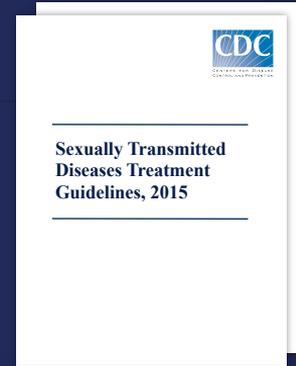


New CDC Vulvovaginal Candidiasis (VVC) Guidelines

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Supported by an unrestricted educational grant from **MONISTAT**[®]

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- Professor of Obstetrics and Gynecology
- Director of the Women's Health Institute and the Associate Dean for Women's Health
- Member of the Rutgers Master Educators' Guild
- Involved in the teaching and clinical practice of medicine as well as in the research aspects as pertains to women's health and wellness
- Internationally known expert with over 150 peer-reviewed publications and over 30 chapters in books
- Data derived from her participation in multiple research trials has added extensively to the literature and to many advances in the field of women's health



Disclosures

This presentation was made possible by an unrestricted educational grant to the Rutgers Women's Health Institute from MONISTAT®

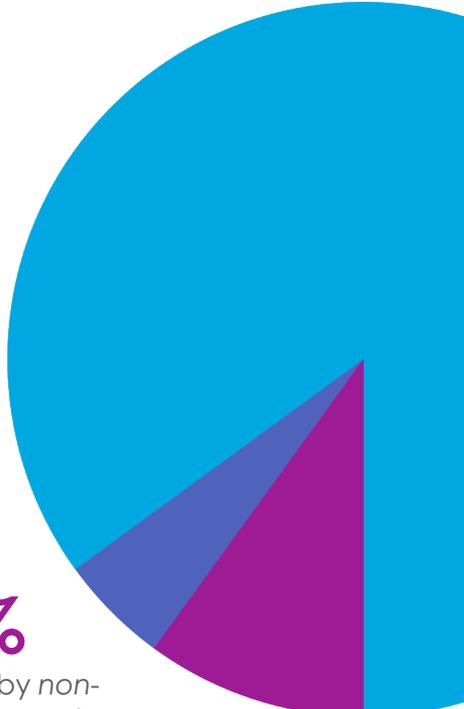
The Pearls

- *Women with previously verified vulvovaginal candidiasis (VVC) can be counseled to pick up an OTC topical azole at their pharmacy*
- *Topical azoles have a broader spectrum of activity vs oral fluconazole*
 - *Intravaginal miconazole treatment has equal efficacy to oral fluconazole*
 - *Intravaginal miconazole treatment relieves symptoms 4x faster than oral fluconazole*
- *Topical azoles are an ideal first-line treatment choice for women seen in the medical office who have confirmed VVC by symptoms, signs, and possibly wet mount*
- *Give patients a simple pearl and a simple vaginal treatment for VVC*

Vulvovaginal Candidiasis (VVC)

CAUSE, SYMPTOMS, INCIDENCE, CLASSIFICATION

- VVC is usually caused by *C. albicans*
 - May occasionally be caused by other *Candida* species of yeast
- Typical “non-specific” symptoms of VVC may include:
 - Pruritus
 - Vaginal soreness
 - Dyspareunia
 - External dysuria
 - Abnormal vaginal discharge

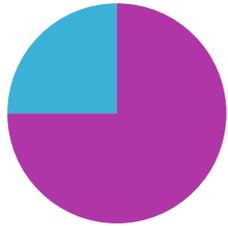


10–15%

of VVC is caused by non-*albicans* *Candida* species

Vulvovaginal Candidiasis (VVC)

CAUSE, SYMPTOMS, INCIDENCE, CLASSIFICATION



Approximately 75% of women have at least one episode of VVC in their lifetime



Approximately 40–45% of women have two or more episodes of VVC in their lifetime



VVC is classified as either uncomplicated or complicated

Approximately 10–20% of women have complicated VVC, which requires special diagnostic and therapeutic considerations

\$3B

In the US, the estimated cost of VVC diagnosis and treatment is \$3 billion

Comparative Symptomatology and Diagnosis of Vaginitis



CRITERIA	NORMAL	VVC	BV	TRICHOMONIASIS	STI
Symptoms	None	Extreme itch, dysuria, thick discharge, vaginal discomfort, soreness, burning, swelling	Odor, itch, discharge, soreness, burning	Odor, itch, discharge, soreness (may be asymptomatic)	
Vaginal Discharge	Clear/white	“Cottage cheese”-like discharge (thick, clumpy, white) if <i>C. albicans</i> ; may have colored discharge if <i>non-albicans species</i>	Thin, milky, “fishy” smelling	Frothy, gray, or yellow/green; foul odor	
Clinical Features		Inflammation (swelling), erythema (redness)	Redness, swelling	“Strawberry cervix” (petechiae: small red or purple spots from bleeding under the skin), swelling	
Vaginal pH	3.8–4.2	Normal: less than or equal to 4.5	>4.5	>4.5	
KOH “Whiff” Test	Negative	Negative	Positive	Often positive	

