Vaginitis

Vaginal Environment

The vagina is a dynamic ecosystem that normally contains approximately 10^9 bacterial colony-forming units per gram of vaginal fluid. The normal vaginal discharge is clear to white, odorless, and of high viscosity. The normal bacterial flora is dominated by lactobacilli, but a variety of other bacteria are also present at lower levels. Lactobacilli convert glycogen to lactic acid, which helps to maintain a normal acidic vaginal pH of 3.8 to 4.5. Some lactobacilli produce H\textsubscript{2}O\textsubscript{2} (hydrogen peroxide), which serves as a host defense mechanism and kills bacteria and viruses.

Vaginitis

Vaginitis is common among women of reproductive age and is usually characterized by a vaginal discharge, vulvar itching and irritation, and a vaginal odor.\[1\] In a retrospective review of studies published between 1966 and 2003, the three most common conditions diagnosed among women with vaginal symptoms presenting in the primary care setting were bacterial vaginosis (22% to 50%), vulvovaginal candidiasis (17 to 39%), and trichomoniasis (4% to 35%).\[2\] In some cases, the etiology may be mixed, and there may be more than one disease present; in approximately 30% of symptomatic women, no etiologic agent is identified.\[3\]

Other causes of vaginal discharge or irritation include the following:

- Normal physiologic variation
- Allergic reactions (e.g., spermicides, deodorants)
- Genital herpes
- Mucopurulent cervicitis
- Atrophic vaginitis
- Vulvar vestibulitis
- Lichen simplex chronicus
- Lichen sclerosis
- Foreign bodies (e.g., retained tampons)
- Desquamative inflammatory vaginitis
Diagnostic Approach

General Principles of Diagnosis

Vaginitis is primarily a clinical diagnosis, but a complete history, physical examination, and laboratory evaluation is necessary for accurate diagnosis. The 2015 STD Treatment Guidelines recommend that clinicians inquire specifically about a woman’s menstrual cycle, sexual history (including gender of sex partners and specific sexual practices), vaginal hygiene practices (such as douching), and any other underlying medical conditions.[4] The following briefly addresses the general approach for evaluating a woman with vaginitis, including the clinical evaluation and diagnostic testing options. A more detailed discussion on the diagnosis and management of specific causes of vaginitis is addressed in the subsequent sections in this module on Bacterial Vaginosis, Trichomoniasis, and Vulvovaginal Candidiasis.

Clinical Evaluation

The evaluation of vaginitis requires visual inspection of the vaginal discharge, the vagina, and the cervix, as well as the collection and evaluation of a discharge specimen under the microscope. Visualization of the cervix is important in order to rule out cervicitis as a source of abnormal vaginal discharge. The following characteristics of the vaginal discharge should be noted during examination:

- Color
- Viscosity
- Adherence to vaginal walls
- Presence of odor

Diagnostic Methods for Initial Evaluation of Vaginitis

Most of the diagnostic methods at the initial evaluation of vaginitis are not organism specific, but can provide valuable information when trying to diagnose the cause of vaginitis[2,3,5]:

Saline Wet Mount

A sample of vaginal fluid should be collected from the lateral wall of the vagina. A specimen slide, referred to as a “wet mount”, can be made with a drop of warm 0.9% saline and a drop of the vaginal discharge specimen. An alternative method of wet mount preparation involves placing the discharge swab into a test tube with less than 1 mL of saline, gently stirring, and then adding a drop from the tube onto a specimen slide. With either method, a cover slip should be placed over the solution on the slide, followed by immediate examination under a microscope at both low (10x) and high (40x) power. The slide should thoroughly be scanned for clue cells and for motile trichomonad organisms. Delays of more than 10 minutes in viewing the wet mount significantly reduce the chance of visualizing motile trichomonads. Visualizing clue cells suggests a diagnosis of bacterial vaginosis.

Potassium Hydroxide (KOH) Preparation and Whiff Test

A second sample of vaginal fluid is placed on a slide and a 10% KOH solution is added. Soon after applying the KOH, bring the slide near the nose to perform the whiff test; the presence of a strong amine "fishy" odor is considered a positive whiff test. A positive whiff test is consistent with a diagnosis of bacterial vaginosis. After performing the whiff test, a cover slip should be placed over the preparation on the slide, followed by immediate examination under a microscope at both low (10x) and high (40x) power. The KOH kills the majority of the cells and bacteria, but does not significantly impact any fungal organisms, thus making it much easier to visualize the presence of yeasts or pseudohyphae. Visualizing fungal organisms is consistent with a diagnosis of vulvovaginal candidiasis.
Litmus Testing for pH of Vaginal Fluid

The pH of the vaginal fluid can be determined by placing a pH litmus paper on the wall of the vagina or directly in pooled vaginal secretions. The normal pH of the vagina is typically between 3.8 and 4.5. A pH greater than 4.5 is consistent with a diagnosis of bacterial vaginosis.

Gram's Stain

Performing an initial Gram's stain can provide useful information in patients with bacterial vaginosis or vulvovaginal candidiasis. With bacterial vaginosis, the abundant gram-positive flora is partially replaced by gram-negative organisms; the Nugent criteria is an established scoring system used for evaluation of bacterial vaginosis on a Gram's stain.[6] In addition, clue cells are sometimes visible on Gram's stain. For patients with vulvovaginal candidiasis, the Gram's stain may show large strongly gram-positive staining yeasts and hyphae, but a wet mount KOH is preferred over the Gram's stain.[5,7]

Point-of-Care Organism Specific Tests

In addition to diagnostic methods that are not organism specific (microscopy, pH determination, and the “whiff test”), other point-of-care tests that are organism specific are available and include the OSOM Trichomonas Rapid Test (detects *T. vaginalis*) and the BD Affirm VPIII Microbial Identification Test (detects *T. vaginalis*, *C. albicans*, and *Gardnerella vaginalis*).[3] The sensitivity, specificity, and clinical utility of these tests are higher than wet mount, but lower than culture.[8,9] Neither the OSOM nor Affirm tests are approved for testing in men.

Culture

Cultures are available for both *T. vaginalis* and *Candida* species. Fungal culture is not usually necessary to make a diagnosis of vulvovaginal candidiasis, but when needed, it is the gold standard. The use of fungal cultures for the diagnosis of candidiasis infection may be especially useful in the management of persistent or recurrent vulvovaginal candidiasis. For the diagnosis of *T. vaginalis*, culture for *T. vaginalis* (using modified Diamond’s medium) is more sensitive than wet mount, but less sensitive than molecular diagnostic methods, such as nucleic acid amplification testing.[10] Culture for bacterial vaginosis is not recommended due to low sensitivity (less than 50%) and potential for mistakenly identifying commensal bacteria as pathogens, resulting in inappropriate treatment.[3]

Nucleic Acid Amplification Tests (NAAT)

The Trichomonas APTIMA test (Gen-Probe) is approved by the U.S. FDA for the diagnosis of vaginal trichomoniasis. This test is highly sensitive and specific and is now the preferred test for the diagnosis of trichomoniasis. The test can be performed on a self-collected or clinician-collected vaginal swab, urine, or liquid endocervical cytology media. This test is the preferred test and is significantly more sensitive than wet mount or culture.[10,11] The APTIMA test appears to have good performance characteristics in penile-meatal swabs but has not yet been FDA-approved for use in men.[10,12] Several NAAT assays are also available that test for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *T. vaginalis* on the same sample.

