

Diagnosis and treatment of vulvovaginal candidiasis

INTRODUCTION

There are a variety of symptoms that are more specific to each form of vaginitis. Therefore, clinicians must get personal with patients and ask very specific questions about their symptoms in order to determine which form of vaginitis they may be presenting with. Obtaining a comprehensive patient history is necessary to enable differentiation between an easily treated condition and one which may require further evaluation. This lesson will focus on the characteristics and management of *vulvovaginal candidiasis* (VVC) including pathophysiology, risk factors, referral criteria, pharmacological and nonpharmacological management options and the role of the clinician in patient consultation. Clinicians play a pivotal role in the management of VVC based on the potential for patient misdiagnosis, easy access to nonprescription medications, possible overuse of over-the-counter (OTC) products and the possibility of nonadherence to treatment regimens leading to resistance.

EPIDEMIOLOGY

Non-prescription antifungals, which are the mainstay of treatment for VVC, are

estimated to rank in the top 10 best-selling OTC products in the United States.² Approximately \$250 million is spent annually on the use of OTC vaginal antifungal creams, ointments and suppositories.² It is estimated that 75 percent of women will have at least one episode of VVC during their reproductive years, and 40 percent to 45 percent will have two or more episodes.^{4,5} Of the two classifications of VVC, complicated and uncomplicated, approximately 10 percent to 20 percent of women will present with complicated infection.⁴ Adequately treating, diagnosing and identifying causes of a first infection is important in order to prevent recurrent vaginal infections. Persistent infections can lead to various complications, depending on the form of vaginitis.

Research has shown that chronic bacterial vaginosis (BV) has been associated with pelvic inflammatory disease resulting in infertility.³ It is suggested that both recurrent BV and trichomonas can lead to an increased risk of HIV transmission, as well as other problems during pregnancy and child-birth, such as preterm labor and delivery. Recurrent VVC may be a sign of an underlying chronic medical condition and can result in chronic vulvar scarring,

skin abrasion, lesions and irritation. In general, vaginitis affects all races, but the highest incidence is observed in African-Americans.⁶ Approximately 50 percent of women presenting with VVC are between the ages of 18 to 23.⁷ Other groups with a high incidence include those who are within their reproductive years, have a sexually active lifestyle and have underlying medical conditions such as HIV, impaired immune system and diabetes.

PATHOPHYSIOLOGY

Under normal physiologic conditions the vagina maintains a balance among microorganisms that make up normal vaginal flora. These microorganisms play a role in regulating vaginal moisture and pH. Normal vaginal flora is predominately comprised of lactobacilli, corynebacteria and yeast, also known as *Candida*. Normally, *Candida* species are found in small amounts in the vagina, causing no symptoms for patients. Other organisms found in the vagina in lower amounts include *streptococcus*, *bacteroides*, *staphylococcus* and *peptostreptococcus*. Normal vaginal flora maintains the low vaginal pH between 3.8 and 4.2 in the healthy female from the time frame of menarche

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Program Goal:
To assist the primary care provider's ability to distinguish vaginal complaints and recommend interventions designed to relieve these concerns.

Learning Objectives
Upon completion of this program, the clinician should be able to:

1. Explain the pathophysiology of vaginal yeast infections.
2. List the risk factors for vaginal yeast infections.
3. Identify those patients who may appropriately be considered for treatment with OTC products.
4. Evaluate the different nonprescription treatment modalities used in the management of vaginal yeast infections and accompanying symptoms.
5. Define his or her role as a clinician in the management of patients who suffer from vaginal yeast infections, including prevention and non-pharmacologic treatments.

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to premenopause. Keeping the pH in this range is necessary in order to inhibit and prevent overgrowth of yeast and other bacteria. In VVC, an alteration to this pH can cause an overgrowth of *Candida*, resulting in a symptomatic discharge. The moist environment of the vagina is maintained by the sweat and apocrine glands found in the epithelium of the vagina and glands of the cervix. Cells of the vaginal epithelium store glycogen, which also helps to maintain the low pH of the vagina. Lactobacilli and corynebacterium maintain the pH by converting glycogen to lactic acid.

The normal physiologic discharge these glands produce is clear to milky white in color, odor-free and non-irritating. As a woman goes through her menstrual cycle and hormone levels fluctuate, the quality and quantity of discharge may change. Rising levels of endogenous estrogen will thicken vaginal epithelium, and decreasing levels will cause epithelium to become thin. This can result in a normal variation from thin, watery discharge to a thicker, cloudy discharge. However, symptoms which are characteristic of VVC include a white odorless vaginal discharge that is cottage cheese in appearance, itching, burning, irritation and pain on urination or intercourse. The amount and consistency of vaginal discharge may vary among women. Therefore, it is not only important for women to know about their normal secretions, but clinicians should feel comfortable inquiring about it, as well. The primary mechanism of action of increasing one's risk of VVC includes alteration of the normal vaginal flora, changes in vaginal pH and thickening of vaginal epithelium.