Vulvovaginal Candidiasis (VVC) Classification

The Centers for Disease Control (CDC) 2015 Vaginitis Guidelines define **Uncomplicated** vs **Complicated** VVC as:

UNCOMPLICATED VVC

Sporadic or infrequent VVC

AND

Mild-to-moderate infection

AND

Non-immunocompromised women

AND

Likely to be *Candida albicans*

COMPLICATED VVC

Recurrent vulvovaginal candidiasis (RVVC)

OR

Severe vulvovaginal candidiasis (Severe VVC)

OR

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

OR

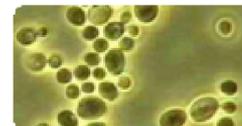
Non-albicans candidiasis

Uncomplicated Vulvovaginal Candidiasis (VVC)

DIAGNOSTIC CONSIDERATIONS FOR CANDIDA VAGINITIS

Diagnosis:

- Signs and symptoms of vaginitis
- Wet preparation (saline, 10% KOH) or gram stain of vaginal discharge demonstrates budding yeasts, hyphae, or pseudohyphae*
- Culture or other tests yield a positive result for a yeast species
 - Note: Identifying *Candida* by culture in the absence of symptoms or signs is not an indication for treatment
 - PCR testing for yeast is not FDA-cleared
- *Candida* vaginitis is associated with a normal vaginal pH (<4.5)



NORMAL



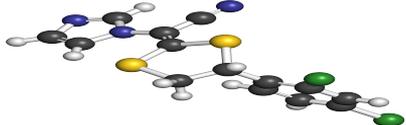
INFECTION

***Note:** If *Candida* cultures cannot be done, empiric treatment can be considered for symptomatic women with any sign of VVC on examination when the wet mount is negative

Azoles: The Antifungals Used to Treat VVC



TYPES OF AZOLES FOR VVC

Imidazoles	miconazole, tioconazole, clotrimazole, butoconazole (Rx topical)	Azole Molecule 
Triazoles	itraconazole, fluconazole (Rx oral), terconazole (Rx topical)	

Mechanism of Action: Achieves antifungal activity by inhibiting ergosterol synthesis in fungal cell membrane through action on cytochrome P450-dependent enzyme lanosterol 14 α -demethylase

Different azole types vary in:

- Pharmacokinetics
- Affinity for target enzymes
- Anti-fungal spectrum of activity

Note: 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.

The creams and suppositories in topical regimens are oil-based and might weaken latex condoms and diaphragms.

Therapeutic Agents

TYPE	ACTIVE INGREDIENT AND DOSAGE FORMS
Rx (Topical)	butoconazole 2% cream 5 g intravaginally in a single application
OTC (Topical)	clotrimazole 1% cream 5 g intravaginally daily for 7–14 days OR clotrimazole 2% cream 5 g intravaginally daily for 3 days OR
OTC (Topical)	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 in a single application for 1 day
OTC (Topical)	tioconazole 6.5% ointment 5 g intravaginally in a single application
Rx (Topical)	terconazole 0.4% cream 5 g intravaginally for 7 days OR terconazole 0.8% cream 5 g intravaginally for 3 days OR terconazole 80 mg vaginal suppository, one suppository for 3 days
Rx (Oral)	fluconazole 150 mg orally in single dose

Special Considerations

ALLERGY, INTOLERANCE, AND ADVERSE REACTIONS

Topical agents

- Risk of systemic side effects low
 - Local burning or irritation

Oral azoles:

- Risk increased from topical agents
 - Occasional nausea, abdominal pain, and headache
 - Associated rarely with abnormal elevations of liver enzymes
 - Interactions may occur with other drugs



Case Study

- A 47-year-old female phones the office complaining of distressing vaginal itching, bleeding, and discharge for the past 2 days
- She notes that her period was over 5 days ago and she is now seeing blood on her undergarments; she has never had these symptoms before
- Her past medical history is remarkable for a sinus infection for which she just completed antibiotic treatment
- She also has a history of genital herpes
- Because of dyslipidemia and a strong family history of cardiovascular disease, she is on atorvastatin

Poll Question

What would you do?

