20% of asymptomatic healthy women, and its mere presence is not an indication for treatment.[26] Likewise, *G. vaginalis* is carried by 30% to 40% of women who do not have bacterial vaginosis.[17,24] Thus, cultures for these latter organisms have no place in the evaluation of asymptomatic women. Vaginal culture for fungi can be useful in the evaluation of a symptomatic or relapsing woman in whom direct microscopy fails to reveal a pathogen.

Table 2. Complications of Bacterial Vaginosis in Pregnant and Nonpregnant Women

Complication	Odds Ratio
Pregnant women	
Chorioamnionitis	1.9 to 6.8
Premature labor and delivery	1.4 to 6.9
Postpartum fever	NA
Postpartum endometritis	5.8
Postpartum salpingitis	3.7
Nonpregnant women	
Endometritis	2.6 to 12.4
Salpingitis	3
Posthysterectomy vaginal cuff or wound infection	3.2 to 6.2

NA = not available.

QUESTION

- **What approach should be used to determine the etiologic agent in patients with suspected vaginitis?**

DISCUSSION

Approach to Testing

When the speculum examination is performed, suitable discharge specimens should be obtained from the cervix and the vagina. The vaginal pH determination and the whiff test should be performed on each patient, because both tests are relatively specific for a diagnosis of bacterial vaginosis or trichomoniasis. Although precise calculations are impossible because of limited data, a positive whiff test and the presence of an elevated pH would effectively rule out either a physiologic discharge or simple vaginal candidiasis. All discharges should be examined microscopically. The wet mount generally provides the most rapid differential diagnosis, but if wet mount microscopy is not available, a dried smear of vaginal material may be sent to the central laboratory for evaluation by Gram stain. However, Gram stain has low sensitivity for the diagnosis of trichomoniasis. Cultures are generally reserved for problem cases.

DIAGNOSIS

During the examination, the patient is found to have a vaginal pH of 5.5, and whiff test is positive. The wet mount reveals a coccobacillary flora and clue cells. No trichomonads are observed, but the number of PMNs is slightly increased. The physician makes a diagnosis of bacterial vaginosis.

QUESTION

- **What are the consequences of untreated bacterial vaginosis, particularly in pregnant patients?**

DISCUSSION

Complications of Bacterial Vaginosis

Bacterial vaginosis has been associated with pregnancy complications, including premature labor and delivery and postpartum endometritis (**Table 2**).[1–4,28–38] A true pathogenic role for bacterial vaginosis in both pregnant and nonpregnant women is supported by the recovery of bacterial vaginosis–associated microorganisms from blood, amniotic fluid, and wound infections. The rate of complications is sufficiently high enough to warrant aggressive treatment of bacterial vaginosis in pregnancy, particularly in late pregnancy.

Although initially regarded as an annoying but benign condition, bacterial vaginosis is now recognized as being associated with complications in nonpregnant women (Table 2). Bacterial vaginosis has been associated with infection of the upper genital tract,[28,30,31] and a particularly strong association with plasma cell endometritis has been documented in a small number of women.[30] In the past this pathologic finding has been most strongly linked to infection with *C. trachomatis*. Thus, bacterial vaginosis should be treated when the patient is symptomatic; treatment should be considered if the patient is to undergo a gynecologic procedure. Many clinicians believe that the condition should be treated even if the patient is asymptomatic, but this opinion is not universally held.[1] This author favors treating asymptomatic women in whom the diagnosis has been made because many women with bacterial vaginosis who initially claim to be asymptomatic note that what they had considered to be their "normal" discharge had resolved upon receiving treatment.

QUESTION

- **Is bacterial vaginosis an STD?**

DISCUSSION

Sexual Transmission and Bacterial Vaginosis

The contribution of sexual transmission to bacterial vaginosis has long been debated (**Table 3**).[17–19,23,24,39–45] Bacterial vaginosis represents a dramatic rearrangement in the vaginal flora, and the factors responsible for this change are incompletely defined. The nonvenereal factors that influence the development of disease have two important consequences for the clinician. First, reappearance of disease does not necessarily imply additional sexual contacts on the part of an infected women or her partner. Second, it is unnecessary to treat male sexual

partners at the time a woman is first diagnosed with bacterial vaginosis.[43,44] Some women with rapidly and frequently recurring disease, however, may benefit from treatment of sexual partners.