Polymerase Chain Reaction

Recently, the FDA has cleared the BD MAX Vaginal Panel test, a molecular test that detects the microorganisms responsible for causing bacterial vaginosis, trichomoniasis, and vulvovaginal candidiasis. The test is a multiplex, real-time PCR assay that amplifies the following DNA targets: *Lactobacillus* species (*L. crispatus* and *L. jensenii*), *Gardnerella vaginalis*, *Atopobium vaginae*, bacterial vaginosis-associated bacteria-2 (BVAB-2), *Megasphaera-1*, *T. vaginalis*, and yeast vaginitis markers *Candida* species (*C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. dubliensis*, *C. glabrata*, and *C. krusei*).
**Additional Tests**

Other commercially available diagnostic tests include indirect testing for enzymatic activity associated with the organisms causing bacterial vaginosis: PIP testing measures proline aminopeptidase activity and BV-blue detects sialidase.[3]
Bacterial Vaginosis

Epidemiology

Bacterial vaginosis is a gynecologic condition that is related to alterations in the normal vaginal flora and is the most common cause of vaginitis among reproductive-age women.[2,13,14] National data show that the prevalence is 29% overall, but the prevalence varies by population, with higher rates reported among sexually active women.[14,15] Racial and socioeconomic disparities also exist, with higher rates of bacterial vaginosis in women of color, lower socioeconomic status, and lower education level.[13,14] Information on the prevalence of BV is limited since bacterial vaginosis is not reportable.

Pathogenesis and Microbiology

Current understanding of the pathogenesis of bacterial vaginosis implicates displacement of the normal lactobacilli in the vagina by anaerobic bacteria, which leads to a subsequent pro-inflammatory response and clinical syndrome.[16] Lactobacilli produce lactic acid from glycogen, a process that maintains the vagina pH as acidic; the low pH environment inhibits the growth of other bacterial species that are normally present in the vagina in low levels. When lactobacilli are lacking, the vaginal flora may become significantly altered with overgrowth of bacterial vaginosis-associated organisms, such as Gardnerella vaginalis, Prevotella bivia, Atopobium vaginae, and Mobiluncus curtisi.[15] Investigators have established that women with bacterial vaginosis clearly have greater bacterial diversity when compared with women without bacterial vaginosis.[17] Recent models for bacterial vaginosis propose a multi-step process that begins as vaginal dysbiosis when G. vaginalis colonizes the vaginal epithelium in place of lactobacili, resulting in enhanced biofilm formation and accumulation of P. bivia.[18,19] The vaginal dysbiosis can progress to bacterial vaginosis, a disorder characterized by mucus degradation, barrier disruption, elevated vaginal pH, and local inflammation.[18,19,20] Vaginal ecology differs among women and is affected by host immune status, as well as many other environmental and behavioral factors; these factors can modulate disease expression and severity.[16] Findings from several studies suggest sexual transmission of anaerobic bacteria may play a key role in the development of bacterial vaginosis, both in heterosexual women and in women who have sex with women.[21,22,23,24,25]

Risk Factors

Bacterial vaginosis has been positively associated with non-white ethnicity, low educational attainment, increasing lifetime sexual partners, and increased frequency of douching.[13,14,26,27] Condoms and oral contraceptive pills are protective.[28,29] Although BV is not classically considered a sexually transmitted disease, increasing evidence suggests that sexual activity is integral to development of the disease; bacterial vaginosis correlates with the frequency of sexual activity, younger age at first sex, practicing anal and oral sex, or using vaginal sex toys.[15,21,25,30,31,32] The role of sexual activity in bacterial vaginosis is supported by indirect evidence, including (1) the absence of BV in women prior to sexual debut, (2) concordant vaginal flora among women in same-sex partnerships, and (3) elevated rates of bacterial vaginosis-associated bacterial colonization (as measured with penile swabs) among men engaging in extramarital sexual relationships have compared with men who are monogamous.[31,33,34,35,36]

Clinical Manifestations

Up to half of all women with bacterial vaginosis have no symptoms.[14] If symptomatic, most women with bacterial vaginosis will have a malodorous (“fishy odor”), homogenous, clear, white or gray vaginal discharge that is reported more commonly after sexual intercourse and after completion of menses; labial and/or vulvar swelling and other signs or symptoms of inflammation are typically absent.[3,16] Symptoms may remit spontaneously. Qualitative studies have shown that bacterial vaginosis can negatively impact self-esteem, sexual relationships, and quality of life.[15,21,37]
Obstetrical and Gynecologic Complications

BV has been linked to several obstetrical and gynecologic complications, including late miscarriage, premature rupture of membranes, premature delivery, low birthweight delivery, development of pelvic inflammatory disease (PID), and post-operation infections after gynecological procedures.[38,39,40,41,42,43,44]

Bacterial Vaginosis and Impact on STD Acquisition

Longitudinal studies have also shown that bacterial vaginosis confers a two-fold increased risk of acquiring sexually transmitted infections—specifically chlamydia, gonorrhea, herpes simplex virus type 2, and HIV.[45,46,47,48,49] Although a recent study showed that periodic treatment of bacterial vaginosis (and other causes of vaginitis) in a clinic setting was associated with a reduced risk of STI acquisition,[50] another study that assessed home-based screening for BV did not have similar findings.[51]

Diagnostic Approach

Amsel’s Criteria

Bacterial vaginosis can be diagnosed using the following Amsel’s criteria.[52] The presence of three of the following four criteria provides sufficient evidence for a clinical diagnosis of bacterial vaginosis:

- Vaginal pH greater than 4.5, which is the most sensitive but least specific sign.
- The presence of “clue cells” (bacterial clumping upon the borders of epithelial cells) on wet mount examination (Figure 1). To meet the criteria for positive clue cells, the clue cells should constitute at least 20% of vaginal epithelial cells viewed on saline microscopy (an occasional clue cell does not fulfill this criterion).[53,54]
- Positive amine, “whiff” or “fishy odor” test (liberation of biologic amines with or without the addition of 10% KOH).
- Homogeneous, nonviscous, milky-white discharge adherent to the vaginal walls.

Gram’s Stain

The gold standard for diagnosis of bacterial vaginosis is vaginal Gram’s stain with Nugent scoring (Figure 2), which is based on the relative concentration of lactobacillus, Bacteroides, Gardnerella, and Mobiluncus species (Figure 3).[6] A normal Gram's stain should show lactobacillus only, or lactobacillus with few Gardnerella morphotypes. Gram's stain showing a more mixed flora with relatively lower numbers of lactobacilli is consistent with bacterial vaginosis.

Polymerase Chain Reaction

The recent FDA-approved BD MAX Vaginal Panel test can detect the microorganisms responsible for causing bacterial vaginosis, trichomoniasis, and vulvovaginal candidiasis. The test is a multiplex, real-time PCR assay that amplifies the following DNA targets: Lactobacillus species (L. crisatus and L. jensenii), Gardnerella vaginalis, Atopobium vaginae, bacterial vaginosis associated bacteria-2 (BVAB-2), and Megasphaera-1. The diagnosis of bacterial vaginosis is based on the relative concentrations of these organisms, with a final determination based on a proprietary algorithm.

