

# Evaluation and Management of Vaginitis



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## CME Activity

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## Abstract

Vaginitis is a common concern for women across the lifespan. Vaginal symptoms may impact quality of life, and clinicians are challenged in the evaluation and management of bacterial vaginosis, Candida vaginitis, trichomoniasis, desquamative inflammatory vaginitis, and genitourinary syndrome of menopause.

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## VAGINAL MICROBIOME

The vaginal microbiome is complex and unique in comparison to that of the skin, mouth, or gut.<sup>1</sup> Its alterations have been linked to endometritis, infertility, preterm birth (PTB), increased risk for acquisition of human immunodeficiency virus (HIV) and other sexually transmitted diseases, and persistence of human

papillomavirus.<sup>1</sup> This microbiome is transiently altered by menses, sexual activity, pregnancy, antimicrobial use, hormonal therapies, perimenopause, and menopause.<sup>1,2</sup> It has been classified into five community states (CSTs) with four of these dominated by lactobacillus (an aerobic, gram-positive rod).<sup>2</sup> Lactobacilli produce lactic acid and hydrogen peroxide, and along

with estrogen during the reproductive years, maintain low vaginal pH (4.5 or lower) to reduce vaginal proinflammatory cytokines and inhibit bacterial overgrowth.<sup>3</sup> A healthy, acidic premenopausal vagina contains 70% to 90% lactobacilli along with a heterogeneous mixture of *Gardnerella vaginalis* (*G. vaginalis*), *Escherichia coli* (*E. coli*), group B streptococcus (GBS), genital *Mycoplasma* species, and *Candida albicans* (*C. albicans*), among other species.<sup>2-4</sup> Community states I, II, and V are considered to be normal microbiome states whereas CST III is different in that it occurs with an abundant polymicrobial vaginal flora.<sup>2</sup> Community state IV is composed of a low concentration or absence of lactobacilli and a high concentration of obligate anaerobes.<sup>2,4</sup> Bacterial vaginosis (BV) is associated with CSTs III and IV (with obligate and facultative anaerobes), whereas desquamative inflammatory vaginitis (DIV) is seen in CST IV colonized with facultative bacteria (as *E. coli*, *S. aureus*, GBS, and *Enterococcus faecalis*).<sup>2,4</sup> The menopausal vagina, with its decreased concentration of lactobacilli, is also consistent with CST IV.<sup>2,5</sup> Systemic and vaginal estrogen increase the concentration of lactobacilli.<sup>6</sup>

## VAGINITIS

Vaginitis is caused by infection, inflammation, or an imbalance in the normal flora.<sup>7,8</sup> Typical symptoms include odor, irritation, burning, pruritus, dysuria, dyspareunia, or a change in vaginal discharge.<sup>7,8</sup> The most common diagnoses are BV, which is not a true vaginitis given an absence of inflammation (22% to 50% of symptomatic women), *Candida* vulvovaginitis (17% to 39%), *Trichomonas vaginalis* (*T. vaginalis*) (4% to 35%), or a mix of these pathogens potentially also including *Mycoplasma* or *Ureaplasma*.<sup>7-9</sup> Vaginitis and cervicitis may be concomitant, with the latter most commonly associated with *Neisseria gonorrhoea* and *Chlamydia trachomatis*. Both conditions should be considered during evaluation.<sup>7,8</sup> An examination with appropriate testing is important to distinguish other causes of vaginal symptoms including vulvar, vaginal,

and cervical cancers; pelvic inflammatory disease (PID); vulvovaginal ulcerative conditions including herpes simplex virus; vaginal fistulas; trauma; and vulvovaginal dermatoses including lichen planus or pemphigoid.<sup>7,8</sup>

Empiric therapy for vaginitis should be avoided to prevent misdiagnosis. Chronic symptoms may require ongoing evaluation and management. We will discuss symptomatology, physical findings, diagnostic criteria, and therapies as recommended by the Centers for Disease Control and Prevention (CDC) and the American College of Obstetricians and Gynecologists (ACOG).<sup>7,10</sup>

## Bacterial Vaginosis

Bacterial vaginosis affects approximately 22 million US premenopausal women yearly with higher rates in Hispanic and Black women, possibly associated with a greater likelihood of vitamin D deficiency and vaginal microbiome dominated by *Lactobacillus iners* (observed in CST III) in these women.<sup>9,11,12</sup> With the shift in the vaginal microbiome to an overgrowth of *G. vaginalis* and *Atopobium vaginae*, a biofilm or scaffolding forms through the vagina and/or endometrium to which anaerobic species adhere resulting in symptomatic odor and transudative discharge.<sup>2,4</sup> A symptomatic counterpart has not been described in men, making it difficult to determine whether BV is sexually transmitted.<sup>4,9</sup> Having new and multiple male and female sexual partners has been linked with BV.<sup>4,7,9</sup> Bacterial vaginosis is prevalent in women having sex with women but is less an issue with a single partner.<sup>7,8</sup> Other risk factors include douching, cigarette smoking, and increased body mass index.<sup>7,8</sup> Bacterial vaginosis can be associated with sexually transmitted infections (STIs) including herpes simplex 2, HIV, gonorrhea, chlamydia, *T. vaginalis*, and human papillomavirus.<sup>4,7,8</sup> The CDC recommends that women positive for BV should be tested for STIs.<sup>10</sup> Because endometrial colonization can occur, BV may be associated with plasma cell endometritis, PID, post-hysterectomy vaginal cuff cellulitis/abscess, postabortion infection, chorioamnionitis, postpartum fever, and PTB.<sup>9,10,13</sup>