QUESTION

- **What is the initial treatment for bacterial vaginosis?**

DISCUSSION

Antimicrobial Therapy for Bacterial Vaginosis

The most effective therapies for bacterial vaginosis, metronidazole and clindamycin (**Table 4**), are directed principally against the anaerobic flora that contributes to disease. In this context, the efficacy of first-generation cephalosporins (cephalexin, cefadroxil) is rather surprising because of their apparent lack of activity in vitro against the relevant pathogens.[46] Several studies document that the single-dose metronidazole treatment, useful for trichomoniasis, is inadequate for bacterial vaginosis[17,47–51] in spite of a recent meta-analysis that claims equivalent efficacy.[39] Standard therapies yield cure rates of approximately 80% to 90%.[39,47–52]

According to the CDC, treatment in pregnant women is the same as treatment in nonpregnant women, and the use of metronidazole is appropriate in any stage of pregnancy.[1] However, clindamycin cream should not be used in pregnant women because of its relative failure to reduce the risk of preterm birth.[1,53,54]

Patients treated with oral metronidazole must be cautioned to avoid alcohol because the drug occasionally induces a disulfiram-like reaction, which can manifest as nausea and flushing. Oral metronidazole is the least expensive regimen that can be used to treat bacterial vaginosis, but its metallic taste is unacceptable to some patients.

Topical preparations[55] are absorbed across the vaginal walls and must be considered very low-dose systemic exposure. In rare cases, oral and even topical clindamycin have been associated with the development of pseudomembranous colitis.[56,57] Vaginal candidiasis can follow any treatment for bacterial vaginosis.[58]

QUESTION

- **Should the patient be assessed for any other conditions?**

DISCUSSION

Polymorphonuclear Leukocytes and Sexually Transmitted Diseases

Physicians do not usually see many PMNs in the vaginal discharge of women with bacterial vaginosis, as demonstrated in the patient in the case study. Although the presence of PMNs in vaginal discharge is not specific for coincident cervicitis[59] and this patient's cervical discharge is mucoid, the possibility of coincident cervical infection should not be overlooked. The contribution of sexual transmission to the overall epidemiology of bacterial vaginosis is sufficiently strong to warrant screening women with bacterial vaginosis for the presence of other sexually transmitted pathogens that may be clinically silent but are of far greater eventual medical significance, including *C. trachomatis, N. gonorrhoeae*, and HIV.

Table 3. Evidence For and Against the Theory of Sexual Transmission of Bacterial Vaginosis

Evidence suggesting that bacterial vaginosis is sexually transmitted
Bacterial vaginosis is more prevalent among women with greater numbers of recent and lifetime sexual partners
Bacterial vaginosis is associated with a higher prevalence of other sexually transmitted diseases, including nongonococcal urethritis and infection with *Chlamydia trachomatis, Neisseria gonorrhoeae,* and human papillomavirus
Symptoms first develop in many women shortly after they become sexually active
Vaginal recolonization with *Gardnerella vaginalis* is far more common in women re-exposed to untreated sexual partners than in women who are not
G. vaginalis is recovered from the urethras of more than 80% of male sexual partners of infected women, and these organisms are almost always the same biotype
Evidence suggesting that bacterial vaginosis is NOT exclusively sexually transmitted
Recurrences of infection are observed in the absence of sexual re-exposure
Bacterial vaginosis has been recognized in virgins
G. vaginalis has been isolated in prepubescent girls and sexually inactive women
Initial simultaneous treatment of sexual partners has not been shown to reduce recurrence rates
The age and racial distribution of bacterial vaginosis differs from that of gonorrhea, being relatively more likely to occur in older white women
The organisms associated with bacterial vaginosis have been cultured from the rectum, from which site it is speculated that the organisms colonize the vagina
Nonvenereal risk factors include douching and use of an intrauterine device

TREATMENT

The patient is treated with metronidazole (500 mg

Table 4. Treatment of Bacterial Vaginosis and Relative Evidence of Effectiveness

Regimen	Supporting Data
Oral agents	
Metronidazole, 500 mg twice daily for 7 days	Strong
Metronidazole, 250 mg three times daily for 7 days	Strong
Metronidazole, 750-mg extended-release tablet once daily for 7 days	Limited
Metronidazole, 2 g as a single dose	Weak
Clindamycin, 300 mg twice daily for 7 days	Strong
Cephalexin, 250 mg four times daily for 7 days	Limited
Cefadroxil, 500 mg twice daily for 7 days	Limited
Vaginal preparations	
Clindamycin 2% cream, 5 g once nightly for 7 days	Strong
Metronidazole 0.75% gel, 5 g twice daily for 5 days	Strong
Metronidazole 0.75% gel, 5 g once nightly for 5 days	Strong
Treatments of negligible or unproven value	
Povidone-iodine, vaginally	Ineffective
Triple sulfa vaginal preparations	Ineffective
Acetic acid gel, vaginally	Ineffective
Yogurt, vaginally	Ineffective
Ampicillin, orally	Ineffective
Lactate gel, vaginally	Variable
Lactobacillus preparations, vaginally	Limited

orally, twice daily for 7 days) and a chlamydia DNA probe from her cervix is obtained. Her odorous discharge resolves, suggesting cure. The DNA probe is positive for *C. trachomatis*. A prescription for a single 1-g dose of oral azithromycin is ordered. The patient is strongly advised to refer her partners for evaluation and treatment for chlamydial infection. The patient is also advised to enroll in a program of prenatal care.