PATIENT SCENARIO 1

Problem

Jasmine is a 22-year-old student who has come into an in-store clinic today. When the clinician asks Jasmine what her concern is, she replies, "Something for an itch, you know, down there."

Assessment

What questions should be part of the clinician's evaluation of this patient?

Although this may be a sensitive subject to some patients, the clinician should ask specific questions to determine the origin of this patient's complaint. The questions should be separated into vaginal discharge symptoms, associated symptoms and potential risk factors. Assessment of vaginal discharge should include onset, duration, presence of odor, color of discharge, blood and previous episodes. Associated symptoms may include presence of itching, irritation, pain of the abdomen, shoulder or pelvis and burning. Assessment of risk factors should include underlying disease states, medication history and lifestyle habits.

Based on Jasmine's responses to the clinician's questions, it is determined that she had one previous episode of VVC two years ago and most recently was diagnosed with a respiratory infection for which she was prescribed an antibiotic. Three days after starting therapy, she noticed an odorless, white cottage cheese-like discharge that causes internal and external vaginal itching and irritation. Examination of the external genitalia and vaginal vault was consistent with VVC.

Recommendation

The clinician's assessment identifies this patient as having uncomplicated (less than or equal to two episodes per year) VVC caused by recent antibiotic use. Jasmine fits the criteria for OTC treatment because she has had one previous episode medically diagnosed and discharge is odorless. Jasmine would be classified as having a secondary sporadic infection caused by *C. albicans* and could be treated with a non-prescription vaginal antifungal.

Jasmine has the choice of four antifungals, including miconazole, butoconazole and tioconazole, all equally efficacious. Depending on her preference and convenience concerns, Jasmine could choose a one- or three-day product. The ovule formulation provides additional convenience for daytime dosing. Being as Jasmine complains of external itching, use of a combination package may be beneficial. Examples of appropriate products for this patient include Monistat-1 Combo, Vagistat-3 Combo and Monistat-3 Combo.

Because all of these products contain miconazole as the active ingredient, Jasmine should be counseled on the potential for weakening of condoms, diaphragms or other contraceptive devices. If Jasmine does not have relief of symptoms within seven days, she should contact her health care provider.

ETIOLOGY

Candida species is typically present in the flora of the vagina, mouth and gastrointestinal tract without causing symptoms. However, the overgrowth of *Candida* can cause patients to be symptomatic. In 90

percent of cases, the causative organism of VVC infection is identified as *Candida albicans*.² According to the Centers of Disease Control and Prevention, those patients with recurrent VVC may have overgrowth of non-albicans *Candida* species. These or-

ganisms may include *C. glabrata*, *C. parapsilosis*, *C. krusei*, *C. tropicalis* and *Saccharomyces cerevisiae*. In comparison, other forms of vaginitis, such as bacterial vaginosis, is caused by *Gardnerella vaginalis*, *Bacteroides*, *Mobiluncus* and *Mycoplasma hominis*.

Trichomonas vaginalis is the primary causative agent of the sexually transmitted infection trichomoniasis. The primary cause of VVC is overgrowth of *Candida* species due to the disruption the normal vaginal flora. This disruption can be caused by multiple risk factors, including antibiotic use, age, hormones, immune system status, sexual activity, underlying chronic disease states and lifestyle habits. Antibiotic use is a primary cause of VVC

as a result of alteration of normal vaginal flora. This alteration reduces or destroys the amount of lactobacillus, while enhancing the growth of *Candida*. Although no particular antibiotic has shown to be of a higher risk, such broad spectrum antibiotics as tetracyclines, cephalosporins and penicillin may have a high incidence.⁷ The risk of developing VVC has shown to increase with the duration of antibiotic use.⁸

Age has proven to be another risk factor of VVC with an increased incidence in one's 20s and a decline after menopause is reached. Although there are various theories of the pathophysiology, pregnancy also has shown to be a common cause of VVC. One theory suggests that the high and fluctuating levels of progesterone and estrogen thickens vaginal epithelium and increases production of glycogen.⁸ Higher levels of glycogen can acidify the vagina further, reducing the amount of normal flora that normally inhibits growth of *Candida*. The thickened epithelial wall also increases the ability of *Candida* to adhere to the vaginal skin cells.

Another theory suggests that *Candida* cells contain progesterone and estrogen receptors, which are stimulated when

hormone levels rise, resulting in *Candida* overgrowth.⁸ Additional situations in which oral hormone intake may predispose a woman to VVC include oral contraceptive use and hormone replacement therapy. Other methods of birth control also may increase the risk of VVC. Use

It is estimated that 75 percent of women will have at least one episode of VVC during their reproductive years, and 40 percent to 45 percent will have two or more episodes.

of diaphragms, sponges and intrauterine devices may contain *Candida* from previous use, irritate the vaginal lining and alter the normal vaginal flora.