Additional Diagnostic Tests

Other diagnostic modalities include the BD Affirm VPIII DNA hybridization probe (which can detect T. vaginalis, C. albicans, and G. vaginalis) and indirect testing for enzymatic activity associated with the organisms causing bacterial vaginosis: PIP testing measures proline aminopeptidase activity and OSOM BV-blue testing measures sialidase.[3,55] Neither culture nor cervical Papanicolaou testing is recommended due to low
sensitivity and specificity. [56, 57, 58, 59]

Screening Recommendations

In general, screening for bacterial vaginosis in asymptomatic women is not recommended. Screening and treatment of women with BV prior to a surgical abortion or hysterectomy can be considered due to decreased rates of postsurgical infections in women pre-treated with metronidazole; cost-comparison studies have found that adding metronidazole to standard surgical prophylaxis, rather than a screen-and-treat approach, is more cost effective. [60, 61, 62, 63] Despite a link between bacterial vaginosis and preterm birth, several studies have concluded that treatment of bacterial vaginosis does not reduce the likelihood of preterm birth. [64, 65, 66, 67, 68] Therefore, the 2015 STD Treatment Guidelines concur with the United States Preventive Services Task Force conclusion that there is insufficient evidence to assess the impact of screening for bacterial vaginosis in asymptomatic pregnant women at high risk (those who have previously delivered a premature infant) or low risk for preterm delivery. [69, 70]

Treatment

Treatment of Bacterial Vaginosis in Nonpregnant Women

The 2015 STD Treatment Guidelines recommend treatment in symptomatic women with bacterial vaginosis. [69] Recommended regimens include metronidazole 500 mg orally twice daily for 7 days; metronidazole gel 0.75%, 2 grams intravaginally once a day for 5 days; or clindamycin cream 2%, 2 grams intravaginally at bedtime for 7 days; alternative regimens include oral tinidazole, oral clindamycin, or intravaginal clindamycin ovules (Table 1).[69] The use of probiotics that target repletion of Lactobacillus species are an attractive concept, but further data are required, and at least one product is under study. [69, 71, 72, 73] Patients should be counseled that consuming alcohol while taking metronidazole or tinidazole could precipitate a disulfiram-like reaction. In addition, patients should not drink alcohol for 24 hours after the last dose of metronidazole and for 72 hours after the last dose of tinidazole.

Secnidazole for Treatment of Bacterial Vaginosis

On September 15, 2017, the U.S. Food and Drug Administration approved secnidazole as a single-dose therapy bacterial vaginosis in adult women. Secnidazole is classified as a 5-nitroimidazole antimicrobial formulated in oral granules that has similar in vitro activity as metronidazole and and tinidazole. [74, 75] In a phase 3, placebo-controlled trial that enrolled 189 women with bacterial vaginosis, a single 2 gram-dose of secnidazole was superior to placebo with respect to clinical cure rates. [76] A phase 2, placebo-controlled trial enrolled women with bacterial vaginosis and compared 1 gram of secnidazole, 2 grams of secnidazole, and placebo and the best clinical cure rates were seen with the 2-gram secnidazole dose. [77] The approved dose for treatment of bacterial vaginosis is a single 2-gram packet of oral granules that should be sprinkled on applesauce, yogurt or pudding and all of the mixture should be ingested within 30 minutes of sprinkling the mixture on food, but without chewing or crunching the granules. Following ingestion of the mixture, the patient can drink a glass of water to help swallowing the granule-food mixture, but note that secnidazole granules should not be dissolved in water for ingestion. Secnidazole is not listed as a treatment option for bacterial vaginosis in the 2015 STD Treatment Guidelines since it was approved in 2017.

Management of Sex Partners

The 2015 STD Treatment Guidelines do not recommend testing and treatment of male sex partners of women with bacterial vaginosis since this has not been shown to impact rates of cure, relapse, or recurrence. [69, 78] Because female sex partners are often concurrent for bacterial vaginosis status, [23] the option of screening and treatment should be considered.

Post-Treatment Follow-Up
Follow-up after treatment of bacterial vaginosis is only necessary if symptoms persist or recur.

**Treatment of Special Populations**

The following special populations require unique consideration when treating bacterial vaginosis.

- **Treatment of Women During Pregnancy**: The 2015 STD Treatment Guidelines recommend treating symptomatic pregnant women with the same oral and intravaginal treatment options as non-pregnant women, except that tinidazole is not recommended during pregnancy due to evidence of fetal harm in animal studies. Metronidazole crosses the placenta and is excreted in breast milk, but it has not been linked to teratogenic effects.\[79,80,81\] Treating symptomatic infection in pregnancy reduces symptoms and may reduce certain adverse obstetrical outcomes, such as late miscarriage. For breastfeeding mothers with symptomatic bacterial vaginosis, metronidazole can be used; some experts recommend deferring breastfeeding (“pump and dump”) for 24 hours after treatment with the higher (2 grams) single dose of metronidazole.\[69,82\]

- **Treatment in Women with HIV Infection**: Women with HIV infection experience higher prevalence and persistence of bacterial vaginosis compared with their HIV-uninfected peers.\[83\] Women with HIV infection and bacterial vaginosis should receive the same treatment as women without HIV infection.\[69\] If clindamycin ovules are used, it is especially important to counsel women with HIV infection that the ovules might weaken latex condoms for up to 72 hours after treatment.\[69\]

- **Treatment of Recurrent Bacterial Vaginosis**: Bacterial vaginosis recurs in approximately 30% of women within the three months following treatment, and in up to 50% of patients after 6 to 12 months.\[84,85\] Women with recurrence can be treated with either the same recommended regimen, or a different recommended regimen.\[69\] If, however, a woman experiences multiple recurrences, options include (1) metronidazole intravaginal gel twice weekly for 4 to 6 months or (2) oral metronidazole 500 mg twice daily (or tinidazole 500 mg twice daily) for 7 days, followed by intravaginal boric acid 600 mg daily for 21 days, followed by intravaginal metronidazole gel (0.75%) twice weekly for 4 to 6 months.\[69,86\] Very little is known about antimicrobial resistance with pathogens that cause bacterial vaginosis and clinical experience suggests that treatment failure from antimicrobial resistance is uncommon.\[21\]

**Patient Counseling and Education**

Patient counseling and education for bacterial vaginosis should cover the nature of the disease, transmission issues, and risk reduction.

**Nature of the Disease**

- Asymptomatic bacterial vaginosis infection is common, and screening of asymptomatic women is not generally recommended.
- BV is caused by a shift in the normal vaginal flora.
- The hallmark of symptomatic bacterial vaginosis is vaginal malodor and discharge.
- BV is associated with several potential obstetric and gynecologic complications, including preterm birth and pelvic inflammatory disease.

**Transmission Issues**

- Sexual behavior is likely implicated in the pathogenesis of the infection, and in some cases, sexual transmission of bacterial vaginosis-associated bacteria may be involved.
- There is a high concordance in female same-sex partnerships.
- Bacterial vaginosis increases a woman’s risk of acquiring sexually transmitted infections, including chlamydia, gonorrhea, genital herpes, and HIV.
- Women with HIV infection and bacterial vaginosis have a higher likelihood of transmitting HIV to their male sexual partners.
Trichomoniasis

Epidemiology

Trichomoniasis is caused by the protozoan parasite *Trichomonas vaginalis* and is one of the most common curable sexually transmitted infections worldwide. An estimated 3.7 million people have trichomoniasis in the United States, with approximately 1.1 million new cases occurring each year.\[87,88,89\] The prevalence of *T. vaginalis* infection among reproductive-age women in the United States is estimated at 3.1%, but rates are at least four times higher among non-Hispanic black women.\[90\] In addition, trichomoniasis prevalence increases with age, is higher among incarcerated women and female sex workers, and yet still afflicts a substantial number of adolescent and young adult women who are tested in the primary care setting.\[90,91,92,93,94,95\] Importantly, many patients are asymptomatic: in one study of women attending STD clinics, prevalence was 26.2% among symptomatic women and 6.5% among asymptomatic women.\[96\] Men are not routinely tested for trichomoniasis; nevertheless, studies have reported rates from 3% to 17% in men attending STD clinics, and as high as 72% among heterosexual men whose female partners are diagnosed with trichomoniasis.\[97,98,99,100,101\] Men who have sex with men appear to be at low risk of acquiring trichomoniasis whereas transmission between female sex partners has been documented.\[98,102\]