The clinical characteristics and diagnostic criteria for BV are listed in Table 1.<sup>4,7,9,14,15</sup> More than 50% of women testing positive for BV may be asymptomatic, with many experts suggesting no treatment is necessary and others associating treatment with lower risk of infertility.<sup>7,9</sup> Vaginal culture for *G. vaginalis* is not recommended for diagnosis nor is cervical cytology given high false-positive and false-negative rates.<sup>4,7,8</sup>

Women with symptomatic BV should be treated.<sup>7-10</sup> Symptomatic partner(s) of women having sex with women should be treated whereas treatment of male partner(s) is not recommended with the possible exception of recurrent BV.<sup>7,9,10</sup> See Table 2 for CDC and ACOG treatment guidelines of acute BV, including standard and alternative therapy for nonpregnant women.<sup>7,9,10</sup> Therapy may decrease STI transmission risk.<sup>7,9,10</sup> Side effects of oral nitroimidazoles, the most common treatment selection, include nausea, vomiting, metallic taste, neutropenia, increased international normalized ratio with warfarin, neuropathy, rash, urticaria, pruritus, and rarely anaphylaxis.<sup>7-9</sup> Intravaginal metronidazole or clindamycin are alternative therapies if troublesome nausea and vomiting occur with oral therapy.<sup>7-10</sup> Condoms, diaphragms, and cervical caps should not be used with clindamycin cream as it may breakdown latex.<sup>7,9</sup> Oral and intravaginal metronidazole are equally efficacious for BV.<sup>7,9</sup> Symptomatic and asymptomatic women with BV undergoing hysterectomy and abortion should be treated.<sup>7,9,10</sup>

ACOG, the US Preventative Services Task Force, and the CDC recommend that only symptomatic pregnant women be tested for BV and treated when positive.<sup>10,13,23</sup> Currently, there is insufficient evidence that screening asymptomatic pregnant women, with or without risk for preterm labor, prevents PTB.<sup>10,13,22,23</sup> Currently available oral and vaginal probiotics are largely ineffective for BV, but a probiotic containing *Lactobacillus Crispatus* which dominates CST I is forthcoming.<sup>24</sup>

### Recurrent Bacterial Vaginosis

Thirty percent of women with initial response to therapy have a recurrence within 3 months whereas 58% recur within 12 months.<sup>7-9</sup> Table 2 outlines preventive therapy for frequent BV (three or more episodes per year).<sup>7,9,10,22,25</sup> Clinical response rates are 50% to 75%.<sup>7,9,25</sup> Although guidelines do not recommend treatment of partners, it is reasonable to consider treating partners in the setting of recurrent BV.<sup>7,9,10</sup> Vaginal microbiome transplant is under investigation for women with recurrent BV.<sup>26</sup>

### Candida Vulvovaginitis

At least 20% of reproductive women and 7% of menopausal women have asymptomatic vaginal candidiasis.<sup>27</sup> Overgrowth of *Candida* is associated with pruritus, discharge, vulvovaginal burning, irritation, soreness, dysuria, and dyspareunia.<sup>7,8</sup> Self-treatment availability limits estimate of true prevalence.<sup>7,27</sup> Progression from asymptomatic colonization to extensive vulvovaginal involvement appears complex, involving host inflammatory responses and yeast virulence factors.<sup>27,28</sup> Although it is often a copathogen with *Gardnerella* or *Lactobacillus* species, vaginal *Candida* does not form a biofilm as seen in BV.<sup>28</sup> *Candida albicans* constitutes 80% to 92% of vulvovaginal candidiasis in the United States whereas *Candida glabrata*, *Candida parapsilosis*, and other strains make up the rest.<sup>7,27</sup> Incidence of a single or sporadic infection increases with age, and Black women are most frequently affected.<sup>27</sup> Risk factors associated with *Candida* include diabetes mellitus, HIV, other immunosuppressive conditions, immunosuppressive or antibiotic use, higher estrogen levels associated with pregnancy, estrogen-containing contraceptives, systemic hormone therapy or vaginal estrogen in menopause, and the use of intrauterine contraception, vaginal sponges, diaphragms, and cervical caps.<sup>7,8,27</sup> Although vulvovaginal *Candida* is not considered sexually transmitted, male partners are more likely to be colonized with the same *Candida* strain.<sup>7,27</sup> Orogenital, rather than anogenital, sex

