Vaginitis

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Module 2: Self-Study Lessons 2nd Edition
Lesson 7: Vaginitis

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Introduction

Vaginitis is common among women of reproductive age and is usually characterized by vaginal discharge, vulvar itching and irritation, and a vaginal odor.[1] A more detailed discussion on the diagnosis and management of specific causes of vaginitis is addressed in the individual sections in this lesson on Bacterial Vaginosis, Trichomoniasis, and Vulvovaginal Candidiasis.

Vaginal Environment

The vagina is a dynamic ecosystem that changes with age. Normal vaginal discharge is clear to white, odorless, and of high viscosity. The normal bacterial microbiota is dominated by *Lactobacillus* spp. (i.e. *L. crispatus*), but a variety of other facultative and strict anaerobic bacteria are also present at much 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_2O_2 (hydrogen peroxide), which serves as a host defense mechanism and kills bacteria and viruses.[Q] Normal Vaginal pH

Vaginitis

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 infection present; in approximately 30% of symptomatic women, no etiologic agent is identified.[3,4] Other causes of vaginal discharge or irritation may include the following:

- Atrophic vaginitis
- Desquamative inflammatory vaginitis
- Foreign bodies (e.g. retained tampons)
- Genital herpes
- Lichen simplex chronicus
- Lichen sclerosis
- Local or systemic allergic reactions (e.g. spermicides, deodorants, drug reactions)
- Mucopurulent cervicitis
- Normal physiologic variation
- Vulvar vestibulitis

Diagnostic Approach for Vaginitis

General Principles of Diagnosis

Vaginitis is primarily a clinical diagnosis, but a complete history, physical examination, and laboratory evaluation are necessary for accurate diagnosis. When evaluating a woman with vaginal symptoms, clinicians should inquire specifically about a woman's menstrual cycle, sexual history (including sex of partners and specific sexual practices), vaginal hygiene practices (such as douching), and any other underlying medical conditions.[5] The following briefly addresses the general approach for evaluating vaginitis, including clinical evaluation and diagnostic testing options.

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[2,3,6]. The following provides a summary of major diagnostic tests used in evaluating women with vaginitis.

- **Saline Wet Mount**: To perform a saline wet mount, begin by collecting a sample of vaginal fluid from the lateral wall of the vagina using a cotton-tipped swab. Next, place a drop of 0.9% saline on a glass slide. Last, mix the vaginal fluid sample with the saline on the slide. Alternatively, place the vaginal swab into a test tube (with less than 1 mL of saline), gently stir, and then extract a drop from the solution in the tube and place it onto a glass slide. With either method, carefully place a coverslip over the mixed solution on the slide and then immediately examine under a microscope at both low (10x) and high (40x) power. Scan the slide thoroughly 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 large motile organisms (trichomonads) is diagnostic for trichomoniasis and observing greater than 20% clue cells per high power field suggests a diagnosis of bacterial vaginosis.
- **Potassium Hydroxide (KOH) Preparation and Whiff Test**: To perform this test, collect a sample of vaginal fluid (using a cotton-tipped swab), place the sample on a glass slide, and add several drops of a 10% KOH solution to the slide. Soon after applying the KOH, the slide should be brought 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 supports the diagnosis of bacterial vaginosis. After performing the whiff test, carefully place a coverslip over the preparation on the slide and immediately examine 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 in a person who is symptomatic is consistent with a diagnosis of vulvovaginal candidiasis.
- **Litmus Testing for pH of Vaginal Fluid**: To determine the pH of the vaginal fluid, place 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. Note that trichomoniasis may occur in the setting of an elevated or normal vaginal pH.

- **Vaginal Gram's Stain**: Performing an initial Gram's stain on a sample from the vagina can provide useful information in women with suspected bacterial vaginosis or vulvovaginal candidiasis. With bacterial vaginosis, the Nugent criteria is an established scoring system used for the evaluation of bacterial vaginosis on a vaginal Gram's stain.[7] In addition, clue cells are visible on the Gram's stain. For women with vulvovaginal candidiasis, the Gram's stain may show large, gram-positive staining yeasts and hyphae, but a wet mount KOH is preferred.[6,8] Trichomoniasis is not diagnosed on Gram's stain.
- **Point-of-Care Organism-Specific Tests**: In addition to point-of-care diagnostic methods that are not organism-specific (microscopy, pH determination, and the "whiff test"), other point-of-care tests have been developed that are organism-specific and have good sensitivity and specificity.[3]
- **Culture**: Cultures can be performed for both *T. vaginalis* and *Candida* species. Fungal culture is not usually necessary to make a diagnosis of vulvovaginal candidiasis but may be needed in cases of recurrent vulvovaginal candidiasis or treatment failure with suspected azole resistance. For the diagnosis of *T. vaginalis*, culture for *T. vaginalis* is more sensitive than a wet mount, but less sensitive than molecular diagnostic methods, such as nucleic acid amplification testing.[9,10] Culture for bacterial vaginosis is not recommended due to low sensitivity (less than 50%) and the potential for mistakenly identifying commensal bacteria as pathogens, resulting in inappropriate treatment.[3]
- **Nucleic Acid Amplification Tests (NAAT)**: There are multiple nucleic acid amplification tests (NAATs) that are available and FDA-cleared for the diagnosis of bacterial vaginosis and trichomoniasis, and candida vulvovaginal candidiasis.[10,11,12,13] Most of these NAATs utilize polymerase chain reaction (PCR)-based technology.

Bacterial Vaginosis

Introduction

Bacterial vaginosis (BV) is a condition characterized by alterations in the normal vaginal microbiota, with a loss of protective lactic-acid producing *Lactobacillus* species in conjunction with increases in the concentration of facultative and strict anaerobic bacteria.[14,15] Bacterial vaginosis can increase the risk of acquiring a number of sexually transmitted infections (STIs), including HIV.[14,16] Further, bacterial vaginosis may contribute to adverse birth outcomes, such as premature birth, low birth weight, and premature rupture of membranes.[17]

Epidemiology

Bacterial vaginosis is the most common cause of vaginal discharge among reproductive-aged women in the United States and worldwide.[2,18,19,20] The estimated prevalence of bacterial vaginosis among reproductive-aged women in the United States has ranged from a low of 17% to a high of 47%, with an overall estimated prevalence of approximately 25 to 30%.[18,20,21] In these studies, many of the women with bacterial vaginosis were asymptomatic. Since bacterial vaginosis is not a reportable infection, data on the prevalence and prevalence trends are limited, with estimates based on published studies. Data on the incidence of bacterial vaginosis are extremely limited. In North America alone, the estimated annual economic burden of treating symptomatic bacterial vaginosis is $1.3 billion, with a global economic burden of $4.8 billion.[20] When taking into account all sequelae associated with bacterial vaginosis, this attributable annual cost in North America increases to approximately $3.7 billion.[20]

Factors Associated with Increased Prevalence

Increased bacterial vaginosis prevalence is associated with a greater number of male sex partners (Figure 1), sex with a female partner, douching (Figure 2), and herpes simplex virus type 2 (HSV-2) infection.[18,19,22,23,24] A reduced risk is associated with condom use, male partners who are circumcised, and oral contraceptive pills.[25,26] Increasing evidence suggests that sexual activity is integral to the development of incident bacterial vaginosis in most persons, as it correlates with the frequency of sexual activity, younger age at sexual debut, participating in anal and oral sex, and use of vaginal sex toys.[21,27,28,29,30,31] The role of sexual activity in bacterial vaginosis is also 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, as compared with men who are monogamous.[30,32,33,34,35]

Pathogenesis and Microbiology

Current understanding of the pathogenesis of bacterial vaginosis suggests loss of normal *Lactobacillus* species in the vagina by multiple facultative and strict anaerobic bacteria, which leads to a subsequent vaginal dysbiosis and a proinflammatory state.[14,16,36] To date, however, the exact etiology of bacterial vaginosis has not been determined, despite extensive research. The following summarizes current step-by-step conceptual models for the pathogenesis of bacterial vaginosis.[14,16,37]

- In the baseline state, in a healthy vaginal microbiome, *Lactobacillus* species are dominant, and they produce lactic acid from glycogen, a process that maintains a low vaginal pH; this acidic pH environment inhibits the growth of other bacterial species that are normally present in the vagina at very low levels.
- The process of vaginal dysbiosis usually begins with colonization of the vagina with a virulent strain of *Gardnerella vaginalis*, typically following a sexual exposure; the proliferation of this organism displaces vaginal lactobacilli and creates a biofilm scaffolding conducive to recruiting *Prevotella bivia*

(and other BV-associated bacteria).
- *Gardnerella vaginalis* and *P. bivia* engage in a synergistic relationship in which proteolysis by *G. vaginalis* produces amino acids that enhance the growth of *P. bivia*. In turn, ammonia produced by *P. bivia* enhances the growth of *G. vaginalis*.
- Sialidase produced by both *P. bivia* and *G. vaginalis* promotes breakdown of the mucin layer of the vaginal epithelium and increase adherence of other strict anaerobes, including *Atopobium vaginae, Megasphaera* type I, and others which join the BV biofilm on the upper layers.
- *Atopobium vaginae* stimulates a strong host immune response from vaginal epithelial cells, leading to localized cytokine and beta-defensin production
- Gradually the healthy normal dominant vaginal lactobacilli are replaced by *G. vaginalis*, *A. vaginae*, bacterial vaginosis-associated bacteria-2 (BVAB-2), and *Megasphaera* type I.
- In the final phase of this transition to bacterial vaginosis, mucus degradation occurs, the vaginal pH is elevated, multiple harmful compounds are produced (biogenic amines, toxic metabolites, and proinflammatory cytokines)—all resulting in a final state of vaginal dysbiosis and inflammation, which may progress to cause vaginal symptoms and adverse outcomes associated with this infection.[16]

[Q] Pathogenesis of Bacterial Vaginosis

[Activity] A. Bacterial Vaginosis - Pathogenesis

Clinical Manifestations

Among women with bacterial vaginosis, approximately 50 to 75% are asymptomatic.[18,38] If symptomatic, most women with bacterial vaginosis will describe vaginal malodor and vaginal discharge.[39] The odor is often described as an unpleasant “fishy smell” that may become more prominent after sexual intercourse and around the time of menstruation; the discharge is typically off-white, thin, and homogenous.[3,36,40] Symptoms may remit spontaneously. Bacterial vaginosis does not typically cause pruritus, burning, dysuria, dyspareunia, vaginal inflammation, or vulvar swelling.[40] Qualitative studies have shown that bacterial vaginosis can negatively impact self-esteem, sexual relationships, and quality of life.[21,28,41]

Obstetrical and Gynecologic Complications

Bacterial vaginosis has been linked to several obstetric complications, including late miscarriage, premature rupture of membranes, premature delivery, and low birth weight at delivery.[17,42,43,44] Bacterial vaginosis has also been associated with gynecologic complications, particularly an increased risk of post-operation infections after gynecological procedures.[45,46] There are some data to suggest bacterial vaginosis may cause additional gynecologic complications, including endometritis, pelvic inflammatory disease, and infertility, but prospective, longitudinal studies are needed to conclusively determine if bacterial vaginosis clearly causes these complications.[47,48]

Impact on Acquisition and Transmission of STIs

Longitudinal studies have also shown that bacterial vaginosis confers a substantially increased risk of acquiring multiple bacterial and viral STIs, including chlamydia, gonorrhea, trichomonas, *Mycoplasma genitalium*, herpes simplex virus type 2, human papillomavirus, and HIV.[49,50,51,52,53,54] Investigators have shown that disruptions of vaginal microbiota with bacterial vaginosis result in high concentrations of specific vaginal bacteria that increase the risk of HIV acquisition in women.[55] The increased risk for HIV acquisition from bacterial vaginosis is thought to occur from the altered bacterial microflora environment causing genital inflammation, impaired vaginal wound healing, and disruptions in the integrity of the mucosal barrier.[56] Additional studies have also shown that bacterial vaginosis increases genital HIV-1 shedding in women and enhances the risk of female-to-male HIV-1 transmission.[57]

Diagnostic Approach

A Gram's stain of a vaginal specimen with Nugent scoring has traditionally been considered the gold standard for diagnosing bacterial vaginosis, but it is primarily used now only in research settings. In the clinical setting, point-of-care testing, such as the Amsel criteria and OSOM BVBlue test, are the most frequently used tests for diagnosing bacterial vaginosis. In addition, in recent years, molecular assays have emerged to play an increasingly important role in the diagnosis of bacterial vaginosis. Making a diagnosis of bacterial vaginosis with vaginal culture or by examining a Papanicolaou smear (Pap test) is not recommended due to low sensitivity and specificity.[58,59,60]

Amsel Criteria

Bacterial vaginosis is most commonly diagnosed clinically using the Amsel criteria.[61] Compared with the traditional gold standard (vaginal fluid Gram's stain with Nugent scoring), the Amsel criteria has a sensitivity in the range of 37 to 70% and specificity of 94 to 99%.[12] In the Amsel criteria, The presence of three of the following four criteria provides sufficient evidence for a clinical diagnosis of bacterial vaginosis:[39,62]

- Vaginal pH greater than 4.5, which is the most sensitive but least specific sign
- The presence of "clue cells" (bacterial clumping that obscures the borders of vaginal epithelial cells) (Figure 3) in at least 20% of vaginal epithelial cells per high power field viewed on saline microscopy
- 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

Vaginal Gram's Stain with Nugent Scoring

The traditional gold standard for diagnosing bacterial vaginosis is a vaginal Gram's stain with Nugent score determination (Figure 4), which is based on the relative concentration of *Lactobacillus*, *Bacteroides*, *Gardnerella*, and *Mobiluncus* species (Figure 5).[7,63] A normal Gram's stain should show *Lactobacillus* species only, or *Lactobacillus* species with only a few *Gardnerella* morphotypes; a Nugent score of 0 to 3 is considered normal and is consistent with a *Lactobacillus*-predominant vaginal microbiota, a score of 4 to 6 indicates intermediate microbiota (emergence of *G. vaginalis*), and 7 to 10 is consistent with bacterial vaginosis.[7,63] Although this test is traditionally considered the gold standard, it is not used often in clinical practice because it is time-consuming, requires training and expertise for interpretation, and results are not typically available during the clinic visit.[12]

Point-of-Care Assays

In addition to the point-of-care methods used to determine the Amsel criteria, there are several assays that have been developed as point-of-care tests for the diagnosis of bacterial vaginosis.