Pathogenesis and Microbiology

The etiologic agent in trichomoniasis is *T. vaginalis*, which is a single-celled flagellated anaerobic protozoan parasite. It is the only known protozoan parasite that infects the genital tract. *T. vaginalis* has four anterior flagella and one flagellum embedded in an undulating membrane (Figure 4).\[103\] The flagella are responsible for the jerky motility of this organism that is seen under a microscope. After attaching to vaginal epithelial cells, this globular, pear-shaped organism transforms into a thin, flat, ameboid shape.\[104\] Trichomoniasis is almost always sexually transmitted; fomite transmission is extremely rare. \[103\] *T. vaginalis* may persist for months to years in epithelial crypts and periglandular areas of the genital tract.\[103\] Distinguishing persistent, subclinical infection from remote sexual acquisition is not always possible.

Risk Factors

Investigators have identified multiple risk factors associated with trichomoniasis that include the following\[105,106,107,108,109,110\]:

- Older age
- Multiple sex partners
- Drug use (marijuana, crack cocaine, alcohol, cigarettes)
- Unprotected sex with non-primary partner
- Presence of STIs at baseline
- Low socioeconomic status
- Douching
- Black race

Clinical Manifestations

Genitourinary Infection in Females

Vaginitis due to acute infection with *T. vaginalis* can have a characteristic "frothy" gray or yellow-green vaginal discharge and pruritus, but many women are asymptomatic.\[103\] Chronic infection may be associated with minimal discharge, mild pruritus and/or dyspareunia.\[103\] The presence of cervical petechiae (Figure 5), often referred to as a "Strawberry cervix", strongly suggests a diagnosis of trichomoniasis, but this occurs in fewer than 5% of women with trichomoniasis.\[103,111\]
Trichomoniasis in Pregnancy

Infection with *T. vaginalis* in pregnant women is associated with both obstetrical and gynecologic adverse outcomes, including premature rupture of membranes and preterm labor; trichomoniasis in pregnancy increases the risk of preterm birth by about 30%.[112,113,114,115] Neonatal trichomoniasis is unusual but can occur.[116,117]

Trichomoniasis and HIV

Trichomoniasis also confers a two- to three-fold risk of acquiring HIV.[118,119,120] Among women with HIV, more than half are coinfected with *T. vaginalis*, and these patients have been shown to have an increased risk for pelvic inflammatory disease and for shedding of HIV in the genital tract.[121,122,123,124,125,126] Importantly, antiretroviral therapy appears to lessen the potentiating effects of trichomoniasis infections on HIV transmission risk.[125] Infection with HIV does not make a woman more likely to have persistent or recurrent trichomoniasis.[127]

Trichomoniasis in Males

*T. vaginalis* may cause up to 11 to 13% of nongonococcal urethritis (NGU) in males, but urethral infection in males is frequently asymptomatic.[128] Men with *T. vaginalis* infection may also present with prostatitis or epididymitis.[126]

Diagnostic Methods

Approach to Diagnosis

In clinical practice, the wet mount preparation has been the most commonly used method for diagnosing trichomoniasis, primarily because of the low cost, convenience, and immediate diagnosis.[89] This approach, however, has a sensitivity that is significantly lower than with newer nucleic acid amplification tests (NAATs).

Wet Mount Preparation

In the clinical setting, the diagnosis of trichomoniasis can be made by microscopic visualization of motile trichomonads on a vaginal wet mount slide (Figure 6).[10,129] Although the wet prep method is inexpensive and relatively simple to perform, it has a sensitivity of at most 60 and is operator-dependent.[10] Once a vaginal fluid sample is collected, it should be stored in saline (for a maximum of one hour) until the operator is ready to perform microscopy.[130] Once the specimen has been placed on the slide, microscopic evaluation is recommended as soon as possible and always within 10 minutes, since the trichomonads will become increasingly sluggish on the wet mount and motility is required for positive identification(Figure 7).[10,129,130]

Culture

Obtaining a culture using modified Diamond’s medium was the previous gold standard for diagnosis of trichomoniasis, and culture is a more sensitive diagnostic tool than wet mount alone. Specialized culture systems (i.e. InPouch) are available to allow for transport of cultures when shipping to an off-site laboratory. Culture may be used for diagnosing *T. vaginalis* in both men and women. According to the 2015 STD Treatment Guidelines, culture in men may be performed on samples from a urethral swab, urine sediment or semen, but testing in women requires sampling of vaginal secretions.[126]

Rapid Testing

Point-of-care tests for diagnosing trichomoniasis in women include the OSOM Trichomonas Rapid Test (an antigen-detection test) and the BD Affirm III Microbial Identification Test (a DNA hybridization probe).[3] The
sensitivity, specificity, and clinical utility of these tests are higher than wet mount but lower than culture.[8,9] Neither the OSOM nor Affirm tests are approved for testing in men.

**Nucleic Acid Amplification Testing (NAAT)**

Several different NAAT-based methods are available, including transcription-mediated amplification (TMA) and polymerase chain reaction (PCR). The Trichomonas APTIMA test is a TMA assay that was approved in 2011 by the U.S. FDA for the diagnosis of vaginal trichomoniasis. This test is highly sensitive and specific, and, in women, can be performed on vaginal swab (self-collected or clinician-collected), urine, or liquid endocervical (in Thin Prep media) specimens(Figure 8).[128,131,132,133,134] This test is considerably more sensitive than wet mount, culture, and the Affirm VPIII point-of-care DNA hybridization probe.[135,136,137] The Trichomonas APTIMA test also appears to be the most sensitive testing method to detect trichomoniasis in asymptomatic women.[136] The APTIMA test may be used to test urine or urethral swabs from men if validated by CLIA regulations; penile-meatal swabs are preferred to urine samples since they improve rates of detection.[126] The FDA-cleared PCR assay for gonorrhea and chlamydia has been modified to test concurrently for *T. vaginalis* in endocervical and urine samples, with high sensitivity and specificity.[94] There are no data to suggest *T. vaginalis* causes anorectal infection and therefore use of NAAT to detect *T. vaginalis* anorectal infection is not recommended.[126,138,139]

**Screening Recommendations**

The 2015 STD Treatment Guidelines recommend diagnostic testing for trichomoniasis in the following three groups: (1) women seeking care for vaginal discharge; (2) persons receiving care in high prevalence settings (STD clinics, correctional facilities), and (3) asymptomatic persons at high risk of infection (i.e. persons with multiple sex partners, persons who exchange sex for money or drugs).[126] Some experts further recommend that all women who receive testing for *C. trachomatis* and *N. gonorrhoeae* should also receive testing for *T. vaginalis*.[109] In addition, due to high rates of prevalent STDs among persons living with HIV infection, guidelines recommend screening all women with HIV for vaginal trichomoniasis.[126,140,141] Because *T. vaginalis* does not infect the pharynx or rectum, screening at these sites is not recommended.[126]

**Treatment**

**Treatment of Vaginal Trichomoniasis**

The 2015 STD Treatment Guidelines recommend all HIV-negative women diagnosed with trichomoniasis receive treatment with either metronidazole 2 grams orally in a single dose or tinidazole 2 grams orally in a single dose (Table 2).[126] Note that tinidazole should be avoided in pregnant women. The alternative regimen is metronidazole 500 mg orally twice daily for 7 days. Compared to metronidazole, tinidazole offers better tolerability and higher cure rates, but it is more expensive. Metronidazole gel (intravaginal) is not effective for the treatment of trichomoniasis and is not recommended. Patients who are allergic to metronidazole can be managed by a desensitization protocol.[142] Patients should be counseled that consuming alcohol while taking metronidazole or tinidazole could precipitate a disulfiram-like reaction.

