**Required Reading**

**Textbook – 19\textsuperscript{th} edition:**

**Vaginal and vulvovaginal disorders (Chapter 8) ★**

- Table 8-1: Differentiation of Common Vaginal Infections
- Figure 8-1: Self-care for vulvovaginal candidiasis
- Table 8-3: Guidelines for Applying Vaginal Antifungal Products
- Patient education box for vulvovaginal candidiasis
- Figure 8-2: Self-care for atrophic vaginitis
Learning Objectives

- Differentiate vulvovaginal candidiasis from other common vaginal infections
- Summarize the key clinical presentation features of genitourinary syndrome of menopause
- Describe the *mechanism of action, efficacy, adverse effects, and cautions/contraindications/interactions* for nonprescription products to self-treat the above conditions
- Explain the possible adverse outcomes associated with the practice of douching
Learning Objectives (continued)

· *Given a patient presenting with vaginal symptoms:*
  · Determine whether the patient is an appropriate candidate for self-treatment
  · Design an appropriate non-prescription treatment plan
  · Provide applicable patient education
Background: Vaginal Environment

- Vagina is a dynamic ecosystem that is colonized by many organisms
- This ecosystem is impacted by several variables:
  - Number and types of endogenous organisms, vaginal pH, glycogen concentration, hormonal fluctuations, drug therapy, douching, sex partners
  - *Lactobacillus* species account for 95% of the vaginal flora
    - These bacteria convert glycogen to lactic acid which helps to maintain a normal acidic vaginal pH of 4-4.5
- Normal vaginal discharge is odorless, clear to white, and of high viscosity
- Secretions are important in cleansing the vaginal tract
Vaginitis Caused by Infection
Common Causes of Vaginitis

- Bacterial Vaginosis (BV) – 33%
- Vulvovaginal Candidiasis (VVC) – 20 to 25%
- TrichomonIASis – 15 to 20%
Other Causes of Vaginal Discharge or Irritation

- Normal physiologic variation
- Allergic reactions
- Herpes simplex virus
- Mucopurulent cervicitis
- Atrophic vaginitis
- Vulvar vestibulitis
- Foreign bodies
- Desquamative inflammatory vaginitis
Differentiation of Common Vaginal Infections

- Important to distinguish VVC from BV and trichomoniasis
  - VVC can be treated with nonprescription vaginal antifungal
  - BV and trichomoniasis require prescription treatment

- Inappropriate use of vaginal antifungal products can lead to:
  - Unnecessary drug use
  - Delay in effective treatment

- Characteristic symptoms can often help us to distinguish infections
JG is a 28 year old woman who presents to the pharmacy seeking nonprescription treatment for her vaginal symptoms. She reports that she started experiencing vaginal itching and irritation yesterday. She also notes that she is having a lot more discharge than usual and it is yellow-green in color.

Based on these symptoms, what is the most likely cause of the patient’s vaginitis?

a. Bacterial vaginosis
b. Trichomoniasis
c. Genitourinary syndrome of menopause
d. Vulvovaginal candidiasis
## Differentiation of Common Vaginal Infections

<table>
<thead>
<tr>
<th></th>
<th><strong>Bacterial Vaginosis</strong></th>
<th><strong>Trichomoniasis</strong></th>
<th><strong>Candidiasis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Etiology</strong></td>
<td>Polymicrobial resulting from imbalance in normal vaginal flora</td>
<td><em>Trichomonas vaginalis</em></td>
<td><em>Candida</em> species (primarily <em>C. albicans</em>) and <em>Saccharomyces</em></td>
</tr>
<tr>
<td><strong>Symptom presentation</strong></td>
<td>Odor, discharge, itch</td>
<td>Itch, discharge, ~50% asymptomatic</td>
<td>Itch, discomfort, dysuria, thick discharge</td>
</tr>
<tr>
<td><strong>Vaginal discharge</strong></td>
<td>Homogenous, adherent, thin, off-white or discolored, sometimes foamy, unpleasant “fishy” odor</td>
<td>Copious, malodourous, yellow-green, frothy</td>
<td>Thick, clumpy, white “cottage cheese”</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td>New sexual partner, African American race, use of IUD, douching, sexual practices, tobacco use, prior pregnancy</td>
<td>Multiple sex partners, new sexual partner, nonuse of barrier contraceptives, presence of other STIs</td>
<td>Medications such as antibiotics and immunosuppressants; no identifiable cause for most infections</td>
</tr>
</tbody>
</table>