Those women with altered immune systems, including AIDS/HIV, corticosteroid use and other immunosuppressants, are estimated to be at a 40 percent to 70 percent increased risk of recurrent VVC.⁸ This group of patients also may be at increased risk of *Candida* infection of the mouth and gastrointestinal tract. The link between VVC and sexual activity is controversial because VVC can still occur in those women who remain abstinent. However those who are sexually active may be at a higher risk because of increased *Candida* entrance to the vagina. According to the CDC, VVC is not acquired through sexual transmission, and research suggests that treatment of the partner has no effect on the women's risk of recurrence.^{4,5,8} Treatment may be considered in partners of those women with recurrent infection, although the studies do not suggest a clinical significant benefit.^{4,5,8}

Underlying chronic disease states, such as diabetes, are a predisposing factor for VVC, especially those patients who are

uncontrolled. Hyperglycemia or diets high in sugar (i.e., sucrose and lactose) may cause thickening of the vaginal epithelial wall and enhanced adherence of *Candida*. It is estimated that patients with uncontrolled diabetes are three times more likely to present with recurrent VVC, as well as

increased vaginal colonization of *Candida*. This incidence has shown to be higher in those with uncontrolled Type 1 diabetes, compared with Type 2 diabetes or those with normal HbA1c levels.⁹ Lifestyle habits also can play a significant role in the development of VVC by introducing bacteria to the vaginal area (i.e., cleansing from the anus toward the vagina), altering normal flora (i.e., douching or perfumed hygiene vaginal products) or increased vaginal moisture and temperature (i.e., poorly ven-

tilated underwear, tight-fitting clothing, sitting for long periods of time, remaining in wet clothes). The clinician should have an understanding of these risk factors in order to provide appropriate counseling on prevention and nonpharmacological management of VVC.

CLASSIFICATION

VVC is classified by recurrence and is categorized as either sporadic or recurrent VVC. Each category is classified then into primary and secondary causes. Sporadic VVC, also known as uncomplicated VVC, is defined as women who have two or fewer episodes per year.^{1,10} Primary sporadic is defined as having no known cause, and secondary sporadic is defined as being caused by pregnancy, antibiotic use or inappropriate lifestyle habits. *Candida albicans* is the primary culprit in 85 percent to 90 percent of sporadic VVC cases.^{1,10} Non-*albicans* *Candida* species, such as *C. glabrata* and *C. parapsilosis*, tend to be the cause of recurrent VVC in approximately 33 percent of patients.²

According to the CDC, recurrent VVC, also known as complicated VVC, is defined as more than four episodes per year or an

infection within two months of a previous treatment regimen. Other sources have defined recurrence when at least four specific episodes occur in one year or more than three episodes unrelated to antibiotic therapy occur in one year.⁸ Primary recurrent are frequent cases with unknown etiology, and secondary recurrent are frequent episodes caused by immune deficiency (i.e., HIV/AIDS, chronic steroid therapy), uncontrolled diabetes, oral hormone intake, resistant strain to antifungal therapy or underlying genital condition.^{1,10} Although the estimates vary, approximately 5 percent of women will experience recurrent VVC infection.² The symptoms of sporadic and recurrent VVC do have some dif-

ferences that can aid the clinician in determining whether self-treatment is appropriate. As previously mentioned, uncomplicated VVC typically presents with a thick, white cottage cheese-like vaginal discharge, discomfort after urination or intercourse, itching and burning. Patients with recurrent VVC may present with more severe symptoms and extreme changes to the vulva upon medical examination, including edema and thickening of skin. A thorough physical examination is essential when a recurrent infection is suspected.

DIAGNOSIS AND REFERRAL

Medical diagnosis of VVC infection is made by the presence of clinical symptoms, evaluation of vaginal pH, microscopic examination and an amine or whiff test. In VVC infection, vaginal pH typically remains normal at less than 4.5, unlike bacterial vaginosis and trichomoniasis, which causes vaginal pH to rise to greater than 4.5.^{2,4,6} Other causes of an alkaline vaginal environment include menstruation, ovulation, recent intercourse, douching and infections.² Presenting with an odorless

discharge is a distinguishing factor of fungal infections. In the amine or whiff test, a drop of 10 percent potassium hydroxide is added to the vaginal secretions. Detecting a fishy odor can differentiate a bacterial infection from a fungal infection. Observing vaginal discharge in a saline solution (wet-mount test) or a 10 percent potassium hy-

droxide preparation under a microscope can help confirm diagnosis of fungal infection. Under the microscope, yeast blastospores and pseudohyphae are characteristic in symptomatic patients.⁷ Being as many women have yeast as part of normal vaginal flora, microscopic evaluation and cultures may have limited value in those who are asymptomatic.² However, any female patient presenting with symptoms of VVC for the first time should always be evaluated by a clinician prior to treatment with a nonprescription antifungal. Table 1 lists additional criteria indicative of the need for evaluation by a clinician.^{1,10}

