Vulvovaginal Candidiasis

VVC usually is caused by *C. albicans* but can occasionally be caused by other *Candida* sp. or yeasts. Typical symptoms of VVC include pruritus, vaginal soreness, dyspareunia, external dysuria, and abnormal vaginal discharge. None of these symptoms is specific for VVC. An estimated 75% of women will have at least one episode of VVC, and 40%–45% will have two or more episodes. On the basis of clinical presentation, microbiology, host factors, and response to therapy, VVC can be classified as either uncomplicated or complicated (Box 3). Approximately 10%–20% of women will have complicated VVC, requiring special diagnostic and therapeutic considerations.

Uncomplicated VVC

Diagnostic Considerations

A diagnosis of *Candida* vaginitis is suggested clinically by the presence of external dysuria and vulvar pruritus, pain, swelling, and redness. Signs include vulvar edema, fissures, excoriations, and thick curdy vaginal discharge. The diagnosis can be made in a woman who has signs and symptoms of vaginitis when either 1) a wet preparation (saline, 10% KOH) or Gram stain of vaginal discharge demonstrates budding yeasts, hyphae, or pseudohyphae or 2) a culture or other test yields a positive result for a yeast species. *Candida* vaginitis is associated with a normal vaginal pH (<4.5). Use of 10% KOH in wet preparations improves the visualization of yeast and mycelia by disrupting cellular material that might obscure the yeast or pseudohyphae.

BOX 3. Classification of vulvovaginal candidiasis

Uncomplicated VVC

- Sporadic or infrequent VVC

AND

- Mild-to-moderate VVC

AND

- Likely to be *Candida albicans*

AND

- Nonimmunocompromised women

Complicated VVC

- Recurrent VVC

OR

- Severe VVC

OR

- Nonalbicans candidiasis

OR

- Women with diabetes, immunocompromising conditions (e.g., HIV infection), debilitation, or immunosuppressive therapy (e.g., corticosteroids)

Abbreviation: HIV = human immunodeficiency virus; VVC = vulvovaginal candidiasis.

Examination of a wet mount with KOH preparation should be performed for all women with symptoms or signs of VVC, and women with a positive result should be treated. For those with negative wet mounts but existing signs or symptoms, vaginal cultures for *Candida* should be considered. If *Candida* cultures cannot be performed for these women, empiric treatment can be considered. Identifying *Candida* by culture in the absence of symptoms or signs is not an indication for treatment, because approximately 10%–20% of women harbor *Candida* sp. and other yeasts in the vagina. PCR testing for yeast is not FDA-cleared; culture for yeast remains the gold standard for diagnosis. VVC can occur concomitantly with STDs. Most healthy women with uncomplicated VVC have no identifiable precipitating factors.

Treatment

Short-course topical formulations (i.e., single dose and regimens of 1–3 days) effectively treat uncomplicated VVC. The topically applied azole drugs are more effective than nystatin. Treatment with azoles results in relief of symptoms and negative cultures in 80%–90% of patients who complete therapy.

Recommended Regimens

Over-the-Counter Intravaginal Agents:

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

OR

Clotrimazole 2% cream 5 g intravaginally daily for 3 days

OR

Miconazole 2% cream 5 g intravaginally daily for 7 days

OR

Miconazole 4% cream 5 g intravaginally daily for 3 days

OR

Miconazole 100 mg vaginal suppository, one suppository daily for 7 days

OR

Miconazole 200 mg vaginal suppository, one suppository for 3 days

OR

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

OR

Tioconazole 6.5% ointment 5 g intravaginally in a single application

Prescription Intravaginal Agents:

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

OR

Terconazole 0.4% cream 5 g intravaginally daily for 7 days

OR

Terconazole 0.8% cream 5 g intravaginally daily for 3 days

OR

Terconazole 80 mg vaginal suppository, one suppository daily for 3 days

Oral Agent:

Fluconazole 150 mg orally in a single dose

The creams and suppositories in these regimens are oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for further information. Intravaginal preparations of clotrimazole, miconazole, and tioconazole are available over-the-counter (OTC). Even women who have previously received a diagnosis of VVC by a clinician are not necessarily more likely to be able to diagnose themselves; therefore, any woman whose symptoms persist after using an OTC preparation or who has a recurrence of symptoms within 2 months after treatment for VVC should be clinically evaluated and tested. Unnecessary or inappropriate use of OTC preparations is common and can lead to a delay in the treatment of other vulvovaginitis etiologies, which can in turn result in adverse outcomes.

Follow-Up

Follow-up typically is not required. However, women in whom symptoms persist or recur after treatment of initial symptoms should be instructed to return for follow-up visits.

Management of Sex Partners

Uncomplicated VVC is not usually acquired through sexual intercourse; thus, data do not support treatment of sex partners. A minority of male sex partners have balanitis, characterized by erythematous areas on the glans of the penis in conjunction with pruritus or irritation. These men benefit from treatment with topical antifungal agents to relieve symptoms.

