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Committee Approvals/Dates:
Clinical Knowledge Management (CKM) Council (Last Periodic Review: 07/27/2017)

Next Review Date: August 2024
A literature review was conducted in August 2021 and there was no compelling evidence to recommend changes to the guideline.
Executive Summary
Guideline Overview
The three diseases most frequently associated with vaginal discharge are bacterial vaginosis, Trichomonas vaginalis, and vulvovaginal candidiasis. This guideline provides recommendations for the diagnosis and treatment of patients with a vagina who report or present with vaginal symptoms.

Key Practice Recommendations
1. A risk-based testing strategy is recommended to promote empiric treatment prior to diagnostic laboratory testing and exam in low risk populations and a full diagnostic work-up in higher risk populations. (UW Health Very low quality evidence, weak/conditional recommendation)

2. Laboratory tests with greater sensitivity are recommended in patients considered to be at higher risk, while less sensitive and less costly tests may be used in lower risk patients. (UW Health Low quality evidence, weak/conditional recommendation)

3. Providers should strive to order as many tests in combination, as clinically appropriate (e.g., may not order a test to evaluate for Trichomoniasis if no risk of sexual transmission). (UW Health Low quality evidence, weak/conditional recommendation)

4. The choice of medication should individualized based on patient preferences, cost, patient compliance, and any presence of allergies, intolerances, or history of response or adverse reactions to prior treatments.1 (UW Health Low quality evidence, strong recommendation)

5. Follow-up evaluation is unnecessary if symptoms of bacterial vaginosis or vulvovaginal candidiasis resolve.2 (UW Health Low quality evidence, strong recommendation)

6. Due to the high rate of reinfection, retesting for T. vaginalis is recommended for all sexually active patients within 3 months following initial treatment regardless of whether they believe their sex partners were treated.2 (UW Health Very low quality evidence, weak/conditional recommendation)
Scope
Disease/Condition(s): Vaginitis including:
- Bacterial Vaginosis
- Vulvovaginal candidiasis
- Trichomoniasis

Clinical Specialty: Urgent Care, Primary Care, OB/GYN, Laboratory

Intended Users: Physicians, Advanced Practice Providers, Nursing Staff, Pharmacists

Objective(s):
- To outline the preferred diagnostic testing methods for symptomatic patients.
- To provide evidence-based recommendations for the treatment of vaginitis and prevention of recurrent symptoms.

Target Population: Patients with a vagina of reproductive age (menarche to menopause) who are symptomatic, with or without a diagnosis of vaginitis confirmed by laboratory testing.

Interventions and Practices Considered:
- Laboratory testing
- Pharmacotherapy
- Sexual activity counseling

Major Outcomes Considered:
- Symptom relief
- Prevention of recurrence
Methodology

Methods Used to Collect/Select the Evidence:
Electronic database searches (e.g., PUBMED) were conducted by the guideline author(s) and workgroup members to collect evidence for review. Expert opinion and clinical experience were also considered during discussions of the evidence.

Methods Used to Formulate the Recommendations:
The workgroup members agreed to adopt recommendations developed by external organizations and/or arrived at a consensus through discussion of the literature and expert experience. All recommendations endorsed or developed by the guideline workgroup were reviewed and approved by other stakeholders or committees (as appropriate).

Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations:
Recommendations developed by external organizations maintained the evidence grade assigned within the original source document and were adopted for use at UW Health.

Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (see Figure 1 in Appendix A).

Rating Scheme for the Strength of the Evidence/Recommendations:
See Appendix A for the rating scheme(s) used within this document.

Recognition of Potential Health Care Disparities:
African American (51.6%) and Mexican American (32.1%) women have significantly higher prevalence of bacterial vaginosis than white non-Hispanic women (23.2%).3 A report by Royce et al. evaluating vaginal flora and vaginal pH of 842 women at 24–29 weeks of gestation, found that vaginal pH and vaginal flora differed significantly by race/ethnicity; African Americans were more likely to have a vaginal pH > or = 4.5, no lactobacilli, small gram-variable and gram-negative rods, and Mobiluncus bacterial species compared to white women after controlling for factors such as sociodemographic, sexual activity, sexually transmitted diseases, health behavior, and sexual hygiene.4

Introduction
Vulvovaginal complaints are one of the most common reasons for women to seek medical advice.5 The diagnosis of bacterial vaginosis, vulvovaginal candidiasis, or Trichomonas vaginalis are often considered clinically and diagnostically as a group because of their overlapping nature. A variety of options are available to diagnose vaginitis, including evaluation for clinical criteria (i.e., Amsel's Diagnostic Criteria) and laboratory testing (e.g., scored Gram stain, microscopy (wet mount), vaginal yeast culture, amplified probe technique, etc.). This guideline provides evidence-based recommendations for the testing and treatment of patients with vulvovaginal symptoms and complaints of vaginal discharge.
Recommendations