- **OSOM BVBlue Test**: The OSOM BVBlue test detects elevated vaginal fluid sialidase, an enzyme that is produced in increased quantities by the bacterial microorganisms (i.e. *G. vaginalis*) that are involved in bacterial vaginosis.[64,65]. This test is a Clinical Laboratory Improvement Amendments (CLIA)-waived, point-of-care test that provides results in about 10 minutes.[12] The test is easy to perform and requires six steps: (1) obtain a vaginal swab sample using the kit swab (either through self-collected or clinician-collected specimens), (2) insert the collection swab into the kit testing vial that contains liquid, (3) wait 10 minutes with the swab in the vial, (4) add one drop of the developer solution to the testing vessel, (5) stir the swab in the vial to mix the test solution with the vial solution, and (6) immediately read the test and interpret based on the color change. Compared with Nugent score, this test has a sensitivity in the range of 88 to 92% and specificity of 92 to 95%.[64,65]
- **Affirm VPIII**: This molecular assay uses a DNA hybridization probe that can detect high concentrations of *G. vaginalis* (greater than 5×10^5 colony-forming units of *G. vaginalis* per mL of vaginal fluid); this assay can also detect *T. vaginalis* and *C. albicans.* The test requires approximately 30 minutes to obtain results. When the Affirm VPIII assay is used alone to diagnose bacterial vaginosis, it has a low sensitivity and specificity when compared with Gram's stain and Nugent

scoring. If, however, this test is used in conjunction with a vaginal pH measurement and presence of amine odor, the test performance improves, with a sensitivity of 97% and specificity of 81%.[12]

- **FemExam Test Card**: The FemExam Test Card measures vaginal pH, proline aminopeptidase, and trimethylamine (a metabolic by-product of *G. vaginalis*).[66] When compared with the Gram's stain and Nugent score, this test has a sensitivity of 91% and specificity of 61%.[63] This test has primarily been used in resource-limited settings, and although it has been reported to be beneficial compared with syndromic management, it is not a preferred diagnosis method for bacterial vaginosis.[66]

Nucleic Acid Amplification Tests

Although multiple nucleic acid amplification tests (NAATs) are commercially available for diagnosing bacterial vaginosis in symptomatic women, only two of these are cleared by the United States Food and Drug Administration (FDA): BD MAX Vaginal Panel and Aptima BV.[12,63] These tests are currently intended only for use in women with vaginitis symptoms, and can be run using a self-obtained or clinician-collected vaginal swab specimens, with results available within 24 hours.[12]

- **BD MAX Vaginal Panel**: The BD MAX Vaginal Panel is a multiplex, real-time PCR assay used to evaluate women with vaginitis symptoms. This assay can detect major *Lactobacillus* species that are present in a healthy vaginal microbiota (*L. crispatus, L. gasseri*, and *L. jensenii*) and prominent bacterial vaginosis-associated bacteria (*G. vaginalis*, *A. vaginae*, BVAB-2, and *Megasphaera* type 1).[63,67] In addition, the BD MAX Vaginal Panel can detect organisms responsible for causing trichomoniasis and vulvovaginal candidiasis.[67] This assay bases the diagnosis of bacterial vaginosis on the relative concentrations of the healthy *Lactobacillus* species and the bacterial vaginosis-causing organisms, with a final determination based on a proprietary algorithm.[63] For the diagnosis of bacterial vaginosis, this test has a reported sensitivity with clinician-collected specimens of 90.5% and specificity of 85.8%; similar results were seen with self-obtained specimens (Figure 6).[67]
- **Aptima BV Test**: The Aptima BV test can be used in symptomatic women to detect certain *Lactobacillus* species (*L.* Crispatus, *L. gasseri* and *L. jensenii*) and bacterial vaginosis-associated bacteria (*G. vaginalis* and *A. vaginae*). This test has a reported sensitivity with clinician-collected specimens of 95.0% and specificity of 89.6%; similar results were seen with self-obtained specimens (Figure 7).[68] [Q] Diagnosis of Bacterial Vaginosis

Screening Recommendations

In general, screening for bacterial vaginosis in asymptomatic women is not recommended. Screening and treatment of women with bacterial vaginosis 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 is more cost-effective than a screen-and-treat approach.[69,70,71,72] 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.[73,74,75,76,77] For pregnant women who do not have vaginal symptoms, routine screening for bacterial vaginosis is not recommended, including women at low risk or high risk for preterm delivery.[63]

Treatment

Treatment of Bacterial Vaginosis in Nonpregnant Women

Women who have vaginal symptoms consistent with bacterial vaginosis should receive treatment.[63] The recommended regimens include metronidazole 500 mg orally twice daily for 7 days; metronidazole 0.75% gel, 5 grams intravaginally once a day for 5 days; or clindamycin 2% cream, 5 grams intravaginally at bedtime for 7 days (Table 1).[63] Accumulating reports have refuted prior warnings that metronidazole (or tinidazole) causes a disulfiram reaction in persons who ingest alcohol while taking these antibiotics.[78,79] Accordingly, experts now consider it unnecessary for persons to refrain from ingesting alcohol when they are taking metronidazole or tinidazole.[63,79] The use of probiotics that target vaginal repletion of *Lactobacillus* species

is an attractive concept for treatment and for prevention of recurrences, but this strategy is not recommended as a primary or adjunctive therapy for the treatment of bacterial vaginosis at this time.[63,80,81,82] [Q] Treatment of Bacterial Vaginosis

Management of Sex Partners

Routine testing or treatment of male sex partners of women diagnosed with bacterial vaginosis is not recommended since multiple trials have failed to show this approach impacts the rates of relapse or recurrence.[63,83] Because female sex partners are often concurrent for bacterial vaginosis status, the option of screening and treatment of female sex partners could be considered, but this approach has not been studied rigorously in clinical trials.[84]

Post-Treatment Follow-Up

Follow-up after treatment of bacterial vaginosis is only necessary if symptoms persist or recur.[63]

Special Considerations

The following situations require unique consideration when treating bacterial vaginosis.

- **Metronidazole (or Tinidazole) Allergy or Intolerance**: For women who are allergic or intolerant to metronidazole (or tinidazole), the preferred option is to treat with clindamycin cream—one full applicator (5 grams) intravaginally at bedtime for 7 days.[63]
- **Treatment of Pregnant Women with Symptomatic Bacterial Vaginosis**: All pregnant women who have symptomatic bacterial vaginosis should receive treatment since symptomatic bacterial vaginosis is clearly associated with adverse pregnancy outcomes.[63] Further, treating symptomatic bacterial vaginosis in pregnancy reduces symptoms and may reduce certain adverse obstetrical outcomes, such as late miscarriage. Any of the recommended bacterial vaginosis treatments for nonpregnant women (oral metronidazole, metronidazole gel, and clindamycin cream) as well as certain alternative regimens (oral clindamycin and clindamycin ovules) can be used to treat women with symptomatic bacterial vaginosis during pregnancy. Metronidazole crosses the placenta and is excreted in breast milk, but it has not been linked to teratogenic effects.[85,86,87] Tinidazole is not recommended during pregnancy due to evidence of fetal harm in animal studies. There are insufficient data in pregnancy to recommend using secnidazole in pregnant women with bacterial vaginosis. Several specific preparations should not be used during pregnancy, including metronidazole 1.3% vaginal gel, the 750-mg vaginal metronidazole tablets, and the Clindesse brand of 2% clindamycin vaginal cream, which is a high-dose single application treatment for bacterial vaginosis. For breastfeeding mothers with symptomatic bacterial vaginosis, metronidazole can be used.[63]
- **Management of Pregnant Women with Asymptomatic Bacterial Vaginosis in Pregnancy**: Since routine screening for bacterial vaginosis is not recommended for pregnant women who do not have vaginal symptoms, the need to address the treatment of asymptomatic bacterial vaginosis during pregnancy should not routinely arise. Available data suggest no benefit for the treatment of asymptomatic bacterial vaginosis in pregnant women who are considered at low risk for preterm delivery.[88] For pregnant women at high risk for preterm delivery, the impact of treating asymptomatic bacterial vaginosis is not clear and available data are conflicting—four studies showed benefit with treatment, two showed no benefit, and one showed harm.[63]
- **Treatment in Women with HIV**: Women with HIV experience higher prevalence and longer persistence of bacterial vaginosis compared to women without HIV.[89] The treatment of bacterial vaginosis in women with HIV should be the same as for women without HIV.[63]

Treatment of Recurrent Bacterial Vaginosis

Bacterial vaginosis recurs in approximately 30% of women within the first 3 months following treatment, and in up to 50% of women after 6 to 12 months.[90,91] Very little is known about antimicrobial resistance with

pathogens that cause bacterial vaginosis, although clinical experience suggests that treatment failure from true antimicrobial resistance is uncommon.[28]

- **Single Recurrence**: Women with a single recurrence can be treated with either the same recommended regimen or a different recommended regimen.[63,92]
- **Multiple Recurrences**: For women who experience multiple recurrences of bacterial vaginosis after completing treatment with a recommended regimen, a different approach from the initial treatment is recommended. Based on available data, the following regimens are suggested as options for these women.[63]
    - Metronidazole gel (0.75%) vaginal suppository twice weekly for at least 3 months.[91]
    - Metronidazole 750 mg vaginal suppository twice weekly for at least 3 months.[93]
    - Metronidazole 500 mg orally twice daily (or tinidazole 500 mg orally twice daily) for 7 days, followed by intravaginal boric acid 600 mg daily for 21 days, followed by suppressive therapy with intravaginal metronidazole gel (0.75%) twice weekly for 4 to 6 months.[94]
    - Metronidazole 2 grams orally once per month plus fluconazole 150 mg orally once per month given over a 12-month timeframe has also been evaluated as periodic presumptive therapy; this approach resulted in fewer episodes of bacterial vaginosis in one study when compared to placebo.[95]
    - Astodrimer 1% gel (a dendrimer-based microbicide) at a dose of 5 grams vaginally every other day for 16 weeks.[96]

Counseling and Education

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

Nature of the Disease

- Asymptomatic bacterial vaginosis is common, and screening of asymptomatic women is not generally recommended.
- Bacterial vaginosis is caused by a shift in the normal vaginal flora microbiota from lactobacillus predominance to predominance of facultative and strict anaerobic bacteria.
- The hallmark of symptomatic bacterial vaginosis is vaginal malodor and discharge.
- Bacterial vaginosis is associated with multiple obstetric and gynecologic complications, including preterm birth and pelvic inflammatory disease, and it is associated with increased risk of acquisition of HIV and other STIs.

Transmission Issues

- Sexual activity is significantly implicated in the pathogenesis of incident bacterial vaginosis; sexual transmission of bacterial vaginosis-associated bacteria may be involved.
- The pathogenesis of recurrent and persistent bacterial vaginosis may be different from incident bacterial vaginosis.
- There is a high concordance for the presence or absence of bacterial vaginosis in partnerships involving women who have sex with women.
- Bacterial vaginosis increases a woman’s risk of acquiring sexually transmitted infections, including chlamydia, gonorrhea, genital herpes, and HIV.
- Women with HIV and bacterial vaginosis have a higher likelihood of transmitting HIV to their sex partners.

Trichomoniasis

Introduction

Trichomoniasis is caused by the protozoan parasite *Trichomonas vaginalis* and is the most common curable STI worldwide. Clinical manifestations associated with trichomoniasis include asymptomatic infection, acute infection, and chronic vaginitis.[97] Trichomoniasis in pregnancy has been associated with obstetrical and gynecologic adverse outcomes.[98,99] A meta-analysis of 17 published studies found that women with *T. vaginalis* were at a two-fold higher risk for developing cervical cancer.[100] In addition to these clinical complications, trichomoniasis also confers a two- to three-fold risk of acquiring HIV.[101,102,103]

Epidemiology

An estimated 3.7 million people have trichomoniasis in the United States, with approximately 1.1 million new cases occurring each year.[104,105,106] The prevalence of *T. vaginalis* infection among women of reproductive age in the United States is estimated at 2.1%, but rates are at least four times higher among non-Hispanic Black women.[107] In contrast to chlamydia and gonorrhea, which have the highest rates in women younger than age 25 years, the prevalence of *T. vaginalis* is lower in women younger than 20 years of age than in women 20 to 50 years of age (Figure 8).[108] Prevalence rates are significantly higher in women with vaginal symptoms: in one study of women attending sexually transmitted diseases (STD) clinics, the trichomonas prevalence was 26.2% among symptomatic women compared to 6.5% among asymptomatic women.[109] Although men are not routinely tested for trichomoniasis, studies have reported rates from 3 to 17% in men attending STI clinics, and as high as 72% among men who have female sex partners diagnosed with trichomoniasis.[110,111,112] Men who have sex with men appear to be at low risk of acquiring trichomoniasis.[113] Transmission of *T. vaginalis* between women who have sex with women has been documented to occur at a substantial rate.[114,115]

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. *Trichomonas vaginalis* has four anterior flagella and one flagellum embedded in an undulating membrane (Figure 9).[97] 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.[116] Trichomoniasis is almost always sexually transmitted. *Trichomonas vaginalis* may persist for months to years in epithelial crypts and periglandular areas of the genital tract.[97] Distinguishing persistent, subclinical infection from remote sexual acquisition is not always possible.

Factors Associated with Increased Prevalence

Investigators have identified multiple factors associated with trichomoniasis, including current or past incarceration, two or more sex partners in the prior year, a diagnosis of bacterial vaginosis, education less than completion of high school, and living below the national poverty level.[117,118,119,120]

Clinical Manifestations

Genitourinary Infection in Women

Vaginitis due to acute infection with *T. vaginalis* can have a characteristic “frothy” gray or yellow-green vaginal discharge (Figure 10) and pruritus, but many women are asymptomatic.[97] Chronic infection may be associated with minimal vaginal discharge, mild pruritus, and/or dyspareunia.[97] The presence of cervical punctate hemorrhages (Figure 11), often referred to as a “strawberry cervix,” strongly suggests a diagnosis of trichomoniasis, but this occurs in fewer than 5% of women with trichomoniasis.[97,121]

[Q] Clinical Manifestations of Trichomoniasis

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%.[98,99,122,123] Neonatal trichomoniasis is unusual but can occur.[124,125]

[Q] Complications of Trichomoniasis

Trichomoniasis in Persons with HIV

Among women with HIV, more than half are coinfected with *T. vaginalis*, and they have been shown to have an increased risk for pelvic inflammatory disease and for shedding of HIV in the genital tract.[126,127,128,129] Antiretroviral therapy appears to lessen the potentiating effects of trichomoniasis infections on HIV transmission risk.[129] Infection with HIV does not make a woman more likely to have persistent or recurrent trichomoniasis.[130]

Trichomoniasis in Men

Trichomonas vaginalis may cause up to 11 to 13% of nongonococcal urethritis (NGU) in men, but urethral infection in men is frequently asymptomatic.[131] Men with *T. vaginalis* infection may also rarely present with prostatitis or epididymitis.[132] Infection with *T. vaginalis* in men may also contribute to impaired sperm motility.

Diagnostic Methods

Diagnostic testing for trichomoniasis should be performed in women seeking evaluation of vaginal discharge.[132] In clinical practice, wet mount preparation has been the most commonly used method for diagnosing trichomoniasis, primarily because of the low cost, convenience, and point-of-care diagnosis.[9,10] This approach, however, has a sensitivity (44 to 68%) that is significantly lower than with newer molecular NAATs.[13] Papanicolaou testing is not considered an appropriate diagnostic tool for trichomoniasis; if *T. vaginalis* infection is identified on routine Papanicolaou testing, a standard trichomonas diagnostic test should be used to verify infection. The following summarizes the major methods used to diagnose trichomoniasis.

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 12).[9,133] Although the wet mount method is inexpensive and relatively simple to perform, it has a sensitivity of only 44 to 68%, and it is operator-dependent.[9] 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.[134] 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 13).[9,133,134]

Culture

Obtaining a culture using modified Diamond’s medium was the previous gold standard for diagnosis of trichomoniasis prior to the availability of highly sensitive NAATs. Culture is a more sensitive diagnostic tool than wet mount alone, but results are not immediately available. Specialized culture systems (i.e. InPouch System [Biomed Diagnostics]) 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. Culture in men may be

performed on samples of urethral secretions, urine sediment, or semen, but testing in women requires sampling of vaginal secretions, as the sensitivity is low in urine culture.[132] *Trichomonas vaginalis* culture is categorized by the Clinical Laboratory Improvement Amendments (CLIA) as moderately complex as it is time-consuming and requires incubation.[13] If *T. vaginalis* is isolated in culture, drug susceptibility testing can be performed, particularly in cases of persistent infection.