**Treatment of Persistent or Recurrent Trichomoniasis**

The most likely reasons for persistent or recurrent trichomoniasis is reinfection from an untreated partner or lack of adherence with treatment, but in patients in whom reinfection and nonadherence is not suspected, antimicrobial-resistant *T. vaginalis* infection should be considered. Currently, rates of metronidazole resistance range from 4 to 10%, and the rate of tinidazole resistance is about 1%.[143,144] For patients who have failed an initial single-dose therapy of metronidazole 2 grams orally, the recommended treatment is metronidazole 500 mg orally twice daily for 7 days. If this 7-day regimen fails, a subsequent 7-day course of higher dose therapy should be administered, with a 7-day oral course of either metronidazole 2 grams given once per day or tinidazole 2 grams once per day. Tinidazole retains activity against many metronidazole-
refractory strains.[145] If this third-line treatment fails, culture should be collected and sent to the CDC for susceptibility testing, in consultation with an expert.[146]

Management of Sex Partners

Communication is an important part of treatment and partner management. Patients should be encouraged to inform their sex partners of the diagnosis of trichomonirosis and to refer them for evaluation, comprehensive STI testing, and presumptive treatment. Expedited partner management (where a clinician provides presumptive antibiotic therapy and educational materials to a patient’s partner) may be considered in states where it is legally permitted (see the CDC Map for the Legal Status of Expedited Partner Therapy).

Resumption of Sexual Activity

Patients should be instructed to avoid sex until they and their sex partners have been treated, and until they no longer have any symptoms of trichomonirosis. This usually takes about 7 days.

Post-Treatment Follow-Up

All sexually active women who are diagnosed and treated for *T. vaginalis* infection (including pregnant women and women with HIV infection) should be retested 3 months after initial treatment to evaluate the possibility of reinfection. Retesting in men is not routinely recommended.

Treatment of Special Populations

- **Treatment of Women During Pregnancy**: The 2015 STD Treatment Guidelines recommend that pregnant women with symptomatic trichomonirosis in any trimester receive treatment with metronidazole 2 grams orally in a single dose. Treatment with the same medication can be considered in asymptomatic patients in whom trichomonirosis is diagnosed. Tinidazole is not recommended during pregnancy or breastfeeding due to limited animal studies suggesting fetal risk. However, treatment for trichomonirosis in pregnancy has not been shown to reduce preterm birth, and one study even demonstrated increased risk of preterm following treatment (which was hypothesized to result from an inflammatory response caused by dying trichomonads).[147]

- **Treatment of Women with HIV**: The 2015 STD Treatment Guidelines recommend treating with a 7-day treatment course of metronidazole 500 mg twice daily in women with trichomonirosis and HIV.[126] This longer course of therapy has been shown to have higher cure rates than single-dose metronidazole therapy in women with HIV infection, possibly due to mechanisms involving underlying immune dysfunction (Figure 9).[122,148,149,150]

Patient Counseling and Education

Patient counseling and education should cover the nature of the disease, transmission issues, and risk reduction.

Nature of the Disease

- Trichomonirosis can be asymptomatic in men and women, and may persist silently for years.
- Untreated trichomonirosis is associated with adverse pregnancy outcomes such as premature rupture of the membranes, preterm delivery, and low birthweight infants.
- Douching may worsen vaginal discharge in patients with trichomonirosis.
- Alcohol consumption is contraindicated with metronidazole and tinidazole.

Transmission Issues

- Trichomonirosis is almost always sexually transmitted.
• Sex partners should be treated.
• Patients should abstain from intercourse until they and their sex partners are cured (about 7 days).
• Trichomoniasis has been associated with increased susceptibility to HIV acquisition and transmission.

**Risk Reduction**

• Individualize risk-reduction plans with each patient.
• Prevention strategies include abstinence, mutual monogamy with an uninfected partner, use of condoms, and limiting the number of sex partners.
• Latex condoms, when used consistently and correctly, can reduce the risk of transmission of *T. vaginalis*.
• Douching should be avoided since it increases the risk for trichomoniasis.
• Male circumcision reduces the risk of trichomoniasis.
Vulvovaginal Candidiasis

Epidemiology

Vulvovaginal candidiasis, caused by Candida species and commonly called a "yeast" infection, affects most females at some time in their lives, with the highest incidence during the reproductive years. Although vulvovaginal candidiasis is not a sexually transmitted disease, it frequently causes clinical manifestations that overlap with several other common sexually transmitted diseases. Candida species may be isolated from the lower genital tract in approximately 20% of asymptomatic women without abnormal discharge, and it is estimated that 70 to 75% of women will experience at least one episode of vulvovaginal candidiasis, 40 to 50% will experience a second episode, and approximately 5 to 10% will develop recurrent vulvovaginal candidiasis, defined as four or more episodes in a single year.[151,152,153] Candidiasis is currently the second most common cause of vaginal infections after bacterial vaginosis, though information on the incidence of vulvovaginal candidiasis is incomplete since vulvovaginal candidiasis is not reportable.[121]

Pathogenesis and Microbiology

Candida species are normal flora of the skin and the vagina and are not considered as sexually transmitted pathogens. Disruption in the host vaginal environment, however, can cause Candida organisms to transition from a commensurate to pathologic role.[151] Yeast blastospores are typically responsible for asymptomatic colonization, whereas mycelia (pseudohyphae or hyphae forms) cause symptomatic vaginitis through overgrowth and adherence to vaginal epithelial cells (Figure 10).[153] Destruction of host tissue by Candida species is mediated by the activity of several hydrolytic enzymes, which promote adhesion and host tissue penetration, as well as other virulence factors, such as biofilm formation and phenotypic switching.[151] In the United States, Candida albicans strains are responsible for 85 to 95% of cases of vulvovaginal candidiasis, with the remainder due to non-albicans isolates, most commonly C. glabrata; in some parts of the world, infections due to non-albicans isolates cause up to 20% of all vulvovaginal candidiasis infections, possibly due to overuse of over-the-counter azole therapies (to which C. albicans is more susceptible than non-albicans species).[151,153]

Risk Factors

Although most patients with vulvovaginal candidiasis do not have specific risk factors associated with risk of developing vulvovaginal candidiasis, those with frequent, complicated, and/or severe vulvovaginal candidiasis have a number of risk factors that have been identified, including predisposing host factors (uncontrolled diabetes, corticosteroids, repeated courses of antibiotics, pregnancy, HIV infection, hormone replacement therapy), behavioral factors (sexual practices, use of oral contraceptives, intrauterine devices, condoms, and spermicide), and genetic predisposition.[151,152,153]

Clinical Manifestations

Classification of Vulvovaginal Candidiasis

On the basis of clinical presentation, and taking into account factors specific to the host and pathogen, vulvovaginal candidiasis is classified as either uncomplicated or complicated.[154] The 2015 STD Treatment Guidelines highlight the importance of this distinction, as it influences treatment decisions.[155] Uncomplicated vulvovaginal candidiasis is defined as infection in an immunocompetent, nonpregnant woman that is mild-to-moderate in severity, recurs less than four times per year, and involves Candida albicans strains that respond to all forms of antifungal therapy.[153,154,155] Complicated vulvovaginal candidiasis, by contrast, is defined as infection that is (1) moderate to severe, (2) associated with pregnancy or other concomitant conditions (i.e. immunosuppression, diabetes mellitus), or (3) recurs more than four times per year in immunocompetent women.[153,154,155] Among women with HIV infection, vulvovaginal candidiasis occurs more frequently than in women without HIV infection.[155,156] With more advanced HIV disease,
vulvovaginal candidiasis often is more severe and may recur more frequently.