All clinicians should feel comfortable talking with female patients about their symptoms in order to eliminate the potential of misdiagnosis or treatment of another form of vaginitis or allowing an underlying condition to go untreated. In order to determine appropriate treatment, clinicians should ask patients specific questions about their discharge and associated symptoms. Questions about discharge should include presence of odor, blood, on-set, duration, amount and pre-

vious episodes. Inquiring about associated symptoms should include complaints of itching, burning, fever and pelvic, abdominal or shoulder pain. Asking about age, pregnancy status and medical, sexual and medication history also should be part of the evaluation. Ideally, pregnant patients should consult with their practitioner, however, non-

prescription antifungal in the appropriate dose, formulation and length of treatment are usually an option for this patient population. Other vaginal conditions, which are noninfectious, could be confused with the symptoms of VVC—specifically complaints of vaginal itching and irritation. These symptoms could be a result of a product hypersensitivity or allergy to latex condoms, spermicides, jellies, use

PHARMACOLOGICAL TREATMENT

The goals of treating VVC infection include relief of symptoms, eradication of infection, re-establishing normal flora and prevention of recurrence. The desired time frame of use of nonprescription antifungals is symptomatic relief within three days, eradication of infection within seven days and no recurrence within two months.^{1,10} Products used in the treatment of noninfectious vaginal irritation should provide relief within a few days, but should not be used for more than seven days.

Vaginal antifungals

There currently are four nonprescription vaginal antifungals available in the imidazole class, including butoconazole, clotrimazole, miconazole and tioconazole (see Table 2).^{1,10,11} Clotrimazole was the first azole brought to the market in 1990, followed by miconazole, butoconazole

TABLE 1
Indicators of need for evaluation

Foul-smelling discharge with an abnormal color
Presence of fever, nausea, vomiting or pain in the abdomen, back, shoulder or pelvis
Pregnant or breastfeeding
Younger than 12 years of age
First infection without physician diagnosis
Already used a product for appropriate length of time with no relief within seven days
More than four specific episodes of VVC per year*
An episode of VVC within the last two months
Underlying medical conditions not currently diagnosed

*or more than three unrelated to antibiotic therapy⁸

and tioconazole. The antifungals work by altering and damaging the fungi membrane, resulting in the death of the organism.¹⁰ Small amounts of the topical antifungals are systemically absorbed, and higher concentrations of the azoles can remain in the vaginal area for longer periods of time. This is observed with the higher concentrations of the one-day preparations.¹⁰

All vaginal antifungals are approved for the treatment of VVC. The products available as combination preparation have an additional indication for the relief of external itching

and irritation due to the infection (i.e., Monistat-1 combo, Mycelex-7 combo). These preparations contain a small tube of antifungal cream and would benefit those patients with complaints of external itching, as well as with internal irritation and itching. The side effect profile of these products is well tolerated with mild itching, irritation and burning. It is important to explain to the patients that these symptoms are side effects of the medication and not a worsening of their condition. Patients may have a tendency to discontinue their medication if they observe a worsening of their symptoms after the start of their treatment. The only product with a drug interaction warning is the ingredient miconazole, which states an increased risk of bleeding in patients taking warfarin or other anticoagulants.^{10,11} Caution should be used in those patients to determine the most appropriate therapy.

Although sexual intercourse during treatment of VVC is discouraged, women who do engage in intercourse should use precaution when using condoms or diaphragms during treatment with a vagi-

TABLE 2
Nonprescription antifungal products

Ingredient	Brand names	Formulation ¹
Butoconazole	Mycelex	Cream (2%)
Clotrimazole ²	Gyne-Lotrimin-3	Cream (2%)
	Gyne-Lotrimin-7	Cream (1%)
	Mycelex-7	Cream (1%)
Miconazole ²	Mycelex-7 combo	Vaginal insert (100mg)/ Cream (1%)
	Monistat-3	Cream (4%)
	Monistat-3 combo	Vaginal insert (200mg)/ Cream (2%)
Tioconazole ²	Monistat-7	Cream (2%)
	Monistat-7 combo	Vaginal insert (200mg)/ Cream (2%)
	Monistat-1 combo	Vaginal insert (1200mg)/ Cream (2%)
Tioconazole ²	Vagistat-3 combo	Vaginal insert (200mg)/ Cream (2%)
	Monistat-1	Ointment (6.5%)
	Vagistat-1	Ointment (6.5%)

1. Products available as pre-filled, disposable or reusable applicators

2. Available as a generic formulation

nal antifungal. Because of the mineral oil contained in these preparations, barrier methods of contraception could be damaged resulting in unexpected pregnancy or exposure to STDs. Clotrimazole is the only azole that does not contain this particular warning as it does not contain mineral oil as an active ingredient. All vaginal antifungal product labels are required by the Food and Drug Administration to include a warning regarding recurrence of symptoms within two months, use during pregnancy or any serious underlying medication condition, such as diabetes and HIV/AIDS.

