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## Vaginitis in Nonpregnant Patients

*Vaginitis is defined as inflammation or infection of the vagina and is associated with a spectrum of symptoms, including vulvovaginal itching, burning, irritation, dyspareunia, “fishy” vaginal odor, and abnormal vaginal discharge. Vaginal symptoms are some of the most frequent reasons for patient visits to obstetrician–gynecologists (1) and may have important consequences in terms of discomfort and pain, days lost from school or work, sexual functioning, and self-image (2). Distinguishing vaginal from vulvar symptoms is important to direct evaluation and treatment. The purpose of this document is to provide updated evidence-based guidance for the diagnosis and treatment of the common causes of vaginitis in nonpregnant patients. Information on the treatment of vaginitis in patients with human immunodeficiency virus (HIV) is covered elsewhere (3). Guidelines are subject to change. For the most up-to-date information on vaginitis diagnosis and treatment, see the Centers for Disease Control and Prevention (CDC) Sexually Transmitted Diseases webpage, which is available at <https://www.cdc.gov/std/>.*

### Background

#### **Etiology**

Vaginitis has a broad differential diagnosis, and successful treatment frequently rests on an accurate diagnosis. The most common causes of vaginitis include vulvovaginal candidiasis, bacterial vaginosis, and trichomoniasis. Among patients with vaginal symptoms, vaginal candidiasis is diagnosed in 17–39% of cases, bacterial vaginosis in 22–50% of cases, and trichomoniasis in 4–35% of cases; however, vaginitis may remain undiagnosed in 7–72% of patients (1, 4). Although vulvovaginal candidiasis, bacterial vaginosis, and trichomoniasis are the most common causes of vaginitis symptoms, other etiologies include vulvar skin diseases, desquamative inflammatory vaginitis, and genitourinary syndrome of menopause (5–9).

#### **Estrogen and the Vaginal Environment**

Estrogen status plays a crucial role in determining the normal state of the vagina. During the reproductive years, the presence of estrogen increases glycogen content in vaginal epithelial cells, which in turn

encourages colonization of the vagina by lactobacilli. This increased level of colonization leads to lactic acid production and a resulting decrease in the vaginal pH to less than 4.5. This acidic environment protects against the growth of pathogenic organisms and is key to maintaining a balanced vaginal ecosystem. The normal vaginal flora remains heterogeneous, and *Gardnerella vaginalis*, *Escherichia coli*, group B streptococci, genital *Mycoplasma* species, and *Candida albicans* are commonly found.

In prepubertal girls and postmenopausal women, the lack of estrogen inhibits normal growth of the vaginal bacterial ecosystem; therefore, microscopy typically shows a paucity of epithelial cells and background bacteria. In addition, the vaginal epithelium is thin and the pH of the vagina is elevated (higher than 4.5) because lactic acid-producing lactobacilli are sparse. Growth of bacteria associated with bacterial vaginosis and yeast forms are less common in an estrogen-depleted environment, thus prepubertal girls and postmenopausal women (not using estrogen) uncommonly have bacterial vaginosis or vaginal candidiasis (10, 11).



## Bacterial Vaginosis

Bacterial vaginosis is not a true infectious or inflammatory state. It represents a change in the normal microbiome of the vagina with an overgrowth of facultative anaerobic organisms (eg, *G vaginalis*, *Bacteroides* species, *Peptostreptococcus* species, *Fusobacterium* species, *Prevotella* species, and *Atopobium vaginae*) and a lack of hydrogen peroxide-producing lactobacilli (12, 13). Bacterial vaginosis is the most common cause of abnormal vaginal discharge in patients of reproductive age and has a higher prevalence in black, Hispanic, and Mexican American women compared with white non-Hispanic women (14, 15). In addition to race and ethnicity, age, douching, and sexual activity are associated with increased risk of bacterial vaginosis (4, 15). Although the occurrence of bacterial vaginosis is associated with sexual activity for both heterosexual (16, 17) and lesbian couples (17, 18), and rarely occurs in patients who have never been sexually active (19), it is not directly caused by the sexual transmission of a single pathogen (17, 20). Nonpregnant patients with bacterial vaginosis are at an increased risk of various infections of the female reproductive tract, including pelvic inflammatory disease (PID) and postprocedural gynecologic infections, and have increased susceptibility to sexually transmitted infections (STIs) such as HIV and herpes simplex virus type 2 (21–24).

Many patients with bacterial vaginosis are asymptomatic (4). However, those who do have symptoms commonly report having an abnormal vaginal discharge and a fishy odor, particularly after vaginal intercourse and menses (4, 12).

## Trichomoniasis

Vaginal trichomoniasis, which is caused by infection with the protozoan parasite *Trichomonas vaginalis*, is the most common nonviral STI in the United States, with approximately 3–5 million cases annually (25, 26). Like bacterial vaginosis, there are prevalence disparities with this vaginal condition. African American women are ten times more commonly affected compared with non-Hispanic white women (26). Other risk factors identified include increased number of sex partners, low socioeconomic status, and douching (26). Trichomoniasis has been found to be associated with PID, posthysterectomy cuff cellulitis, HIV, and other STIs (20, 27). More than 50% of patients with trichomoniasis are asymptomatic or have minimal symptoms; however, symptomatic patients with trichomoniasis may report an abnormal vaginal discharge, itching, burning, or postcoital bleeding (26, 28).