**Clinical Findings**

Vulvovaginal candidiasis classically presents with symptoms such as pruritus (the most common symptom), vaginal soreness, dyspareunia, vulvar burning, external dysuria, and abnormal vaginal discharge.\(^2,153\) Vulvar and labial erythema, fissures, and satellite papular lesions may be present.\(^{153}\) Symptoms associated with vulvovaginal candidiasis tend to flare prior to the onset of menses. Vaginal discharge is usually described as thick, white, and clumpy (“cottage-cheese-like”) (Figure 11), but it may be watery, minimal, or not present, and there is typically little, if any, associated odor.\(^{153}\)

**Diagnostic Methods**

The clinical symptoms of vulvovaginal candidiasis overlap with other causes of vaginitis, so diagnostic evaluation is recommended. Most patients with symptomatic vulvovaginal candidiasis can be readily diagnosed on the basis of a microscopic examination of vaginal secretions.

**Vaginal pH**

The vaginal pH should be normal (3.8 to 4.5) in the setting of candidiasis. If the pH is abnormally high (greater than 4.5), it suggests an alternative diagnosis of bacterial vaginosis or trichomoniasis, or a mixed infection.

**Potassium Hydroxide (KOH) and Saline Wet Mount Preparation and Microscopy**

Visualization under microscopy of pseudohyphae (mycelia) and/or budding yeast (conidia) on 10% KOH wet prep examination (Figure 12) or saline wet mount (Figure 13) can confirm the diagnosis of vulvovaginal candidiasis; use of the 10% KOH preparation dissolves many of the host cells and thus improves the sensitivity compared with the saline wet mount.\(^{153}\) Microscopy is also useful in differentiating candidiasis from bacterial vaginosis and *T. vaginalis*. Most patients with vulvovaginal candidiasis do not have abundant white blood cells visualized on microscopy. Large numbers of white blood cells indicates a diagnosis other than vulvovaginal candidiasis, or a mixed infection.

**Gram's Stain**

Performing an initial Gram's stain can provide useful information in patients with vulvovaginal candidiasis, but a wet mount KOH is preferred over the Gram's stain. For patients with vulvovaginal candidiasis, the Gram's stain may show large strongly gram-positive staining yeasts, and in some instances, hyphae (Figure 14).\(^{5,7}\)

**Culture**

Fungal cultures are not useful for the routine diagnosis of vulvovaginal candidiasis since positive cultures may detect colonization rather than clinically significant infections. In some circumstances, however, fungal culture may be useful to detect non-albicans species (since *C. glabrata* only forms blastospores and is easily missed on microscopy) or resistant organisms in women with recurrent disease, and is recommended before initiating suppressive therapy for vulvovaginal candidiasis.\(^{154}\) Fortunately, *C. albicans* azole resistance is still considered uncommon; nonetheless, susceptibility testing should be performed in patients with complicated disease.\(^{155,157,158}\)

**Treatment**

**Treatment of Uncomplicated Vulvovaginal Candidiasis Infections**

The 2015 STD Treatment Guidelines recommend a variety of short-course intravaginal antifungal agents to
treat uncomplicated vulvovaginal candidiasis (Table 3).[155] Many of the treatment options are available in over-the-counter formulations, and prescription intravaginal medications are also available. The recommendations include one option for patients who prefer oral therapy: fluconazole 150 mg orally in a single dose. The short-course topical formulations are effective in treating uncomplicated vulvovaginal candidiasis and azole drugs are more effective than topical nystatin. An estimated 80 to 90% of patients with vulvovaginal candidiasis who complete treatment with an azole have a relief in symptoms and negative cultures.

**Treatment of Recurrent Vulvovaginal Candidiasis**

For patients who develop recurrent vulvovaginal candidiasis (four or more episodes within 1 year), the 2015 STD Treatment Guidelines recommend a strategy of using a longer 7 to 14 day initial course of therapy to achieve clinical remission, followed by a 6 month maintenance regimen. The longer course initial therapy options include topical therapy for 7 to 14 days or oral fluconazole given as a 100 mg, 150 mg, or 200 mg oral dose every third day (day 1, 4, and 7) for a total of 3 doses; the goal of the intensive initial therapy is to achieve mycologic remission before using maintenance therapy. The preferred maintenance therapy consists of oral fluconazole (100, 150, or 200 mg) given weekly for 6 months; maintenance therapy has been demonstrated to reduce episodes of vulvovaginal candidiasis, but symptoms recur in about 30 to 50% of women once maintenance therapy is stopped. For patients who cannot take oral fluconazole maintenance therapy, topical azole therapy given intermittently can be used as an alternative.

**Treatment of Severe Vulvovaginal Candidiasis**

Severe disease, which can involve significant skin breakdown, fissuring, and edema, requires treatment with 7 to 10 days of topical azole therapy or two doses of oral fluconazole 150 mg given 72 hours apart. Low-dose topical steroid preparations may also provide immediate symptomatic relief.

**Treatment of Non-** *albicans* **Vulvovaginal Candidiasis**

Unfortunately, the optimal therapy for non-*albicans* vulvovaginal candidiasis is not known. The 2015 STD Treatment Guidelines indicate that treatment of non-*albicans* vulvovaginal candidiasis may require longer courses of a non-fluconazole azole, either oral or topical.[155] If this approach fails, intravaginal boric acid (600 mg in a type O gelatin capsule inserted nightly for one week or longer) is a reasonable option.[155,159,160] If all of these measures fail, specialist consultation is advised.

**Management of Sex Partners**

Vulvovaginal candidiasis is not sexually transmitted so there is no treatment necessary for asymptomatic sex partners of infected women. Balanitis caused by *Candida* species is an uncommon finding in men and may be due to risk factors other than penile-vaginal sex, including age over 40, diabetes mellitus, or uncircumcised status.[161] Men with candidal balanitis should be treated with 1 to 2 weeks of topical antifungal therapy, or one day of oral antifungal therapy.[161]

**Post-Treatment Follow-Up**

Follow-up after treatment of uncomplicated vulvovaginal candidiasis is not necessary. Women should seek reevaluation if symptoms persist or recur, since this could indicate complicated disease.

**Treatment of Special Populations**

- **Treatment of Women During Pregnancy**: The 2015 STD Treatment Guidelines recommend that pregnant women use topical (intravaginal) azole medications for 7 days during pregnancy. Oral fluconazole should not be used in pregnancy due to concern about possible teratogenicity based on several case reports; in 2011, the FDA changed the pregnancy category from C to D to reflect this
concern. However, a large Danish cohort study counters this conclusion, finding that fluconazole use in the first trimester confers a small risk of tetralogy of Fallot, but otherwise is not associated with an excess risk of birth defects overall.[162]

**Treatment of Women with HIV Infection:** The 2015 STD Treatment Guidelines recommend women with HIV infection and vulvovaginal candidiasis receive the same treatment as women without HIV infection.[155] If topical therapies are chosen, it is especially important to counsel women with HIV infection that the available creams and suppositories are oil-based and might weaken latex condoms. With more advanced HIV disease, vulvovaginal candidiasis often is more severe and may recur more frequently, but primary prophylactic fluconazole therapy is not recommended in these women.[155,163]

### Patient Counseling and Education

Patient counseling and education about vulvovaginal candidiasis should cover the nature of the disease, transmission issues, and risk reduction.