Risk Stratification & Diagnostic Testing

When making decisions regarding a diagnostic strategy, providers must consider the local prevalence of each diagnosis, individual patient history and physical examination results, laboratory testing characteristics, and cost. Unfortunately, an optimal diagnostic strategy is not clearly defined in the literature. Many expert consensus groups and several low quality studies question the accuracy and benefit of prescribing empiric therapy based on history and/or physical exam alone due to the risks of misdiagnosis or missed diagnoses, high coinfection rate, potential adverse effects from incorrect or delayed treatment, and overall lack of trust in the accuracy of patient-reported symptoms. On the contrary, two low quality research studies have challenged the utility of laboratory testing and have offered successful demonstrations of telephone triage protocols. At UW Health, a risk-based testing strategy (Figure 1) can be considered to promote empiric treatment prior to diagnostic evaluation in low risk populations and a full diagnostic work-up in higher risk populations. (UW Health Very low quality evidence, weak/conditional recommendation)

A complete description of symptoms and medical history should be obtained in all patients, regardless of encounter type (e.g., office visit, telephone). (UW Health Moderate quality evidence, strong recommendation) The medical history should include information on sexual behaviors and practices, gender of sex partners, menses, vaginal hygiene practices (e.g., douching), and any self-treatment with medications available over-the-counter (OTC). (UW Health Low quality evidence, strong recommendation)

All patients who present in the office with vulvovaginal symptoms, regardless of risk, should receive a full physical examination and diagnostic testing prior to receiving vaginitis treatment. (UW Health Low quality evidence, strong recommendation)

Patients who report vulvovaginal symptoms via a telephone encounter, MyChart encounter, or e-Visit should be evaluated for the presence of any high risk factors (Table 1). Patients who exhibit any risk factors should not be treated for vaginitis without first having a full medical history, physical examination, and laboratory testing performed. (UW Health Low quality evidence, strong recommendation)

<table>
<thead>
<tr>
<th>Table 1. High Risk Factors for Evaluation Prior to Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Age &lt; 25 years¹¹,¹⁴</td>
</tr>
<tr>
<td>• Systemic symptoms (e.g., fever, chills, body aches, etc.)¹³-¹⁵</td>
</tr>
<tr>
<td>• Abdominal or pelvic pain¹³,¹⁴</td>
</tr>
<tr>
<td>• New low back pain</td>
</tr>
<tr>
<td>• Pain with sexual intercourse⁵</td>
</tr>
<tr>
<td>• Unusual bleeding¹³</td>
</tr>
<tr>
<td>• Suspected exposure to a sexually transmitted infection or symptomatic sexual partner¹⁴</td>
</tr>
<tr>
<td>• New or multiple sexual partners²,⁵,¹⁴</td>
</tr>
<tr>
<td>• Over-the-counter or prescription treatment for vaginitis in the last 3 months⁵</td>
</tr>
<tr>
<td>• Previously prescribed empiric treatment over the telephone, MyChart, or e-Visit (max 2 per year)⁶</td>
</tr>
<tr>
<td>• Immunocompromised (e.g., HIV infection, uncontrolled diabetes mellitus)²,⁵</td>
</tr>
<tr>
<td>• Symptoms suggesting an alternative diagnosis (e.g., changes in skin condition or sores on the genitals, presence of vaginal and urinary symptoms)</td>
</tr>
<tr>
<td>• Pregnancy or possible pregnancy*</td>
</tr>
</tbody>
</table>

*Special consideration should be given in this population; providers should decide individually based on patient characteristics, history, and provider comfort whether to prescribe treatment without a full diagnostic evaluation.
In the absence of any high risk factors (Table 1) or other symptoms, patients who report classic symptoms of bacterial vaginosis or vulvovaginal candidiasis (Table 2) via a telephone encounter, MyChart encounter, or e-Visit may receive empiric treatment prior to diagnostic evaluation.\(^8,13\) (UW Health Very low quality evidence, weak/conditional recommendation) An office visit should be scheduled in either patient population for a complete physical examination and diagnostic evaluation if there is no resolution of symptoms within 2 weeks of treatment initiation.\(^13\) (UW Health Low quality evidence, strong recommendation)

### Table 2. Signs and Symptoms of Vaginitis\(^5\)

<table>
<thead>
<tr>
<th>Symptoms and Clinical Signs</th>
<th>Bacterial vaginosis</th>
<th>Vulvovaginal candidiasis</th>
<th>Trichomoniasis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Discharge</strong></td>
<td>Malodorous; homogenous; clear, white, or gray; fishy odor</td>
<td>White, thick, lack of odor</td>
<td>Green-yellow, frothy</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td>Not primary symptom</td>
<td>Burning, dysuria, dyspareunia</td>
<td>Pain with sexual intercourse, vaginal soreness, dysuria</td>
</tr>
<tr>
<td><strong>Pruritus</strong></td>
<td>Not primary symptom</td>
<td>Frequent</td>
<td>Not primary symptom</td>
</tr>
<tr>
<td><strong>Vagina</strong></td>
<td>No signs of inflammation</td>
<td>Signs of inflammation, edema</td>
<td>Signs of inflammation, “strawberry cervix”</td>
</tr>
<tr>
<td><strong>Vulva</strong></td>
<td>Unaffected</td>
<td>Excoriations</td>
<td>Vestibular erythema may be present</td>
</tr>
</tbody>
</table>