Although trichomoniasis is an STI, because asymptomatic carriage can occur for prolonged periods in men

and women, a recent diagnosis of trichomoniasis does not necessarily establish recent acquisition unless the patient has had documented negative *Trichomonas* testing results in the recent past.

## Vulvovaginal Candidiasis

Vulvovaginal candidiasis represents inflammation and infection of the vagina with *Candida* species. It is the second most common cause of vaginitis behind bacterial vaginosis (20), and 29–49% of females report at least one lifetime episode (29). Physical manifestations of vulvovaginal candidiasis range from asymptomatic colonization to severe vulvovaginal symptoms such as burning, itching, edema, dysuria, dyspareunia, and an abnormal discharge (20). In one study of the vaginal and endocervical environment in nonpregnant patients, 12% of asymptomatic patients were culture positive for *Candida* species (10, 30). Vulvovaginal candidiasis is uncommon in prepubescent girls and postmenopausal women (not using estrogen) and is often over-diagnosed in these populations (30).

## Clinical Considerations and Recommendations

### ► What is the recommended initial evaluation for patients with symptoms of vaginitis?

A complete medical history, physical examination of the vulva and vagina, and clinical testing of vaginal discharge (ie, pH testing, a potassium hydroxide [KOH] “whiff test,” and microscopy) are recommended for the initial evaluation of patients with vaginitis symptoms (20).

### History

Evaluation of patients with vaginitis symptoms should include a focused history. Patients may have difficulty distinguishing vulvar and vaginal symptoms, thus it is important to elicit information about the location of symptoms (vulva, vagina, anus), description of symptoms, and duration of symptoms. Additionally, the clinician should inquire about the following to yield important insights into the likely etiology (20):

- sexual history (including number and gender identification of sex partners and specific sexual practices)
- self-treatment with over-the-counter medications or prescription medications
- vulvovaginal hygiene practices (eg, shaving, douching)



- underlying medical conditions (eg, diabetes, HIV status, inflammatory bowel disease)
- relation of symptoms to the menstrual cycle

### **Physical Examination**

Because many patients with vaginitis have vulvar manifestations, the physical examination should begin with a thorough evaluation of the vulva and skin surrounding the anus. Patients with vulvar dermatosis may have erythema, hypopigmentation, papules and plaques, melanosis, edema, or architectural changes that suggest chronic inflammation. Bacterial vaginosis does not affect the vulva and is not an inflammatory condition, whereas candidiasis and trichomoniasis may lead to vulvar erythema and edema in addition to vaginal findings. Fissures may be present in severe vulvovaginal candidiasis (31).

During speculum examination, samples of vaginal discharge collected from the vaginal walls or fornix should be obtained for clinical testing. Evaluation of the physical appearance of the discharge may provide some clues as to the diagnosis but are not diagnostic alone (Table 1). It is important that the swab for pH evaluations be obtained from the mid-portion of the vaginal side wall to avoid false elevations in pH results caused by cervical mucus, blood, semen, lubricants, or other substances.

### **Clinical Testing**

Office-based testing of samples of vaginal discharge to determine the likely cause of vaginal symptoms includes pH testing, a KOH whiff test (ie, amine odor test), and microscopic examination with 0.9% saline and 10% KOH (Table 1). Commercial tests that have been approved by the U.S. Food and Drug Administration (FDA) for the diagnosis of vaginitis can be used as an alternative to clinical testing in settings where pH paper, KOH, and microscopy are not available (20). Diagnosis of each of the most common causes of vaginitis is discussed in detail in the following sections.

#### ► **How is bacterial vaginosis diagnosed and treated?**

### **Diagnosis**

Bacterial vaginosis presents with a watery gray homogeneous discharge that often is accompanied by an amine (“fishy”) odor. Other initial evaluation findings that are suggestive of bacterial vaginosis are included in Table 1. The use of Amsel clinical criteria or Gram stain with Nugent scoring is recommended for the diagnosis of bacterial vaginosis (20, 32). Because the normal vaginal flora is heterogeneous, routine bacterial culture of the vagina is not specific for bacterial vaginosis. For this

reason, bacterial culture is not recommended for the diagnosis (20, 32). In research settings, Gram stain with Nugent scoring (33) is considered the criterion standard for diagnosing bacterial vaginosis; however, it is impractical for most clinical practitioners and, therefore, Amsel criteria typically are used for the diagnosis of bacterial vaginosis. Overdiagnosis of bacterial vaginosis is common and clinical correlation is necessary to avoid overtreatment of a condition that is usually asymptomatic.

### **Amsel Criteria**

Bacterial vaginosis can be diagnosed based on the presence of three of the following four Amsel criteria (20, 34):

1. Homogeneous, thin, white-gray discharge that smoothly coats the vaginal walls
2. More than 20% clue cells (eg, vaginal squamous cells studded with adherent coccobacilli) on saline microscopy
3. A pH of vaginal fluid greater than 4.5
4. Positive KOH whiff test result (ie, detection of an amine or fishy odor before or after a sample of vaginal discharge is mixed with the addition of 10% KOH).

Detection of three of four of these Amsel criteria has been correlated with results by Gram stain with Nugent scoring, which is considered the reference standard (20). Amsel clinical criteria have a reported sensitivity of 92% and a specificity of 77% compared with Gram stain with Nugent scoring (35, 36).

If microscopy is not available, Amsel criteria can still be fulfilled by using the patient report of vaginal discharge, elevated pH, and positive whiff test result. One observational study correlated two of the Amsel criteria (elevated pH and whiff test) with equal sensitivity and specificity as the standard three Amsel criteria (36).