QUESTION

- **Should medication be prescribed for the patient's sexual partners?**

DISCUSSION

Medication for the Sexual Partner

Some physicians prescribe medications for sexual partners, but this practice has some disadvantages and risks. The disadvantage lies in the physician's inability to examine both partners because several conditions (eg, nongonococcal urethritis) are more easily diagnosed in men than in women. The risk lies in the possibility that the partner may have an adverse reaction to the prescribed drug. Such an outcome can be avoided if the prescribing physician interviews the patient directly.

FOLLOW-UP VISIT

The patient presents 5 days after her initial presentation and notes vulvar irritation and external dysuria. She is found to have diffuse vulvar erythema. The vagina contains a normal amount of discharge. The vaginal pH is 4.5, and whiff test is negative. Wet mount reveals a flora of rods and a moderate excess of PMNs. Potassium hydroxide preparation reveals no fungal elements.

QUESTION

- **What is the patient's current diagnosis?**

DISCUSSION

Diagnosis

The return of a normal flora of rods, presumably lactobacilli, has been accompanied by the expected return of the vaginal pH to the normal range. Because the hydrogen-peroxide–producing lactobacilli have suppressed the anaerobic flora, the whiff test has reverted to negative. Apparently, the patient's bacterial vaginosis has resolved. Part of the value of metronidazole in the treatment of bacterial vaginitis stems from its ability to permit recolonization of the vagina with lactobacilli during treatment.[60] Other less effective regimens such as amoxicillin/clavulanate suppress lactobacilli during therapy. Clindamycin suppresses lactobacilli, but only transiently.[60] Vulvovaginal candidiasis occurs in the presence of a lactobacillary flora; the findings on wet mount are consistent with this diagnosis.

QUESTIONS

- **What factors predispose a woman to vulvovaginal candidiasis?**
- **What is the role of sexual transmission in vulvovaginal candidiasis?**
- **Why is evidence of the current infection lacking on microscopy?**

DISCUSSION

Risk Factors for Acute Vulvovaginal Candidiasis

This patient's risk factors include her recent use of

two different antimicrobials and her pregnancy.[17,58,61] High estrogen levels favor the growth of *Candida.* The mechanism of estrogenic predisposition is unclear, although some investigators have suggested that increased vaginal glycogen stores may play a role[17] or that estrogens influence vaginal pH in a way that makes the milieu more hospitable to the fungi.[26] Estrogens induce changes in vaginal epithelial cells that increase the adherence of yeasts and may directly affect the organism. An estrogen receptor is found in the cytosol of *C. albicans,* and estrogens induce formation of the more pathogenic, filamentous forms.[62] The mechanism of increased glycogen stores has also been adduced to explain the association of vaginal candidiasis with poorly controlled diabetes mellitus; tight glycemic control decreases the frequency of symptomatic infection. However, testing for diabetes in women with recurrent vaginal candidiasis is not cost-effective.[61]

Severe, refractory vaginal candidiasis plagues some women with AIDS.[63] Whereas some studies have failed to support an increased incidence of vaginal candidiasis in this population,[64] it seems appropriate to consider AIDS in women with severe, frequently recurring, or persistent disease. Although there is no need to screen for HIV infection on the basis of a single episode of acute vaginal candidiasis, the patient in this case study should be encouraged to undergo HIV testing because she has multiple sexual partners and has been diagnosed with other sexually transmitted infections. The presence of an STD should always be considered a marker for high-risk behavior and should therefore prompt an attempt to rule out coincident infection with HIV.[1]

Sexual Transmission and Vulvovaginal Candidiasis

Sexual transmission appears to play only a small role in the overall epidemiology of vaginal candidiasis.[1] Some studies have noted that the vaginal carriage of yeasts is not significantly altered by the onset of sexual activity, whereas others have described an increased incidence of symptomatic vulvovaginal candidiasis at this time.[64–66] It should be noted, however, that the incidence of vulvovaginal candidiasis is increased among users of oral contraceptives,[61,62,67] the contraceptive sponge,[64] and the intrauterine device,[64] any of which might act as a confounder of the observation. The male sexual partners of infected women do not need to be treated.