#### Nature of the Disease

- Asymptomatic colonization with *Candida* species is common and does not require treatment.
- Symptomatic vulvovaginal candidiasis is caused by a disruption of the normal vaginal flora by various factors, including pregnancy, hormonal contraception, sexual activity, and immunosuppressive conditions.
- Women with symptomatic vulvovaginal candidiasis should be treated with antifungal therapy.
- Women with complicated vulvovaginal candidiasis typically require longer courses of antifungal therapy.

#### Transmission Issues

- VVC is not considered a sexually transmitted infection, although there are some cases of male sexual partners developing candidal balanitis as a result of penile-vaginal sex.

#### Risk Reduction

- Avoid douching.
- Avoid unnecessary antibiotic use.
- Avoid repeated courses of self-administered, over-the-counter antifungal therapy in settings where no laboratory diagnosis has been confirmed.
- Complete the full course of any prescribed therapy.
- Optimize the management of other concurrent illnesses, such as diabetes mellitus and HIV infection.
Summary Points

- The three most common conditions diagnosed among women with vaginal symptoms presenting in the primary care setting are bacterial vaginosis, vulvovaginal candidiasis, and trichomoniasis.
- Vaginitis is primarily a clinical diagnosis, but a wide variety of diagnostic tests are available, including point-of-care tests, culture, molecular detection methods (PCR, NAAT), and indirect testing for enzymatic activity.
- Clinical manifestations of vaginitis depend on the organism causing infection: bacterial vaginosis is typically characterized by a “fishy”, homogenous, clear, white or gray vaginal discharge; trichomoniasis has a characteristic "frothy" gray or yellow-green vaginal discharge and pruritus; and vulvovaginal candidiasis classically presents with symptoms of pruritus, vaginal soreness, dyspareunia, vulvar burning, external dysuria, and abnormal vaginal discharge.
- Both bacterial vaginosis and trichomoniasis have been linked to several obstetrical and gynecologic complications, including premature rupture of membranes and preterm labor as well as an increased risk of HIV acquisition and transmission.
- *Candida* species may be isolated from the lower genital tract in approximately 20% of asymptomatic women without abnormal discharge, and it is estimated that 70% to 75% of women will experience at least one episode of vulvovaginal candidiasis.
- Bacterial vaginosis should be treated with oral or intravaginal metronidazole, oral tinidazole (not recommended in pregnancy), or oral or intravaginal clindamycin.
- Trichomoniasis treatment consists of single-dose metronidazole or tinidazole therapy, except in women with HIV infection who require 7 days of metronidazole therapy.
- Uncomplicated vulvovaginal candidiasis can be treated with a wide array of short-course topical antifungal agents or oral fluconazole.
Citations

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Figures

Figure 1 Bacterial Vaginosis—Clue Cells

Illustration by Jared Travnicek, Cognition Studio
**Figure 2 Nugent's Score and Gram's Stain of Vaginal Smears**

This image shows multiple gram-stained vaginal smears from women and the Nugent Scoring for each smear. Normal vaginal flora (A and B); Intermediate vaginal flora (C and D); Bacterial vaginosis (E and F). (A) 4+ lactobacillus morphotypes, no small gram-negative or gram-variable rods (score = 0); (B) 3+ lactobacillus morphotypes, 1+ *Gardnerella* spp. morphotypes (score = 2); (C) 3+ lactobacillus morphotypes and 3+ small gram-variable rods (score = 4); (D) 2+ lactobacillus morphotypes and 4+ small gram-negative and gram-variable rods (score = 6); (E) no lactobacilli and 4+ gram-negative and gram-variable rods (score = 8); note clue cells on left; (F) no lactobacilli and 4+ gram-negative rods and curved rods (score = 10); note the *Mobiluncus* spp. morphotypes on the clue cell (center of field).

**Figure 3 Nugent Scoring System for Bacterial Vaginosis**

The Nugent scoring is based on morphotypes per high power field of a gram-stained vaginal swab sample.


<table>
<thead>
<tr>
<th>Score</th>
<th>Lactobacillus morphotypes</th>
<th>Gardnerella and Bacteroides morphotypes</th>
<th>Curved gram-variable rods</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>3+</td>
<td>1+</td>
<td>1+ or 2+</td>
</tr>
<tr>
<td>2</td>
<td>2+</td>
<td>+</td>
<td>3+ or 4+</td>
</tr>
<tr>
<td>3</td>
<td>1+</td>
<td>3+</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>4+</td>
<td>-</td>
</tr>
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</table>

**Scoring Based on Morphotypes per High Power Field:** 0 = 0; 1+ = <1; 2+ = 1-4; 3+ = 5-30; 4+ = ≥30

**Total Score:** 0-3 Normal; 4-6 Intermediate; 7-10 Bacterial Vaginosis
Figure 4 *Trichomonas vaginalis*

*Trichomonas vaginalis* is a pear-shaped flagellated protozoan parasitic organism that is approximately 10 by 7 micrometers. The organism achieves a quivering motion via the anterior flagella and the undulating membrane. After attaching to vaginal epithelial cells, the organism takes on a more ameboid-like appearance.

Illustration by Jared Travnicek, Cognition Studio
Figure 5 Trichomoniasis and Cervical Petechiae

This photograph shows multiple petechiae on the cervix of a woman with trichomoniasis. This manifestation in a woman with vaginal discharge strongly suggests a diagnosis of trichomoniasis and is often referred to as a ‘strawberry cervix’.

Source: Claire Stevens, University of Washington
Figure 6 *Trichomonas vaginalis* on Wet Mount

This photomicrograph taken of a vaginal discharge wet mount sample shows numerous oval *Trichomonas vaginalis* protozoan parasites; the black arrow on left indicates two characteristic *T. vaginalis* organisms (the thin flagellum can be faintly seen).

Source: Centers for Disease Control and Prevention Public Health Image Library (Joe Miller, 1975).
**Figure 7 Time to Loss of Trichomonad Motility with Wet-mount Microscopy**

Investigators collected samples for wet-mount preparations of vaginal discharge. Specimens were examined immediately with microscopy for evidence of motile trichomonads; all positive samples were then viewed every 10 minutes thereafter. As shown in the graph, for the 65 initial positive specimens, the wet mount diagnostic yield declined significantly over time.

Figure 8 Performance of Aptima for Diagnosis of Trichomonas

This graphic shows the sensitivity and specificity of the Aptima nucleic acid amplification test (NAAT) in 933 women. Among the women enrolled, 60% were symptomatic, most often with vaginal discharge.


| Clinical Performance of Automated Aptima Trichomonas vaginalis Assay in 1,025 Asymptomatic and Symptomatic Women |
|--------------------------------------------------|------------------|------------------|
|                             | Sensitivity      | Specificity      |
| Urine                        | 95.2             | 98.9             |
| Vaginal swab                 | 100              | 99               |
| Endocervical swab            | 100              | 99.4             |
| ThinPrep                     | 100              | 99.6             |
In this trial, investigators randomized women with trichomoniasis and HIV infection to receive either a 7-day course of metronidazole (500 mg twice daily) or a single 2-gram dose of metronidazole. More treatment failures occurred in women who received single dose therapy.