TABLE 1. Common Characteristics and Diagnoses of BV, Candida, Trichomoniasis, DIV, and GSM<sup>a,b</sup>

Vaginitis subtype	Symptoms	Signs	Diagnosis
BV	Milky, gray thin homogenous discharge (d/c) and "fishy" odor No dysuria, dyspareunia, pruritus, burning unless copathogen present	White, gray thin d/c with odor. No vaginal inflammation, $\pm$ vulvar irritation from d/c	Amsel criteria, $\geq 3$ present: (1) homogenous, thin, white-gray discharge, (2) pH $>4.5$ , (3) +KOH whiff test (with 10% KOH added to d/c), and (4) wet prep with $\geq 20\%$ clue cells (epithelial cells coated with bacteria), absence of lactobacilli and WBCs (Sensitivity 92%, Specificity 77%); BV gram stain (Sensitivity 70%, Specificity 94%), uses Nugent criteria to score bacterial morphotypes; Rapid chromogenic point of care assay (OSOM BV Blue Test, FemExam Card) (Sensitivity 88% to 91%, Specificity 62% to 95%), detects enzymatic sialidase activity of pathogens; DNA probe assay/Affirm VPill vaginitis panel (Sensitivity 90%, Specificity 86% to 97%), detects pathogenic levels of <i>G. vaginalis</i> along with Candida and Trichomonas; Single swab multiplex, real-time PCR/NAAT (NuSwab, BD Max, MDL BV, Aptima BV) (Sensitivity 91% to 99%, Specificity 86% to 94%), amplifies DNA or RNA targets, detecting ratio of lactobacilli to BV bacteria; can detect multiple infections
Candida	Pruritus, thick, curd-like d/c, (premenopause), $\pm$ odor, burning, irritation/soreness, dysuria, dyspareunia D/c may be thin, watery in menopause, also thin with <i>C. glabrata</i> , <i>C. parapsilosis</i>	Vulvar erythema (satellite lesions), excoriations/fissures, edema, vaginal erythema, thick white/yellow to thin watery d/c, normal pH 4.0 to 4.5	KOH wet prep budding yeast, hyphae, or pseudohyphae (Sensitivity 50% to 70%); Vulvar or vagina culture (can speciate Candida strain especially in recurrent or refractory disease); DNA probe assay/Affirm VPill vaginitis panel (Sensitivity 76% to 91%, Specificity 94% to 99%); Multiplex PCR (BD Max) to check for BV, Trichomonas, and 6 strains of Candida: <i>C. albicans</i> , <i>C. tropicalis</i> , <i>C. parapsilosis</i> , <i>C. dubliniensis</i> , <i>C. glabrata</i> , and <i>C. krusei</i> (Sensitivity 90%, Specificity 94%); Aptima CV/TV (detects specific Candida strains) (Sensitivity 85% to 92%, Specificity 95% to 99%)

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TABLE 1. Continued

Vaginitis subtype	Symptoms	Signs	Diagnosis
Trichomoniasis	Thin to profuse, purulent, malodorous, white/gray/yellow/green d/c; burning, pruritus, dysuria, frequency, dyspareunia	Vulvar erythema, edema; d/c thin to frothy, purulent odorous white/gray/yellow/ green	Wet prep motile trichomonads (flagellated, undulating), increased WBCs (Sensitivity 50% to 60%); Antigen point-of-care assay (AmpliVue, Solana, OSOM Trichomonas assays) (Sensitivity 88%, Specificity 99%); DNA probe assay/Affirm VPill vaginitis panel (Sensitivity 93%, Specificity 99%); NAAT/multiplex PCR/DNA probe (Sensitivity 93% to 99%, Specificity 99%)
DIV	Copious vaginal d/c, clear/gray, purulent yellow or green without odor, severe vaginal or introital pain, burning, irritation, pruritus, dyspareunia	Copious d/c, introital or vestibule erythema, edema, marked vaginal and cervical inflammation with focal or diffuse ecchymosis, erythema, petechiae, erosions, pH>4.5	Wet prep increased parabasal cells and inflammatory cells, WBC-to-epithelial cell ratio >1:1 (often a marked increase in polymorphonuclear WBCs); exclusion of other vaginitis, STIs
GSM	Vulvovaginal dryness, burning, irritation, dyspareunia, dysuria, urgency, recurrent UTIs, postcoital spotting	Clitoral atrophy, phimosis of prepuce, labial atrophy, urethral caruncle, prolapse, or polyps, introital/vaginal dryness, introital narrowing, vagina friable, pale to erythematous, petechiae, ulcerations, fissures, pH≥5.0 to 5.5	Wet prep or cytology >1 WBC per epithelial cells, immature vaginal cells with enlarged nuclei (parabasal cells), decreased or absent superficial vaginal squamous cells

<sup>a</sup>BV, bacterial vaginosis; CV, candida vaginitis; d/c, discharge; DIV, desquamative inflammatory vaginitis; GSM, genitourinary syndrome of menopause; KOH, potassium hydroxide; PCR, polymerase chain reaction; NAAT, nucleic acid amplification testing; STI, sexually transmitted infection; UTI, urinary tract infection; WBC, white blood cell.