### **Gram Stain With Nugent Scoring**

Although Gram stain with Nugent scoring is the reference standard for the diagnosis of bacterial vaginosis, its use generally is limited to research settings. Nugent scoring assigns a value to different bacterial morphotypes seen on Gram stain of vaginal secretions. Scores 0–3 are interpreted as normal flora; scores reported as 4–6 are intermediate flora; and scores valued 7–10 are interpreted as bacterial vaginosis flora. If an intermediate score is obtained, then Amsel criteria are assigned to dispute or accept the diagnosis of bacterial vaginosis (33). Clue cells on microscopy correlate well with Gram stain findings and are the most reliable indicator of bacterial vaginosis (12).



**Table 1. Clinical Features of Vaginitis**

Condition	Symptoms/Discharge	Examination Findings	pH Level	Microscopy/KOH Test Results	Diagnostic Tests
Normal physiologic discharge	White and creamy or clear discharge	White discharge in vaginal fornix and adherent to vaginal walls	3.5–4.5	Mature squamous cells, rare PMN, background bacteria dominated by lactobacillus	N/A
Bacterial vaginosis	Increased thin, watery, white-gray vaginal discharge often with fishy odor. Most are asymptomatic.	Thin, white-gray homogenous discharge	More than 4.5	Clue cells (more than 20%), no PMNs, a positive KOH “whiff” test result.  Decreased or absent lactobacilli and increased cocci, and small curved rods	Recommended: • Amsel criteria • Gram stain with Nugent scoring  Alternative: • FDA-approved commercial tests
Trichomoniasis	Yellow-to-green frothy vaginal discharge, abnormal vaginal odor, pruritus, irritation, and dysuria. More than half are asymptomatic.	Yellow, frothy vaginal discharge; vaginal or cervical-vaginal erythema with petechiae	More than 4.5	Motile trichomonads, abundant PMNs, bacteria with both bacillus and cocci, variable KOH “whiff” test results	Recommended: • NAAT  Alternative: • FDA-approved commercial tests • Culture
Vulvovaginal candidiasis	Normal-appearing discharge or thick, white vaginal discharge, pruritus, burning, dyspareunia and dysuria	Thick, white, curd-like vaginal discharge. In severe vulvovaginal candidiasis, erythema, edema, excoriations, and fissures may be present.	3.5–4.5	Branching pseudohyphae, budding pseudohyphae (10x), or spores (40x) with 10% potassium hydroxide.  Mature squamous cells, rare PMNs, bacteria dominated by lactobacillus	Recommended: • Microscopy • Yeast culture  Alternative: • FDA-approved commercial tests

Abbreviations: NAAT, nucleic acid amplification test; PMN, polymorphonuclear leukocytes.

Data from Nyirjesy P. Management of Persistent Vaginitis: A Clinical Expert Series. *Obstet Gynecol* 2014; 124:1135–46; and Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. Centers for Disease Control and Prevention [published erratum appears in *MMWR Recomm Rep* 2015;64:924]. *MMWR Recomm Rep* 2015;64(RR-03):1–137.

## Commercial Tests

Although microscopy with Amsel criteria and Gram staining with Nugent scoring remain the preferred methods and the most cost-effective way to diagnosis bacterial vaginosis, some newer commercially available diagnostic tests show promise for use in the clinical setting and may be considered when microscopy is unavailable.

Data from studies that have evaluated commercially available tests such as direct DNA probe assays for *G vaginalis* or chromogenic point-of-care assays that detect the presence of sialidase activity show that these tests have acceptable performance against the reference standards for bacterial vaginosis diagnosis, Amsel criteria and Nugent scoring (20, 37–39). However, because a single sentinel organism has not been found that accurately identifies patients with bacterial vaginosis, the diagnostic

utility of a test that identifies only a single organism (eg, *G vaginalis*) is still being investigated and is not currently supported (20, 40).

Polymerase chain reaction (PCR) has been used in research settings for the detection of *G vaginalis* as well as a variety of organisms associated with bacterial vaginosis; however, until recently, its use as a clinical diagnostic test for bacterial vaginosis was still investigational (20). An advanced single-swab panel test that combines multiplex PCR and DNA probe technology can diagnose bacterial vaginosis by determining the ratio of lactobacilli species (“good bacteria”) to several bacterial vaginosis-associated bacterial species (“bad bacteria”) in a patient-collected or physician-collected single-swab sample and has demonstrated comparable diagnostic sensitivity and specificity to Nugent scoring and Amsel criteria (41–43).



This multiplex PCR panel also can detect other common causes of vaginitis, such as trichomoniasis and candidiasis (41). Although the clinical utility of PCR testing for the diagnosis of bacterial vaginosis is still being evaluated (20), this single-swab multiplex test may be a promising alternative to microscopy (41).

## **Treatment**

Symptomatic patients with bacterial vaginosis should receive treatment, which works by reducing the overgrowth of the patient's endogenous facultative and anaerobic bacteria and enabling the lactobacilli to become dominant. Treatment of bacterial vaginosis also may decrease a patient's risk of transmission and acquisition of other STIs, including chlamydial infection, gonorrhea, trichomoniasis, HIV, and herpes simplex virus type 2 (24, 44, 45). Currently, the CDC recommends that patients with bacterial vaginosis also be tested for HIV and other STIs (20).