Nucleic Acid Amplification Testing (NAAT)

Several NAAT-based methods are available for diagnosis of *T. vaginalis*, including transcription-mediated amplification and polymerase chain reaction (PCR). 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.[132,135,136]

- **Aptima *Trichomonas vaginalis* Assay (Becton Dickinson)**: This assay uses transcription-mediated amplification for detection of *T. vaginalis* RNA.[131,137] This test is FDA-cleared for detection of *T. vaginalis* in symptomatic and asymptomatic women.[132] The test can be performed on clinician-collected vaginal swabs, clinician-collected endocervical swabs, female urine specimens, or liquid endocervical Pap smear specimens collected in PreservCyt Solution.[131,138] The Aptima *Trichomonas vaginalis* assay has a sensitivity of 95.3 to 100% and specificity of 95.2 to 100%, which are considerably higher than wet mount or culture (Figure 14).[131,139,140,141] The Aptima *Trichomonas vaginalis* assay is not FDA-cleared for use in men, but it may be used to test urine or urethral swabs from men if the assay is internally validated in accordance with CLIA regulations.[132]
- **Probe Tec TV Qx Amplified DNA Assay (Becton-Dickinson)**: This assay uses Strand Displacement Amplification technology and is FDA-cleared for detection of *T. vaginalis* from vaginal swabs (clinician-collected or self-collected), endocervical swabs (clinician-collected), and female urine specimens.[132] This assay can be used to detect *T. vaginalis* in symptomatic and asymptomatic females. The Probe Tec TV Qx Amplified DNA assay has a sensitivity of 98.3% and specificity of 99.6% for detecting *T. vaginalis*.[142]
- **GeneXpert TV (Cepheid)**: This PCR-based NAAT is FDA-cleared for detection of *T. vaginalis* genomic DNA using self-collected or clinician-collected vaginal specimens, female urine specimens, clinician-collected endocervical swab specimens, and male urine specimens.[132,143] With this assay, the results are available within 63 minutes; for samples that have a clear positive result after 45 PCR cycles have been completed, the Early Assay Termination function will provide the positive result earlier, typically within 40 minutes.[143] The GeneXpert TV has a sensitivity of 99.5 to 100% and a specificity of 99.4 to 99.9%.[67]
- **Max CTGCTV2 Assay (Becton Dickinson)**: This FDA-cleared PCR assay for gonorrhea and chlamydia has been modified to test concurrently for *T. vaginalis*.[144] This test is FDA-cleared for detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *T. vaginalis* from vaginal specimens (self-collected or clinician-collected), female urine specimens, and male urine specimens.[132] The Max CTGCTV2 Assay has a sensitivity of 96.2 to 100% and specificity of 99.1 to 100% for detecting *T. vaginalis*.[67]
- **Cobas TV/MG (Roche Diagnostics)**: This PCR-based NAAT is FDA-cleared for detection of *T. vaginalis* and *M. genitalium* using vaginal specimens (self-collected or clinician-collected), clinician-collected endocervical swab specimens, female urine specimens, male urine specimens, and clinician-collected meatal specimens.[145] This assay is FDA-cleared for both symptomatic and asymptomatic patients. The Cobas TV/MG has a sensitivity and specificity greater than 99.5%.[145,146]

Point-of-Care Testing

There are multiple point-of-care tests available for diagnosing trichomoniasis in women.[147]

- **Osom Trichomonas Rapid Test (Sekisui Diagnostics)**: This is an antigen-detection point-of-care test for use with clinician-collected vaginal samples. The test requires about 10 to 15 minutes for test results to become available; this test has a sensitivity of 82 to 95% and a specificity of 97 to

100%.[148,149] The Osom Trichomonas Rapid Test is not FDA-cleared for use in men.
- **Solana Trichomonas Assay (Quidel)**: This point-of-care test uses isothermal Helicase-Dependent Amplification technology to detect *T. vaginalis* DNA from asymptomatic and symptomatic female urine specimens or clinician-collected vaginal specimens, with a sensitivity greater than 92% for urine specimens and greater than 98% for vaginal samples.[150] Results are available within 40 minutes. This test is not FDA-cleared for use in men.
- **Sexual Health Click Test (Visby Medical)**: This point-of-care PCR test is a single-use, disposable test that can detect chlamydia, gonorrhea, and trichomonas using self-collected vaginal swabs.[151] The compact test device provides results within 30 minutes. In an analysis of self-collected vaginal swabs obtained in 1,449 women, this test had a sensitivity of 99.2% and specificity of 96.9% for detection of *T. vaginalis*.[151] This assay received FDA clearance and a CLIA waiver in August 2021.

Screening Recommendations

Routine urogenital screening for trichomoniasis may be considered for (1) women receiving care in high trichomonas prevalence settings (STI clinics or correctional facilities), and (2) asymptomatic women at high risk of acquiring *T. vaginalis* (e.g. women with multiple sex partners, persons who exchange sex for money or drugs, or a history of STIs or incarceration).[132,152] Screening for trichomoniasis is recommended in all sexually active women with HIV (when they enter care and then annually thereafter).[132,152] Screening for *T. vaginalis* of the pharynx or rectum is not recommended, primarily because these infections are uncommon, and the cost-effectiveness for screening at these sites has not been established.[132] Screening for trichomoniasis is not recommended for men.[152]

Treatment

Treatment of Trichomoniasis

All women diagnosed with trichomoniasis, regardless of HIV or pregnancy status, should receive treatment with metronidazole 500 mg twice daily for 7 days.[132] All men diagnosed with trichomoniasis, regardless of HIV status, should receive treatment with a single dose of 2 grams of oral metronidazole (Table 2).[132] These specific recommendations for men and women are based on two studies conducted in women, most of whom were symptomatic, that demonstrated oral metronidazole given for 7 days was more effective at curing infection than a single 2-gram oral dose.[153,154] Tinidazole 2-gram oral dose is the alternative for both women and men, but it should be avoided in pregnant women.[132] Experts now consider it unnecessary for persons to refrain from ingesting alcohol when they are taking metronidazole or tinidazole.[132] Metronidazole gel (intravaginal) is not effective for the treatment of trichomoniasis and is not recommended. Persons who are allergic to metronidazole should be referred to an allergy specialist; if this is not possible, additional options are limited but would include intravaginal paromomycin cream or intravaginal boric acid.[132,155,156,157].[Q] Treatment of Trichomoniasis

Treatment of Persistent or Recurrent Trichomoniasis

The most likely reasons for persistent or recurrent trichomoniasis are reinfection from an untreated partner or lack of adherence with treatment, but in some individuals, antimicrobial-resistant *T. vaginalis* infection can occur. Currently, rates of metronidazole resistance range from 4 to 10%, and the rate of tinidazole resistance is about 1%.[158,159] Tinidazole retains activity against many metronidazole-refractory strains. The following summarizes the approach to treatment in persons with persistent or recurrent trichomoniasis.[132]

- **Treatment Failure with Reexposure**: For women and men who received standard treatment for trichomoniasis and have treatment failure due to reexposure from an untreated partner, retreatment should consist of the same regimen they initially received.[132]
- **Treatment Failure without Reexposure**: For men who have treatment failure after receiving an initial single-dose therapy of metronidazole 2 grams orally (and reexposure has not occurred), the recommended retreatment is metronidazole 500 mg orally twice daily for 7 days.[132] For women

who have failed the initial regimen of metronidazole 500 mg twice daily for 7 days and have not been reexposed, repeat treatment should be given with a 7-day regimen of either metronidazole 2 grams given once per day or tinidazole 2 grams once per day.[132] Tinidazole should not be used in pregnant women.

- **Treatment Failure after Second-Line Treatment without Reexposure**: If an individual experiences persistent infection after receiving treatment with a second-line regimen (and reexposure to a partner with trichomoniasis has not occurred), the clinician should request a special kit from the Centers for Disease Control and Prevention for 5-nitroimidazole drug-resistance testing (*Trichomonas* Susceptibility Testing).[132,160]
- **Treatment of 5-Nitroimidazole-Resistant Trichomonas**: If drug-resistance testing reveals nitroimidazole resistance and treatment with a 7-day regimen of either metronidazole 2 grams given once per day or tinidazole 2 grams once per day has been unsuccessful, then the next option is oral tinidazole 2 grams daily plus intravaginal tinidazole 500 mg twice daily for 14 days.[132,161] If this option fails, then consider using high-dose oral tinidazole (1 gram 3 times daily) plus intravaginal paromomycin (4 grams of 6.25% intravaginal paromomycin cream nightly) for 14 days.[132,157] Note that tinidazole should not be used in pregnant women. Intravaginal boric acid has been used to treat trichomoniasis in women allergic to nitroimidazole and thus could be considered as an option for women with treatment-refractory nitroimidazole-resistant trichomoniasis.[132,156,162]

Management of Sex Partners

All persons diagnosed with trichomoniasis should refer all sex partners in the prior 60 days for evaluation, comprehensive STI testing, HIV testing and presumptive treatment of trichomoniasis. 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

Persons diagnosed with trichomoniasis should be instructed to avoid sex until they and their sex partners have been treated and until they no longer have any symptoms of trichomoniasis. This usually takes about 7 days after completion of treatment.[132]

Post-Treatment Follow-Up

All sexually active women who are diagnosed and treated for *T. vaginalis* infection (including pregnant women and women with HIV) should be retested 3 months after initial treatment to evaluate the possibility of reinfection. Retesting in men is not routinely recommended.[132]

Treatment of Special Populations

- **Treatment of Women During Pregnancy**: Pregnant women with symptomatic trichomoniasis, in any trimester, should receive treatment with metronidazole 500 mg orally twice daily for 7 days.[132] Treatment of asymptomatic trichomoniasis in pregnancy, however, has not been shown to reduce preterm birth.[163] Both metronidazole and tinidazole are secreted in breast milk. Some clinicians advise deferring breastfeeding by 12-24 hours after taking a dose of metronidazole.[132,164] Tinidazole is not recommended during pregnancy due to limited animal studies suggesting fetal risk; women who are breastfeeding should wait 72 hours after taking tinidazole before breastfeeding.[132]
- **Treatment of Women with HIV**: Women with HIV who are diagnosed with trichomoniasis should receive a 7-day treatment course of metronidazole 500 mg twice daily.[132,165] This longer course of therapy has been shown to have higher cure rates than single-dose metronidazole therapy in women with HIV (Figure 15).[126,165,166,167]

Patient Counseling and Education

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

Nature of the Disease

- Trichomoniasis can be asymptomatic in men and women, and it may persist silently for years.
- Untreated trichomoniasis is associated with adverse pregnancy outcomes such as premature rupture of membranes, preterm delivery, and low birth weight infants.
- Infection with *T. vaginalis* in women has been associated with an increased risk of cervical cancer.
- Douching may worsen vaginal discharge in patients with trichomoniasis.

Transmission Issues

- Trichomoniasis is almost always sexually transmitted.
- Current and recent sex partners should undergo evaluation and receive empiric treatment for trichomoniasis.
- Persons diagnosed with trichomoniasis 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, consistent condom use, and limiting the number of sex partners.
- Douching should be avoided since it increases the risk for trichomoniasis.
- Male circumcision reduces the risk of trichomoniasis.[168,169]

Vulvovaginal Candidiasis

Introduction

Vulvovaginal candidiasis is caused by an abnormal proliferation of one or more *Candida* species in the vaginal tract. Vulvovaginal candidiasis is commonly referred to as a “yeast” infection. Globally, about 138 million women have vulvovaginal candidiasis on an annual basis.[170,171] Although vulvovaginal candidiasis is not a sexually transmitted infection, it frequently causes clinical manifestations that overlap with other sexually transmitted infections and vaginal conditions.

Epidemiology

An estimated 70 to 75% of women will experience at least one episode of vulvovaginal candidiasis in their lifetime, 40 to 50% will experience a second episode, and approximately 5 to 10% will develop recurrent vulvovaginal candidiasis (defined as three or more symptomatic episodes in one year).[171,172,173] Overall, candidiasis is responsible for about 15 to 30% of all cases of vaginitis.[174] Candidiasis is 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.[175] Women with HIV have more frequent episodes of vulvovaginal candidiasis than women without HIV.[176,177] In addition, with more advanced HIV disease, vulvovaginal candidiasis often is more severe and may recur more frequently.

Pathogenesis and Microbiology

Candida species are normal flora of the vagina and are not considered a sexually transmitted pathogen. Indeed, an estimated 20% of healthy women who have no vulvovaginal symptoms, will have *Candida* species isolated from their vagina.[171] Disruption in the host vaginal environment, however, can cause *Candida* organisms to transition from a commensal to a pathogenic role.[172] 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 16).[171] Destruction of host tissue by *Candida* species is mediated by hydrolytic enzymes that promote adhesion and host tissue penetration, as well as other virulence factors, such as biofilm formation and phenotypic switching.[172] 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 Candida* isolates, most commonly *C. glabrata*.[171] Fluconazole resistance is most often associated with significant prior azole exposure.[178,179]

[Q] Microbiology of Vulvovaginal Candidiasis

Factors Associated with Vulvovaginal Candidiasis

Although most women with vulvovaginal candidiasis do not have specific risk factors associated with vulvovaginal candidiasis, those with frequent, complicated, and/or severe vulvovaginal candidiasis have a number of factors that have been identified, including host factors (uncontrolled diabetes, corticosteroids, repeated courses of antibiotics, pregnancy, HIV, hormone replacement therapy), behavioral factors (sexual practices, use of oral contraceptives, intrauterine devices, condoms, and spermicide), and genetic predisposition.[171,172,173]

Classification of Vulvovaginal Candidiasis

On the basis of clinical presentation, host immunity, and pathogen factors, vulvovaginal candidiasis is classified as either uncomplicated or complicated (Table 3).[177,180,181] Among all women who develop vulvovaginal candidiasis, approximately 10 to 20% will have complicated vulvovaginal candidiasis. Distinguishing uncomplicated from complicated vulvovaginal candidiasis is important, as it influences treatment decisions in most instances. The management of complicated vulvovaginal candidiasis requires

unique diagnostic and treatment considerations.[177] [Q] Classification of Vulvovaginal Candidiasis

Clinical Manifestations

Vulvovaginal candidiasis characteristically manifests with multiple vaginal symptoms that may include pruritus, vaginal soreness, dyspareunia, external vulvar burning, external dysuria, and, in some, abnormal vaginal discharge.[2,171,174] When vaginal discharge is present, it is typically described as odorless, thick, white, and clumpy (“cottage-cheese-like”) (Figure 17), but it may be thin or watery.[171] Vulvar and labial erythema, fissures, and satellite papular lesions may also be present.[171] Symptoms associated with vulvovaginal candidiasis tend to flare prior to the onset of menses.

Diagnostic Methods

The clinical symptoms of vulvovaginal candidiasis overlap with other causes of vaginitis, so diagnostic evaluation is recommended. Most women with symptomatic vulvovaginal candidiasis can be readily diagnosed on the basis of a microscopic examination of vaginal secretions. Vaginal Gram’s stain is not recommended for the diagnosis of vulvovaginal candidiasis.

- **Vaginal pH**: The vaginal pH is typically normal (less than 4.5) in the setting of vulvovaginal candidiasis. If the pH is abnormally high (greater than 4.5), it suggests an alternative diagnosis of bacterial vaginosis, trichomoniasis, or a mixed vaginal infection.
- **Potassium Hydroxide (KOH) and Saline Wet Mount**: Visualization under microscopy of pseudohyphae (mycelia) and/or budding yeast (conidia) on 10% KOH wet prep examination (Figure 18) or saline wet mount (Figure 19) can confirm the diagnosis of candidiasis. Use of the 10% KOH preparation dissolves many of the host cells and thus improves sensitivity when compared with the saline wet mount.[171] Microscopy is also useful in differentiating candidiasis from bacterial vaginosis and *T. vaginalis*. Most women with vulvovaginal candidiasis do not have abundant white blood cells visualized on microscopy. Large numbers of white blood cells indicate a mixed infection or a diagnosis other than vulvovaginal candidiasis.
- **Culture**: For those with negative wet mounts but existing signs or symptoms worrisome for vulvovaginal candidiasis, fungal culture for *Candida* species should be considered. Identifying *Candida* species by fungal culture in the absence of symptoms or signs is not an indication for treatment because approximately 10 to 20% of healthy women harbor *Candida* species in the vagina.[171] In women with complicated vulvovaginal candidiasis, however, fungal cultures are indicated to confirm the diagnosis and to detect non-*albicans* species; this is particularly important for identifying *C. glabrata* since this organism only forms blastospores and is easily missed on microscopy.[177] In addition, fungal cultures (with resistance testing) should be performed in women with recurrent vulvovaginal candidiasis who have persistent symptoms while receiving maintenance antifungal therapy.[177,179] Because non-*albicans* species are present in about 10 to 20% of women with recurrent vulvovaginal candidiasis, some experts would obtain vaginal fungal cultures prior to initiating suppressive therapy for vulvovaginal candidiasis.[180]
- **Polymerase Chain Reaction (PCR)**: Most PCR tests for yeast are not FDA approved and are not recommended for diagnosing vulvovaginal candidiasis. Medical providers who use these tests should be familiar with the performance characteristics of the specific test used.