<sup>b</sup>The information in this table has been obtained from other sources.<sup>4,6-10,14-18</sup>

appears linked with vulvovaginal candidiasis.<sup>7,27</sup>

Characteristics and diagnostic criteria of *Candida* are listed in Table 1.<sup>7,8,27</sup> Cervical cytology is positive in 25% of women with culture-positive, symptomatic candidiasis, but screening with this modality is insensitive and not recommended.<sup>7</sup>

Vulvovaginal *Candida* infections are regarded as uncomplicated when *C. albicans* symptoms are mild to moderate, occur three or fewer times yearly, and *C. albicans* occurs in healthy immunocompetent and nonpregnant women.<sup>7,27</sup> Complicated infections are associated with severe symptoms, non-*albicans* species occurring three or more times yearly in women with uncontrolled diabetes, immune compromise or HIV, immunosuppressive therapy, debilitation, or pregnancy.<sup>7,8,10,27</sup>

Table 2 lists treatment regimens using oral and vulvovaginal azoles for uncomplicated versus complicated candida vulvovaginal infections.<sup>10,19</sup> *C. glabrata* and *C. krusei* infections are often fluconazole resistant.<sup>10,19</sup> Pregnant women should avoid fluconazole given case reports regarding craniofacial and cardiac abnormalities with dosages of 400 to 800 mg daily and conflicting data regarding miscarriage.<sup>10,19</sup> Fluconazole allergy incidence is unknown, but if angioedema or severe rash occur, topical azoles are preferred.<sup>10,19</sup>

### Trichomoniasis

Trichomoniasis is the most common global nonviral STI and is caused by the mobile anaerobic protozoan *Trichomonas vaginalis*.<sup>29</sup> It is often present with other STIs and is especially prevalent in women with HIV.<sup>7,8,29</sup> Trichomoniasis affects

TABLE 2. Vaginitis Treatment Options (Non-Pregnant and Pregnancy)<sup>a,b</sup>

Vaginitis	Nonpregnant	Pregnant or breastfeeding treatment
Bacterial vaginosis (first-line treatment)	<p>Metronidazole 500 mg BID by mouth x7 d</p> <p>OR</p> <p>Metronidazole 0.75% vaginal gel QD x5 d</p> <p>OR</p> <p>Clindamycin 2% vaginal cream QD x7 d</p> <p>OR</p> <p>Alternative therapies:</p> <p>Tinidazole 2 g QD by mouth x2 d</p> <p>OR</p> <p>Tinidazole 1 g QD by mouth x5 d</p> <p>OR</p> <p>Secnidazole 2 g by mouth single dose</p> <p>OR</p> <p>Clindamycin 300 mg BID by mouth x7 d</p> <p>OR</p> <p>Clindamycin 100 mg vaginal ovules QD x3 d, no condoms</p> <p>**Alcohol no longer needs to be avoided with oral nitroimidazoles (metronidazole, tinidazole, or secnidazole)</p>	<p>Metronidazole: not contraindicated in pregnancy, no known teratogenic effects. Defer breastfeeding during and for 12 to 24 hours after last dose;</p> <p>Tinidazole: limited data in pregnancy. CDC advises avoiding in pregnancy. Defer breastfeeding during and for 72 hours after last dose;</p> <p>Secnidazole: not contraindicated in pregnancy but data limited. Defer breastfeeding for 96 hours after dose</p>
Bacterial vaginosis (recurrent)	<p>Change antibiotic from that initially used</p> <p>OR</p> <p>Extend course of antibiotic</p> <p>OR</p> <p>Metronidazole vaginal gel 0.75% 2 times weekly x16-24 weeks after treatment of the acute episode</p> <p>OR</p> <p>Boric acid 600 mg vaginal capsules (never oral) at bedtime x21 d; followed by metronidazole vaginal gel twice weekly x16-24 weeks</p> <p>OR</p> <p>Metronidazole 2 g by mouth + fluconazole (Diflucan) 150 mg by mouth once monthly</p> <p>OR</p> <p>Initial course of nitroimidazole x7-10 d by mouth followed by metronidazole vaginal gel twice weekly x16-24 weeks</p> <p>OR</p> <p>Initial course of nitroimidazole by mouth + boric acid 600 mg vaginal capsules (never oral) at bedtime x21 d (same time), followed by metronidazole vaginal gel twice weekly x16-24 weeks</p>	<p>Metronidazole: Not contraindicated in pregnancy, no known teratogenic effects. Defer breastfeeding during &amp; for 12-24 hours after last dose;</p> <p>Tinidazole: Limited data in pregnancy. CDC advises avoiding in pregnancy. Defer breastfeeding during &amp; for 72 hours after last dose;</p> <p>Secnidazole: Not contraindicated in pregnancy but data limited. Defer breastfeeding for 96 hours after dose</p>
Vaginal candidiasis	<p>Uncomplicated infection</p> <p>Clotrimazole (Gyne-Lotrimin)</p> <p>1% vaginal cream 1 applicator (5 g) daily x7 d</p> <p>OR</p> <p>2% vaginal cream 1 applicator (5 g) daily x3 d;</p> <p>Miconazole (Monistat)</p> <p>2% vaginal cream 1 applicator (5 g) daily x7 d</p> <p>OR</p> <p>4% vaginal cream 1 applicator (5 g) daily x3 d</p> <p>OR</p> <p>100 mg vaginal suppository daily x7 d</p> <p>OR</p> <p>200 mg vaginal suppository daily x3 d (kit may include 2% cream for external use)</p>	<p>Vaginal clotrimazole or miconazole x7 days, repeat if needed</p>