When performing diagnostic tests, it is more cost-effective to perform a combination of laboratory tests which assess for all three diagnoses rather than ordering tests sequentially.\(^16\) Providers should strive to order as many tests in combination as clinically appropriate (e.g., may not need to order a test for Trichomoniasis if no risk of sexual transmission). (UW Health Very low quality evidence, weak/conditional recommendation)

Various testing strategies are recommended to evaluate for the presence of bacterial vaginosis, vulvovaginal candidiasis, and Trichomoniasis based on the clinical scenario (Table 3). Wet mount microscopy performed by a skilled microscopist is the preferred testing method in most symptomatic patients, due to the low cost and rapid availability of results at the point of care.\(^5\) (UW Health Low quality evidence, weak/conditional recommendation)

The low sensitivity of wet mount and risk for missed diagnoses has been challenged across the literature, especially for *T. vaginalis* infection as it is associated with relatively significant health consequences including increased risk for HIV acquisition, pelvic inflammatory disease, and adverse pregnancy outcomes (e.g., premature rupture of membranes, preterm delivery, low birth weight).\(^2,5,17\) Therefore, reflex testing for Trichomoniasis using a highly sensitive nucleic acid amplification test (NAAT) is recommended in patients with a negative wet mount result to improve the diagnostic sensitivity.\(^2,18,19\) (UW Health Low quality evidence, weak/conditional recommendation) Concurrent screening for other sexually transmitted infections (e.g., chlamydia, gonorrhea) should be considered in patients who are tested for *T. vaginalis*, and may even be able to be performed from a single vaginal sample.\(^17,20\) (UW Health Low quality evidence, weak/conditional recommendation)

Diagnostic tests with the highest sensitivity are recommended in patients who have failed empiric therapy within 2 weeks of initiation or in patients with recurrent symptoms.\(^19,21,22\) (UW Health Low quality evidence, weak/conditional recommendation) Unlike less sensitive testing
methods, molecular testing (for bacterial vaginosis and *Trichomonas*) and culture (for *Candidiasis*) can help to negate concerns for the risks associated with delays in appropriate treatment and also provide the opportunity to identify organisms, such as *C glabrata* and *C krusei*, which have demonstrated resistance to fluconazole and would require alternative regimens.10

Researchers continue to evaluate the concordance between provider-collected and patient-collected vaginal samples to diagnose vaginal infections. Self-obtained swabs have been used successfully to diagnose other conditions, such as chlamydia and gonorrhea, and a high degree of acceptability has been reported by patients.20,23 Although several studies have demonstrated similar performance between self-collected and clinician-collected swabs, the anticipated benefits of efficiency and cost savings with self-collection are not believed to outweigh the risk for missed diagnoses.10,11,18,23,24 A comparison of “testing-only” visits with standard care visits at three sexually transmitted disease clinics revealed 10.8% of symptomatic women would remain undiagnosed with *Trichomoniasis* and 52.2% of BV/VVC cases would be missed using “testing-only” visits.11 Furthermore, wet mounts prepared using patient-collected samples demonstrated an even lower sensitivity than those prepared using a provider-collected sample.18,25

### Table 3. Preferred Strategy by Clinical Scenario

<table>
<thead>
<tr>
<th>Scenario(s)</th>
<th>Bacterial vaginosis</th>
<th>Vulvovaginal candidiasis</th>
<th>Trichomoniasis**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low risk</strong></td>
<td>If classic symptoms, consider treatment before lab testing. Patients with atypical symptoms should be considered higher risk and evaluated in the office.</td>
<td>If classic symptoms, consider treatment before lab testing. Patients with atypical symptoms should be considered higher risk and evaluated in the office.</td>
<td>N/A – Patients with risk factors for <em>Trichomonas</em> are considered high risk</td>
</tr>
<tr>
<td>Low risk</td>
<td>Saline Wet Prep with pH5 (provider or lab performed)</td>
<td>KOH Wet Prep5 (provider or lab performed)</td>
<td>Collect multiple swabs: Saline Wet Prep5 (provider or lab performed)</td>
</tr>
<tr>
<td>Low risk</td>
<td>Saline Wet Prep with pH5 (provider or lab performed)</td>
<td>KOH Wet Prep5 (provider or lab performed)</td>
<td>If negative, consider reflex with <em>Trichomonas vaginalis</em> by Amplified Probe Technique19</td>
</tr>
<tr>
<td><strong>High risk</strong></td>
<td>Saline Wet Prep with pH5 (provider or lab performed)</td>
<td>KOH Wet Prep5 (provider or lab performed)</td>
<td>Collect multiple swabs: Saline Wet Prep5 (provider or lab performed)</td>
</tr>
<tr>
<td>High risk</td>
<td>Saline Wet Prep with pH5 (provider or lab performed)</td>
<td>KOH Wet Prep5 (provider or lab performed)</td>
<td>If negative, consider reflex with <em>Trichomonas vaginalis</em> by Amplified Probe Technique19</td>
</tr>
<tr>
<td>Failed initial treatment for BV or VVC after 2 weeks (Never tested)</td>
<td>Gram stain, vaginal for bacterial vaginosis21</td>
<td>Vaginal Yeast Culture with Smear22</td>
<td>N/A – Patients with risk factors for <em>Trichomonas</em> are considered high risk</td>
</tr>
<tr>
<td>Recurrent infection or symptoms</td>
<td>Gram stain, vaginal for bacterial vaginosis21</td>
<td>Vaginal Yeast Culture with Smear22</td>
<td><em>Trichomonas vaginalis</em> by Amplified Probe Technique19</td>
</tr>
</tbody>
</table>