IUD, intrauterine device; STI, sexually transmitted infection
Diagnosis

- Patient history
- Visual inspection of internal/external genitalia
- Appearance of discharge
- Collection and evaluation of specimen
  - Saline wet mount, KOH and whiff test, vaginal pH
Vulvovaginal Candidiasis (VVC)
Epidemiology

- Estimated that 70 to 75% of women will experience at least one episode of VVC
- Highest incidence during the reproductive years
- Most cases caused by *C. albicans* (85 to 95%)
Pathogenesis

**Microbiology**

- Disruption of host vaginal environment
- *Candida* organisms transition from a commensurate to pathologic role
  - *Candida* species are not considered to be sexually transmitted pathogens
- Symptomatic clinical infection occurs with excessive growth of yeast

**Predisposing Factors**

- Pregnancy
- High-dose combined oral contraceptives
- Estrogen therapy
- History of diabetes
- Recent use of systemic antibiotics
- Immunosuppression
Clinical Presentation and Symptoms

- Vulvar pruritus is most common symptom
- Thick, white, curdy vaginal discharge ("cottage cheese-like")
- Erythema, irritation, occasional erythematous "satellite" lesions
- External dysuria and dyspareunia
- Normal vaginal pH (3.8 to 4.5)
ML is a 32-year-old woman who presents to the pharmacy seeking treatment for her vaginal symptoms. She reports vaginal itching and white “cottage-cheese” like discharge. She had these same symptoms 12 months ago and was seen by a medical provider who diagnosed her with VVC. She has no significant PMH. She takes a daily multivitamin and had Nexplanon® implanted 2 years ago.

How would you classify this patient’s VVC?

a. Complicated
b. Uncomplicated
c. Recurrent
d. Severe
## Classification of VVC

<table>
<thead>
<tr>
<th>Uncomplicated</th>
<th>Complicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Sporadic or infrequent</td>
<td>- Recurrent VVC</td>
</tr>
<tr>
<td>- Mild-to-moderate symptoms</td>
<td>- Severe symptoms (edema, excoriation/fissure formation)</td>
</tr>
<tr>
<td>- Likely to be <em>C. albicans</em></td>
<td>- Non-albicans candidiasis</td>
</tr>
<tr>
<td>- Non-immunocompromised women</td>
<td>- VVC in women who are pregnant, have uncontrolled diabetes, or are immunosuppressed</td>
</tr>
</tbody>
</table>

Responds to short course regimen

Should be evaluated by healthcare provider. May require longer duration of treatment and/or systemic treatment
Treatment Goals

- Relieve patient symptoms
- Eradicate infection
- Reestablish normal vaginal flora
Exclusions For Self-Treatment

- Pregnancy
- Girls <12 years of age
- Concurrent symptoms: fever or pain in the pelvic area, lower abdomen, back, or shoulder
- Medications that can predispose to VVC: corticosteroids, antineoplastics
- Medical disorders that can predispose to VVC: diabetes, HIV infection
- Recurrent VVC (>3 episodes per year or vaginal infection in past 2 months)
- First vulvovaginal episode
### Treatment: Nonprescription Pharmacologic Therapy

- **Vaginal Antifungals** - recommended for initial therapy for uncomplicated VVC and relief of external vulvar itching and irritation associated with infection

<table>
<thead>
<tr>
<th>Class</th>
<th>• Imidazoles</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOA</td>
<td>• Alter fungi membrane permeability through decreased synthesis of the fungal sterol ergosterol</td>
</tr>
<tr>
<td>OTC drugs</td>
<td>• Clotrimazole, miconazole, and tioconazole</td>
</tr>
<tr>
<td>Dosage Forms</td>
<td>• Vaginal cream, vaginal suppositories, and vaginal tablets</td>
</tr>
</tbody>
</table>
## Selected Nonprescription Products