Vaginal antifungals are available as one-day, three-day or seven-day preparations. They also are available in several formulations, including cream, ointment and ovule, sometimes referred to as vaginal inserts or suppositories. Currently, tioconazole is the only vaginal antifungal available as an ointment formulation, and its higher concentration allows for one-day use. The cream-based products may be purchased as prefilled, disposable or reusable applicators. Product selection for the antifungals is based on cost, length of

treatment, formulation, convenience and ease of use. The price does vary among the products depending on the type of formulation and length of treatment, however, all products except butoconazole are available in generic.

A common question is which length of therapy should the patient choose, and is one better than the other. Numerous studies have concluded that efficacy among one-, three- and seven-day preparations is comparable in providing symptomatic relief within three days and eradication within seven days.⁴ Approximately 80

percent to 90 percent of patients will have relief of symptoms and cure of infection with any of the available non-prescription antifungals.¹⁰ Therefore, overall product selection is based on patient preference and convenience of the chosen treatment, which is typically the one- and three-day preparations. According to the CDC, the only specific product recommendation is made for pregnant women who should use a seven-day product because they provide a lower concentration of medication over several days.⁴

Whether to use a cream or ovule is another factor to consider when selecting a vaginal antifungal. Each formulation has advantages and disadvantages. When choosing among the cream formulations, patients have the choice of various applicators, such as prefilled medication applicators, which provide additional convenience so the patient does not have to touch the cream. The reusable applicators should be washed with soap and water to prevent reinfection, therefore prefilled applicators tend to be preferred. Creams should be used at bedtime with a minipad to prevent

any leaked medication from staining bedclothes or sheets. In comparison, vaginal inserts or ovules allow for day-time administration with less incidence of staining. This formulation is more convenient for patients, but studies have shown comparable efficacy between the ovule and cream products.

In a study by Upmalis et al, a single-dose miconazole ovule was compared with seven-day miconazole cream in patients with uncomplicated VVC. Overall, cure rates were comparable between the ovule and miconazole cream (i.e., 71.7 percent versus 70.1 percent, respectively).¹² The time to symptom relief and complete relief was significantly higher in the ovule group compared with the cream (i.e., four versus five days, $p=0.008$ and three versus four days, $p=0.025$, respectively). However, overall safety results were comparable.¹² The products were concluded to be equally efficacious, with the ovule providing additional convenience and was therefore the preferred treatment among patients. Fluconazole is a commonly prescribed one-day oral dose prescription medication used in the treatment of VVC infection. Numerous studies have concluded similar safety and efficacy between the use of oral fluconazole and topical nonprescription antifungals.

In a study by Sobel et al, a single dose fluconazole was compared with a seven-day intravaginal clotrimazole therapy in patients with uncomplicated VVC. There were no clinically significant differences in the cure rates observed among the two groups. Although additional side effects were reported with the oral treatment, both regimens were equally efficacious. A health care provider seeing a patient with a first VVC infection should base medical treatment on drug costs, convenience, patient preference and side effect profiles.¹³ Additional counseling points during treatment with vaginal antifungals

includes avoiding sexual intercourse, avoiding douching to prevent washing out medication, no use of tampons (which may absorb medication), no use of condoms or diaphragms (which may become damaged and ineffective), the ability to use during menstrual flow and that patients should continue to use for full treatment duration even if symptoms improve.

Recurrent VVC

According to the CDC, recurrent episodes of VVC respond well to a longer duration (i.e., seven to 14 days) of therapy of either oral (i.e., fluconazole) or topical azole therapy for acute infection.⁴ After the acute episode has been treated, it is then recommended to initiate maintenance for approximately six months with medications including ketoconazole, terconazole, prescription butoconazole (Gynazole-1) or itraconazole.² Patients who have uncontrolled diabetes, are immunosuppressed, present with treatment resistance to *C. albicans* or with

non-albicans type may be candidates for maintenance therapy. Unfortunately, it is estimated that 30 percent to 40 percent of patients will develop recurrences once therapy is discontinued.⁴

One study evaluating maintenance regimens included a randomization of patients with recurrent VVC to placebo group, 400 mg ketoconazole for five days after menses for six months or 100 mg ketoconazole daily for six months.⁸ At the six month follow-up, recurrence rates were significantly lower in the daily ketoconazole group compared with the 400 mg group and placebo (i.e., 5 percent, $p=0.001$ versus 29 percent, $p=0.01$ versus 71 percent).⁸ The study also observed high relapse rates after discontinuation of maintenance therapy with high-dose (43 percent, $p=0.05$) and low-dose ketoconazole (52.4 percent, $p=0.05$).⁸ Patients who require longer maintenance therapy should be evaluated to determine the most appropriate regimen, taking into consideration drug cost, side effect profile, cost of monitor-

PATIENT SCENARIO 2

Problem

Mrs. Jones is a 46-year-old obese woman with complaints of vaginal itching and an odorless, white curd-like discharge. She has had these symptoms four times within the last year, and her last infection was less than two months ago. Additional complaints include frequent urination, hunger and thirst. She also has noticed increased fatigue, dry mouth, blurred vision and prolonged healing time of small wounds. She currently is being treated for hypertension and hyperlipidemia. She would like your recommendation.