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TABLE 2. Continued

Vaginitis	Nonpregnant	Pregnant or breastfeeding treatment
	<p>OR</p> <p>1200 mg vaginal suppository x1 dose (kit may include 2% cream for external use);</p> <p>Terconazole (Terazol)</p> <p>0.4% vaginal cream 1 applicator (5 g) at bedtime x7 nights</p> <p>OR 0.8% vaginal cream 1 applicator (5 g) at bedtime x3 nights</p> <p>OR</p> <p>80 mg vaginal suppository at bedtime x3 nights;</p> <p>Tioconazole (Vagistat)</p> <p>6.5% vaginal ointment 1 applicator (5 g) x1 dose bedtime</p> <p>OR</p> <p>Butoconazole (Gynazole)</p> <p>2% vaginal cream 1 applicator (5 g) x1 dose bedtime</p> <p>OR Fluconazole</p> <p>150 mg by mouth x1 dose (not recommended in pregnancy)</p> <p>OR</p> <p>Alternative Antifungal: Itraconazole 200 mg BID by mouth x1 d; in HIV-infected women 200 mg QD for 3-7 d;</p> <p><b>Complicated infection:</b> Fluconazole</p> <p>150 mg by mouth every 72 h x2-3 doses</p> <p>OR</p> <p>Vaginal azole as above daily x7-14 days with low-potency topical corticosteroid such as Triamcinolone 0.1% vaginal ointment bid x48 h for vulvar irritation**New alternative non-azole antifungal Ibrexafungerp (Brexafemme) 150 mg 2 by mouth BID x 1 d;</p> <p><b>Recurrent candidiasis:</b></p> <p>Fluconazole 150 mg by mouth every 72 h x3 doses, then 1 tablet by mouth weekly x6 mo</p> <p>OR</p> <p>Vaginal azole x 10-14 d (or alternative itraconazole 200 mg QD by mouth for 3-7 d) followed by topical clotrimazole 200 mg 2% vaginal cream twice weekly OR 500 mg vaginal suppository weekly x 6 mo;</p> <p><b>Non-albicans candida vaginitis:</b></p> <p><i>C. Glabrata:</i> vaginal boric acid 600 mg daily x14 d (never oral) OR Nystatin 100,000 vaginal insert or suppository daily x14 d; if fails, 17% flucytosine vaginal cream (5 g) nightly x14 d alone or in combination with 3% Amphotericin B vaginal cream x14 d;</p> <p><i>C. Krusei:</i> intravaginal clotrimazole, miconazole, or terconazole x7-14 d;</p> <p>All other species: conventional dose fluconazole;</p> <p>Compromised host (poorly controlled diabetes mellitus, immunosuppression, debilitation) and <i>Candida</i> isolate susceptible to azoles: by mouth or topical therapy x7-14 d</p>	
Trichomoniasis	<p>Metronidazole 500 mg BID by mouth x7 d recommended in women</p> <p>OR</p> <p>Metronidazole 2 g by mouth single dose (single dose in men)</p> <p>OR alternative</p> <p>Tinidazole 2 g by mouth single dose (either gender)</p> <p>In refractory disease:</p> <p>Tinidazole 2 g by mouth single dose or daily x7 d</p>	<p>Metronidazole 500 mg BID by mouth x 7 d recommended in pregnancy, defer during breastfeeding and for 12-24 h after last dose;</p> <p>As for BV, tinidazole should be avoided in pregnancy and breastfeeding deferred during and for 72 hours after last dose</p>