** Consider screening for other sexually transmitted infections (e.g., chlamydia, gonorrhea, etc.).
Figure 1. Management of Symptomatic Vaginitis Patients based on Risk

Patient reports vulvovaginal symptoms

- Obtain description of symptoms and medical history

  - Presentation in clinic?
    - Yes: Perform physical examination and diagnostic testing.
      - BV: Saline wet prep with pH (provider or lab performed)
      - VVC: KOH wet prep (provider or lab performed)
      - TV: Saline wet prep (provider or lab performed).
      - If wet prep negative, order Trichomonas vaginalis by Amplified Probe Technique
    
    - No: Present to schedule office visit

  - Presence of any high risk factors?
    - Yes: Schedule office visit
    
    - No: Outside guideline scope; manage as appropriate.

  - Classic BV symptoms?
    - Yes: Prescribe treatment
    
    - No: Outside guideline scope; manage as appropriate.

  - Classic VVC symptoms?
    - Yes: Recommend OTC treatment or prescribe treatment
    
      - Resolution of symptoms within 2 weeks?
        - Yes: No follow-up needed.
        
        - No: Schedule office visit to perform physical examination and diagnostic testing.
          - BV: Gram stain, vaginal
          - VVC: Vaginal yeast culture with smear
          - TV: Trichomonas vaginalis by Amplified Probe Technique
        
        - Prescribe treatment as clinically indicated.

  - Outside guideline scope; manage as appropriate.

- Prescribe treatment as clinically indicated.

BV = bacterial vaginosis; VVC = vulvovaginal candidiasis; TV: Trichomoniasis vaginalis; OTC = over-the-counter
Treatment & Follow-up

Complementary and Alternative Therapies

Complementary and alternative therapies are commonly used to treat vulvovaginal symptoms. These may include lactobacillus formulations or probiotics, yogurt, garlic, tea tree oil, a low carbohydrate diet, or hormonal manipulation with depot medroxyprogesterone. Insufficient evidence exists to consistently evaluate the benefits and harms of these modalities as related to improving patient outcomes for treatment and symptom relief. For example, some low quality studies of probiotics have demonstrated safety and efficacy in prevention or treatment of bacterial vaginosis and vulvovaginal candidiasis, however, additional high quality evidence is desired prior to routine application by clinicians in practice. Vaginal douching is not recommended. Some studies illustrate an increased risk of vaginal infections with douching, and no data exists to support the use of douching as treatment or in relief of symptoms.

Bacterial Vaginosis

The established benefits of therapy for bacterial vaginosis include relief of vaginal symptoms and signs of infection. Other potential benefits in symptomatic nonpregnant patients include reduction in risk for acquiring C. trachomatis, N. gonorrhoeae, T. vaginalis, HIV, and herpes simplex type 2.

Treatment of Initial Infection

The choice of medication should be individualized based on patient preferences, cost, patient compliance, and any presence of allergies, intolerances, or history of response or adverse reactions to prior treatments. Suggested treatment regimens for symptomatic patients with bacterial vaginosis are outlined in Table 4. Clindamycin and metronidazole have been found to be equally effective, achieving clinical cure rates of 91% and 92% respectively after 2-3 weeks of treatment. A comparison of tinidazole with metronidazole in 593 women with bacterial vaginosis also did not reveal significant differences in cure rates or side-effect profiles between the two medications. Multiple studies and meta-analyses have failed to demonstrate an association between metronidazole use during pregnancy and teratogenic or mutagenic effects in newborns. Symptomatic pregnant patients can be treated with either of the oral or vaginal metronidazole or clindamycin regimens recommended for non-pregnant patients. However, tinidazole should be avoided during pregnancy as animal data suggests this medication poses moderate risk. Alcohol consumption should be avoided during treatment with nitroimidazoles. It is recommended to continue alcohol abstinence 24 hours after completion of metronidazole or 72 hours after completion of tinidazole to reduce the risk for a disulfiram-like reaction.

Management of Sexual Partners

Patients should be advised to refrain from sexual activity or use condoms consistently and correctly during the treatment regimen.
Clindamycin cream and ovules may weaken latex condoms and diaphragms. Therefore, use of these products is not recommended within 72 hours following treatment with clindamycin ovules or within 5 days following treatment with clindamycin cream.