Special Considerations

Allergy, Intolerance, and Adverse Reactions

Topical agents usually cause no systemic side effects, although local burning or irritation might occur. Oral azoles occasionally cause nausea, abdominal pain, and headache. Therapy with the oral azoles has been associated rarely with abnormal elevations of liver enzymes. Clinically important interactions can occur when oral azoles agents are administered with other drugs *(722)*.

Complicated VVC

Diagnostic Considerations

Vaginal cultures should be obtained from women with complicated VVC to confirm clinical diagnosis and identify unusual species, including nonalbicans species. *C. glabrata* does not form pseudohyphae or hyphae and is not easily recognized on microscopy. Although *C. albicans* azole resistance is possibly becoming more common in vaginal isolates *(723,724)*, susceptibility testing is usually not warranted for individual treatment guidance.

Recurrent Vulvovaginal Candidiasis

Recurrent Vulvovaginal Candidiasis (RVVC), usually defined as four or more episodes of symptomatic VVC within 1 year, affects a small percentage of women (<5%). The pathogenesis of RVVC is poorly understood, and most women with RVVC have no apparent predisposing or underlying conditions. *C. glabrata* and other nonalbicans *Candida* species are observed in 10%–20% of women with RVVC. Conventional antimycotic therapies are not as effective against these nonalbicans species as against *C. albicans*.

Treatment

Each individual episode of RVVC caused by *C. albicans* responds well to short duration oral or topical azole therapy. However, to maintain clinical and mycologic control, some specialists recommend a longer duration of initial therapy (e.g., 7–14 days of topical therapy or a 100-mg, 150-mg, or 200-mg oral dose of fluconazole every third day for a total of 3 doses [day 1, 4, and 7]) to attempt mycologic remission before initiating a maintenance antifungal regimen.

Oral fluconazole (i.e., 100-mg, 150-mg, or 200-mg dose) weekly for 6 months is the first line maintenance regimen. If this regimen is not feasible, topical treatments used intermittently can also be considered. Suppressive maintenance therapies are effective in reducing RVVC. However, 30%–50% of women will have recurrent disease after maintenance therapy is discontinued. Symptomatic women who remain culture-positive despite maintenance therapy should be managed in consultation with a specialist.

Severe VVC

Severe vulvovaginitis (i.e., extensive vulvar erythema, edema, excoriation, and fissure formation) is associated with lower clinical response rates in patients treated with short courses of topical or oral therapy. Either 7–14 days of topical azole or 150 mg of fluconazole in two sequential oral doses (second dose 72 hours after initial dose) is recommended.

Nonalbicans VVC

Because at least 50% of women with positive cultures for nonalbicans *Candida* might be minimally symptomatic or have no symptoms and because successful treatment is often difficult, clinicians should make every effort to exclude other causes of vaginal symptoms in women with nonalbicans yeast *(725)*. The optimal treatment of nonalbicans VVC remains unknown. Options include longer duration of therapy (7–14 days) with a nonfluconazole azole regimen (oral or topical) as first-line therapy. If recurrence occurs, 600 mg of boric acid in a gelatin capsule is recommended, administered vaginally once daily for 2 weeks. This regimen has clinical and mycologic eradication rates of approximately 70% *(726)*. If symptoms recur, referral to a specialist is advised.

Management of Sex Partners

No data exist to support the treatment of sex partners of patients with complicated VVC. Therefore, no recommendation can be made.

Special Considerations

Compromised Host

Women with underlying immunodeficiency, those with poorly controlled diabetes or other immunocompromising conditions (e.g., HIV), and those receiving immunosuppression therapy (e.g., corticosteroid treatment) do not respond as well to short-term therapies. Efforts to correct modifiable conditions should be made, and more prolonged (i.e., 7–14 days) conventional treatment is necessary.

Pregnancy

VVC occurs frequently during pregnancy. Only topical azole therapies, applied for 7 days, are recommended for use among pregnant women.

HIV Infection

Vaginal *Candida* colonization rates among women with HIV infection are higher than among seronegative women with similar demographic and risk behavior characteristics, and the colonization rates correlate with increasing severity of immunosuppression. Symptomatic VVC is also more frequent in women with HIV infection and similarly correlates with severity of immunodeficiency. In addition, among women with HIV infection, systemic azole exposure is associated with the isolation of nonalbicans *Candida* species from the vagina.

On the basis of available data, therapy for uncomplicated and complicated VVC in women with HIV infection should not differ from that for seronegative women. Although long-term prophylactic therapy with fluconazole at a dose of 200 mg weekly has been effective in reducing *C. albicans* colonization and symptomatic VVC *(727)*, this regimen is not recommended for women with HIV infection in the absence of complicated VVC *(247)*. Although VVC is associated with increased HIV seroconversion in HIV-negative women and increased HIV cervicovaginal levels in women with HIV infection, the effect of treatment for VVC on HIV acquisition and transmission remains unknown.