Figure 10 *Candida albicans* Yeast and Hyphae Forms

Illustration with 3D rendering of *Candida albicans* showing yeasts and hyphae forms.

Figure 11 Vulvovaginal Candidiasis—Intravaginal View

This photograph was taken during pelvic examination with speculum inserted into the vagina. The thick white clumps visible on the cervix and vaginal wall indicate vaginal candidiasis.

Source: Public Health—Seattle & King County STD Clinic
Figure 12 Vulvovaginal Candidiasis and Potassium Hydroxide Preparation of Vaginal Wet Mount

This photograph is taken of a vaginal wet mount sample that has been prepared with 10% potassium hydroxide. Abundant yeasts and hyphae are visible in tangled mass. Magnification 10x.

Source: Public Health—Seattle & King County STD Clinic
Figure 13 Vulvovaginal Candidiasis and Saline Vaginal Wet Mount

This photograph taken of a saline vaginal wet mount sample shows multiple yeast forms (blue arrows) and hyphae forms (red arrow on right). Magnification 40x.

Source: Public Health—Seattle & King County STD Clinic
Figure 14 Vulvovaginal Candidiasis and Gram's Stain of Vaginal Discharge

This photograph is taken of a Gram's stain of a vaginal discharge specimen. The specimen has abundant Candida that are evident as large, oval, gram-positive yeast cells. The black arrow points to a representative cluster of yeast cells.

Source: Centers for Disease Control and Prevention Public Health Image Library (Joe Miller, 1975).
Table 1. 2015 STD Treatment Guidelines: Bacterial Vaginosis

### Treatment of Bacterial Vaginosis

<table>
<thead>
<tr>
<th>Recommended for Treatment of Bacterial Vaginosis</th>
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<tbody>
<tr>
<td><strong>Metronidazole</strong></td>
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<tr>
<td>500 mg orally twice a day for 7 days</td>
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<tr>
<td>Note: Alcohol consumption should be avoided during treatment with nitroimidazoles. To reduce the possibility of a disulfiram-like reaction, abstinence from alcohol use should continue for 24 hours after completion of metronidazole.</td>
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<tr>
<th>Recommended for Treatment of Bacterial Vaginosis</th>
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<tbody>
<tr>
<td><strong>Metronidazole</strong></td>
</tr>
<tr>
<td>gel 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days</td>
</tr>
<tr>
<td>Note: Alcohol consumption should be avoided during treatment with nitroimidazoles. To reduce the possibility of a disulfiram-like reaction, abstinence from alcohol use should continue for 24 hours after completion of metronidazole.</td>
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<tr>
<th>Recommended for Treatment of Bacterial Vaginosis</th>
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<tbody>
<tr>
<td><strong>Clindamycin</strong></td>
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<tr>
<td>cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days</td>
</tr>
<tr>
<td>Note: Clindamycin cream is oil-based and might weaken latex condoms and diaphragms for 5 days after use (refer to clindamycin product labeling for additional information).</td>
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<tr>
<th>Alternative for Treatment of Bacterial Vaginosis</th>
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<tbody>
<tr>
<td><strong>Tinidazole</strong></td>
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<tr>
<td>2 g orally once daily for 2 days</td>
</tr>
<tr>
<td>Note: Alcohol consumption should be avoided during treatment with nitroimidazoles. To reduce the possibility of a disulfiram-like reaction, abstinence from alcohol use should continue for 72 hours after completion of tinidazole.</td>
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<tr>
<td><strong>Clindamycin</strong></td>
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<tr>
<td>300 mg orally twice daily for 7 days</td>
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<tr>
<td><strong>Clindamycin</strong></td>
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<tr>
<td>ovules 100 mg intravaginally once at bedtime for 3 days</td>
</tr>
<tr>
<td>Note: Clindamycin ovules use an oleaginous base that might weaken latex or rubber products (e.g., condoms and vaginal contraceptive diaphragms). Use of such products within 72 hours following treatment with</td>
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</table>
clindamycin ovules is not recommended.

### Table 2. 2015 STD Treatment Guidelines: Trichomoniasis

**Treatment of Trichomoniasis**

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<td><strong>Metronidazole</strong></td>
<td>2 g orally in a single dose</td>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metronidazole</strong></td>
<td>500 mg orally twice a day for 7 days</td>
</tr>
<tr>
<td>Note: Alcohol consumption should be avoided during treatment with metronidazole. To reduce the possibility of a disulfiram-like reaction, abstinence from alcohol use should continue for 24 hours after completion of metronidazole.</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. 2015 STD Treatment Guidelines: Vulvovaginal Candidiasis
Treatment of Uncomplicated Vulvovaginal Candidiasis

<table>
<thead>
<tr>
<th>Recommended: Over-the-Counter Intravaginal Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clotrimazole 1% cream</strong></td>
</tr>
<tr>
<td>5 g intravaginally daily for 7-14 days</td>
</tr>
<tr>
<td>Note: This cream is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommended: Over-the-Counter Intravaginal Agents</th>
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</thead>
<tbody>
<tr>
<td><strong>Clotrimazole 2% cream</strong></td>
</tr>
<tr>
<td>5 g intravaginally daily for 3 days</td>
</tr>
<tr>
<td>Note: This cream is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommended: Over-the-Counter Intravaginal Agents</th>
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</thead>
<tbody>
<tr>
<td><strong>Miconazole 2% cream</strong></td>
</tr>
<tr>
<td>5 g intravaginally daily for 7 days</td>
</tr>
<tr>
<td>Note: This cream is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Recommended: Over-the-Counter Intravaginal Agents</th>
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</thead>
<tbody>
<tr>
<td><strong>Miconazole 4% cream</strong></td>
</tr>
<tr>
<td>5 g intravaginally daily for 3 days</td>
</tr>
<tr>
<td>Note: This cream is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Recommended: Over-the-Counter Intravaginal Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Miconazole 100 mg vaginal suppository</strong></td>
</tr>
<tr>
<td>one suppository daily for 7 days</td>
</tr>
<tr>
<td>Note: This suppository is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommended: Over-the-Counter Intravaginal Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Miconazole 200 mg vaginal suppository</strong></td>
</tr>
<tr>
<td>one suppository daily for 3 days</td>
</tr>
<tr>
<td>Note: This suppository is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommended: Over-the-Counter Intravaginal Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Miconazole 1,200 mg vaginal suppository</strong></td>
</tr>
<tr>
<td>one suppository for 1 day</td>
</tr>
<tr>
<td>Note: This suppository is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommended: Over-the-Counter Intravaginal Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tioconazole 6.5% ointment</strong></td>
</tr>
<tr>
<td>5 g intravaginally in a single application</td>
</tr>
<tr>
<td>Note: This ointment is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.</td>
</tr>
</tbody>
</table>
Recommended : Prescription Intravaginal Agents

Butoconazole 2% cream (single dose bioadhesive product)
5 g intravaginally in a single application

Note: This cream is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.

Recommended : Prescription Intravaginal Agents

Terconazole 0.4% cream
5 g intravaginally daily for 7 days

Note: This cream is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.

Recommended : Prescription Intravaginal Agents

Terconazole 0.8% cream
5 g intravaginally daily for 3 days

Note: This cream is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.

Recommended : Prescription Intravaginal Agents

Terconazole 80 mg vaginal suppository
One suppository daily for 3 days

Note: This suppository is oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information.

Recommended : Oral Agent

Fluconazole
150 mg orally in a single dose