<table>
<thead>
<tr>
<th>Primary Ingredient</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clotrimazole Products</strong></td>
<td></td>
</tr>
<tr>
<td>Cream: Clotrimazole 1%</td>
<td>Insert cream into vagina daily for 7 days; apply to vulva twice daily as needed for itching</td>
</tr>
<tr>
<td>Tablet: Clotrimazole 100 mg Cream: Clotrimazole 1%</td>
<td>Insert tablet into vagina daily for 7 days; apply cream to vulva twice daily as needed for itching up to 7 days</td>
</tr>
<tr>
<td>Cream: Clotrimazole 2%</td>
<td>Insert cream into vagina daily for 3 days; apply to vulva twice daily for itching</td>
</tr>
<tr>
<td><strong>Miconazole Products</strong></td>
<td></td>
</tr>
<tr>
<td>Cream: miconazole 2% cream Supp: miconazole 1200 mg</td>
<td>Apply cream to vulva twice daily as needed for itching up to 7 days; insert suppository into vagina daily for 1 day</td>
</tr>
<tr>
<td>Cream: miconazole 2% cream Supp: miconazole 200 mg</td>
<td>Apply cream to vulva twice daily as needed for itching up to 7 days; insert suppository into vagina daily for 3 days</td>
</tr>
<tr>
<td>Cream: miconazole 2% Supp: miconazole 100 mg</td>
<td>Apply cream to vulva twice daily as needed for itching up to 7 days; insert suppository into vagina daily for 7 days</td>
</tr>
<tr>
<td>Cream: miconazole 4%</td>
<td>Insert cream into vaginal daily for 3 days; apply to vulva twice daily as needed for itching</td>
</tr>
<tr>
<td><strong>Tioconazole Products</strong></td>
<td></td>
</tr>
<tr>
<td>Ointment: tioconazole 6.5%</td>
<td>Insert ointment into vagina daily for 1 day</td>
</tr>
</tbody>
</table>
Examples of Nonprescription Products
Side effects are uncommon and generally mild

- Vulvovaginal burning, itching, and irritation (3-7%)
  - More likely to occur with initial application
  - May be dose-related
- Penile irritation and allergic reactions (3-7%)
- Abdominal cramps (3%)
- Headache (9%)

Creams and suppositories in these regimens are oil-based and may weaken latex condoms and diaphragms. Refer to condom product labeling for further information.
Drug-Drug Interactions

- Limited systemic absorption
- Possible drug-drug interaction between miconazole suppositories and warfarin
  - Both metabolized by CYP2C9
  - Increased risk for bleeding
Product Selection: Special Populations

- Pediatrics (<12 years) – exclusion for self-treatment
- Pregnant women – exclusion for self-treatment
- Lactating women – miconazole or clotrimazole
- Older adults – treat same as other adults
Product Selection Considerations

- **Pharmacotherapeutic Comparison:**
  - Studies have shown imidazoles to be equally effective (~80-90% effectiveness rates)
  - Single-dose and 7-day treatments have shown similar overall cure rates. However, faster symptom relief with single-dose group
Product Selection Considerations

- **Pharmacotherapeutic Comparison:**
  - Studies have shown imidazoles to be equally effective (~80-90% effectiveness rates).
  - Single-dose and 7-day treatments have shown similar overall cure rates. However, faster symptom relief with single-dose group.
Administration – refer to guidelines for administering vaginal antifungal products (Table 8-3)

- For women who have external vulvar symptoms in addition to vaginal symptoms, external topical application of cream is usually beneficial.
Patient Education

When to seek further medical attention:

- Symptoms persist > 1 week after treatment
- Symptoms recur within 2 months
- Vaginal symptoms worsen or change
Patient Education

Relief of symptoms:
- Within **3 days** but may take a week for complete resolution
- Important to complete full course of treatment even if symptom relief is sooner
Patient Education

Miscellaneous -- refer to Patient Education box:

- Tampon use
  - “How long do I need to wait to use a tampon after taking a vaginal medication?”
  - Response: ________________________________