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TABLE 2. Continued

Vaginitis	Nonpregnant	Pregnant or breastfeeding treatment
	OR Tinidazole 2-3 g by mouth in divided dose x14 d (if failure again, consult CDC and refer to infectious disease specialist); Partners should ideally be treated same time	
DIV	Clindamycin 2% vaginal cream daily at hs x1-3 weeks, then 1-2 times weekly x2-6 mo OR Vaginal hydrocortisone 300-500 mg daily at hs x3 weeks, then 1-2 times weekly x2-6 months OR Clobetasol 0.05% vaginal cream daily at hs x1 week, longer use not evidence based Additional recommendations with above: Fluconazole 150 mg 1 tablet by mouth weekly Vaginal estrogen 2 times weekly	Not commonly seen in pregnancy Clindamycin 2% cream intravaginally daily at hs x1-3 weeks, then 1-2 times weekly x2-6 mo OR Hydrocortisone 300-500 mg intravaginally daily at hs x3 weeks, then 1-2 times weekly x2-6 mo OR Clobetasol intravaginally daily at hs x1 week, longer use not evidence based Vaginal estrogen 2 times weekly
Mycoplasma and Ureaplasma Treatment recommended for symptomatic nongonococcal urethritis, cervicitis, or PID	Nonpregnant treatment for uncomplicated genital infections: <b>M. hominis:</b> Doxycycline 100 mg BID by mouth x 7-14 d Alternatives: Clindamycin 300-450 mg QID by mouth x 7-14 d OR Ciprofloxacin 500 mg BID by mouth x 7-14 d OR Levofloxacin 500 mg daily by mouth x 7-14 d <i>M. hominis</i> is often resistant to macrolides as erythromycin or azithromycin <b>Ureaplasma:</b> Doxycycline 100 mg BID by mouth x 7-14 d Alternatives: Azithromycin 1 g by mouth single dose OR Azithromycin 500 mg by mouth day 1, then 250 mg by mouth days 2-5  Ureaplasma often resistant to clindamycin <b>M. genitalium:</b> Doxycycline 100 mg BID by mouth x7 d, then azithromycin 1 g by mouth followed by 500 mg by mouth days 2-4 **Test of cure recommended for <i>M.genitalium</i> 21 days after completion of therapy If macrolide resistant: Doxycycline 100 mg BID by mouth x7 d, then moxifloxacin 400 mg daily by mouth x7 d	Pregnant or breastfeeding: <b>M. hominis:</b> Clindamycin 300-450 mg QID by mouth for 7 to 14 d <b>Ureaplasma:</b> Azithromycin 500 mg by mouth day 1, 250 mg by mouth days 2-5 OR Azithromycin 1 g by mouth day 1, then 500 mg by mouth days 2-4 Avoid doxycycline and fluoroquinolones in this population if possible
GSM	Organic-based lubricants and moisturizers; Vaginal estrogen or DHEA: Premarin 0.5-1 g nightly x2 weeks, then 2 times weekly OR Estrace 0.5-1 g nightly x2 weeks, then 2 nights weekly OR Vagifem or Yuvaferm 10 µg nightly x2 weeks, then 2 nights weekly OR Imvexxy 4 or 10 µg nightly x2 weeks, then 2 nights weekly	Not generally a cause of vaginitis but can apply to women who are breastfeeding and have symptoms of vaginal dryness Vaginal estrogen: Premarin 0.5-1 g nightly x2 weeks, then 2 times weekly OR Estrace 0.5-1 g nightly x2 weeks, then 2 nights weekly OR Vagifem or Yuvaferm 10 µg nightly x2 weeks, then 2 nights weekly

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TABLE 2. Continued

Vaginitis	Nonpregnant	Pregnant or breastfeeding treatment
	May alternatively give the above twice weekly without an initial burst nightly x2 weeks	OR
	Estring 2 mg vaginal ring every 3 months	Imvexxy 4 or 10 µg nightly x2 weeks, then 2 nights weekly
	OR	
	Intrarosa (DHEA, Prasterone) 6.5 mg intravaginal insert suppository nightly	
	OR	
	Oral SERM	
	Ospemifene (Osphena) 60 mg by mouth daily	

<sup>a</sup>BID, twice daily; BV, bacterial vaginitis; CDC, Centers for Disease Control and Prevention; DHEA, dehydroepiandrosterone; GSM, genitourinary syndrome of menopause; PID, pelvic inflammatory disease; QD, once daily; QID, four times daily; SERM, selective estrogen receptor modulator.