- A. Immediately send the patient for a pelvic ultrasound due to this irregular bleeding, and then have her come into the office for a pelvic exam and endometrial biopsy?
- B. Tell this patient to take her anti-viral Rx, as this may be a herpes infection, and if symptoms do not resolve, ask her to come into the office for a herpes culture?
- C. Tell the patient to come into the office for a vaginal exam and wet prep before prescribing?
- D. Prescribe an anti-fungal Rx over the phone?

Poll Answer

C. Tell the patient to come into the office for a vaginal exam and wet prep before prescribing.

She is bleeding and this is her first episode of fungal-like symptoms.

On evaluation her pelvic exam is remarkable for erythema of the vulva with excoriation from where she had scratched. The excoriated area bleeds with light touch. On speculum exam there is a thick, white, clumpy discharge with a pH of 4.2. On wet prep hyphae are noted.

Case Study

Diagnosis: Vulvovaginal candidiasis

- After full counseling that these symptoms were caused by a vulvovaginal yeast infection, the patient was told to pick up OTC miconazole at the pharmacy
- She was told that the blood noted on her undergarments was caused from the excoriated vulvar skin due to scratching
- When she asked about an oral antifungal, it was advised that there was a risk of interaction with her statin medication if she were given fluconazole
- She also was counseled that the vaginal medication would provide more rapid relief of symptoms

Poll Question

If this last patient were a 27-year-old pregnant patient, what **duration and type of therapy** would you have recommended?

- A. One dose of oral fluconazole 150 mg
- B. 1-day, 3-day, or 7-day topical azole
- C. 7-day topical azole
- D. Both A and C

Poll Answer

If this last patient were a 27-year-old pregnant patient, what **duration and type of therapy** would you have recommended?

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- B. 1-day, 3-day, or 7-day topical azole
- C. 7-day topical azole**
- D. Both A and C

Special Considerations

PREGNANCY

- Only topical azole therapies, applied for 7 days, are recommended for use in pregnancy
 - VVC occurs frequently during pregnancy



Vulvovaginal Candidiasis (VVC) Classification

The Centers for Disease Control (CDC) Vaginitis Guidelines 2015 define **Uncomplicated** vs **Complicated** VVC as:

UNCOMPLICATED VVC	COMPLICATED VVC
Sporadic or infrequent vulvovaginal candidiasis	Recurrent vulvovaginal candidiasis (RVVC)
AND	OR
Mild-to-moderate infection	Severe vulvovaginal candidiasis (Severe VVC)
AND	OR
Non-immunocompromised women	Women with diabetes, immunocompromising conditions (e.g., HIV infection), debilitation, or immunosuppressive therapy (eg, steroids)
AND	OR
Likely to be <i>Candida albicans</i>	<i>Non-albicans candidiasis</i>

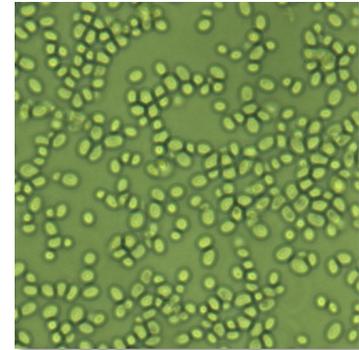
Complicated Vulvovaginal Candidiasis (VVC)

DIAGNOSTIC CONSIDERATIONS

- Vaginal cultures should be obtained to confirm the clinical diagnosis and to identify other species, including *non-albicans* species*
 - *Candida glabrata* (does not form pseudohyphae or hyphae and is not easily recognized on microscopy)

***Note:** Currently, *azole-resistant C. albicans* appears to be more common in vaginal isolates

- Susceptibility testing is usually **not** warranted



Non-albicans species

Complicated Vulvovaginal Candidiasis (VVC)

RECURRENT VULVOVAGINAL CANDIDIASIS (RVVC)



Definition and Background

- Four or more episodes of symptomatic VVC
 - Annually affects small percentage of women (<5%)
 - Seen in compromised host: underlying immunodeficiency, uncontrolled diabetes, other immunocompromising conditions (e.g., HIV), those receiving immunosuppression therapy (e.g., corticosteroid treatment)
 - Pathogenesis poorly understood
 - Considered severe when extensive vulvar erythema, edema, excoriation, and fissure formation present

Species

- *C. glabrata* and other *non-albicans Candida* species observed in 10–20% of women
 - *Non-albicans Candida* species more difficult to diagnose and treat

Management

- Lower clinical response rates in patients treated with short courses of topical or oral therapy
 - Does not respond well to short-term therapies