Routine prescription of treatment for sexual partners is not recommended. \textit{(UW Health Moderate quality evidence, strong recommendation)} In several high quality studies, treatment of male sexual partners with antibiotics, when compared with placebo, did not increase the rate of clinical or symptomatic improvement of their partner diagnosed with BV. Furthermore, antibiotic treatment of the sexual partner does not appear to demonstrate effect on the recurrence ofBV up to 12 weeks after treatment, but did increase the frequency of minor adverse effects reported by the sexual partner.

\textbf{Follow-up}

Follow-up evaluation is unnecessary if symptoms resolve. \textit{(UW Health Low quality evidence, strong recommendation)} As persistent or recurrent infections are common, patients should be advised to return for evaluation if symptoms recur. \textit{(UW Health Low quality evidence, strong recommendation)}

\textbf{Persistent or Recurrent Infection}

Use of oral contraceptives may have a protective affect against BV recurrences, whereas the following risk factors have been associated with recurrence:

- Sexual activity, specifically with increased numbers of sexual partners, inconsistent condom use, and women who have sex with women
- Vaginal douching
- Cigarette smoking
- Increased body mass index

Suggested treatment regimens for patients with persistent or recurrent bacterial vaginosis are outlined in Table 4. Detection of certain BV-associated organisms has been associated with antimicrobial resistance and might be predictive of risk for subsequent treatment failure. In patients with persistent or recurrent BV after the first occurrence, retreatment with the same recommended regimen is acceptable. \textit{(UW Health Low quality evidence, weak/conditional recommendation)}

For patients with multiple recurrences after completion of a recommended regimen, 0.75% metronidazole gel twice weekly for 4–6 months has been shown to reduce recurrences, although this benefit might not persist when suppressive therapy is discontinued. \textit{(UW Health Low quality evidence, weak/conditional recommendation)}

Limited data suggest that an oral nitroimidazole (metronidazole or tinidazole 500 mg twice daily for 7 days) followed by intravaginal boric acid 600 mg daily for 21 days and then suppressive 0.75% metronidazole gel twice weekly for 4–6 months for those women in remission might be an option for women with recurrent BV. \textit{(UW Health Low quality evidence, weak/conditional recommendation)} Monthly oral metronidazole 2 g administered with fluconazole 150 mg has also been evaluated as suppressive therapy; this regimen reduced the incidence of BV and promoted colonization with normal vaginal flora. \textit{(UW Health Low quality evidence, weak/conditional recommendation)}
**Trichomoniasis**
The benefits of therapy for *Trichomoniasis vaginalis* include a reduction of symptoms and signs, and possible reduction in transmission.\(^2\) With treatment, the likelihood of adverse outcomes in patients with HIV is also reduced.\(^2\)

**Treatment of Initial Infection**
The choice of medication should individualized based on HIV infection status, patient preferences, cost, patient compliance, and any presence of allergies, intolerances, or history of response or adverse reactions to prior treatments.\(^1\) *(UW Health Low quality evidence, strong recommendation)* Treatment regimens for symptomatic patients with *T. vaginalis* are outlined in Table 5.\(^2\)

Nitroimidazoles are the only class of antimicrobial medications known to be effective against *T. vaginalis* infections.\(^2\) Tinidazole is generally more expensive, reaches higher levels in serum and the genitourinary tract, has a longer half-life and has fewer gastrointestinal side effects than metronidazole.\(^2\) Cure rates differ slightly between metronidazole and tinidazole, approximately 84-98% and 92-100% respectively.\(^2\)

Multiple studies and meta-analyses have failed to demonstrate an association between metronidazole use during pregnancy and teratogenic or mutagenic effects in newborns.\(^2\) Symptomatic pregnant patients can be treated with either of the oral or vaginal metronidazole or clindamycin regimens recommended for non pregnant patients.\(^2\) *(UW Health Moderate quality evidence, weak/conditional recommendation)* Tinidazole should be avoided during pregnancy, and breastfeeding should be deferred for 72 hours following a single 2-g dose.\(^2\) *(UW Health Very low quality evidence, strong recommendation)*

Alcohol consumption should be avoided during treatment with nitroimidazoles.\(^2,33\) It is recommended to continue alcohol abstinence 24 hours after completion of metronidazole or 72 hours after completion of tinidazole to reduce the risk for a disulfiram-like reaction.\(^2\)

**Management of Sexual Partners**
Trichomoniasis is a sexually transmitted infection, requiring treatment of both the patient and their sexual partner. Patients should be advised to abstain from sexual activity until they and their sex partners are treated (i.e., when therapy has been completed and any symptoms have resolved).\(^2\) *(UW Health Low quality evidence, strong recommendation)*

In Wisconsin, expedited partner therapy (EPT) can be given to the patient to provide to any partner(s) with whom the patient has had sex in the 60 days prior to the onset of symptoms or a positive test.\(^2,33\) *(UW Health Low quality evidence, weak/conditional recommendation)* Partners with reported or known severe allergies to antibiotics should not receive EPT.\(^33\) *(UW Health Low quality evidence, strong recommendation)* The recommended regimen for EPT is metronidazole 2 grams by mouth in a single dose (once).\(^33\) *(UW Health Low quality evidence, strong recommendation)* Common side effects include dizziness, headache, diarrhea, nausea, stomach pain, and change in taste sensitivity or dry mouth.\(^33\)