Treatment of Uncomplicated Vulvovaginal Candidiasis

Treatment Options

There are multiple recommended short-course, over-the-counter, and prescription formulations for intravaginal antifungal treatments for women with uncomplicated vulvovaginal candidiasis (Table 4).[177] For women who prefer oral therapy, fluconazole 150 mg orally in a single dose is an option.[177] Of note, the recommended antifungal creams and suppositories are oil-based and might weaken latex condoms.[177] 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 women with vulvovaginal candidiasis who complete treatment with an azole have relief in symptoms and negative fungal cultures. The topical intravaginal azole creams and suppositories are oil based and may potentially weaken latex condoms and diaphragms.[177] Thus, women receiving treatment with a topical antifungal intravaginal cream should abstain from sex during treatment or use a form of birth control that does not rely on a condom or diaphragm.[Q] Treatment of Vulvovaginal Candidiasis

Management of Sex Partners

Since vulvovaginal candidiasis is not sexually transmitted, there is no treatment necessary for asymptomatic sex partners of women with uncomplicated vulvovaginal candidiasis. Balanitis caused by *Candida* species is an uncommon finding in men and may be due to factors other than penile-vaginal sex, including age over 40, diabetes mellitus, or uncircumcised status.[182] Men with *Candida* balanitis should be treated with 7 days of topical antifungal therapy, or a single 150-mg dose of oral fluconazole.[182,183]

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 Complicated Vulvovaginal Candidiasis

Treatment of Severe Vulvovaginal Candidiasis

Severe disease, which can involve significant skin breakdown, fissuring, and edema, requires treatment with 7 to 14 days of topical azole therapy or two doses of oral fluconazole 150 mg given 72 hours apart.[177]

Treatment of Recurrent Vulvovaginal Candidiasis

Recurrent vulvovaginal candidiasis—defined as three or more episodes within one year—occurs in fewer than 5% of women with vulvovaginal candidiasis.[170] Among women with recurrent disease, approximately 10 to 20% will have non-*albicans* species, including *C. glabrata*, isolated from vaginal cultures. Although most women with recurrent vulvovaginal candidiasis have no predisposing or underlying conditions, some will have a risk factor, such as frequent antibiotic use, diabetes mellitus, or immunosuppression. If culture results show *C. albicans*, the recommended approach is to use a longer 7- to 14-day initial course of therapy to achieve clinical remission, followed by a 6-month maintenance regimen.[177]

- **Initial Therapy**: The 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 (days 1, 4, and 7) for a total of 3 doses; the goal of the intensive initial therapy is to achieve mycologic remission before initiating maintenance therapy.
- **Maintenance Regimen**: 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 women who cannot take oral fluconazole maintenance therapy, topical azole therapy given intermittently can be used as an alternative.

Treatment of Non-*albicans* Vulvovaginal Candidiasis

There are limited data on the treatment of non-*albicans* vulvovaginal candidiasis, and the optimal treatment approach is not known.[184] Strategies usually employ treatment of non-*albicans* vulvovaginal candidiasis with a 7- to 14-day course of a non-fluconazole azole, either oral or topical.[177] If this approach fails, intravaginal boric acid (600 mg in a gelatin capsule inserted nightly for 3 weeks) is a reasonable option, with

expected high clinical and mycologic response rates.[177,184,185] If all of these measures fail, consultation with a specialist is advised.

Treatment of Immunocompromised Women

Women with diabetes, underlying immunodeficiency, or immunosuppressive therapy (e.g. chronic corticosteroids), should receive longer courses of antifungal therapy—typically a course lasting 7 to 14 days.[177]

Treatment of Women with HIV

Women with HIV and vulvovaginal candidiasis (complicated or uncomplicated) should receive the same treatment as women without HIV.[177] If topical therapies are chosen, it is especially important to counsel women with HIV 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.[177,186]

Treatment of Women During Pregnancy

The recommended treatment of vulvovaginal candidiasis in pregnant women is a 7-day course of a topical (intravaginal) azole cream.[177] Oral fluconazole should not be used in pregnancy due to several reports that suggested a possible association of oral fluconazole with spontaneous abortion and possible teratogenicity.[187,188]

Management of Sex Partners

Insufficient data exist regarding treatment of sex partners of women who have complicated vulvovaginal candidiasis. Accordingly, there are no recommendations for or against treatment of male sex partners in this setting.[177]

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 microbiota by various factors, including pregnancy, diabetes, 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

- Vulvovaginal candidiasis is not considered a sexually transmitted infection, although there are some cases of male sex partners developing *Candida* 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.

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.
- The normal vagina has abundant and dominant *Lactobacillus* species and a pH that is less than 3.8 to 4.5.
- 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.
- Women with symptomatic bacterial vaginosis typically present with a homogenous, white or gray vaginal discharge that often has a “fishy” odor. Bacterial vaginosis has been linked to several obstetrical and gynecologic complications.
- The preferred treatments for bacterial vaginosis are oral metronidazole (500 mg twice daily for 7 days), 0.75% metronidazole gel (5 grams applied intravaginally once daily for 5 days), or intravaginal 2% clindamycin cream (5 grams applied intravaginally at bedtime for 7 days).
- Women with symptomatic trichomoniasis usually have a characteristic “frothy” gray or yellow-green vaginal discharge and pruritus. Trichomoniasis increases the risk of premature rupture of membranes and preterm labor.
- The preferred treatment for trichomoniasis in women is a 7-day course of oral metronidazole (500 mg twice daily); for men, the preferred treatment is a single 2-gram dose of oral metronidazole.
- Vulvovaginal candidiasis characteristically presents with symptoms of pruritus, vaginal soreness, dyspareunia, vulvar burning, external dysuria, and abnormal vaginal discharge.
- Vulvovaginal candidiasis is classified as either uncomplicated or complicated based on clinical presentation, host immunity, and pathogen factors.
- Uncomplicated vulvovaginal candidiasis can be treated with a wide array of short-course topical antifungal agents or a single 150 mg dose of oral fluconazole.

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Figures

Figure 1 Prevalence of Bacterial Vaginosis in the United States, 2001–2004: Number of Lifetime Sex Partners

Source: Koumans EH, Sternberg M, Bruce C, et al. The prevalence of bacterial vaginosis in the United States, 2001-2004; associations with symptoms, sexual behaviors, and reproductive health. Sex Transm Dis. 2007;34:864-9.

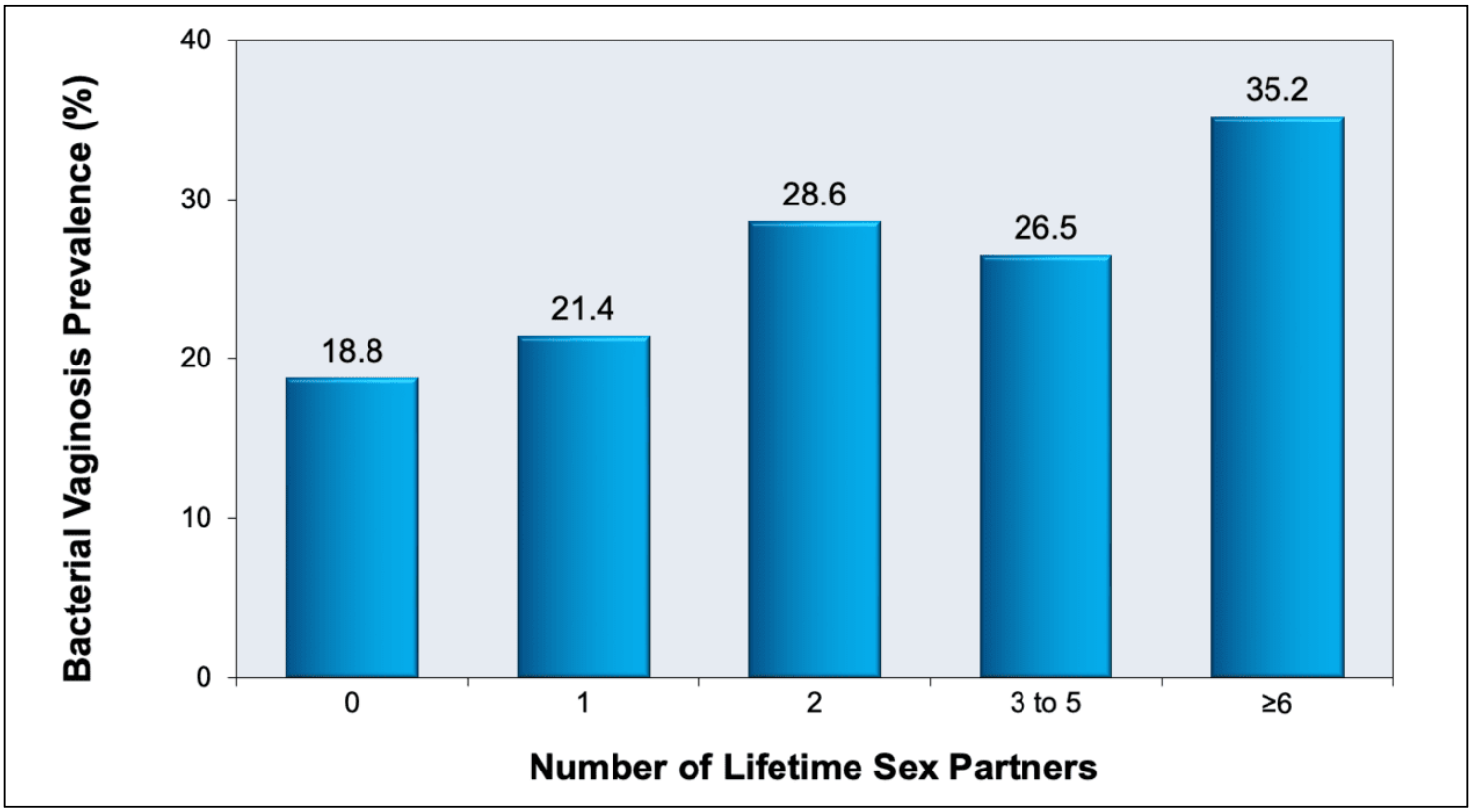

Figure 2 Prevalence of Bacterial Vaginosis in the United States, 2001–2004: Frequency of Vaginal Douching in Prior 6 Months

Source: Koumans EH, Sternberg M, Bruce C, et al. The prevalence of bacterial vaginosis in the United States, 2001-2004; associations with symptoms, sexual behaviors, and reproductive health. Sex Transm Dis. 2007;34:864-9.

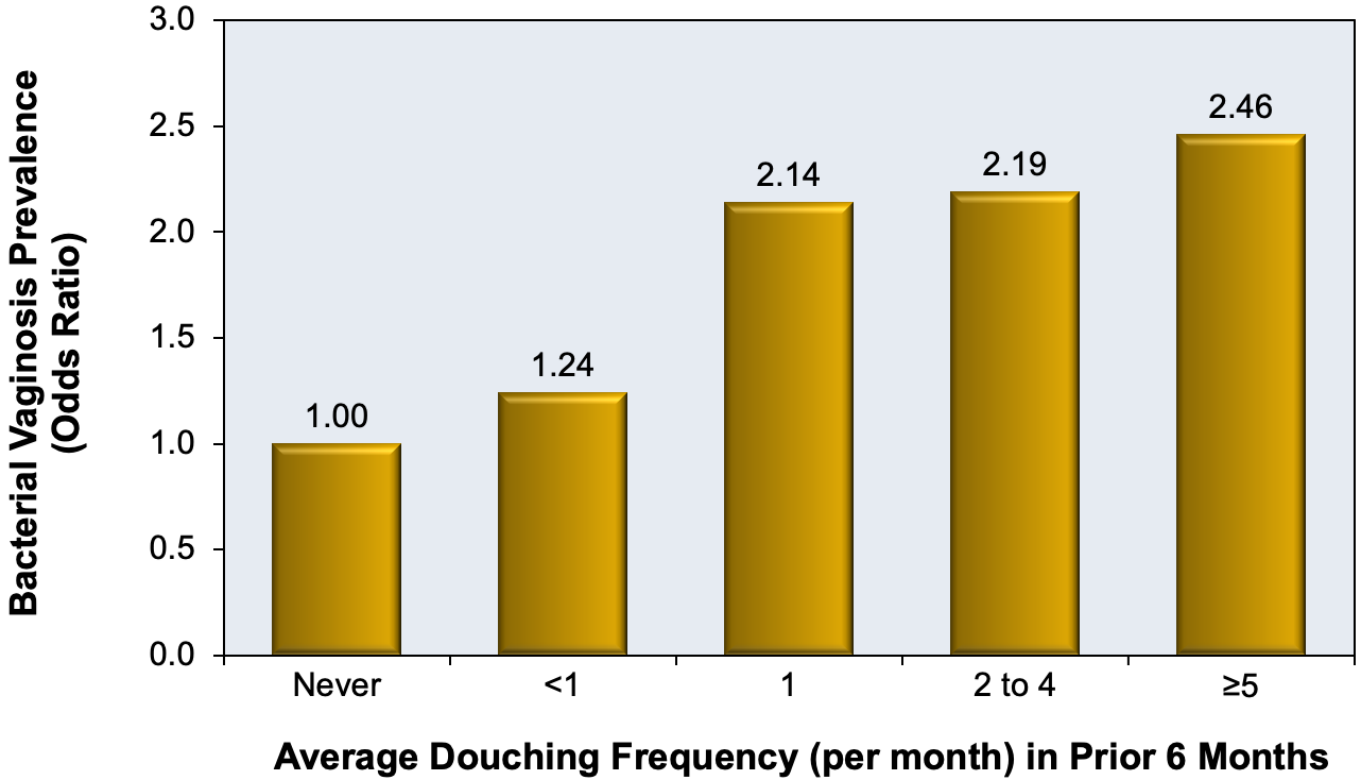

Figure 3 Bacterial Vaginosis—Clue Cells

This illustration shows a microscopic examination of a vaginal smear. Normal vaginal epithelial cells with overlying scattered bacteria are shown on the left, and the clue cells on the right illustrate vaginal epithelial cells covered with abundant bacteria.