Some male partners of women with vaginal candidiasis develop *Candida balanitis,* which manifests as erythematous, moist, pruritic plaques on the penile glans and shaft.[68] This condition may be considered sexually transmitted but does not have the same significance as other, more traditional STDs.

Table 5. Treatment of Vulvovaginal Candidiasis

Oral regimens
Single dose
Fluconazole, 150 mg
1-day
Itraconazole, 200 mg twice daily*
3-day
Itraconazole, 200 mg once daily*
Ketoconazole, 200 mg twice daily*
Ketoconazole, 200 mg once daily*
Vaginal regimens
Single dose
Miconazole, 1200-mg suppository
Clotrimazole, 500-mg suppository
Clotrimazole 10% cream, 5 g
Tioconazole 6.5% cream, 4.6 g
3-day
Butoconazole 2% cream, 5 g once nightly
Clotrimazole, 200-mg suppository once nightly
Econazole, 150-mg suppository once nightly
Miconazole, 200-mg suppository once nightly
Terconazole 0.8% cream, 5 g once nightly
Terconazole, 80-mg suppository once nightly
Tioconazole 2% cream, 5 g once nightly
7-day
Clotrimazole, 100-mg suppository once nightly
Clotrimazole 1% cream, 5 g once nightly
Fenticonazole 2% cream, 5 g once nightly
Miconazole 2% cream, 5 g once nightly
Miconazole, 100-mg suppository once nightly
Terconazole 0.4% cream, 5 g once nightly
14-day
Nystatin, 100,000-U suppository once nightly

*Not approved by United States Food and Drug Administration.

Laboratory Diagnosis of Vulvovaginal Candidiasis

The wet mount, even with the use of potassium hydroxide, fails to demonstrate the presence of yeasts in 30% to 50% of infected women.[26] Much of the inflammatory response in vulvovaginal candidiasis is immunologically mediated, and very small numbers of yeasts may be present even in severe disease. A commercially

available latex agglutination test has a disappointingly low sensitivity of only approximately 60%.[69] Thus, a patient with risk factors and a consistent clinical picture should never be denied treatment for vulvovaginal candidiasis on the basis of a failure to demonstrate the organism. Culture may be useful in cases of recurrent disease or those cases in which the diagnosis is in doubt.

QUESTION

- **What treatment is appropriate at this time?**

DISCUSSION

Therapy for Acute Vulvovaginal Candidiasis

Currently available therapies for vaginal candidiasis are essentially equivalent (**Table 5**).[17,70–72] The choice between these treatments may be made on the basis of patient preference and price. Some studies suggest marginally lower cure rates with the single-dose topical regimens. Of considerable current interest are the oral therapies, which are being used with increasing frequency. Only single-dose fluconazole is currently approved by the United States Food and Drug Administration and has adequate supporting data.[73–76] Oral therapy may be particularly useful when the diagnosis is in doubt, because oral medication avoids the potentially confounding effect of the soothing carriers in which the topical regimens are applied. Some women report a transient decrease in symptoms while they are using topical therapies, even though they have a vaginal process of another etiology. The oral regimen is also of particular value in the setting of coincidental vulvovaginal candidiasis and genital herpes, when covering herpetic lesions with an antifungal might delay healing. Longer-course (ie, 7 day) regimens may be of use in patients whose vulvovaginal candidiasis is caused by *Candida (Torulopsis) glabrata*, which is relatively resistant to the imidazole-triazole antifungals.[77]

The high incidence of infectious vaginitis has given rise to a large number of nonprescription preventive and therapeutic products. To use them effectively, however, patients must make an accurate etiologic diagnosis on the basis of symptoms alone, a practice that is treacherous even for trained clinicians because of the great variability of vaginitis symptoms. For example, a woman may believe she has vulvovaginal candidiasis and decide to use a nonprescription topical antifungal, when, indeed, she has a vaginitis of a different etiology.[78] The antifungal may nonspecifically reduce or mask vaginal symptoms during use, further deluding the patient into thinking that she has a simple mycotic infection. More ominously, such women may actually have a cervical discharge that exits through the introitus, but the patient may think that this infection is a vaginal process. In such cases, use of nonprescription products can delay the patient's decision to seek treatment for clinically serious conditions.[78]

TREATMENT AND RESOLUTION OF SYMPTOMS

The patient is treated with a 7-day regimen of clotrimazole, which completely relieves her symptoms. She suffers one recurrence of vulvovaginal candidiasis during the third trimester of her pregnancy, which is successfully treated with a topical antifungal preparation. **HP**

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