EPT for Trichomoniasis is not legal in Illinois.\(^34\)

**Follow-up**
Due to the high rate of reinfection, retesting for *T. vaginalis* is recommended for all sexually active patients within 3 months following initial treatment regardless of whether they believe
their sex partners were treated.2 (UW Health Very low quality evidence, weak/conditional recommendation)

Testing by nucleic acid amplification can be conducted as soon as 2 weeks after treatment.2,35

**Persistent or Recurrent Infection**

It is important to consider the cause for persistent or recurrent infections and to distinguish the possibility of simply reinfection from an untreated sex partner from other causes (e.g., antimicrobial resistance, nonadherence to treatment, treatment failure).2,35 (UW Health Low quality evidence, strong recommendation) Repeat infections are common, ranging from 5-31% in HIV negative women and 18-37% in HIV positive women.35 Rates of metronidazole resistance is relatively low (ranging from 2.2-9.6%), and typically resolved with repeat treatment at the same or higher dosage.35 Treatment failure has been seen in 7-10% of cases (and can be even higher among HIV positive patients).35 Suggested treatment regimens for truly persistent or recurrent *T. vaginalis* are outlined in Table 5.2

Single-dose therapy should be avoided for treating recurrent trichomoniasis that is not likely a result of reinfection.2 (UW Health Low quality evidence, strong recommendation) If treatment failure has occurred with metronidazole 2 g single dose and reinfection is excluded, the patient (and their partner[s]) can be treated with metronidazole 500 mg orally twice daily for 7 days.2 (UW Health Low quality evidence, weak/conditional recommendation) If this regimen fails, clinicians should consider treatment with metronidazole or tinidazole at 2 g orally for 7 days.2 (UW Health Low quality evidence, weak/conditional recommendation)

If several 1-week regimens have failed in a person who is unlikely to have nonadherence or reinfection, consider nitroimidazole resistance and consult an Infectious Disease specialist.2 (UW Health Low quality evidence, weak/conditional recommendation)

**Vulvovaginal candidiasis**

**Treatment of Initial Infection**

The choice of medication should individualized based on patient preferences, cost, patient compliance, and any presence of allergies, intolerances, or history of response or adverse reactions to prior treatments.1 (UW Health Low quality evidence, strong recommendation) Factors Treatment regimens for patients with vulvovaginal candidiasis are outlined in Table 6.2

No statistically significant differences were found in clinical cure rates of anti-fungals administered by the oral and intravaginal routes.36 However, in April 2016, FDA released a warning for the use of fluconazole in patients who are pregnant. Therefore, intravaginal creams and suppositories are recommended in this patient population.2,37 (UW Health Low quality evidence, weak/conditional recommendation)

Although shorter duration therapy is available and recommended by national guidelines, avoidance of over-the-counter medications with a shorter duration of therapy is suggested. (UW Health Very low quality evidence, weak/conditional recommendation) These agents are believed to cause a greater number of side effects (e.g., burning, irritation) and often do not meet patient expectations for immediate symptom resolution which can prompt repeated contacts, concern for reinfection, and overall dissatisfaction.38

**Management of Sexual Partners**

Uncomplicated vulvovaginal candidiasis is not usually acquired through sexual intercourse, therefore data does not support treatment of sex partners.2 Patients should be advised that the
creams and suppositories may weaken latex condoms and diaphragms.\textsuperscript{2} \textit{(UW Health Low quality evidence, strong recommendation)}

**Follow-up**
Follow-up evaluation is unnecessary if symptoms resolve.\textsuperscript{2} \textit{(UW Health Low quality evidence, strong recommendation)} However, patients should be advised to return for evaluation if symptoms recur.\textsuperscript{2} \textit{(UW Health Low quality evidence, strong recommendation)}

**Persistent or Recurrent Infection**
Recurrent Vulvovaginal Candidiasis, usually defined as four or more episodes of symptomatic VVC within 1 year, affects a small percentage of patients (< 5\%).\textsuperscript{2} Suggested treatment regimens for truly persistent or recurrent \textit{T. vaginalis} are outlined in Table 6.\textsuperscript{2}

Oral fluconazole (i.e., 100 mg, 150 mg, or 200 mg) weekly for 6 months is the first line maintenance regimen.\textsuperscript{2-39} \textit{(UW Health Low quality evidence, weak/conditional recommendation)}

If recurrence of nonalbicans \textit{Candida} occurs, 600 mg of boric acid in a gelatin capsule is recommended, administered vaginally once daily for 2 weeks.\textsuperscript{2} \textit{(UW Health Low quality evidence, weak/conditional recommendation)} This regimen has clinical and mycologic eradication rates of approximately 70\%.\textsuperscript{2} If symptoms recur, referral to an Infectious Disease specialist is recommended.\textsuperscript{2} \textit{(UW Health Low quality evidence, weak/conditional recommendation)}
### Table 4. Treatment of Bacterial Vaginosis