Illustration by Jared Travnicek, Cognition Studio

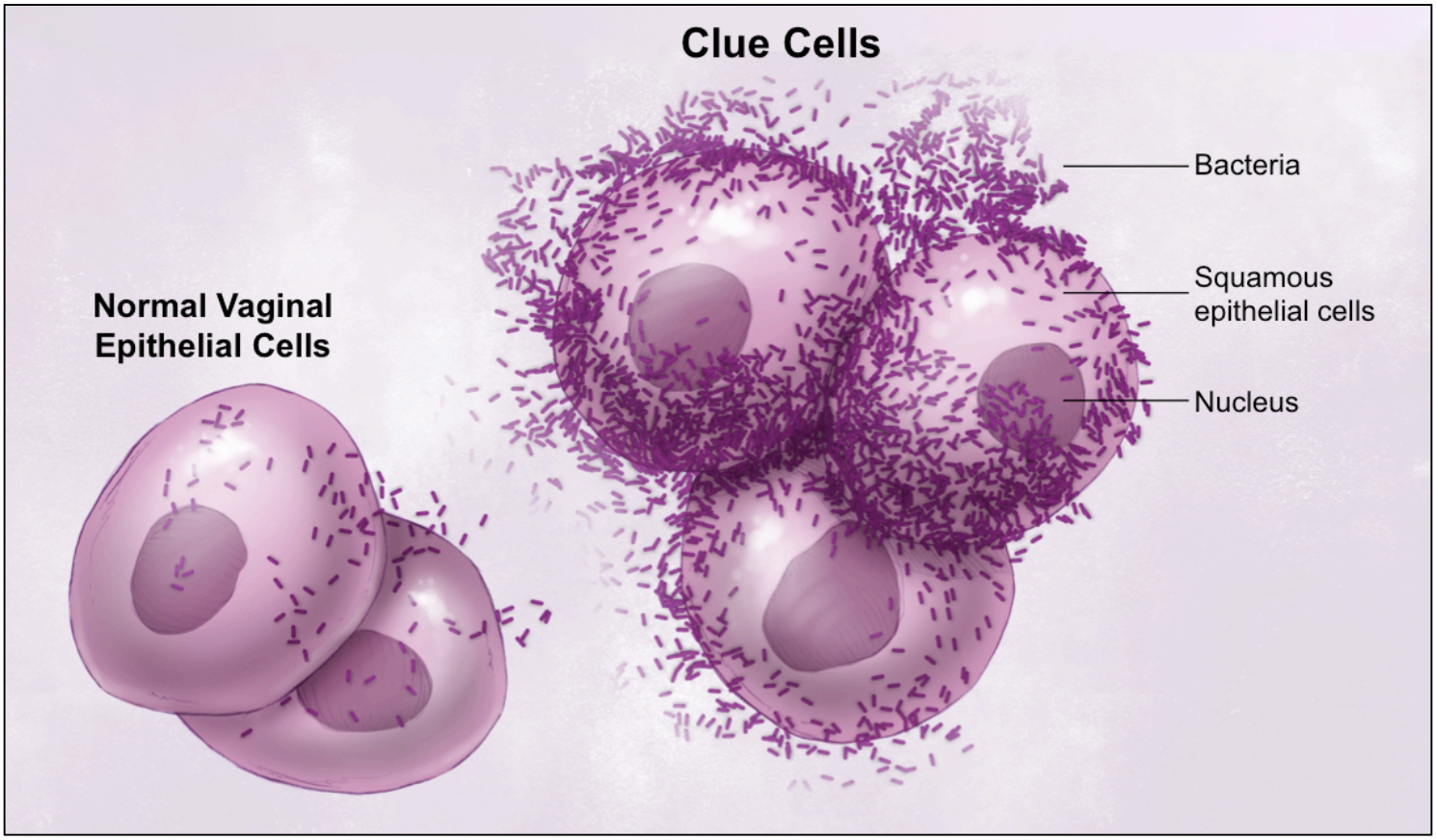

Figure 4 Nugent's Score and Gram's Stain of Vaginal Smears

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).

Source: Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. J Clin Microbiol. 1991;29:297-301. Reproduced with permission from the American Society of Microbiology.

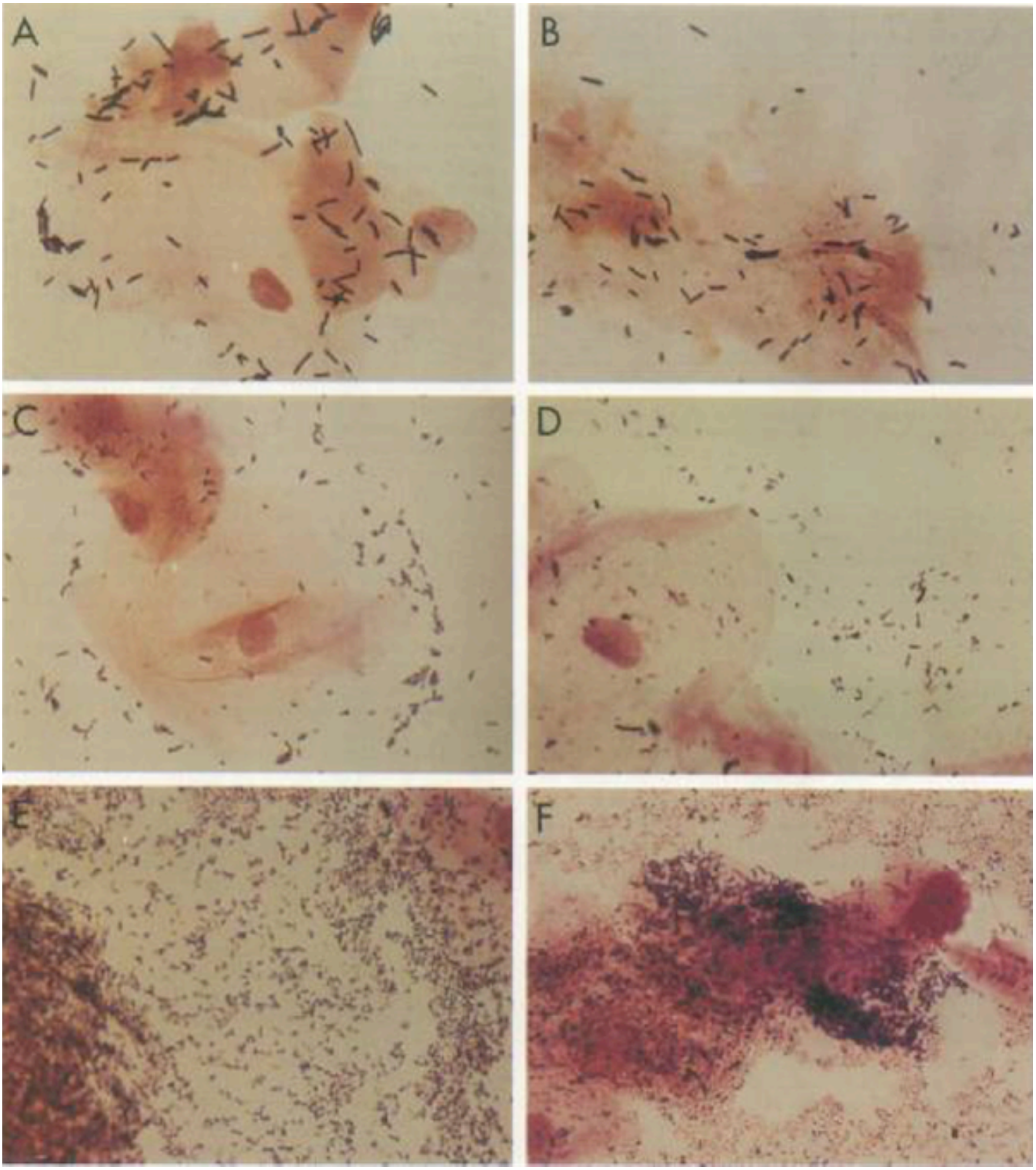
A
B
C
D
E
F

Figure 5 Nugent Scoring System for Bacterial Vaginosis

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

Source: Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. J Clin Microbiol. 1991;29:297-301.

Nugent Scoring System (0-10) for Gram-Stained Vaginal Smears

Score	*Lactobacillus* morphotypes		*Gardnerella* and *Bacteroides* morphotypes		Curved gram-variable rods
0	4+		0		0
1	3+		1+		1+ or 2+
2	2+	+	2+	+	3+ or 4+
3	1+		3+		-
4	0		4+		-

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 6 Performance of BD-MAX Vaginal Panel for the Diagnosis of Bacterial Vaginosis

Source: Gaydos CA, Beqaj S, Schwebke JR, et al. Clinical validation of a test for the diagnosis of vaginitis. Obstet Gynecol. 2017;130:181-9.

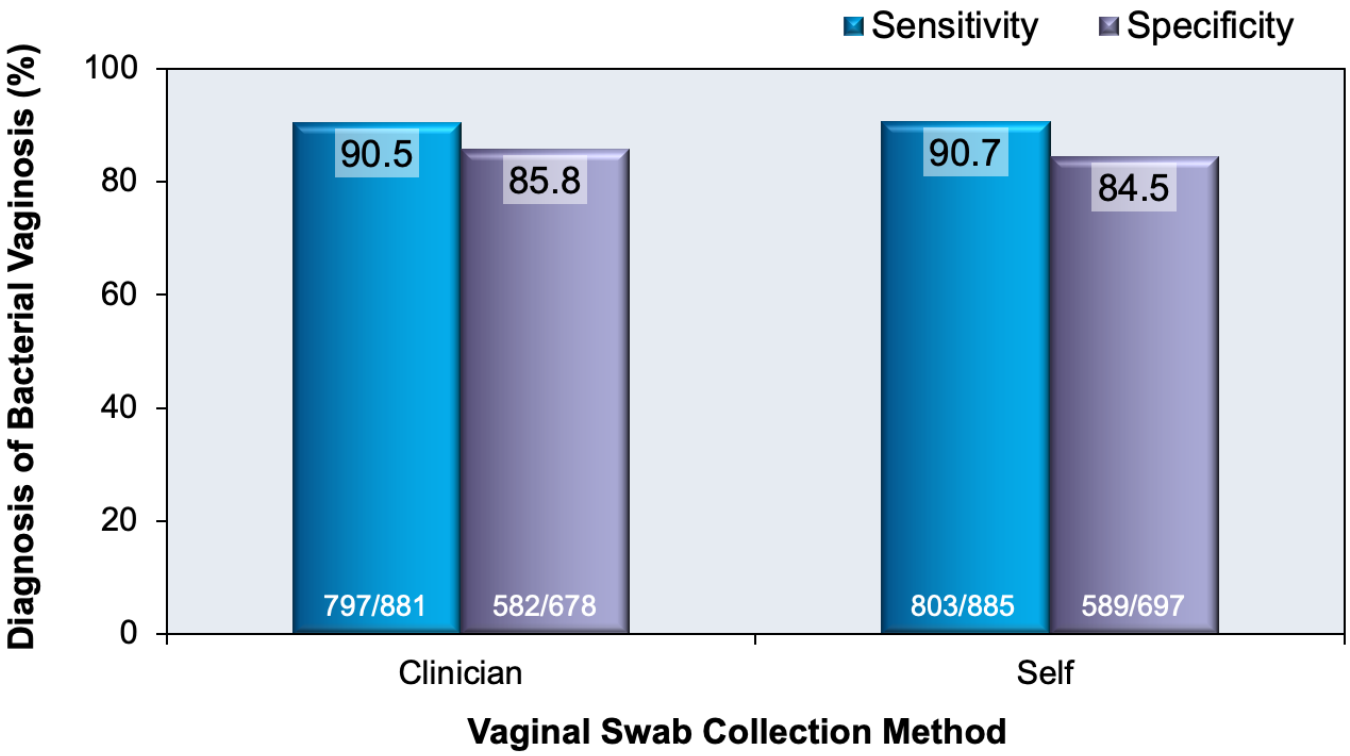

Figure 7 Performance of Aptima Vaginal Panel for the Diagnosis of Bacterial Vaginosis

Source: Schwebke JR, Taylor SN, Ackerman R, et al. Clinical validation of the Aptima bacterial vaginosis and Aptima *Candida/Trichomonas* vaginitis assays: results from a prospective multicenter clinical study. J Clin Microbiol. 2020;58:e01643-19.

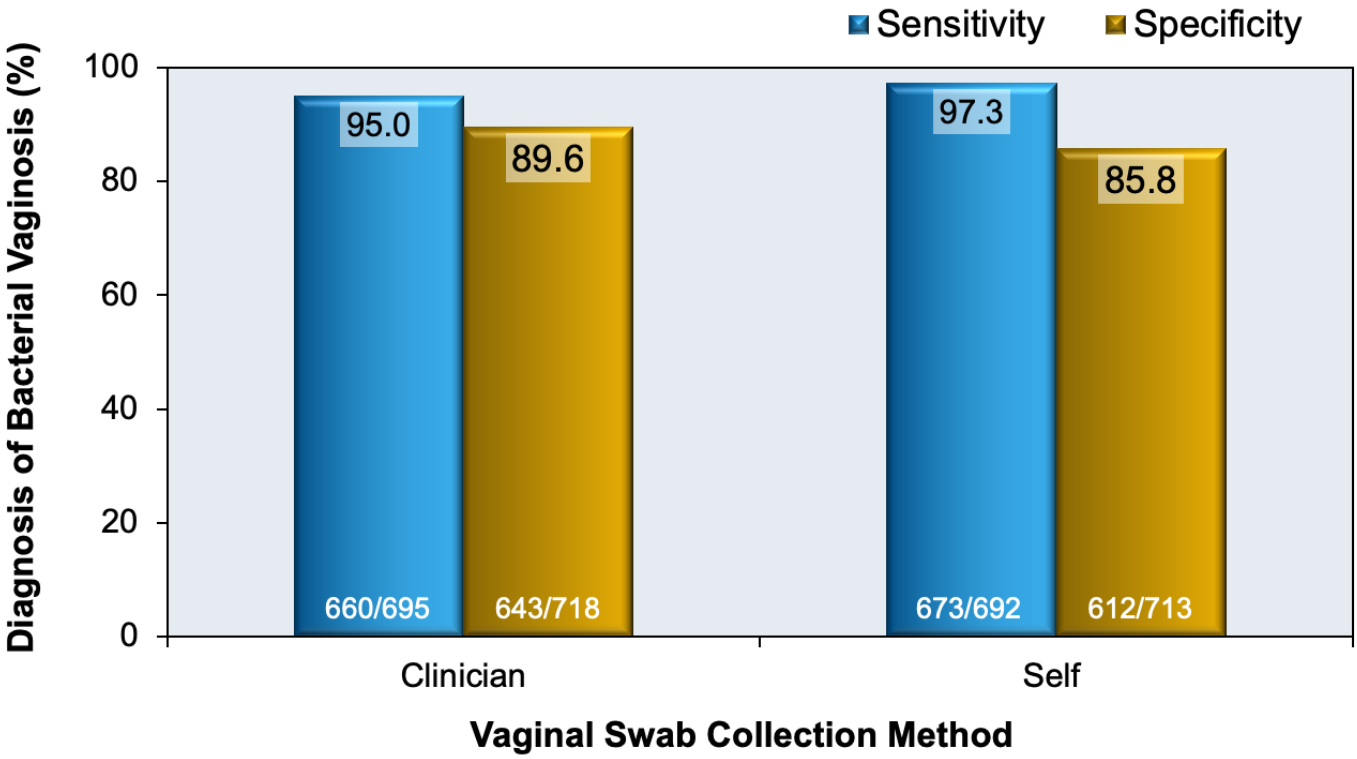

Figure 8 Prevalence of *Trichomonas vaginalis* Among Civilian, Noninstitutionalized Females Aged 14 to 59 Years: United States, 2013 to 2016

Source: Flagg EW, Meites E, Phillips C, Papp J, Torrone EA. Prevalence of *Trichomonas vaginalis* among civilian, noninstitutionalized male and female population aged 14 to 59 years: United States, 2013 to 2016. Sex Transm Dis. 2019;46:e93-e96.