Oral or intravaginal metronidazole or intravaginal clindamycin is recommended for the treatment of bacterial vaginosis. Alternative treatments include oral secnidazole, oral tinidazole, or oral clindamycin (Table 2). Because these treatments have comparable safety and efficacy profiles, the choice of therapy should be individualized based on factors such as patient preference, cost, convenience, adherence, ease of use, and history of response or adverse reactions to previous treatments (20, 46–49). Patients who are unable to tolerate oral metronidazole because of gastrointestinal adverse effects may find that the intravaginal metronidazole gel is tolerable. Secnidazole is a newer FDA-approved agent for the treatment of bacterial vaginosis that in randomized clinical trials has been found to be superior to placebo and comparable to metronidazole in treating bacterial vaginosis (50, 51).

Abstaining from alcohol use during treatment with oral nitroimidazoles and for 24 hours after completion of metronidazole treatment or 72 hours after treatment with tinidazole is currently recommended by the drug manufacturers because of a theoretical concern of a disulfiram-like reaction that may occur with the use of nitroimidazoles (52, 53). Patients also should refrain from sexual activity during bacterial vaginosis treatment unless condoms are used. Experts advise that patients who are using an intravaginal product to treat a vaginal infection may want to avoid use of tampons during treatment to ensure adequate dispersion of the medication.

## **Management of Recurrent Bacterial Vaginosis**

If symptoms have resolved, follow-up with rescreening for bacterial vaginosis is not necessary. However, following treatment, bacterial vaginosis may recur in

up to 30% of patients within 3 months and 58% within 12 months (12, 54, 55). Potential factors associated with recurrent bacterial vaginosis include douching, frequent sexual activity, a previous history of bacterial vaginosis, persistence of pathogenic bacteria, or failure to reestablish a lactobacillus-predominant vaginal flora. Patients identified to have at least three documented, separate episodes in 1 year meet the criteria for recurrent bacterial vaginosis and may be offered twice weekly suppressive metronidazole gel for 16 weeks after treatment for the acute episode (20, 56, 57). Changing the antibiotic or extending the course of the antibiotic also may be effective in patients with recurrent bacterial vaginosis (Table 2) (20). For more information, see the CDC Sexually Transmitted Diseases webpage at [www.cdc.gov/std/](http://www.cdc.gov/std/).

### ► **How is trichomoniasis diagnosed and treated?**

## **Diagnosis**

Trichomoniasis is associated with an elevated pH level and inflammatory discharge that may be green–yellow in color and bubbly in consistency. A highly sensitive and specific test such as nucleic acid amplification is the preferred diagnostic test for *T vaginalis* infection (20) because microscopy has limited sensitivity (50–60%) for the detection of *T vaginalis* (58–60). Alternative diagnostic options include FDA-approved commercial tests or vaginal culture (20).

## **Nucleic Acid Amplification Testing**

Nucleic acid amplification testing (NAAT) is recommended for the diagnosis of trichomoniasis (20). Nucleic acid amplification testing is highly sensitive compared with microscopy and is the recommended diagnostic method for trichomoniasis (12, 20, 61). Nucleic acid amplification testing can be performed on vaginal, cervical, or urine specimens with equal sensitivity (95.3–100%) and specificity (95.2–100%) (62–64).

## **Commercial Tests**

Using DNA probe technology, vaginal secretions can be tested for the presence of *T vaginalis*. In one study that compared NAAT to DNA probe technology, the sensitivity and specificity were significantly greater in the NAAT kit compared with the direct DNA probe, 98% versus 46.3%, respectively (40). A newer multiplex PCR panel test that combines direct DNA probe and DNA amplification technology has a sensitivity (93%) and specificity (99%) for *T vaginalis* that is comparable to reference standards (ie, wet mount microscopy and culture) and has the ability to screen for the other two



**Table 2. Treatment Options for Vaginitis in Nonpregnant Patients**

Condition	Recommended Treatment Regimens	Alternative Treatment Regimens
Bacterial vaginosis	Metronidazole, 500 mg orally twice daily for 7 days* or Metronidazole gel 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days* or Clindamycin cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days	Secnidazole, 2 g orally in a single dose or Tinidazole, 2 g orally once daily for 2 days* or Tinidazole 1 g orally once daily for 5 days* or Clindamycin, 300 mg orally twice daily for 7 days or Clindamycin ovules, 100 mg intravaginally once at bedtime for 3 days†
Trichomoniasis	Metronidazole, 500 mg orally twice a day for 7 days*	Tinidazole, 2 g orally in a single dose*
Uncomplicated vulvovaginal candidiasis	<b>Over-the-counter intravaginal agents:</b> Clotrimazole 1% cream, 5 g intravaginally daily for 7–14 days or Clotrimazole 2% cream, 5 g intravaginally daily for 3 days or Miconazole 2% cream, 5 g intravaginally daily for 7 days or Miconazole 4% cream, 5 g intravaginally daily for 3 days or Miconazole, 100-mg vaginal suppository, one suppository daily for 7 days or Miconazole, 200-mg vaginal suppository, one suppository for 3 days or Miconazole, 1,200-mg vaginal suppository, one suppository for 1 day or Tioconazole 6.5% ointment, 5 g intravaginally in a single application  <b>Prescription intravaginal agents:</b> Butoconazole 2% cream (single-dose bioadhesive product), 5 g intravaginally in a single application or Terconazole 0.4% cream, 5 g intravaginally daily for 7 days or Terconazole 0.8% cream, 5 g intravaginally daily for 3 days or Terconazole, 80-mg vaginal suppository, one suppository daily for 3 days  <b>Oral agent:</b> Fluconazole, 150 mg orally in a single dose	N/A

Abbreviations: OTC, over-the-counter; N/A, not applicable.