#### INITIAL INFECTION

<table>
<thead>
<tr>
<th>Recommended Regimens</th>
<th>Considerations</th>
</tr>
</thead>
</table>
| **Metronidazole** | • Preferred first line agent in most patients  
• Oral route is preferred in pregnant patients  
• Avoid alcohol\(^2\)  
• Oral route may be associated with significant gastrointestinal symptoms\(^1\)  
• Consider gel if patient does not tolerate oral medications\(^2\) |
| 500 mg tab orally twice a day for 7 days  
0.75% gel, one full applicator (5 g) intravaginally, once a day for 5 days |  |
| **Clindamycin** | • Preferred in patients with an allergy or intolerance to metronidazole or tinidazole\(^2\)  
• May weaken latex condoms and diaphragms\(^2\) |
| 2% cream, one full applicator (5 g) intravaginally at bedtime for 7 days |  |

#### Alternative Regimens

<table>
<thead>
<tr>
<th><strong>Clindamycin</strong></th>
<th>• Ovules may weaken latex condoms and diaphragms; avoid use of products within 72 hours following treatment(^2)</th>
</tr>
</thead>
</table>
| 300 mg capsule orally twice daily for 7 days  
100 mg ovules intravaginally once at bedtime for 3 days |  |
| **Tinidazole** | • Avoid alcohol\(^2\)  
• Avoid during pregnancy\(^2\)  
• Lower dose for longer duration may cause less side effects  
• Typically more expensive than metronidazole |
| 2 g tab orally daily for 2 days  
1 g tab orally once daily for 5 days |  |

#### PERSISTENT OR RECURRENT INFECTION

<table>
<thead>
<tr>
<th>Retreat with same recommended regimen (see above)</th>
<th>• Acceptable after first occurrence(^2)</th>
</tr>
</thead>
</table>
| **Metronidazole** | • Recommended in patients with multiple recurrences\(^2\)  
• Avoid alcohol\(^2\) |
| 0.75% gel twice weekly for 4-6 months |  |
| **Metronidazole or Tinidazole + Boric acid + Metronidazole** | • Option for patients with multiple recurrences\(^2\)  
• Tinidazole is typically more expensive than metronidazole  
• Avoid alcohol with use of nitroimidazoles\(^2\)  
• Avoid tinidazole during pregnancy\(^2\)  
• A specialty pharmacy may need to compound the boric acid  
• Suppressive therapy may be considered in patients in remission\(^2\) |
| 500 mg tab twice daily for 7 days  
600 mg intravaginally daily for 21 days  
0.75% gel intravaginally twice weekly for 4-6 months |  |
| **Metronidazole + Fluconazole** | • Consider use as suppressive therapy\(^2\)  
• High dose of metronidazole may cause significant gastrointestinal side effects |
| 2 g tab orally monthly  
150 mg tab orally monthly |  |
Table 5. Treatment of *Trichomoniasis vaginalis*\textsuperscript{2,17}

<table>
<thead>
<tr>
<th>INITIAL INFECTION</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended Regimens</strong></td>
<td><strong>Metronidazole</strong> 2 g tab orally in a single dose</td>
</tr>
</tbody>
</table>
|  | • Preferred first line agent in most patients  
|  | • Recommended for expedited partner therapy\textsuperscript{33}  
|  | • Avoid alcohol\textsuperscript{1,2}  
|  | • Common side effects include dizziness, headache, diarrhea, nausea, stomach pain, and change in taste sensitivity or dry mouth\textsuperscript{33}  
|  | • If significant gastrointestinal symptoms, consider 1 g tab orally for 2 doses Q12 hours  
| **Tinidazole** 2 g tab orally in a single dose |  
|  | • Available first line agent  
|  | • More expensive than metronidazole (approximately ten times retail price)\textsuperscript{17}  
|  | • Slightly higher cure rate than metronidazole  
|  | • Fewer gastrointestinal side effects than metronidazole  
| **Alternative Regimen** | **Metronidazole** 500 mg tab orally twice a day for 7 days |  
|  | • Preferred for patients with HIV infection\textsuperscript{2}  
|  | • Lower rates of side effects (nausea and vomiting) than single dose\textsuperscript{35}  
|  | • Avoid alcohol\textsuperscript{1,2}  

| PERSISTENT OR RECURRENT INFECTION – EXCLUDE REINFECTION |  
| **Metronidazole** 500 mg tab orally twice daily for 7 days |  
|  | • Recommended for initial treatment failure of metronidazole 2 g single dose\textsuperscript{2}  
|  | • Consider for partner therapy  
| **Metronidazole or Tinidazole** 2 g tab orally for 7 days |  
|  | • Option for failure of metronidazole 500 mg tab twice daily for 7 days  
| **Consult Infectious Disease specialist** |  
|  | • Consider in cases of suspected nitroimidazole resistance or continued infection  