Complicated Vulvovaginal Candidiasis (VVC)

RECURRENT VULVOVAGINAL CANDIDIASIS (RVVC)



Initial Therapy

- Individual episodes of RVVC caused by *C. albicans* respond to short-duration oral or topical azole therapy
- To maintain clinical and mycologic control, longer duration of initial therapy preferred to attempt mycologic remission before initiating a maintenance regimen
 - 7–14 days of topical therapy
 - 100 mg, 150 mg, or 200 mg oral fluconazole every third day for a total of 3 doses (days 1, 4, and 7)

Maintenance Therapy

- Oral fluconazole (i.e., 100 mg, 150 mg, or 200 mg dose) weekly for 6 months
- If this regimen is not feasible, weekly intravaginal application of a topical preparation
- 30–50% will have recurrent disease after maintenance therapy discontinued

Symptomatic women who remain culture-positive despite maintenance therapy: suggest consultation with gynecologic infectious disease specialist

Case Study

- A 20-year-old college female home for spring break phones the office
- She reports that she is sure she has another vaginal yeast infection
- She wants to know if she should come in for an evaluation
- She explains that she is a competitive swimmer who's in the pool at least 5 days/week
- She notes that she has exercise-induced asthma, for which she uses a daily steroid inhaler
- Lastly she states that she's had 3 episodes of vulvovaginal candidiasis over the past 12 months, all confirmed at the student health center
- She asks you to send in an Rx to the pharmacy for an oral antifungal

Poll Question

What would you do?

- A. Send the Rx for an oral antifungal to her pharmacy?
- B. Have her come into the office for a pelvic exam, wet prep, and cultures?
- C. Tell her to go to the local pharmacy for an OTC antifungal?
- D. Have her come in for a pelvic exam, wet prep, cultures, and an HIV work-up to be sure that she is not immunocompromised?

Poll Answer

C. You tell her to go to the local pharmacy for an OTC antifungal

- Since she is otherwise healthy and the cause of her vaginal infection is known, she is an ideal candidate to use an OTC antifungal vaginal preparation
 - You may also suggest that she test her pH with an OTC pH detecting vaginal swab (if the swab turns blue-green, her pH is high and she should be seen for further evaluation)
- While on the phone, she is counseled that she should use an OTC antifungal vaginal preparation as soon as symptoms are present
- She also is warned that if symptoms don't resolve after self-diagnosis and treatment or if the frequency of infection increases, she should schedule a follow-up for further evaluation and management
- Finally, for this patient with established vulvovaginal candidiasis (VVC) or any patient with VVC diagnosed in the office, consider an OTC anti-fungal. Data suggest equal efficacy and faster relief when compared to treatment with oral fluconazole

ACCELERATE Study Data

- In a randomized, double-parallel group study, 300 women were treated with either miconazole 1 ovule combination pack or fluconazole 150 mg
- There was a statistically significant difference in time to onset of relief of itching, irritation, and overall symptoms between treatment groups

SYMPTOM	MICONAZOLE 1 HOURS (N=122)	FLUCONAZOLE HOURS (N=135)	P**
Itching	1.0	4.0	0.0001
Burning	1.0	4.0	0.0894
Irritation	1.0	4.0	0.0071
Combined symptoms	4.0	16.0	0.0010

For the individual symptoms, miconazole 1 ovule combination pack provided statistically significant faster onset of relief of itching and irritation than systemic fluconazole oral therapy.

For the combined symptoms, miconazole 1 ovule combination pack delivered **4x faster onset of relief of symptoms when compared to systemic fluconazole oral therapy (4 hours vs 16 hours).**

**Kaplan-Meier analysis based on overall time to event curves

Complicated Vulvovaginal Candidiasis (VVC): Other Scenarios

Women with Severe VVC:

Either 7–14 days of topical azole or 150 mg of fluconazole in two sequential oral doses (second dose 72 hours after initial dose)

Women with Special Medical Conditions:

- Efforts to correct modifiable conditions should be made
- Consider more prolonged (i.e., 7–14 days) conventional treatment

Poll Question

What **duration and type of therapy** is recommended first-line for patients with suspected or confirmed *non-albicans* vulvovaginal candidiasis?

- A. Oral fluconazole 150 mg every 3 days (days 1, 4, 7)
- B. Longer duration of intra-vaginal therapy (7–14 days) with a non-fluconazole azole
- C. Oral fluconazole 150 mg once weekly for 2 weeks
- D. Intravaginal azole therapy for 3 days
- E. Both 2 and 4

Poll Answer

What **duration and type of therapy** is recommended first-line for patients with suspected or confirmed *non-albicans* vulvovaginal candidiasis?