\*Abstaining from alcohol during treatment with nitroimidazoles and for 24 hours after completion of oral metronidazole treatment or 72 hours after treatment with oral tinidazole is currently recommended by the drug manufacturers because of a theoretical concern about a disulfiram-like reaction that may occur with the use of nitroimidazoles (Pfizer Inc. 2018. Flagyl [metronidazole] tablets. New York, NY: Available at: <http://labeling.pfizer.com/showlabeling.aspx?id=570>, and Mission Pharmaceutical Company. 2004. Tindamax (tinidazole) tablets. San Antonio, TX. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2007/021618s0031bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2007/021618s0031bl.pdf)).

†Clindamycin ovules use an oleaginose base that might weaken latex or rubber products (eg, condoms and vaginal contraceptive diaphragms). Use of such products within 72 hours after treatment with clindamycin ovules is not recommended.

Data from Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. Centers for Disease Control and Prevention [published erratum appears in MMWR Recomm Rep 2015;64:924]. MMWR Recomm Rep 2015;64(RR-03):1–137; Kissinger P, Muzny CA, Mena LA, Lillis RA, Schwabke JR, Beauchamps L, et al. Single-dose versus 7-day-dose metronidazole for the treatment of trichomoniasis in women: an open-label, randomised controlled trial. *Lancet Infect Dis*. 2018 Nov;18(11):1251–1259; and Elghazaly SM, Hamam KM, Badawy MM, Yakoub Agha NA, Samy A, Abbas AM. Efficacy and safety of single dose of oral secnidazole 2 g in treatment of bacterial vaginosis: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol* 2019;238:125–31.



organisms most commonly associated with vaginitis (*G vaginalis* and *C albicans*) with one probe (41).

Antigen-detection testing is a commercial point-of-care option to test for *Trichomonas*. A *Trichomonas* rapid test is the most widely used antigen-detection method and can be performed in approximately 10 minutes in the office, providing immediate results and expedited treatment. The test has a sensitivity of 88.3% and a specificity of 98.8% (58, 65, 66).

## Culture

*Trichomonas* culture was considered the most sensitive and the preferred method for the detection of *T vaginalis* in patients (20, 65) until molecular detection methods were introduced (67). Additionally, culture is inconvenient, takes at least 5 days, and often requires preemptive discussion with a local microbiology laboratory with special media (68).

## Treatment

Treatment options for uncomplicated trichomoniasis (ie, women not infected with HIV) are listed in Table 2. Oral nitroimidazoles are recommended for the treatment of trichomoniasis (20). Although a single dose of metronidazole has been the preferred treatment regimen for trichomoniasis, recent data from a randomized controlled trial show that a 7-day course of metronidazole is more effective (69). Tinidazole single-dose therapy (20, 70) is an acceptable alternative to the metronidazole regimen. Metronidazole often is less expensive than tinidazole but has more gastrointestinal adverse effects (20, 71). Associated adverse effects are similar, including a theoretical concern about a disulfiram-like effect with alcohol consumption, thus the drug manufacturers recommend that alcohol should be avoided during treatment with nitroimidazoles and for 24 hours after metronidazole use and 72 hours after tinidazole use (52, 53). Metronidazole gel is not effective in treating *T vaginalis* infections. In cases of metronidazole allergy, patients should be referred for metronidazole desensitization (20, 28, 72).

Although high-level resistance to metronidazole is considered rare, low-level in vitro resistance may be as high as 4–10% (73–75). Nonetheless, in suspected cases of metronidazole resistance, patients should be interviewed carefully to exclude the possibility of nonadherence with the medication regimen or reinfection from an untreated partner. In cases of suspected metronidazole resistance, tinidazole may be an effective treatment. For example, a series of 33 cases demonstrated that treatment with high-dosage tinidazole (500 mg four times daily or more for 14 days) was well tolerated and effective in more than 90% of metronidazole-resistant cases

(76). Another series of three resistant cases showed that a lower dose of tinidazole (500 mg three times daily for 7 days) also was effective (77). If re-treatment with the same regimen has failed and adherence has been assured (78), sending a culture of the potential resistant isolate to a reference laboratory that can perform susceptibility testing should be considered to help guide the choice of therapy and dosage (20). Patients should be retested within 3 months after treatment for *T vaginalis* because of the high rates of infection recurrence (20). For more information, see the CDC Sexually Transmitted Diseases webpage, which is available at <http://www.cdc.gov/std>.

## ► How is vulvovaginal candidiasis diagnosed and treated?

### Diagnosis

Candidiasis is often associated with abnormal discharge. However, vulvovaginal candidiasis cannot be reliably diagnosed based on clinical symptoms alone (1, 32). In a symptomatic patient, diagnosis of vulvovaginal candidiasis requires one of the following two findings: 1) visualization of spores, pseudohyphae, or hyphae on wet-mount microscopy or 2) vaginal fungal culture or commercial diagnostic test results positive for *Candida* species (20).

### Microscopy

Although microscopy is convenient, cost effective, and commonly used in clinical practice, its sensitivity to yeast (ie, *C albicans*) is approximately 50–70%, and a substantial percentage of patients with symptomatic vulvovaginal candidiasis are missed (79–81). Microscopy also may be limited by self-treatment before evaluation, making it more difficult for the health care provider to visualize yeast on microscopy (82).