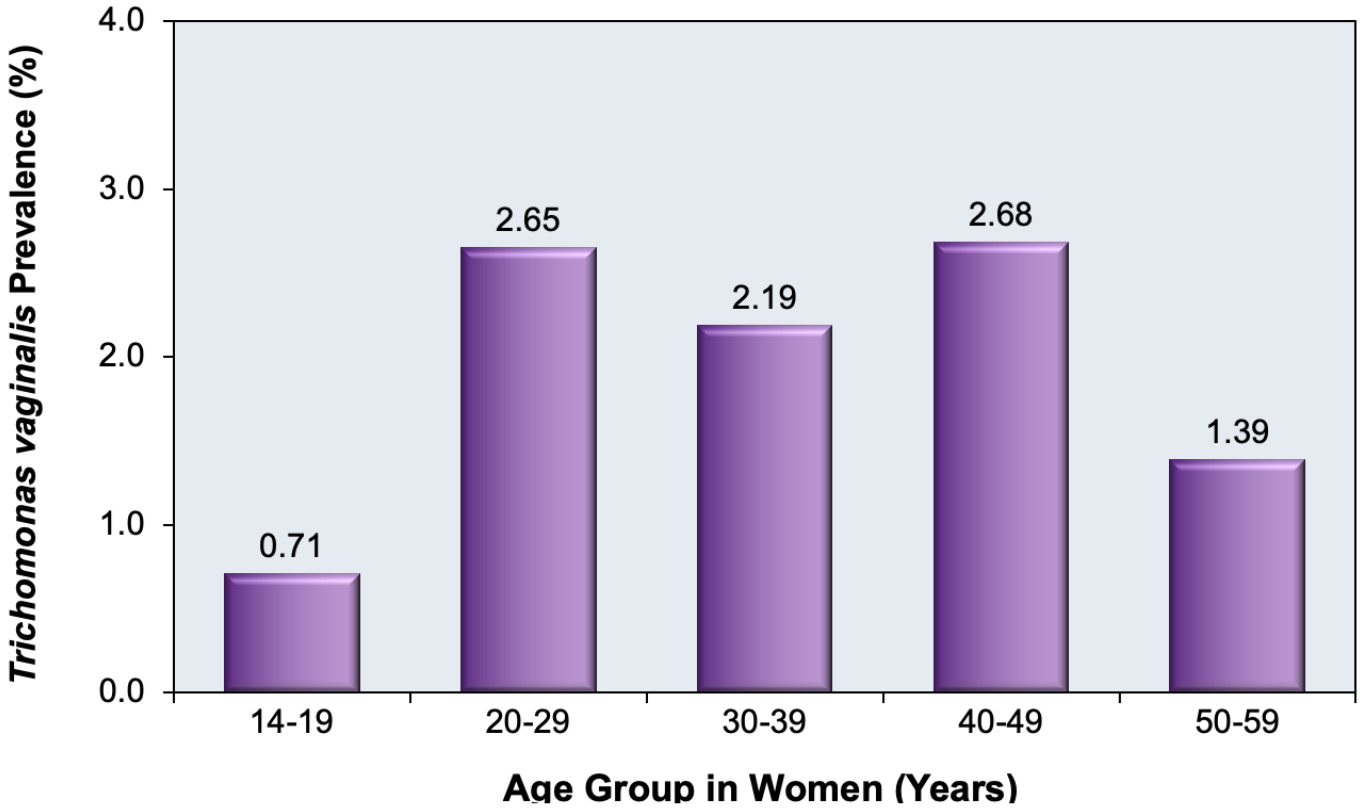

Figure 9 *Trichomonas vaginalis*

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

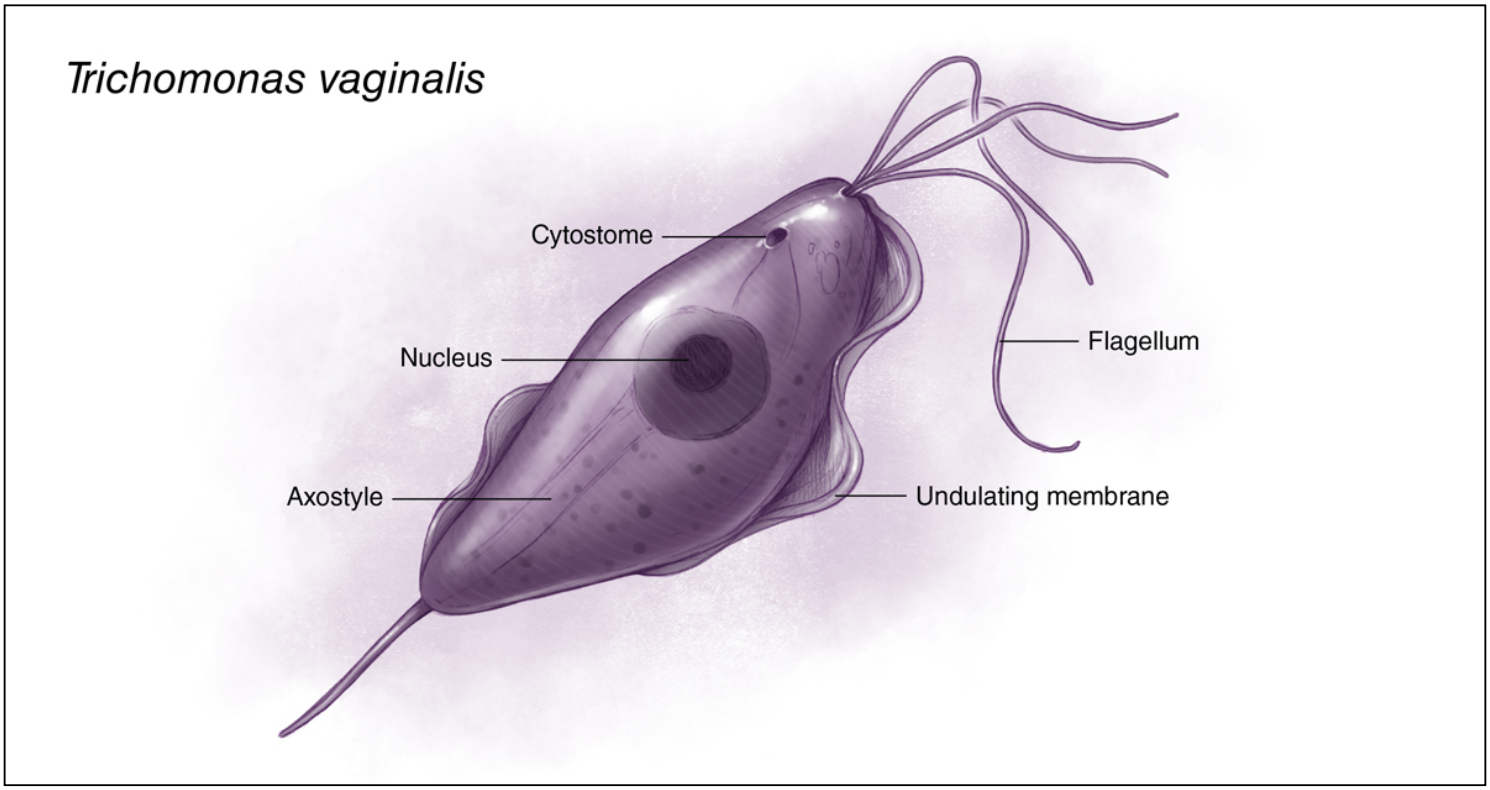

Figure 10 Cervical Discharge with Trichomoniasis

Illustration by Jared Travnicek, Cognition Studio

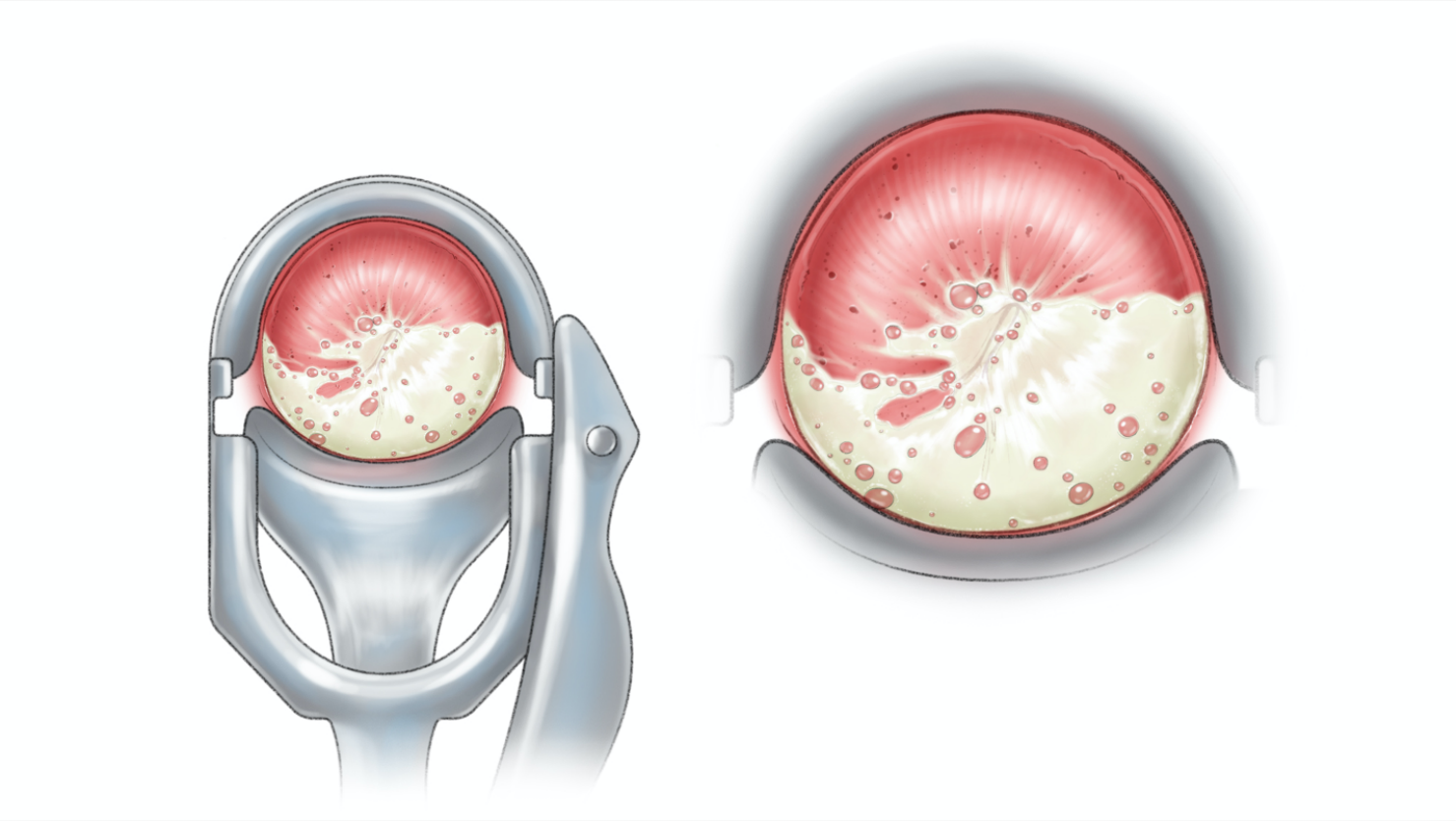

Figure 11 Trichomoniasis and Cervical Petechiae

This photograph shows multiple petechiae on the cervix of a woman with trichomoniasis (the petechiae are prominent in upper part of the image). This suggests a diagnosis of trichomoniasis and is often referred to as a "strawberry cervix".

Source: Claire Stevens, University of Washington

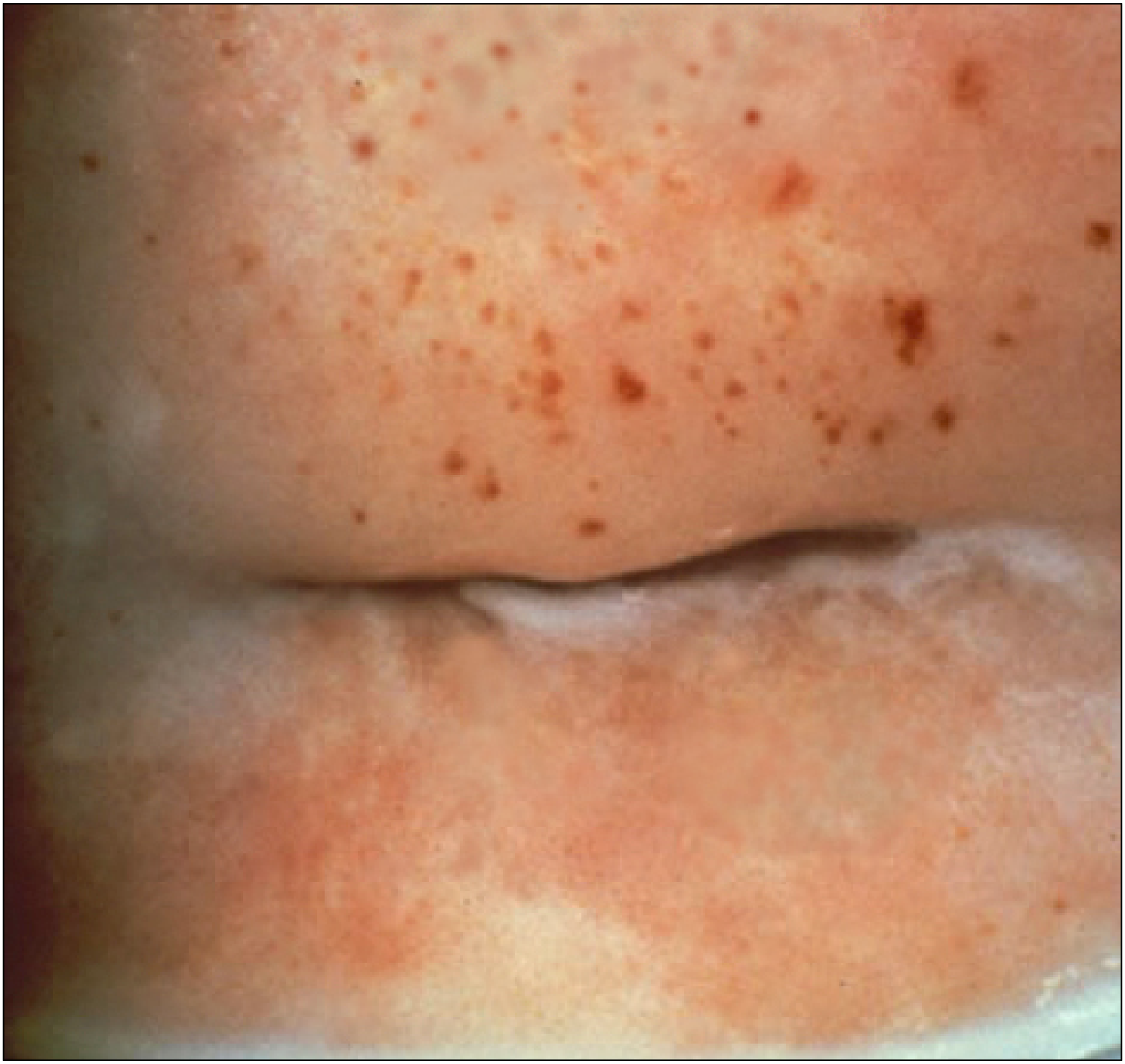

Figure 12 *Trichomonas vaginalis* on Wet Mount

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).