<sup>b</sup>The information in this table has been obtained from other sources.<sup>4,6-10,19-22</sup>

approximately 3.7 million people yearly in the United States.<sup>20,29</sup> Coinfection rate in partners is 30% to 80%, and prevention includes having fewer partners, using condoms and spermicide, and avoiding douching.<sup>20,29</sup> *T. vaginalis* occurs mainly in premenopausal and perimenopausal women.<sup>16</sup> Non-Hispanic Black women are affected more frequently than White women.<sup>20,29</sup> Trichomoniasis is associated with cervical dysplasia, post-hysterectomy cuff cellulitis/abscess, PID, infertility, and potential acquisition and transmission of HIV.<sup>7,10,30</sup> In pregnant women with *T. vaginalis*, there is an increased risk of premature rupture of membranes, PTB, fetal growth restriction, and potential for neonatal infection.<sup>13</sup>

Women range from being asymptomatic to symptomatic with characteristics and diagnostic criteria as per Table 1.<sup>7,8,17,20,29</sup> Per the CDC, screening should be performed yearly in HIV-positive women, including during their initial prenatal visits.<sup>10,20,29</sup> Women without HIV who have new or multiple sexual partners or those with other STIs need screening.<sup>10,29</sup>

Treatment of *T. vaginalis* should be prescribed in symptomatic and asymptomatic women and their partners as in Table 2.<sup>10,20,22</sup> It is important to evaluate for other STIs.<sup>10,20</sup> Sexual partners should be evaluated for other STIs even if expedited partner therapy is provided.<sup>10</sup> It is recommended that women avoid intercourse

for approximately 1 week after they and their partner(s) have been treated.<sup>7,10</sup> Treating trichomoniasis found on cervical cytology is not recommended.<sup>7</sup>

For recurrent trichomoniasis, consider noncompliance and treat partner(s).<sup>7,10,22</sup> In recurrent disease or suspected failure of single-dose therapy, follow guidelines in Table 2 for refractory disease.<sup>10,22</sup> If these guidelines fail, in vitro culture and susceptibility are recommended and available through the CDC with referral to an infectious disease expert recommended.<sup>10</sup>

Pregnant or nursing women with symptoms must be tested and treated as per Table 2.<sup>10,22</sup> Pregnant women should avoid intercourse until asymptomatic for 1 week and all partners have completed therapy.<sup>10</sup> Test of cure should be obtained in pregnant and nonpregnant women within 3 months, although nucleic acid amplification testing (NAAT) can be performed as early as 2 weeks after completing therapy.<sup>10,15</sup>

### Desquamative Inflammatory Vaginitis

Desquamative inflammatory vaginitis is a poorly understood, chronic inflammatory vaginitis without a specific pathogen identified.<sup>4</sup> It may be frustrating for both patients and clinicians in that women have intermittent symptoms despite multiple therapies before diagnosis. Women with DIV have a CST IV vaginal microbiome with colonization by facultative anaerobes (such as *E. coli*, *S. aureus*, GBS, or *E. faecalis*)

consistent with “aerobic vaginitis.”<sup>2,4,18</sup> The DIV microbiome is notable for vaginal inflammation, increased white blood cells (WBCs), and nearly absent lactobacilli.<sup>2,4,18</sup> Proposed etiologies include estrogen deficiency, a toxic reaction to bacteria such as *S. aureus*, *E. coli*, *E. faecalis*, GBS, or an immunologic abnormality.<sup>2,4,18</sup> Desquamative inflammatory vaginitis presents in pre- and perimenopause, with copious vaginal discharge and irritative vulvovaginal symptoms.<sup>4,18</sup> Desquamative inflammatory vaginitis has been linked with increased risk of STIs, premature rupture of membrane, PTB, chorioamnionitis, and miscarriage.<sup>4</sup> It might also increase the risk of *E. coli* urinary tract infection (UTI) and neonatal GBS infection.<sup>2,4,18</sup>

Table 1 lists characteristics and diagnoses of DIV.<sup>4,18</sup> The differential diagnosis includes genitourinary syndrome of menopause (GSM), erosive lichen planus, pemphigus vulgaris, and cicatricial pemphigoid.<sup>4,18</sup> All of the following criteria must be present: (1) at least 1 present—vaginal discharge, dyspareunia, pruritus, burning, and irritation; (2) vaginal inflammation (spotted ecchymosis or petechiae, erythema, focal or linear erosions); (3) vaginal pH greater than 4.5; and (4) saline microscopy showing increased parabasal and inflammatory cells, leukocyte-to-epithelial cell ratio greater than 1:1, and exclusion of BV, trichomoniasis, gonorrhea, and chlamydia.<sup>4,18,21</sup>

Treatments are summarized in Table 2, although they have not been studied in randomized controlled trials.<sup>4,21</sup> Clindamycin treats the facultative bacteria linked to DIV and acts as an anti-inflammatory agent as does intravaginal hydrocortisone for several weeks followed by maintenance therapy to reduce flare-ups.<sup>4,18,21</sup> Topical estrogen for a heavy parabasal-cell component may be helpful to reduce symptom duration.<sup>18,21</sup>