### Culture

When microscopy results are negative, yeast cultures are the preferred method for confirming the presence of yeast in symptomatic patients. Speciation is particularly helpful since *C albicans* constitutes 90% of all vulvovaginal *Candida* infections and is usually susceptible to over-the-counter azoles and oral fluconazole (20, 83). Cultures are useful to evaluate recurrent or resistant vulvovaginal candidiasis (80, 83, 84). In patients with complicated vulvovaginal candidiasis, identifying the species of yeast with culture is the first step in creating a treatment plan. Although culture delays diagnosis more than microscopy or commercial tests, it is useful for the detection of non-*albicans Candida* species, particularly *Candida glabrata*, which may be difficult to recognize on microscopy



because of the presence of blastospores instead of pseudohyphae. Cultures may be positive for yeast forms in as many as 30% of asymptomatic patients at any given time (32). Thus, clinical correlation is important before a culture is collected.

## Commercial Tests

Polymerase chain reaction testing for *Candida* species offers results within a few hours compared with culture and has comparable sensitivity and specificity (97.7% and 93.2%, respectively) (40). However, these PCR tests often are considerably more expensive than fungal culture and have not been FDA approved for the detection of yeast despite their frequent use in clinical practice.

One commonly used test is a commercially available DNA probe technology kit that tests for the presence of several *Candida* species (40). However, a limitation of this test is the lack of *Candida* speciation because it reports results only as positive or negative. A newer DNA probe test with PCR technology is available that further divides the species of *Candida* genus into three groups: 1) *Candida* group (*C albicans*, *C tropicalis*, *C parapsilosis*, and *C dubliniensis*) (sensitivity 90.9% and specificity 94.1%), 2) *C glabrata* (sensitivity 75.9% and specificity 99.7%), and 3) *Candida krusei* (41). This newer DNA probe with PCR provides a level of sophistication greater than its predecessor and may prove to be useful in the diagnosis of complicated yeast infection.

## Classification and Treatment

Vulvovaginal candidiasis is classified as uncomplicated or complicated based on clinical presentation, microbiology, host factors, and response to initial therapy (Box 1) (20). Nonpregnant patients with complicated vulvovaginal candidiasis require more aggressive treatment to achieve relief of symptoms.

### Uncomplicated Vulvovaginal Candidiasis

Intravaginal azole therapy or oral fluconazole is recommended for the treatment of uncomplicated vulvovaginal candidiasis. Because uncomplicated vulvovaginal candidiasis is effectively and safely treated with a variety of oral and topical treatments that are often available as over-the-counter and as short-course topical treatments (Table 2), the choice of therapy should be individualized based on factors such as patient preference, cost, convenience, adherence, ease of use, and history of response or adverse reactions to previous treatments. Symptomatic relief and mycologic cure are greater than 90% (20, 85). Imidazole creams and suppositories are available over-the-counter (Table 2) and are easy for most patients to acquire even though most patients prefer a single oral tablet of fluco-

### Box 1. Classification of Vulvovaginal Candidiasis

#### Uncomplicated (presence of ALL of the following):

- Sporadic or infrequent episodes
- Mild-to-moderate symptoms or findings
- *Candida albicans* infection (suspected or proven)
- Non-immunocompromised patients

#### Complicated (presence of ANY of the following):

- Recurrent episodes (four episodes or more per year)
- Severe symptoms or findings
- Non-*C albicans* candidiasis (suspected or proven)
- Diabetes, immunocompromising conditions (eg, HIV), debilitation, or immunosuppressive therapy (eg, corticosteroids)

Modified from Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. Centers for Disease Control and Prevention [published erratum appears in MMWR Recomm Rep 2015;64:924]. MMWR Recomm Rep 2015;64(RR-03):1–137.

nazole (86, 87). Topical treatments may cause local adverse effects, such as burning and irritation. Oral fluconazole is well tolerated and affordable and is equally effective in treating vulvovaginal candidiasis as an intravaginal product (86, 87). Occasionally, oral therapy may cause systemic adverse effects, such as gastrointestinal intolerance, headache, and liver function test elevations; however, these effects usually are mild and self-limited (88). Allergic reactions to oral therapy are rare.

### Complicated Vulvovaginal Candidiasis

*Complicated vulvovaginal candidiasis* is defined as recurrent vulvovaginal candidiasis (ie, four or more infections in 12 months); an infection with severe symptomatology; an infection with any non-*albicans Candida* species; or an infection in a woman who is immunocompromised (eg, HIV, immunosuppressive medications, or diabetes) (20). For information on treatment of vulvovaginal candidiasis in patients with HIV, see ACOG Practice Bulletin No. 167 (3).

Objective information in the form of culture is important to identify the yeast species and correlate with symptoms (82, 89). Most infections are secondary to *C albicans*, which is responsive to both topical and oral azoles. Oral fluconazole is an effective and convenient





treatment for complicated infections with *C albicans*. Although rare, the growing resistance of *C albicans* to oral fluconazole has been documented (90). Culture and susceptibility testing should be considered when a patient remains clinically symptomatic after treatment or when non-*albicans* isolates are identified because these species often are intrinsically resistant to most azole agents.