Assessment

Following examination of the urogenital area, the patient's clinical presentation is consistent with VVC. Given her history, the clinician should evaluate for the presence of concomitant disease states, in particular diabetes, that could be contributing to the VVC.

Recommendation

This patient fits the criteria for further evaluation based on a possible underlying condition. Uncontrolled diabetes is a risk factor for recurrent VVC and should be treated to prevent future episodes. It would not be appropriate for Mrs. Jones to attempt to self-treat with over-the-counter products. Mrs. Jones also should be counseled on avoiding a diet high in sugars, as well as avoiding scented vaginal products, wearing tight clothing or sitting in wet clothing for a prolonged period of time.

ing, drug interactions, adherence concerns and ease of administration.

Vaginal antipuritics

As previously mentioned, patients may present with noninfectious vaginal irritation that is the result of inadequate hygiene or allergy to vaginal products. Symptoms may mimic VVC, however the predominant symptom is external itching, soreness and discharge that resembles the physiologic type. Patients should not use these products for more than one week and should be re-evaluated if symptoms worsen or do not improve with treatment. Ingredients used for vaginal irritation include anesthetics (i.e., benzocaine), external analgesics (i.e., resorcinol) and antipuritic (i.e., hydrocortisone) (see Table 3).^{1,10} Povidone-iodine is another ingredient found in various douche formulations, which may have bactericidal and fungicidal properties. Because of the potential risks of excessive douching, this may not be a preferred product. Frequent douching can reduce the amount of normal flora and increase a patient's risk of developing VVC, bacterial vaginosis, as well as other gynecological problems. Vitamin A, D, E and aloe vera are additional ingredients that may be found in combination products that relieve the symptoms associated with vaginal irritation.

Complementary therapies

Alternative therapies, such as boric acid, *Lactobacillus acidophilus* and homeopathic remedies also may have benefit in treatment of itching and irritation associated with VVC infection. Lactobacillus is a pro-

biotic, which is a micro-organism that has activity against pathogens living within the body. In VVC infection, lactobacillus works by re-establishing normal vaginal flora and inhibiting overgrowth of *Candida*. Lactobacillus can be found in oral supplements or in dietary sources, such as yogurt with live cultures or milk fortified with lactobacillus. Because of limited studies, there is conflicting data on

participants in these studies, the clinical significance remains questionable.

Additional research is warranted before specific recommendations for use of lactobacillus can be made. In the meantime, clinicians should explain to patients that lactobacillus is part of the normal vaginal flora and although it may not prevent infection, it will not be harmful and it can re-establish the normal flora. Homeopathic

products also are available for the relief of symptoms associated with VVC or noninfectious vaginal irritation. Homeopathic medicine uses the theory of treating certain conditions with very small diluted doses of similar natural substances. Because of the limited data on the benefits and safety of these products, patients should use the same precautions when using homeopathic remedies as with other natural vaginal preparations. Boric acid is a natural remedy that may provide benefit in the prevention of

recurrent VVC episodes and the associated symptoms of itching and irritation. Boric acid works to acidify the vagina and help restore natural lactobacillus by vaginally inserting a 600 mg suppository.⁸ Other ingredients found in boric acid preparations include such herbs as Oregon grape root and calendula, which may help with irritation, inflammation and repairing of the tissues of the vagina. Boric acid suppositories should not be used during pregnancy or on damaged or irritated skin.

Guaschino et al studied the use of boric acid in comparison with oral itraconazole in patients with recurrent VVC. The study concluded that there was no clinically sig-

TABLE 3
Selected products for vaginal itching and irritation

Ingredients	Brand
Benzocaine 5%, resorcinol 2%	Vagi-Gard Advanced Sensitive Cream
Benzocaine 20%, resorcinol 3%	Vagi-Gard Maximum Strength Cream
Benzocaine, benzalkonium chloride	Vagi-Gard cream
Hydrocortisone 0.5%	Massengill Towelette
Hydrocortisone 1%	Gynecort Cream
Povidone-iodine 0.3%	Betadine Douche; Massengill Douche; Summer's Eve Douche
Pulsatilla, <i>Candida Albicans</i> , <i>Candida Parapsilosis</i> ¹	Yeast-Gard suppository
Natrum Muriaticum, <i>C. Albicans</i> , Kreosotum, Carboilic Acidum	Hyland's Vaginitis
Boneset, Mistletoe Leaf containing <i>Lactobacillus Sporogenes</i> ¹	Azo Yeast
Boric Acid, Oregon Grape Root, Calendula	Yeast Arrest
Cornstarch, aloe, mineral oil	Summer's Eve Feminine Powder; Vagisil Feminine Powder

1. Indicated for the relief of symptoms associated with VVC

whether lactobacillus taken prophylactically can prevent a VVC infection.