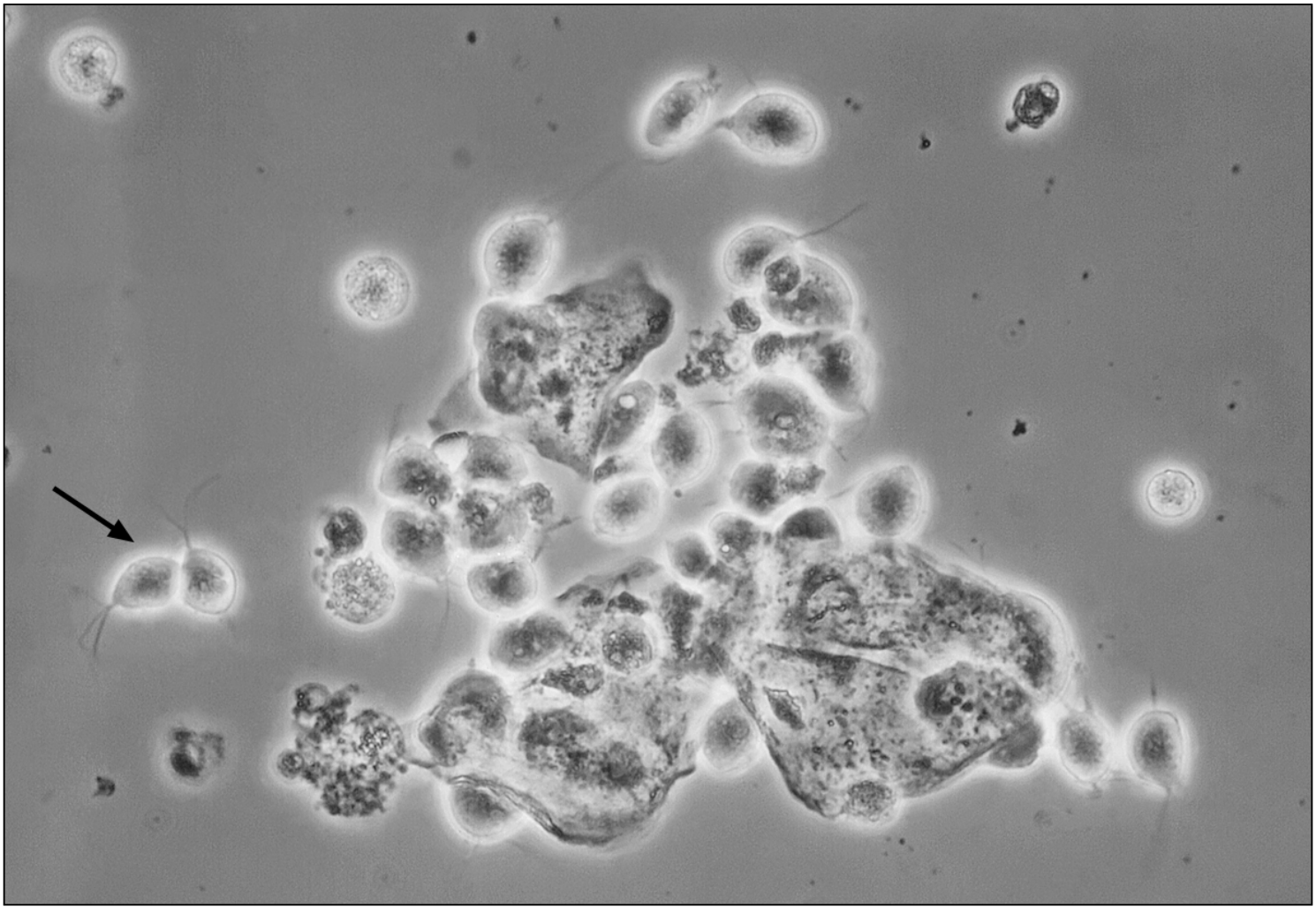

Figure 13 Time to Loss of Trichomonad Motility with Wet Mount Microscopy

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.

Source: Kingston MA, Bansal D, Carlin EM. 'Shelf life' of *Trichomonas vaginalis*. Int J STD AIDS. 2003;14:28-9.

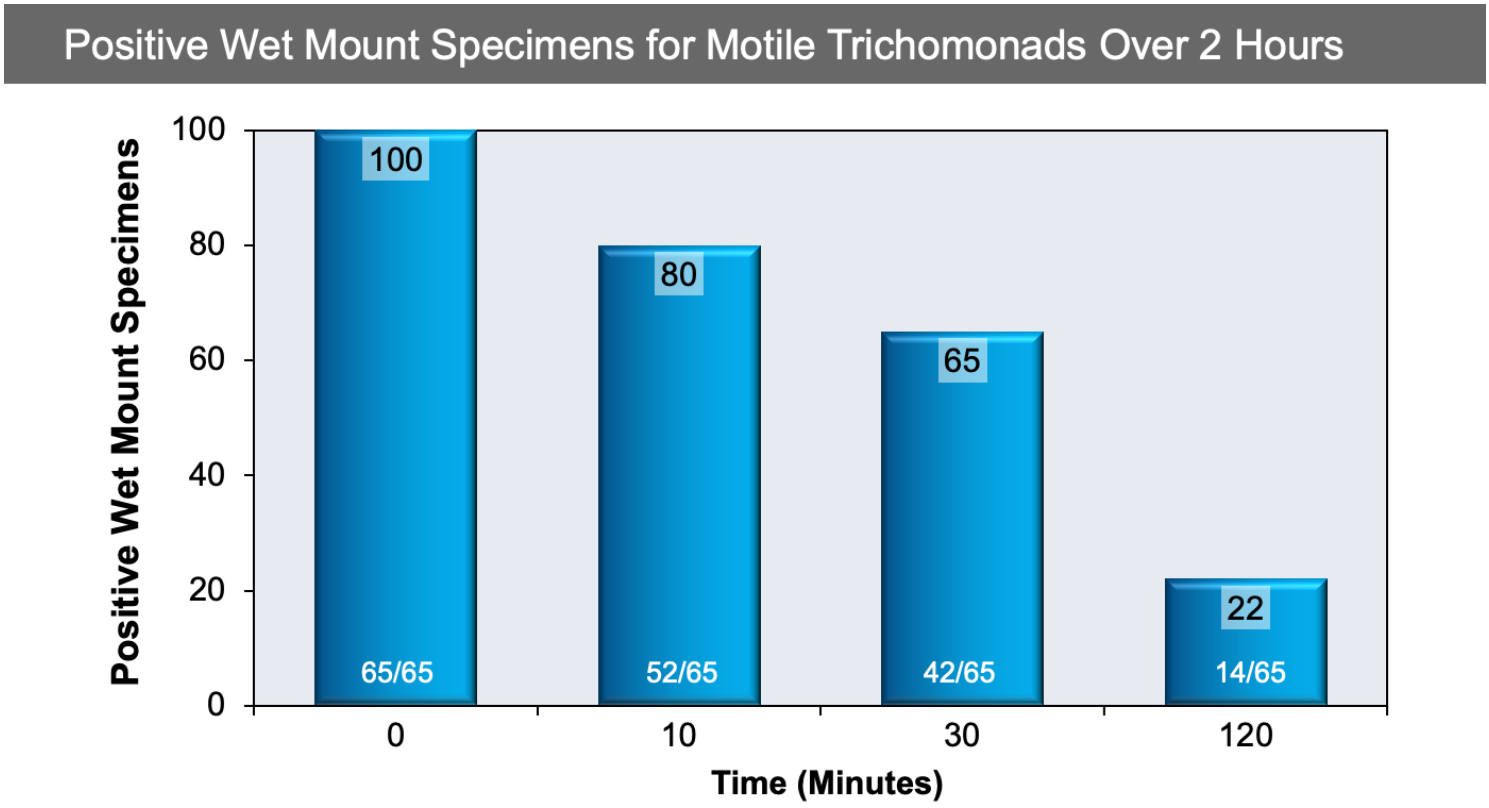

Figure 14 Performance of Aptima for Diagnosis of Trichomonas

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

Source: Schwebke JR, Hobbs MM, Taylor SN, et al. Molecular testing for *Trichomonas vaginalis* in women: results from a prospective U.S. clinical trial. J Clin Microbiol. 2011;49:4106-11.

Clinical Performance of Automated Aptima *Trichomonas vaginalis* NAAT 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

Figure 15 Treatment of Trichomoniasis in Women with HIV

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.

Source: Kissinger P, Mena L, Levison J, et al. A randomized treatment trial: single versus 7-day dose of metronidazole for the treatment of *Trichomonas vaginalis* among HIV-infected women. J Acquir Immune Defic Syndr. 2010;55:565-71.

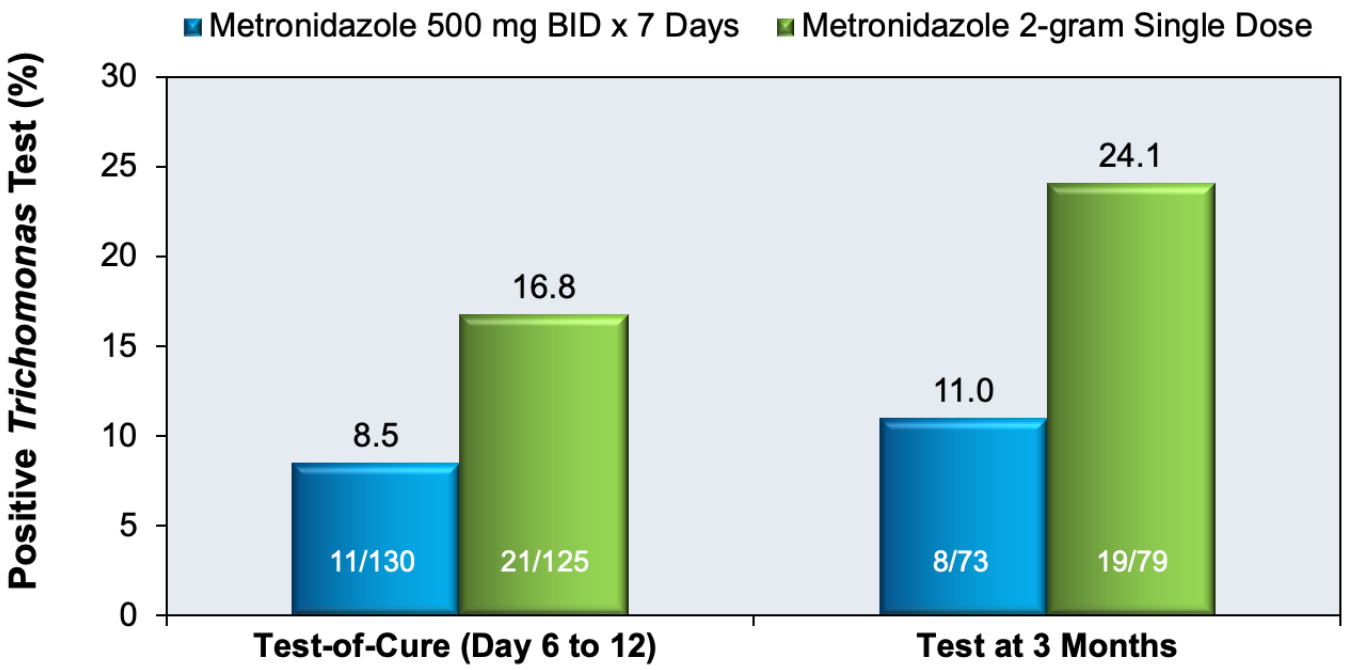

Figure 16 *Candida albicans* Yeast and Hyphae Forms

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

Illustration by 306/Shutterstock.com. Image used under license from Shutterstock.com.

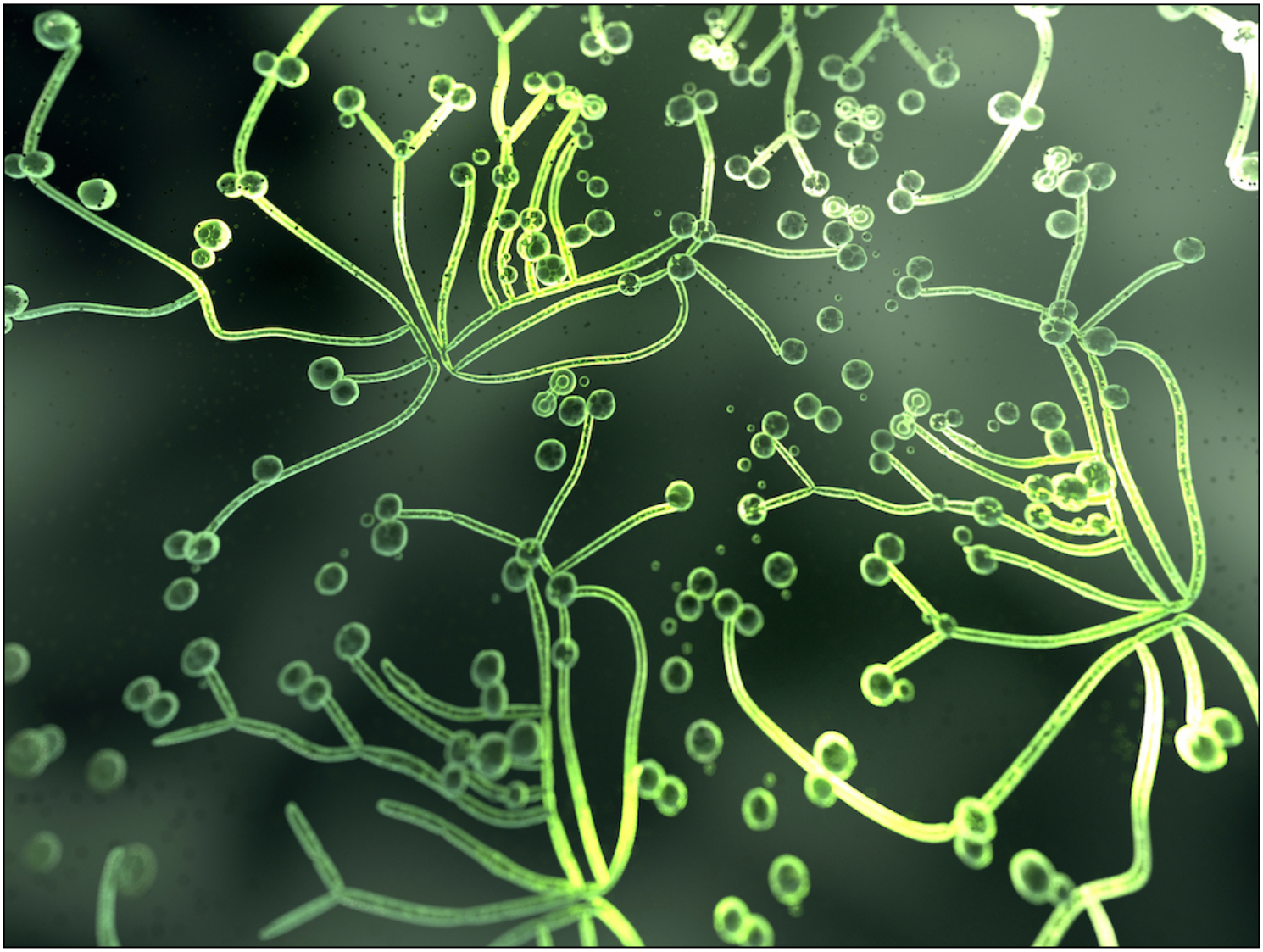

Figure 17 Vulvovaginal Candidiasis—Intravaginal View

This photograph was taken during a pelvic examination with a speculum inserted into the vagina. There are thick white clumps visible on the cervix (image center) and vaginal wall.