**Recurrent vulvovaginal candidiasis.** The diagnosis of recurrent vulvovaginal candidiasis should be determined by documentation of infections with objective data, including yeast speciation by culture (91–93). A yeast culture remains the preferred diagnostic method for recurrent vulvovaginal candidiasis (20, 32). Extended antifungal treatment is recommended for patients with recurrent vulvovaginal candidiasis to reduce the likelihood of persistent symptoms. After initial treatment of the acute infection, suppressive therapy with weekly doses of either an intravaginal or oral azole improves cure rates and decreases recurrence rates (85, 94). Prolonged antifungal treatment with fluconazole (150 mg weekly for 6 months) successfully controlled more than 90% of recurrent symptomatic episodes. A prolonged protective effect was observed in approximately 50% of patients with recurrent vulvovaginal candidiasis secondary to *C albicans* (94). For patients who are unable or unwilling to take fluconazole, prolonged therapy with intermittent topical agents, such as clotrimazole (500 mg weekly or 200 mg twice a week), are acceptable options (20). A confirmatory yeast culture is recommended for patients with suspected fluconazole-resistant vulvovaginal candidiasis, and referral to a subspecialist should be considered (20, 95).

**Severe vulvovaginal candidiasis.** Patients with severe vulvovaginal candidiasis manifest symptoms on the vulva that include erythema, erosion, fissure, and edema. These patients require a prolonged course with a topical intravaginal azole for 10–14 days or two to three doses of oral fluconazole taken orally 3 days apart. Suppressive weekly doses are not necessary in this population of patients (20). An acute infection is treated with an extended course of a topical or oral azole. Topical agents listed in Table 2 can be extended to a 10–14-day intravaginal course (20). Oral fluconazole can be prescribed every 3 days for 2–3 doses (days 1, 4, and 7) (20, 96). One placebo-controlled randomized trial of patients with severe vulvovaginal candidiasis found that a second dose of fluconazole (150 mg given 3 days after the first dose) increased the cure rate from 67% to 80% (96).

**Non-*albicans* *Candida* species.** Although much less common than *C albicans*, approximately 5–10% of vulvovaginal

candidiasis is caused by non-*albicans* *Candida* species, particularly *C glabrata*. Non-*albicans* *Candida* species are less likely to respond to topical imidazole therapy or oral fluconazole and should be suspected in any woman with ongoing symptoms after treatment for uncomplicated vulvovaginal candidiasis. Vaginal fungal culture can identify the species and is recommended for the diagnosis of resistant or recurrent vulvovaginal candidiasis (91–93). Therapy with intravaginal boric acid (600-mg capsules daily for a minimum of 14 days) is effective for *C glabrata* and other atypical *Candida* species (92, 97). Patients with non-*albicans* *Candida* vulvovaginal candidiasis in whom boric acid therapy is ineffective should be referred to a subspecialist for further management. Boric acid can be fatal if ingested orally and patients should be well counseled to use it only intravaginally, to place it out of the reach of children, and to use reliable contraception. Topical flucytosine, 5 g nightly for 2 weeks, is another effective treatment for *C glabrata*. However, the cost of flucytosine is often prohibitive for most patients (97, 98).

► ***When is it appropriate to provide treatment for vaginitis without an examination?***

Self-diagnosis of common vaginitis is not recommended because of its limited accuracy and the nonspecific nature of vulvovaginal symptoms. Patients with vaginitis symptoms should present to a clinician for evaluation, particularly patients who have self-treated for presumed vulvovaginal candidiasis with a nonprescription antifungal medication and still have symptoms (82, 89). Patients who are already in the office and report vulvovaginal symptoms should receive an examination before being treated for vaginitis.

► ***Are there adverse effects of nonprescription antifungal use?***

In general, topical nonprescription antifungal medication use is associated with cure rates and adverse effects that are similar to prescription therapy (20, 88). A patient with vulvovaginal candidiasis who uses a nonprescription antifungal agent should respond to therapy. Failure to respond to initial treatment should prompt clinical evaluation. Contact dermatitis, presenting as localized burning and irritation, may occur in approximately 5% of users (1). If used for the wrong condition or if the patient has vulvovaginal candidiasis but does not respond to treatment, antifungal medication use may delay accurate diagnosis and appropriate treatment. Although such a delay may have a minimal effect on vulvovaginal symptoms (eg, itching or discharge), it may be of greater concern if a patient who self-treats has a more serious infection such as PID, an STI, or a urinary tract infection



(89). Furthermore, patients who use numerous courses of nonprescription antifungal therapy and do not have vulvovaginal candidiasis may incur significant financial costs.

- **What is the appropriate management of findings consistent with vulvovaginal candidiasis, bacterial vaginosis, or trichomoniasis on a cervical cytology report in an asymptomatic patient?**

Pap tests are not reliable for the diagnosis of vaginitis (20, 32). Diagnostic confirmation is recommended for incidental findings of vulvovaginal candidiasis, bacterial vaginosis, or trichomoniasis on a Pap test (20, 99, 100).

### **Vulvovaginal Candidiasis**

Vaginal *Candida* species are present in 20–30% of asymptomatic patients (32, 101). Treatment of asymptomatic candidiasis on a Pap test is not indicated. Symptomatic patients with Pap results that show the presence of *Candida* infection should be evaluated with confirmatory diagnostic testing (Table 1).

### **Bacterial Vaginosis**

The Pap test is an unreliable tool to diagnose bacterial vaginosis (20), with a sensitivity of 49% and specificity of 93% (102). In symptomatic patients with suggestive bacterial vaginosis on a Pap test, confirmatory diagnostic testing should be performed (Table 1). Asymptomatic patients with Pap test findings suggestive of bacterial vaginosis do not need evaluation or treatment.