- Menstrual period
  - “What should I do if I start my menstrual period while taking a vaginal medication?”
  - Response: ________________________________

- Sexual intercourse
  - “Is it okay to have sex while using a vaginal medication?”
  - Response: ________________________________
Treatment: Nonpharmacologic Measures

- **Sodium bicarbonate sitz bath**
  - May provide quick, temporary relief of vulvar irritation

- **For recurrent infections**
  - Yogurt (1 cup per day of live culture yogurt)
  - Decrease dietary sugar and refined carbohydrates

1. Add 1 teaspoon sodium bicarbonate to 1 pint of water.
2. Add 2–4 tablespoons of the solution to 2 inches of bath water.
3. Sit in the sitz bath or bathtub for 15 minutes as needed for symptom control.
Other Nonprescription Vaginal Preparations

**Products**

- **Benzocaine Products**
  - Vagisil Anti-Itch – Benzocaine 5%; resorcinol 2%
  - Vagisil Maximum Strength – Benzocaine 20%; resorcinol 3%

- **Hydrocortisone Products**
  - Cortizone-10 Feminine Relief – Hydrocortisone 1%

**Patient education**

- May provide relief of itching but **DO NOT** treat the underlying cause
- Generally not recommended given benefits of imidazole antifungals
Complementary Therapies

- **Lactobacillus preparations**
  - Proposed mechanism: reestablish normal vaginal flora and inhibit overgrowth of *Candida* organisms
  - Data on effectiveness is limited and inconsistent

- **Vaginal tea tree oil**
  - Proposed mechanism: antibacterial and antifungal properties
  - Effectiveness not established
  - Allergic dermatitis may occur

- **Gentian violet**
  - A tampon may be soaked in dye and inserted into the vagina for several hours or overnight
  - Sometimes used for resistant *Candida* infections

- **Boric acid vaginal suppository**
  - May be useful for non-*C. albicans* infections
  - Can be compounded in community pharmacies
  - Pregnant women should not use
Atrophic Vaginitis now Genitourinary Syndrome Of Menopause (GSM)
Genitourinary Syndrome of Menopause (GSM)

- Board of Directors of the International Society for the Study of Women’s Sexual Health and Board of the North American Menopause Society (NAMS) approved change of terminology from vulvovaginal atrophy and atrophic vaginitis in 2014

- Vaginal atrophy can lead to genital, sexual, and urinary symptoms
  - GSM terminology better describes vaginal atrophy and its accompanying symptoms
Atrophic vaginitis occurs secondary to:

a. Excess douching
b. Decreased estrogen levels
c. Oral contraceptive use
d. Pelvic inflammatory disease
Pathophysiology

- Decreased estrogen levels lead to decreased vaginal lubrication and thinning of the vaginal epithelium
- Primarily occurs in postmenopausal women
  - Up to 45% of postmenopausal women may experience symptoms, but only 25% may seek treatment
- Can also occur in women who may have decreased estrogen from other causes:
  - Postpartum period, breastfeeding
  - Decreased ovarian estrogen production
  - Drugs (antiestrogenic drugs, aromatase inhibitors)
Clinical Presentation

Vaginal & Sexual Symptoms

- Vaginal dryness – most common
- Dyspareunia
- Vaginal irritation
- Itching
- Vaginal tenderness
- Vaginal bleeding/spotting during intercourse

Urinary Symptoms

- Dysuria
- Urgency
- Frequency
- Nocturia
- Urinary incontinence
- Recurrent urinary tract infection
Treatment Goals

- Reduce symptoms
  - Vaginal dryness
  - Burning
  - Itching
- Reduce dyspareunia
Exclusions for Self-Treatment

- Symptoms of severe vaginal dryness, dyspareunia, or bleeding
- Symptoms that are not localized
- Vaginal dryness or dyspareunia not relieved by vaginal moisturizers or lubricants
Treatment: Vaginal Moisturizers & Lubricants

- Vaginal moisturizers and lubricants can be used to relieve symptoms by temporarily moistening the vaginal tissues
- Multiple water-soluble products available
- Can be applied both externally and internally
- Quantity and frequency of use can be tailored to specific patient needs
## Comparison of Moisturizers and Lubricants