Source: Public Health—Seattle & King County Sexual Health Clinic

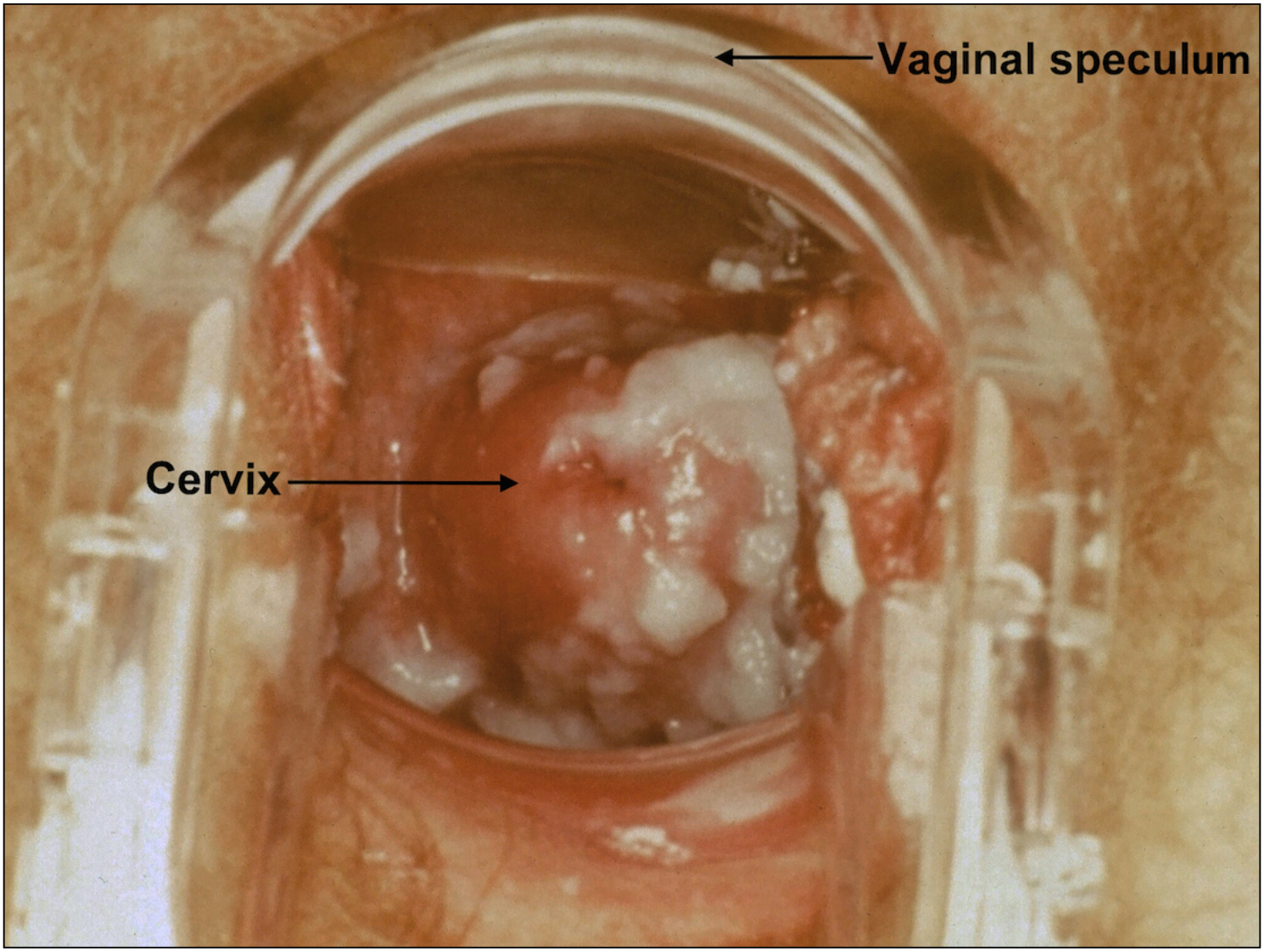

Figure 18 Vulvovaginal Candidiasis and Potassium Hydroxide Preparation of Vaginal Wet Mount

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 a tangled mass. Magnification 10x.

Source: Public Health—Seattle & King County Sexual Health Clinic

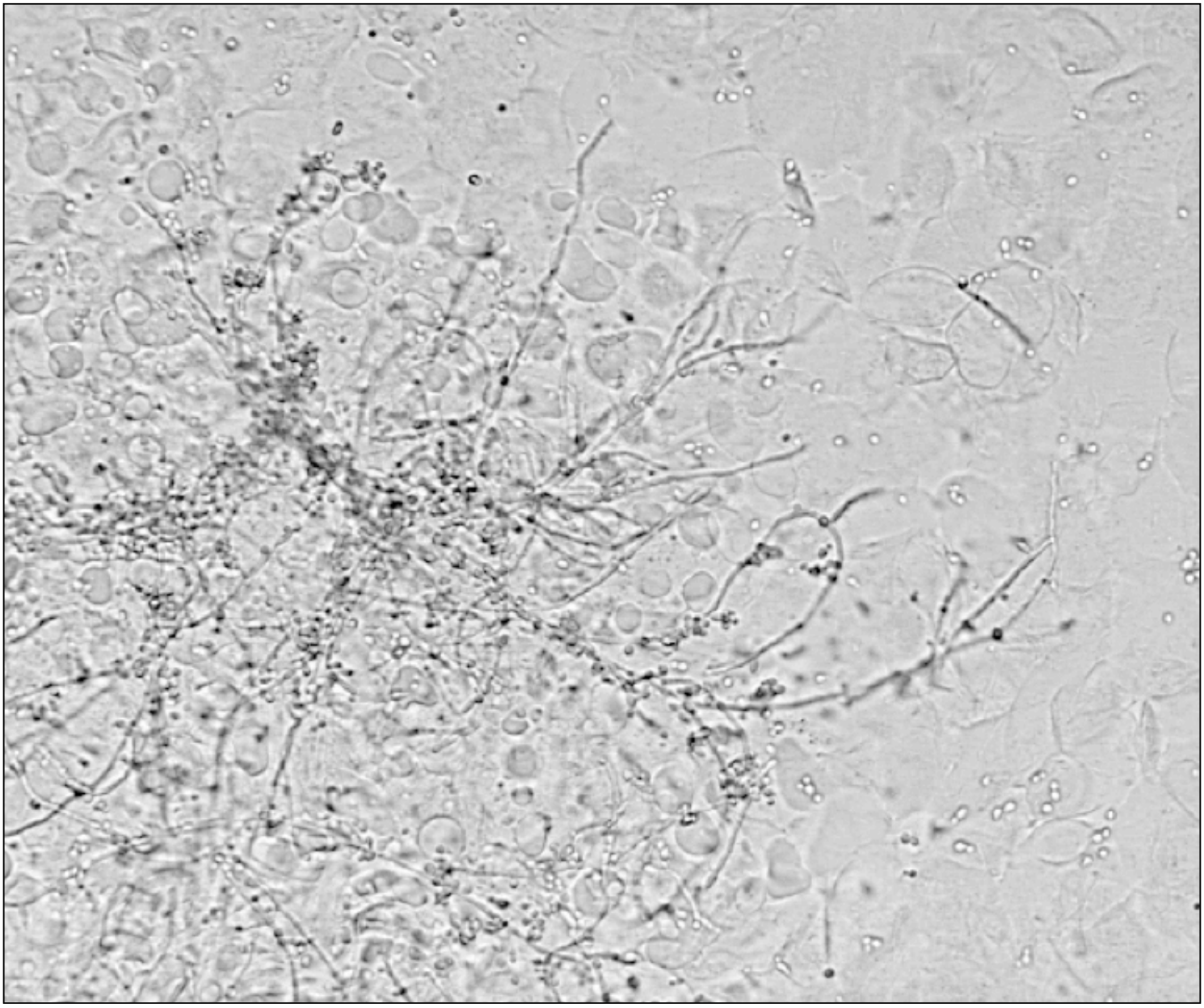

Figure 19 Vulvovaginal Candidiasis and Saline Vaginal Wet Mount

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 Sexual Health Clinic

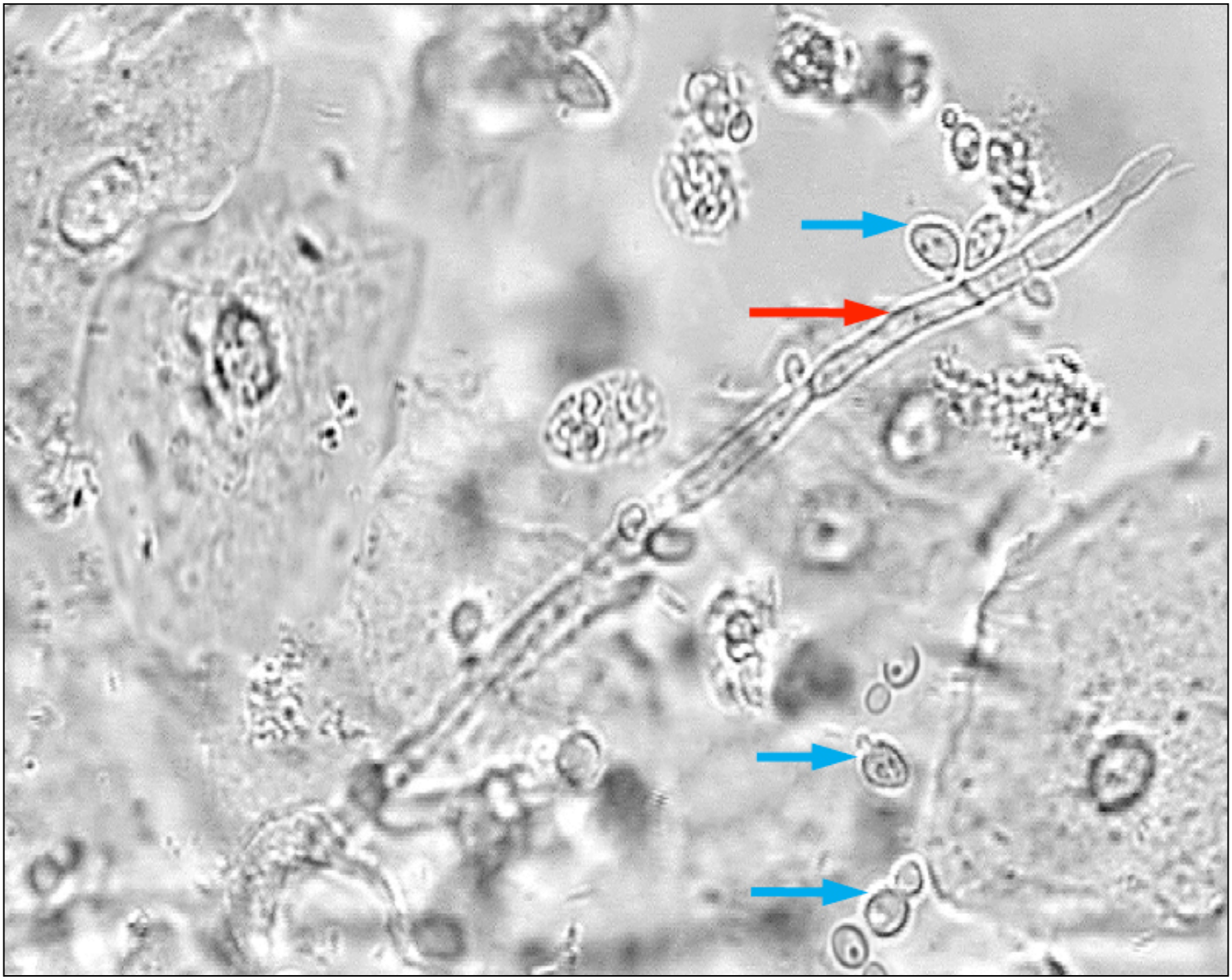

Table 1. 2021 STI Treatment Guidelines: Bacterial Vaginosis
Treatment of Bacterial Vaginosis

Recommended Regimens

Metronidazole
500 mg orally twice a day for 7 days

Recommended Regimens

Metronidazole gel 0.75%
one full applicator (5 g) intravaginally, once a day for 5 days

Recommended Regimens

Clindamycin vaginal cream 2%
one full applicator (5 g) intravaginally at bedtime for 7 days

Note: Clindamycin cream is oil based and might weaken latex condoms and diaphragms for 5 days after use.

Alternative Regimens

Clindamycin
300 mg orally twice daily for 7 days

Alternative Regimens

Clindamycin ovules
100 mg intravaginally once at bedtime for 3 days

Note: Clindamycin ovules use an oleaginous base that might weaken latex or rubber products (e.g. condoms and diaphragms). Use of such products within 72 hours after treatment with clindamycin ovules is not recommended.

Alternative Regimens

Secnidazole
2 g oral granules in a single dose

Note: Oral granules should be sprinkled onto unsweetened applesauce, yogurt, or pudding before ingestion. A glass of water can be taken after administration to aid in swallowing.

Alternative Regimens

Tinidazole
2 g orally once daily for 2 days

Alternative Regimens

Tinidazole
1 g orally once daily for 5 days

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Diseases characterized by vaginal itching, burning, irritation, odor or discharge: bacterial vaginosis. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Table 2. 2021 STI Treatment Guidelines: Trichomoniasis
Treatment of Trichomoniasis

Recommended Regimen for Women
Metronidazole *500 mg orally twice a day for 7 days*

Recommended Regimen for Men
Metronidazole *2 g orally in a single dose*

Alternative Regimen for Women and Men
Tinidazole *2 g orally in a single dose*

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Diseases characterized by vaginal itching, burning, irritation, odor or discharge: trichomoniasis. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Table 3.

Classification of Vulvovaginal Candidiasis

Abbreviation: HIV = human immunodeficiency virus.
Uncomplicated Vulvovaginal Candidiasis
• Sporadic or infrequent vulvovaginal candidiasis *and* • Mild-to-moderate vulvovaginal candidiasis *and* • Likely to be *Candida albicans* *and* • Nonimmunocompromised women
Complicated Vulvovaginal Candidiasis
• Recurrent vulvovaginal candidiasis (three or more episodes of symptomatic vulvovaginal candidiasis in <1 year) *or* • Severe vulvovaginal candidiasis *or* • Non-*albicans* candidiasis *or* • Women with diabetes, immunocompromising conditions (e.g., HIV), underlying immunodeficiency, or immunosuppressive therapy (e.g. corticosteroids)

Source:

- Sobel JD, Faro S, Force RW, et al. Vulvovaginal candidiasis: epidemiologic, diagnostic, and therapeutic considerations. Am J Obstet Gynecol. 1998;178:203-11. [PubMed Abstract]
- Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Diseases characterized by vaginal itching, burning, irritation, odor or discharge: vulvovaginal candidiasis. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Table 4. 2021 STI Treatment Guidelines: Vulvovaginal Candidiasis
Treatment of Uncomplicated Vulvovaginal Candidiasis

Recommended Regimens: Over-the-Counter Intravaginal Agents

Clotrimazole 1% cream
5 g intravaginally daily for 7–14 days

Recommended Regimens: Over-the-Counter Intravaginal Agents

Clotrimazole 2% cream
5 g intravaginally daily for 3 days

Recommended Regimens: Over-the-Counter Intravaginal Agents

Miconazole 2% cream
5 g intravaginally daily for 7 days

Recommended Regimens: Over-the-Counter Intravaginal Agents

Miconazole 4% cream
5 g intravaginally daily for 3 days

Recommended Regimens: Over-the-Counter Intravaginal Agents

Miconazole 100 mg vaginal supository
one suppository daily for 7 days

Recommended Regimens: Over-the-Counter Intravaginal Agents

Miconazole 200 mg vaginal suppository
one suppository daily for 3 days

Recommended Regimens: Over-the-Counter Intravaginal Agents

Miconazole 1,200 mg vaginal suppository
one suppository for 1 day

Recommended Regimens: Over-the-Counter Intravaginal Agents

Tioconazole 6.5% ointment
5 g intravaginally in a single application

Recommended Regimens: Prescription Intravaginal Agents

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

Recommended Regimens: Prescription Intravaginal Agents

Terconazole 0.4% cream
5 g intravaginally daily for 7 days

Recommended Regimens: Prescription Intravaginal Agents

Terconazole 0.8% cream
5 g intravaginally daily for 3 days

Recommended Regimens: Prescription Intravaginal Agents

Terconazole 80 mg vaginal suppository
one suppository daily for 3 days

Recommended Regimen: Oral Agent

Fluconazole
150 mg orally in a single dose

Note: the creams and suppositories in these regimens are oil based and might weaken latex condoms and diaphragms. Patients should refer to condom product labeling for further information.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Diseases characterized by vaginal itching, burning, irritation, odor or discharge: vulvovaginal candidiasis. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]