A study by Pirota et al researched the effects of lactobacillus in the prevention of post-antibiotic VVC.¹⁴ Participants took a 10-day course (six days during antibiotic treatment and four post-treatment) of either oral or vaginal lactobacillus or placebo. Symptoms of post-antibiotic VVC and microscopic evaluation of VVC were the primary outcome measurements at day 14. Overall, the use of lactobacillus was not supported by this study, and more patients would be required to detect any significant differences among the treatment groups.¹³ Other studies have shown some benefit. However, because of the small number of

nificant difference among treatment groups with respect to symptomatic improvement and mycological cure rates.¹⁵

The authors did observe relapse of VVC infection following treatment discontinuation in both groups, which is common in patients with recurrent

episodes. Tea tree oil, cinnamon, carvacrol and garlic are examples of herbs that may provide benefit to women with VVC infection. When counseling on natural or herbal remedies, clinicians should explain to patients that these products are not evaluated by the FDA and are not meant to treat, prevent or cure disease.

PATIENT COUNSELING

Prevention and appropriate administration of non-prescription medications is an important part of the management of VVC episodes (see Table 4). When patients are using these preparations, clinicians should reiterate to patients that they should not rely on condoms, diaphragms or other barrier devices as they can weaken their effectiveness. It is advised that patients abstain from sexual intercourse during treatment of VVC infection. It also is recommended that patients avoid the use of tampons during treatment, as they may absorb medication and decrease product efficacy. This may cause the patient to have recurrent episodes and require additional therapy. Patients should be encouraged to wear pads to avoid vaginal leakage and soiling of undergarments that can occur with cream formulations. Medication should never be doubled, but used immediately if a dose is missed or skipped if it's close to the next dose. When using the non-prescription antifungals for uncomplicated VVC infection, patients should continue the medication even if symptoms resolve quickly. In addition, patients should be counseled that their symptoms may worsen before they get better because of the side effects that mimic VVC. If being treated for recurrent VVC infection, patients should adhere to their regimen and

TABLE 4
Use of vaginal antifungal products

1. Wash hands
2. Fill applicator with cream or ovule OR use prefilled applicator with cream
3. Place applicator tip into vagina
4. Depress plunger until all cream or ovule is released from applicator
5. Throw away applicator OR wash reusable applicator
6. Wash hands

complete their entire course of therapy even if they don't present with symptoms.

Tips for prevention of future cases include avoidance of tight clothing, synthetic undergarment materials and/or pantyhose for long periods of time, as all of these can cause irritation to the vaginal area. Patients should thoroughly dry the vaginal region after showering or swimming and immediately change out of wet clothes to prevent a favorable environment for yeast. Counseling also should include avoidance of douching, scented tampons or other vaginal hygiene products. Appropriate hygiene should be encouraged, including wiping from front to back and cleansing the area regularly.

CONCLUSION

Vaginitis presents with a variety of symptoms, and clinicians should be educated on the types of infection, risk factors, management and prevention. In patients presenting with a foul-smelling discharge and greater than or equal to four specific episodes per year or an episode within two months of a previous treatment evaluation must consider the potential for bacterial

vaginosis, trichomoniasis or other gynecological problems. Although VVC is a form of vaginitis that currently is not considered sexually transmitted, women should avoid intercourse if they suspect infection. A first infection should always be medically diagnosed

prior to treatment with OTC medications, and those who are pregnant or have underlying medical conditions should consult with their primary care provider.

The primary treatment of choice for the management of sporadic VVC is the non-prescription azole antifungals. Product selection should be based on cost, duration of treatment, formulation and ease of administration. Overall, there are no differences in efficacy among the one-, three- and seven-day treatment courses, and numerous studies have concluded that treatment duration can be based on patient convenience. Patients should follow proper medication guidelines to ensure optimal absorption or efficacy. Noninfectious vaginal irritation and itching also can be relieved with non-prescription ingredients, but should not be used for more than seven days. Although not a proven benefit, use of lactobacillus and yogurt with live cultures for prevention of VVC infection may provide some relief for patients who are at high risk. This may include those with antibiotic ingestion, uncontrolled diabetes or altered immune system.

PRACTICE POINTS

VVC is a form of vaginitis characterized by an odorless, white, curd-like discharge with internal and external vaginal itching and irritation.

VVC is classified as sporadic (< two episodes yearly) and recurrent (> four episodes yearly) or reinfection within two months.

Risk factors for VVC infection include underlying disease states, lifestyle, habits, antibiotic use, hormonal changes, age and sexual activity.

The four main ingredients found in OTC products for VVC infection include butocanazole, miconazole, clotrimazole and tioconazole.

Nonpharmacological management includes avoidance of scented vaginal hygiene products, douching and tight, wet or damp clothing.

Diagnosis and treatment of vulvovaginal candidiasis

Learning Assessment

Successful completion of "Diagnosis and treatment of vulvovaginal candidiasis" is worth 1.5 contact hours of credit. To obtain credit, answer the following questions and complete the evaluation online at www.retailclinician.com.