### Mycoplasma and Ureaplasma

*Mycoplasma hominis* and *Ureaplasma* species are found in the normal genital flora of up to 50% and 80%, respectively, of sexually active, healthy asymptomatic women, whereas *Mycoplasma genitalium* is found in

1% to 6%.<sup>31</sup> They are unlikely pathogens on their own but may be symbiotic with other pathogens in various genitourinary tract infections, such as *M. hominis* in PID and *Ureaplasma* in nongonococcal urethritis, and complications of pregnancy.<sup>31,32</sup> *M. genitalium*, although often asymptomatic, may cause cervicitis and PID.<sup>31</sup> Colonization with *Ureaplasma* (35% to 90%) and *M. hominis* (5% to 80%) is high in the normal pregnant population.<sup>32</sup> Routine testing for *M. hominis* and *Ureaplasma* in nonpregnant and pregnant women who are asymptomatic or have uncomplicated genital infections is not recommended.<sup>31,32</sup> Testing for *M. genitalium* is recommended for symptomatic women with cervicitis and PID.<sup>22,31</sup> Testing is by vaginal NAAT, polymerase chain reaction (PCR), or culture and treatment initiated for symptomatic nongonococcal urethritis, cervicitis, or PID.<sup>22,31,32</sup> Treatment is summarized in Table 2.<sup>10,22,31</sup>

### Genitourinary Syndrome of Menopause

Genitourinary syndrome of menopause is vulvovaginal atrophy affecting 27% to 84% of postmenopausal women.<sup>6,33</sup> Symptoms include vaginal dryness, burning, irritation, dyspareunia, urgency, dysuria, and recurrent UTIs.<sup>6,33</sup> Unfortunately, 50% of women never seek therapy even though GSM significantly impacts sexual health and quality of life.<sup>33</sup> The microbiome of the menopausal vagina is consistent with CST IV and generally decreased lactobacilli and increased pH (5.0 to 5.5 or greater) without increased pathogens.<sup>2,5</sup> Wet prep microscopy shows greater than 1 WBC per epithelial cell, immature vaginal epithelial cells with relatively large nuclei termed parabasal cells, and decreased or absent superficial vaginal cells.<sup>6</sup>

Diagnostic criteria is detailed in Table 1.<sup>6</sup> Genitourinary syndrome of menopause increases the likelihood of trauma, pain, recurrent UTIs, postcoital bleeding, and decline in sexual activity.<sup>6,33</sup>

Therapies include regular use of vaginal moisturizers and lubricants for intercourse.<sup>6</sup> Table 2 lists therapies for moderate to severe GSM.<sup>6</sup> For women with a history of breast or

endometrial cancer, vaginal estrogen therapy (ET) and dehydroepiandrosterone (DHEA) may be appropriate with minimal risk.<sup>6,34</sup> However, shared decision making with a woman and her oncologist is recommended.<sup>6,34</sup> Product labeling for vaginal ET contains risks associated with systemic ET (coronary heart disease, stroke, venous thromboembolism, breast, and endometrial cancer), although these risks are highly unlikely given minimal systemic absorption and reassuring findings from clinical studies.<sup>6,34</sup> Based on observational studies, a progestogen is unnecessary with low-dose vaginal ET.<sup>6,34</sup> Although routine endometrial assessment is not recommended, transvaginal ultrasound or intermittent progestogen therapy may be considered for women at risk of endometrial cancer.<sup>6,34</sup> Vaginal bleeding in postmenopausal women requires evaluation that may include transvaginal ultrasound, endometrial biopsy, and/or office hysteroscopy.<sup>6</sup>

Energy-based therapies such as vaginal laser and radiofrequency devices require long-term, sham-controlled safety and efficacy studies before use may be recommended.<sup>6,35</sup> Platelet-rich plasma has been suggested, but prospective randomized controlled trials have not been completed.<sup>36</sup> Genitourinary syndrome of menopause therapy can be continued long-term with appropriate follow-up to avoid bothersome symptoms.<sup>6</sup>

## SUMMARY

Vaginitis remains challenging for both women and clinicians. Although vaginal microbiome research and innovative treatments are evolving, there are clinically proven, effective therapies available for symptom management after careful evaluation. Importantly, women with recurrent or complicated vaginitis should be referred to clinicians with vaginitis expertise rather than treated empirically.

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**Abbreviations and Acronyms:** **ACOG**, American College of Obstetricians and Gynecologists; **BV**, bacterial vaginosis; **CDC**, Centers for Disease Control and Prevention; **CST**, community state; **DIV**, desquamative inflammatory vaginitis; **ET**, estrogen therapy; **GBS**, group B streptococcus; **GSM**, genitourinary syndrome of menopause; **HIV**, human immunodeficiency virus; **NAAT**, nucleic acid amplification test; **PID**, pelvic inflammatory disease; **PTB**, preterm birth; **STI**, sexually transmitted infection; **UTI**, urinary tract infection

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