Sexually Transmitted Infections Treatment Guidelines, 2021

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Bacterial Vaginosis

BV is a vaginal dysbiosis resulting from replacement of normal hydrogen peroxide and lactic-acid–producing Lactobacillus species in the vagina with high concentrations of anaerobic bacteria, including G. vaginalis, Prevotella species, Mobiluncus species, A. vaginae, and other BV-associated bacteria. A notable feature is the appearance of a polymicrobial biofilm on vaginal epithelial cells (970). Certain women experience transient vaginal microbial changes, whereas others experience them for longer intervals (971). BV is a highly prevalent condition and the most common cause of vaginal discharge worldwide (972). However, in a nationally representative survey, the majority of women with BV were asymptomatic (310).

BV is associated with having multiple male sex partners, female partners, sexual relationships with more than one person (973), a new sex partner, lack of condom use (974), douching (975,976), and HSV-2 seropositivity (977). Male circumcision reduces the risk for BV among women (978). In addition, BV prevalence increases during menses (979,980). Women who have never been sexually active are rarely affected (981). The cause of the microbial alteration that precipitates BV is not fully understood, and whether BV results from acquisition of a single sexually transmitted pathogen is unknown. BV prevalence has been reported to increase among women with copper-containing IUDs (972,982). Hormonal contraception does not increase risk for BV (983) and might protect against BV development (983,984). Vitamin D deficiency has not been reported to be a risk factor for BV (985).

Women with BV are at increased risk for STI acquisition, such as HIV, N. gonorrhoeae, C. trachomatis, T. vaginalis (977), M. genitalium (986), HPV (987), and HSV-2 (988); complications after gynecologic surgery; complications of pregnancy; and recurrence of BV (971,989–991). BV also increases HIV infection acquisition (992) because specific BV-associated bacteria can increase susceptibility to HIV (993,994) and the risk for HIV transmission to male sex partners (187). Evaluation of short-term valacyclovir suppression among women with HSV-2 did not decrease the risk for BV, despite effective suppression of HSV-2 (995).

Although BV-associated bacteria can be identified on male genitalia (996,997), treatment of male sex partners has not been beneficial in preventing the recurrence of BV (998). Among WSW, a high level of BV concordance occurs between sex partners (292); however, no studies have evaluated treatment of female sex partners of WSW to prevent BV recurrence.

Diagnostic Considerations

BV can be diagnosed by using clinical criteria (i.e., Amsel's diagnostic criteria) (999) or by determining the Nugent score from a vaginal Gram stain (1000). Vaginal Gram stain, considered the reference standard laboratory method for diagnosing BV, is used to determine the relative concentration of lactobacilli (i.e., long gram-positive rods), small gram-negative and gram-variable rods (i.e., G. vaginalis or Bacteroides), and curved gram-negative rods (i.e., Mobiluncus) characteristic of BV. A Nugent score of 0–3 is consistent with a Lactobacillus-predominant vaginal microbiota, 4–6 with intermediate microbiota (emergence of G. vaginalis), and 7–10 with BV. Clinical diagnosis of BV by Amsel criteria requires at least three of the following four symptoms or signs:

- Homogeneous, thin discharge (milklike consistency) that smoothly coats the vaginal walls
- Clue cells (e.g., vaginal epithelial cells studded with adherent bacteria) on microscopic examination
- pH of vaginal fluid >4.5
- A fishy odor of vaginal discharge before or after addition of 10% KOH (i.e., the whiff test)

Detection of at least three Amsel criteria has been correlated with results by Gram stain (1001). The sensitivity and specificity of the Amsel criteria are 37%–70% and 94%–99%, respectively, compared with the Nugent score (1002).

In addition to the Amsel criteria, multiple POC tests are available for BV diagnosis. The Osom BV Blue test (Sekisui Diagnostics) detects vaginal sialidase activity (1003,1004). The Affirm VP III (Becton Dickinson) is an oligonucleotide probe test that detects high concentrations of G. vaginalis nucleic acids (>5 x 10^5 CFU of G. vaginalis/mL of vaginal fluid) for diagnosing BV, Candida species, and T. vaginalis. This test has been reported to be most useful for symptomatic women in conjunction with vaginal pH measurement and presence of amine odor (sensitivity of 97%); specificity is 81% compared with Nugent. Finally, the FemExam Test Card (Cooper Surgical) measures vaginal pH, presence of trimethylamine (a metabolic by-product of G. vaginalis), and proline aminopeptidase (1005). Sensitivity is 91% and specificity is 61%, compared with Nugent. This test has primarily been studied in resource-poor settings (1005), and although it has been reported to be beneficial compared with syndromic management, it is not a preferred diagnostic method for BV diagnosis.

Multiple BV NAATs are available for BV diagnosis among symptomatic women (1002). These tests are based on detection of specific bacterial nucleic acids and have high sensitivity and specificity for BV (i.e., G. vaginalis, A. vaginae, BVAB2, or Megasphaera type 1) (1006) and certain lactobacilli (i.e., Lactobacillus crispatus, Lactobacillus jensenii, and Lactobacillus gasseri). They can be performed on either clinician- or self-collected vaginal specimens with results available in <24 hours, depending on the availability of the molecular diagnostic platform (1002). Five quantitative multiplex PCR assays are available: Max Vaginal Panel (Becton Dickinson) (1007), Aptima BV (Hologic), NuSwab VG (LabCorp) (1008), OneSwab BV Panel PCR with Lactobacillus Profiling by qPCR (Medical Diagnostic Laboratories) (1009), and SureSwab BV (Quest Diagnostics). Two of these assays are FDA cleared (BD Max Vaginal Panel and Aptima BV), and the other three are laboratory-developed tests.