<table>
<thead>
<tr>
<th></th>
<th>Moisturizers</th>
<th>Lubricants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing:</strong></td>
<td>Typically used on a chronic basis</td>
<td>Typically used with sexual activity</td>
</tr>
<tr>
<td><strong>Ingredients:</strong></td>
<td>Generally contain active ingredients like polycarbophil</td>
<td>Usually water-based or silicone-based</td>
</tr>
<tr>
<td><strong>Administration:</strong></td>
<td>Inserted into upper vagina and releases water and electrolytes into vaginal epithelium</td>
<td>Designed to be applied directly to genitals of both partners at time of sexual activity</td>
</tr>
<tr>
<td><strong>Duration:</strong></td>
<td>One application may provide benefit for 2-3 days</td>
<td>Silicone-based products last longer than water-based products</td>
</tr>
<tr>
<td><strong>Example products:</strong></td>
<td>Replens®</td>
<td>Water-based:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- K-Y Jelly®, Astroglide®</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Silicone-based:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- K-Y Liquibeads®</td>
</tr>
</tbody>
</table>
## Patient Assessment Using QuEST SCHOLAR

<table>
<thead>
<tr>
<th>QUickly and accurately assess the patient</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
<td>Are the symptoms stable or changing?</td>
</tr>
<tr>
<td><strong>History</strong></td>
<td>What has the patient done so far to try to relieve the symptoms?</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>When did the condition start? Is the patient peri- or post-menopausal? Recent childbirth? Breastfeeding? New medications?</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>Where are the symptoms? Localized to vagina?</td>
</tr>
<tr>
<td><strong>Aggravating factors</strong></td>
<td>What makes it worse? Sexual intercourse?</td>
</tr>
<tr>
<td><strong>Remitting factors</strong></td>
<td>What makes it better?</td>
</tr>
<tr>
<td><strong>Establish that the patient is an appropriate self-care candidate</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Suggest appropriate self-care strategies</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Talk with the patient</strong></td>
<td></td>
</tr>
</tbody>
</table>
Patient Education

- **Duration of symptoms**
  - Postpartum or breastfeeding → short-term
  - Perimenopausal or postmenopausal → long-term treatment may be necessary

- **When to expect relief of symptoms**
  - May be apparent within hours after first dose
  - Typically improve within a few days

- **Miscellaneous**
  - Some leakage of the product may occur and a sanitary napkin or panty liner can be used if desired

- **When to seek medical attention**
  - If no response within one week
  - Worsening symptoms (or vaginal bleeding)
Douching
Prevalence of Douching

- Centers for Disease Control and Prevention (CDC) reports that about 1 in 5 women practice douching.

- Most frequently stated reason for douching is to achieve good vaginal hygiene.
Potential Adverse Effects of Douching

- Local irritation and/or sensitization from ingredients
- Pelvic inflammatory disease
- Reduced fertility
- Ectopic pregnancy
- Bacterial vaginosis
- Sexually transmitted infections
- Preterm delivery
- Cervical cancer
Patient Education

- Douching is unnecessary
- Douching has many potential adverse effects
- Contraindicated during pregnancy
- Should be delayed at least 6-8 hours after sexual intercourse if vaginal spermicide was used as contraceptive agent
Case Study

LF is a 55-year-old woman who comes to the pharmacy to pick up her prescription for venlafaxine ER 75 mg once daily for hot flashes. While counseling the patient, you inquire about other menopausal symptoms. The patient reports that sexual intercourse has been more painful over the last several months and overall her vagina feels dry and irritated.

Which of the following options would be the most appropriate recommendation at this time?

a. Recommend vaginal moisturizer (Replens®) three times weekly and vaginal lubricant (Astroglide®) before sexual intercourse

b. Recommend miconazole 4% cream intravaginally for 3 days and vaginal lubricant (Astroglide®) before sexual intercourse

c. Recommend vaginal lubricant (K-Y Jelly®) applied 4 to 5 times daily and before sexual intercourse

d. Refer patient to primary care provider for further evaluation
References