Effective 08/03/2021. Contact CCKM@uwhealth.org for previous versions.
Table 6. Treatment of Vulvovaginal candidiasis\(^2\)

<table>
<thead>
<tr>
<th>INITIAL INFECTION</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended Regimens</strong></td>
<td><strong>Considerations</strong></td>
</tr>
</tbody>
</table>
| Clotrimazole | 1% cream 5 g intravaginally daily for 7-14 days 2% cream 5 g intravaginally daily for 3 days | • Clotrimazole, miconazole, and tioconazole are available over-the-counter  
• Butoconazole and terconazole are only available via prescription  
• Local side effects (burning, irritation)\(^1\)  
• Clotrimazole has best reported tolerance \(^3\)  
• Longer duration therapy is recommended if concerns for patient expectations or side effects  
• Immunocompromised patients do not respond as well to short-term therapies; recommend more prolonged treatment (i.e., 7-14 days)\(^2\) |
| Miconazole | 2% cream 5 g intravaginally daily for 7 days 100 mg vaginal suppository, one daily for 7 days 200 mg vaginal suppository, one daily for 3 days | |
| Tioconazole | 6.5% ointment 5 g intravaginally in a single application | |
| Butoconazole | 2% cream 5 g intravaginally in a single application | |
| Terconazole | 0.4% cream 5 g intravaginally daily for 7 days 0.8% cream 5 g intravaginally daily for 3 days 80 mg vaginal suppository, one suppository daily for 3 days | |
| Fluconazole | 150 mg tab orally in a single dose | • Avoid in pregnancy (FDA warning)\(^3\) \(^7\)  
• Effective in mild or moderately severe VVC, additional doses (max every 72 hours for 2-3 doses) may be required for severe infections\(^3\) \(^8\)  
• Systemic side effects (gastrointestinal intolerance, headache)\(^1\) \(^2\)  
• Immunocompromised patients do not respond as well to short-term therapies; recommend more prolonged treatment (i.e., 7-14 days)\(^2\)  
• Only available via prescription |

<table>
<thead>
<tr>
<th>PERSISTENT OR RECURRENT INFECTION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluconazole</td>
<td>100, 150, 200 mg tab orally each week for 6 months</td>
</tr>
<tr>
<td>Boric acid</td>
<td>600 mg gelatin capsule vaginally once daily for 2 weeks</td>
</tr>
<tr>
<td>Consult Infectious Disease specialist</td>
<td>• Consider in cases of suspected resistance or continued infection</td>
</tr>
</tbody>
</table>
UW Health Implementation

Potential Benefits:
- Reduction in practice variation across legacy UWHC and UWMF clinics
- Improved patient experience and satisfaction
- Reduction in health care costs; more efficient treatment and diagnosis

Potential Harms:
- Delay in appropriate treatment/diagnosis if using OTC medication or prescription first
- Prenatal or infant exposure to medications if patient pregnant or in postpartum period
- Adverse reactions to pharmacotherapy
- Psychosocial implications of recurrent disease including distress, embarrassment, lack of control, or avoidance of daily activities due to fear of others detecting vaginal odor

Pertinent UW Health Policies & Procedures
1. UWHC Policy #13.04: Communicable Disease Reporting

Patient Resources
1. Healthwise- Vaginitis
2. Healthwise- Vaginal Yeast Infections
3. Healthwise- Vaginal Yeast Infections: Should I Treat It Myself?
4. Healthwise- Trichomoniasis

Guideline Metrics
1. % of patients treated first who required diagnostic testing within 2 weeks
2. Frequency of laboratory testing by clinic
3. Rate of orders placed individually vs. in combination

Implementation Plan/Clinical Tools
1. Guideline will be posted on uConnect in a dedicated location for Clinical Practice Guidelines.
2. Release of the guideline will be advertised in the Physician/APP Briefing newsletter.
3. Content and hyperlinks within clinical tools, documents, or Health Link related to the guideline recommendations (such as the following) will be reviewed for consistency and modified as appropriate.

Delegation Protocols
Treatment of Sexually Transmitted Infections or Genital Infections – Adult/Pediatric – Ambulatory [27]

Order Sets & Smart Sets
Vaginitis/STD/Pelvic SX [98]
OP – Treatment of Sexually Transmitted Infections (STIs) or Genital Infections Delegation Protocol – Adult/Pediatric – Ambulatory [5264]

Disclaimer
Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician’s judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.
Appendix A. Evidence Grading Scheme(s)

Figure 2. GRADE Methodology adapted by UW Health

GRADE Ranking of Evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>We are confident that the effect in the study reflects the actual effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.</td>
</tr>
<tr>
<td>Low</td>
<td>The true effect may differ significantly from the estimate.</td>
</tr>
<tr>
<td>Very Low</td>
<td>The true effect is likely to be substantially different from the estimated effect.</td>
</tr>
</tbody>
</table>

GRADE Ratings for Recommendations For or Against Practice

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong</td>
<td>The net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.</td>
</tr>
<tr>
<td>Weak/conditional</td>
<td>Recommendation may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.</td>
</tr>
</tbody>
</table>
References