- A. Oral fluconazole 150 mg every 3 days (days 1, 4, 7)
- B. Longer duration of intra-vaginal therapy (7–14 days) with a non-fluconazole azole**
- C. Oral fluconazole 150 mg once weekly for 2 weeks
- D. Intravaginal azole therapy for 3 days
- E. Both 2 and 4

Non-albicans Vulvovaginal Candidiasis (VVC)

Management of *non-albicans Candida* is often difficult and optimal treatment is not confirmed:

- At least 50% of women positive for *non-albicans Candida* may be minimally symptomatic or asymptomatic
- First-line treatment recommendation for *non-albicans VVC*: non-fluconazole azole agent for longer duration of therapy (7–14 days)
 - Topical azoles, like miconazole, treat a broader spectrum of yeast species than oral fluconazole
- If recurrence occurs after extended use of topical therapy: consider boric acid 600 mg intravaginally daily for 2 weeks (clinical and mycologic eradication rates of approximately 70%)



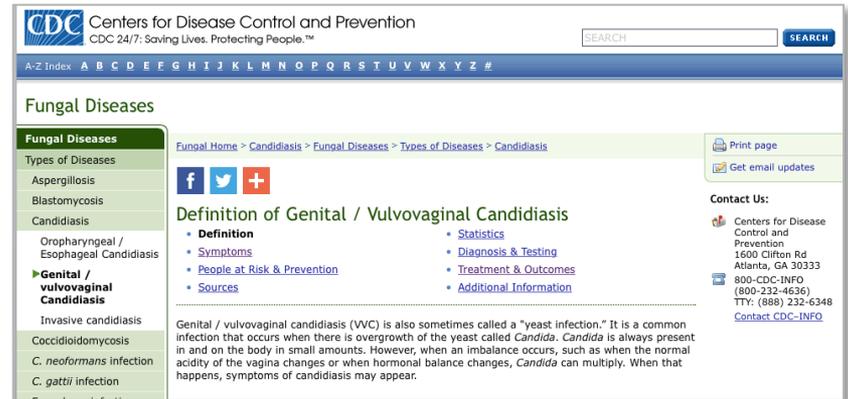
The Pearls

- *Women with previously verified vulvovaginal candidiasis (VVC) can be counseled to pick up an OTC topical azole at their pharmacy*
- *Topical azoles have a broader spectrum of activity vs oral fluconazole*
 - *Intravaginal miconazole treatment has equal efficacy to oral fluconazole*
 - *Intravaginal miconazole treatment relieves symptoms 4x faster than oral fluconazole*
- *Topical azoles are an ideal first-line treatment choice for women seen in the medical office who have confirmed VVC by symptoms, signs, and possibly wet mount*
- *Give patients a simple pearl and a simple vaginal treatment for VVC*



Message from the US National Library of Medicine and the CDC (Education)...

- The information that a patient responds to varies from person to person
- Keep your assessment of the patient in mind and consider literacy and culture as you develop a plan
- Focus on the benefits of education and tell your patient what to pay special attention to
- Review materials with the patient since no resource is a substitute for one-on-one patient teaching



The screenshot shows the CDC website page for "Genital / Vulvovaginal Candidiasis". The page header includes the CDC logo and the text "Centers for Disease Control and Prevention" and "CDC 24/7: Saving Lives. Protecting People.™". A search bar is located in the top right corner. Below the header, there is a navigation menu with letters A-Z and a search button. The main content area is titled "Fungal Diseases" and includes a breadcrumb trail: "Fungal Home > Candidiasis > Fungal Diseases > Types of Diseases > Candidiasis". A sidebar on the left lists various fungal diseases, with "Genital / vulvovaginal Candidiasis" highlighted. The main content area features a "Definition of Genital / Vulvovaginal Candidiasis" section with links for "Definition", "Symptoms", "People at Risk & Prevention", "Sources", "Statistics", "Diagnosis & Testing", "Treatment & Outcomes", and "Additional Information". A "Contact Us" section on the right provides contact information for the Centers for Disease Control and Prevention, including the address, phone number, and TTY number. Social media icons for Facebook, Twitter, and YouTube are also visible.

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CDC Patient Education/VVC; <http://www.cdc.gov/fungal/diseases/candidiasis/genital/index.html>, accessed 7/1/15.



When you decide to recommend an OTC anti-fungal, how do you handle the conversation with the patient?

Send your ideas or additional questions to: Lori Lonczak RPh, at lorilonczak@gmail.com

Thank you for participating!

Stay tuned for the next webinar in the series