- 1. Complications of recurrent VVC infection include which of the following?**

 - Increased risk of HIV transmission
 - Pelvic inflammatory disease
 - Vulvar scarring and lesions
 - Preterm labor
- 2. A 30-year-old pregnant female presenting with two VVC episodes this year and more than two months apart would be classified as having which type of VVC?**

 - Primary sporadic
 - Secondary sporadic
 - Primary recurrent
 - Secondary recurrent
- 3. Which of the following patients requires clinical intervention for VVC infection?**

 - Female < 12 years of age
 - Pregnancy and breastfeeding
 - No relief within seven days of treatment
 - All of the above
- 4. A patient prescribed warfarin should avoid which vaginal azole antifungal?**

 - Butoconazole
 - Miconazole
 - Clotrimazole
 - Tioconazole
- 5. The CDC recommends which preparation for use in pregnant women?**

 - 1-day
 - 3-day
 - 7-day
 - Any of the above would be appropriate
- 6. The recommended time frame for the treatment of recurrent VVC infection following resolution of an acute episode is _____ months?**

 - three
 - six
 - nine
 - 12
- 7. Which nonprescription antifungal ingredient has also shown benefit in the treatment of recurrent VVC infection?**

 - Butoconazole
 - Miconazole
 - Clotrimazole
 - Tioconazole
- 8. Which of the following nonprescription ingredients has shown to have bacterial and fungicidal properties in the relief of symptoms associated with noninfectious vaginal irritation?**

 - Resorcinol
 - Benzocaine
 - Povidone-iodine
 - Hydrocortisone
- 9. Patients should be counseled to avoid which of the following during treatment of VVC infection due to the mineral oil content of antifungal products?**

 - Use of scented hygiene products
 - Use of tampons
 - Use of condoms
 - Use of douches
- 10. Which of the following nonpharmacological counseling points should be included in the prevention of VVC infection?**

 - Immediately change out of wet clothes
 - Avoid synthetic undergarments
 - Appropriate cleansing of the vaginal area
 - All of the above

¹Pray WS. Female Genital Conditions. In *Nonprescription Product Therapeutics*. Lippincott: Philadelphia, PA. Second edition. Chapter 23. ²Nyirjesy P. Chronic Vulvovaginal Candidiasis. *Am Fam Physician* 2001;63:697-702. ³National Institute of Allergy and Infectious Diseases (NIAID). US Department of Health and Human Services. Vaginitis Due to Vaginal Infections: NIAID Fact Sheet. October 2004. Available at www.niaid.nih.gov Accessed June 2006. ⁴Centers for Disease Control and Prevention (CDC). Sexually Transmitted Diseases Treatment Guidelines 2002: Disease Characterized by Vaginal Discharge. Available at www.cdc.gov Accessed June 2006. ⁵Mitchell H. Vaginal discharge-causes, diagnosis, and treatment. *BMJ* 2004;328:1306-1308. ⁶Ching S. vaginitis. eMedicine. November 25, 2004. Available at www.emedicine.com Accessed on June 2006. ⁷Samra O. Vulvovaginitis. eMedicine. July 20, 2005. Available at www.emedicine.com Accessed on June 2006. ⁸Ringdahl EN. Treatment of Recurrent Vulvovaginal Candidiasis. *Am Fam Physician* 2000;61:3306-12. ⁹Leon E, Jacober SJ, Sobel JD, et al. Prevalence and risk factors for vaginal Candida colonization in women with type 1 and type 2 diabetes. *BMC Infectious Diseases* 2002;2:1 ¹⁰Shimp LA. Vaginal and Vulvovaginal Disorders. In: *Handbook of Nonprescription Drugs*. 14th Ed. Washington D.C., American Pharmaceutical Association (APHA) 2002: Chapter 8. ¹¹Women's Healthcare Topics. Yeast Infection Diagnosis and Treatment. 2004-2006 Available at www.womenshealthcare-topics.com Accessed on June 2006. ¹²Upmalis DH, Cone FL, Lamia CA, et al. Single-dose miconazole nitrate vaginal ovule in the treatment of VVC: two single-blind, controlled studies versus miconazole nitrate 100mg cream for 7 days. *J Womens Health Gen Based Med* 2000;9(4):421-429. ¹³Sobel JD, Brooker D, Stein GE, et al. Single oral dose fluconazole compared with conventional clotrimazole topical therapy of Candida vaginitis. Fluconazole Vaginitis Study Group. *Am J Obstet Gynecol* 1995;172(4 Pt 1):1263-8. ¹⁴Pirotta M, Gunn J, Chondros P, et al. Effect of lactobacillus in preventing post-antibiotic vulvovaginal candidiasis: a randomized controlled trial. *BMJ* 2004;329:548-553. ¹⁵Guaschino S, De Seta F, Sartore A, et al. Efficacy of maintenance therapy with topical boric acid in comparison with oral itraconazole in the treatment of recurrent vulvovaginal candidiasis *Am J Obstet Gynecol*. 2001;184(4):598-602.