The Max Vaginal Panel provides results by an algorithmic analysis of molecular DNA detection of Lactobacillus species (L. crispatus and L. jensenii) in addition to G. vaginalis, A. vaginae, BVAB2, and Megasphaera type 1. This test has 90.5% sensitivity and 85.8% specificity for BV diagnosis, compared with Amsel criteria and Nugent score. It also provides results for Candida species and T. vaginalis. The Aptima BV detects G. vaginalis, A. vaginae, and certain Lactobacillus species including L. crispatus, L. jensenii,

and L. gasseri, with sensitivity and specificity ranging from 95.0% to 97.3% and 85.8% to 89.6%, respectively (using either clinician- or patient-collected vaginal swabs). The three laboratory-developed tests (NuSwab VG, OneSwab BV Panel PCR with Lactobacillus Profiling by qPCR, and SureSwab BV) have to be internally validated before use for patient care yet have good sensitivity and specificity, similar to FDA-cleared assays. BV NAATs should be used among symptomatic women only (e.g., women with vaginal discharge, odor, or itch) because their accuracy is not well defined for asymptomatic women. Despite the availability of BV NAATs, traditional methods of BV diagnosis, including the Amsel criteria, Nugent score, and the Affirm VP III assay, remain useful for diagnosing symptomatic BV because of their lower cost and ability to provide a rapid diagnosis. Culture of G. vaginalis is not recommended as a diagnostic tool because it is not specific. Cervical Pap tests have no clinical utility for diagnosing BV because of their low sensitivity and specificity.

Treatment

Treatment for BV is recommended for women with symptoms. Established benefits of therapy among nonpregnant women are to relieve vaginal symptoms and signs of infection. Other potential benefits of treatment include reduction in the risk for acquiring C. trachomatis, N. gonorrhoeae, T. vaginalis, M. genitalium, HIV, HPV, and HSV-2 (971,986–988,990,1010). No data are available that directly compare the efficacy of oral and topical medications for treating BV.

Recommended Regimens for Bacterial Vaginosis

Metronidazole 500 mg orally 2 times/day for 7 days

OR

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

OR

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

A review regarding alcohol consumption during metronidazole treatment reported no in vitro studies, animal models, reports of adverse effects, or clinical studies providing convincing evidence of a disulfiram-like interaction between alcohol and metronidazole (1011). The previous warning against simultaneous use of alcohol and metronidazole was based on laboratory experiments and individual case histories in which the reported reactions were equally likely to have been caused by alcohol alone or by adverse effects of metronidazole.

Metronidazole does not inhibit acetaldehyde dehydrogenase, as occurs with disulfiram. Ethanol alone or ethanol-independent side effects of metronidazole might explain the suspicion of disulfiram-like effects. Thus, refraining from alcohol use while taking metronidazole (or tinidazole) is unnecessary. 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).

Women should be advised to refrain from sexual activity or to use condoms consistently and correctly during the BV treatment regimen. Douching might increase the risk for relapse, and no data support use of douching for treatment or symptom relief.

Alternative Regimens

Clindamycin 300 mg orally 2 times/day for 7 days

OR

Clindamycin ovules 100 mg* intravaginally once at bedtime for 3 days

OR

Secnidazole 2 g oral granules in a single dose†

OR

Tinidazole 2 g orally once daily for 2 days

OR

Tinidazole 1 g orally once daily for 5 days

* 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.

† 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 include secnidazole oral granules (1012–1014), multiple oral tinidazole regimens (1015), or clindamycin (oral or intravaginal) (1016). In a phase 3 clinical trial of secnidazole 2 g oral granules versus placebo, BV clinical cure rates at days 21–30 were 53% in the secnidazole arm compared with 19% in the placebo arm ($p<0.001$) (1013). Secnidazole is listed as an alternative regimen, due to its higher cost and lack of long-term outcomes compared with recommended BV treatments. A patient savings card for secnidazole is available at https://www.solosec.com/savings-card.

Additional BV treatment regimens include metronidazole 1.3% vaginal gel in a single dose (1017,1018) and clindamycin phosphate (Clindesse) 2% vaginal cream in a single dose (1019). In a phase 3 clinical trial of metronidazole 1.3% vaginal gel versus placebo, BV clinical cure rates at day 21 were 37.2% in the metronidazole 1.3% vaginal gel arm, compared with 26.6% in the placebo arm ($p = 0.01$) (1018). A patient savings card for metronidazole 1.3% vaginal gel is available at https://nuvessa.com/nuvessa_files/19_Nuvessa_WEB_Card_032819.pdf. In a multicenter, randomized, single-blind, parallel-group study of Clindesse 2% vaginal cream single dose versus clindamycin 2% vaginal cream at bedtime for 7 days among 540 women with BV, no statistically significant difference existed between groups in clinical cure at days 21–30 (64.3% versus 63.2%; $p = 0.95$) (1019); however, this study had methodologic problems. A patient savings card for Clindesse 2% vaginal cream is available at https://www.clindesse.com/pdf/CLINDESSE_SavingsCard.pdf.

BV biofilm disrupting agents (i.e., TOL-463) (1020) are being investigated to determine their role in enhancing the likelihood of BV cure relative to approved therapies. Studies have evaluated the clinical and microbiologic efficacy of intravaginal Lactobacillus and other probiotic formulations to treat BV and restore normal vaginal microbiota (1021–1025); overall, no studies support these products as an adjunctive or replacement therapy for women with BV.