### **Trichomoniasis**

As with wet-mount microscopy, the Pap test has a low sensitivity for the detection of trichomonads (55–60%). In patients with Pap test results that suggest the presence of trichomonads, confirmatory diagnostic testing should be performed (Table 1) (100, 101). Patients with confirmed trichomoniasis should be treated with a recommended therapy (20) (Table 2).

- **Are probiotics or nonmedical approaches effective for the treatment or prevention of vaginitis?**

Probiotics (vaginal or oral) and nonmedical therapies are not recommended for the treatment or prevention of vaginitis (20).

### **Vulvovaginal Candidiasis**

Use of lactobacilli products, such as *Lactobacillus acidophilus*, *Lactobacillus rhamnosus* GR-1, and *Lactobacillus fermentum* RC-14 orally or vaginally, is not effective for treatment or prevention of vulvovaginal candidiasis

(103–105). Other nonmedical therapies proposed for the treatment of candidiasis include yogurt, garlic, tea tree oil, a low carbohydrate diet, and douching. However, these commercially available products are not FDA regulated, and there are insufficient data on their efficacy.

### **Bacterial Vaginosis**

Probiotics (vaginal or oral) are not recommended for the treatment of bacterial vaginosis, to augment antimicrobial therapy, or to maintain a balanced vaginal ecosystem (20). Some studies have evaluated the use of vaginal lactobacillus supplements, particularly *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 (106, 107) either alone or with oral antibiotics, for the treatment of bacterial vaginosis (108, 109) and found no benefit.

### **Trichomoniasis**

Nitroimidazoles (metronidazole and tinidazole) are the only recommended and only effective treatment for *T vaginalis* infection. For patients who are intolerant or allergic to nitroimidazoles, referral to a specialist should be made for desensitization (20). Anecdotal use of intravaginal paromomycin in combination with high-dose tinidazole and intravaginal boric acid has been reported when desensitization is unsuccessful (20, 78, 110–112).

- **Should the sex partners of patients with confirmed vaginitis be treated as well?**

Whenever trichomoniasis is confirmed, current sex partners should be referred for presumptive therapy and counseled to refrain from sexual activity until they have completed therapy and are asymptomatic (20). Typically, this is a full 7 days since taking the last antibiotic dose. Management of sex partners helps to decrease transmission of trichomoniasis to other sex partners and reduce recurrence (20). Data show that expedited partner therapy might have a role in partner management for trichomoniasis; however, no single partner management intervention has been shown to be more effective than any other in reducing trichomoniasis reinfection rates (20, 113).

For bacterial vaginosis, data do not support that treatment of sex partners affects rates of relapse or remission (114). Additionally, no studies address whether simultaneous treatment of both women in a lesbian couple decreases recurrence rates of bacterial vaginosis.

In episodes of uncomplicated vulvovaginal candidiasis, treatment of sex partners is not warranted (20). Randomized studies of partner treatment among heterosexual couples also have failed to show a decrease in the risk of recurrence of bacterial vaginosis or vulvovaginal candidiasis (55, 114–117).



# Summary of Recommendations

## Recommendations based on good and consistent scientific evidence (Level A)

- ▶ The use of Amsel clinical criteria or Gram stain with Nugent scoring is recommended for the diagnosis of bacterial vaginosis.
- ▶ Oral or intravaginal metronidazole or intravaginal clindamycin is recommended for the treatment of bacterial vaginosis. Alternative treatments include oral secnidazole, oral tinidazole, or oral clindamycin.
- ▶ Nucleic acid amplification testing is recommended for the diagnosis of trichomoniasis.
- ▶ Oral nitroimidazoles are recommended for the treatment of trichomoniasis.
- ▶ In a symptomatic patient, diagnosis of vulvovaginal candidiasis requires one of the following two findings: 1) visualization of spores, pseudohyphae, or hyphae on wet-mount microscopy or 2) vaginal fungal culture or commercial diagnostic test results positive for *Candida* species.
- ▶ Extended antifungal treatment is recommended for patients with recurrent vulvovaginal candidiasis to reduce the likelihood of persistent symptoms.

## Recommendations based on limited or inconsistent scientific evidence (Level B)

- ▶ Patients should be retested within 3 months after treatment for *T vaginalis* because of the high rates of infection recurrence.
- ▶ Pap tests are not reliable for the diagnosis of vaginitis. Diagnostic confirmation is recommended for incidental findings of vulvovaginal candidiasis, bacterial vaginosis, or trichomoniasis on a Pap test.

## Recommendations based primarily on consensus and expert opinion (Level C)

- ▶ A complete medical history, physical examination of the vulva and vagina, and clinical testing of vaginal discharge (ie, pH testing, a potassium hydroxide [KOH] “whiff test,” and microscopy) are recommended for the initial evaluation of patients with vaginitis symptoms.
- ▶ Intravaginal azole therapy or oral fluconazole is recommended for the treatment of uncomplicated vulvovaginal candidiasis.
- ▶ Self-diagnosis of common vaginitis is not recommended because of its limited accuracy and the nonspecific nature of vulvovaginal symptoms.

- ▶ Probiotics (vaginal or oral) and nonmedical therapies are not recommended for the treatment or prevention of vaginitis.
- ▶ Whenever trichomoniasis is confirmed, current sex partners should be referred for presumptive therapy and counseled to refrain from sexual activity until they have completed therapy and are asymptomatic.

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The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000 and July 2019. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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