

Conquering Resistant Vulvovaginitis

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Learning Objectives

At the end of this presentation, the participant will:

- Understand “itis” versus “osis”
- Understand the various forms of vaginitis
- Be comfortable diagnosing and treating recurrent/resistant vaginitis
- Recognize unusual conditions that resemble vaginitis

I have no relevant financial relationships with any commercial interest relative to the subject of this lecture.

Vaginitis is a common problem seen daily in different care provider's offices. It accounts for over 10,000,000 office visits each year. The most prevalent infections are bacterial vaginosis (50%), candidiasis (30%) and trichomoniasis (20%). Less common causes of vaginitis include, foreign body, desquamative inflammatory vaginitis, and streptococcal vaginitis (very uncommon). Other conditions that cause vaginitis symptoms include collagen vascular disease, Behçet's syndrome, pemphigus and idiopathic conditions. The patient with chronic vaginitis is often frustrated, encounters difficulty in personal relationships, may suffer economic losses and at times, develops depression. A sense of hopelessness may exist.

NORMAL INHABITANTS OF THE LOWER GENITAL TRACT

Lactobacillus	Klebsiella
Corynebacterium	Prevotella
Diphtheroids	Peptostreptococcus
Enterococcus	Eubacterium
Escherichia	Proteus enterobacteria
Staphylococcus	Fusobacterium
Streptococcus	Morganella bacteroides

Pelvic examination

The pH of the vaginal discharge can easily and inexpensively be determined using pH strips. The pH paper should range from 3.5 to 7.0. The sample should be obtained approximately one third to midway down the lateral vaginal wall. It should not be contaminated with cervical mucus (pH=7.0). An aliquot of the diluted vaginal discharge should be examined microscopically (40x magnification). A drop or two of the discharge should be mixed with a drop of concentrated potassium hydroxide and whiffed to detect the presence of amines ("whiff test"). A positive test is detected by the presence of a fish-like odor which indicates the presence of bacterial vaginosis and/or anaerobes. The same specimen should be examined microscopically for the presence of fungal hyphae and/or budding yeast cells, which are resistant to alkali.

Potential causes for elevated vaginal pH include menses, heavy cervical mucus, semen, ruptured membranes, hypoestrogenism, trichomoniasis, bacterial vaginosis, foreign body with infection, Streptococcal vaginitis (group A) (rare), desquamative inflammatory vaginitis.

Bacterial vaginosis.

Various terms have existed throughout time for bacterial vaginosis. These include non-specific vaginitis, Hemophilus vaginitis, Corynebacterium vaginitis, Gardnerella vaginalis vaginitis, and anaerobic vaginosis. Bacterial vaginosis represents a complex change in vaginal flora. It is characterized by a reduction in the prevalence and concentration of hydrogen peroxide producing lactobacilli and an increase in the prevalence and concentration of Gardnerella vaginalis (found in 40% of women normally, found in 95% of women with bacterial vaginosis), mobiluncus species, Mycoplasma hominis, anaerobic gram negative rods belonging to the genera prevotella, porphyromonas, bacteroides, and peptostreptococcus species. Treatment of bacterial vaginosis (BV) is based on the understanding that it is not a disease but an unbalance of the vaginal ecosystem. This is an important concept because the imbalance is not due to a single bacterium or pathogen, but a disturbance in the ecosystem that allows the non-dominant symptom causing bacteria to become dominant.

The patient presents with a foul, "fishy" odor, more noticeable following intercourse and during menses. There is an increased or different vaginal discharge. Vulvar itching and/or irritation are present. The undergarments are stained at times.

Bacterial vaginosis may be diagnosed with other laboratory methods such as the use of DNA probes. These are expensive, but may be useful to practitioners unable to perform microscopy. Cultures have been used at times, but they are not useful since they are positive in 40-60% of asymptomatic females.

A new technique that includes nucleic acid probes for high concentrations of G. Vaginalis has become available (Affirm VPIII Microbial Identification Test).

Etiology of vaginal odor in BV

- anaerobic bacteria concentrations increase 100-1000x with BV
 - anaerobic metabolism produces amines (cadaverine, putrescine, trimethylamine)
 - alkalinity volatilizes amines causing the sharp odor associated with BV

Treatment (from 2006 CDC STD Treatment Guidelines)

<http://www.cdc.gov/std/treatment/2006/toc.htm>

Recommended Regimens

Metronidazole 500 mg orally twice a day for 7 days

OR

Metronidazole gel, 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days

OR

Clindamycin cream, 2%, one full applicator (5 g) intravaginally at bedtime for 7 days

NOTE: Patients should be advised to avoid consuming alcohol during treatment with metronidazole and for 24 hours thereafter. Clindamycin cream and ovules are oil-based and might weaken latex condoms and diaphragms. Refer to condom product labeling for additional information.

Alternative Regimens

Clindamycin 300 mg orally twice a day for 7 days

OR

Clindamycin ovules 100 g intravaginally once at bedtime for 3 days

Studies are currently underway to evaluate the efficacy of vaginal lactobacilli suppositories in addition to oral metronidazole for the treatment of BV. No data support the use of non-vaginal lactobacilli or douching for the treatment of BV.

Follow-Up

Because recurrence of BV is not unusual, women should be advised to return for additional therapy if symptoms recur. A treatment regimen different from the original regimen may be used to treat recurrent disease. However, women with multiple recurrences should be managed in consultation with a specialist. One randomized trial for persistent BV indicated that metronidazole gel 0.75% twice per week for 6 months after completion of a recommended regimen was effective in maintaining a clinical cure for 6 months. (Sobel JD, Ferris D, Schwebke J, et al. Suppressive antibacterial therapy with 0.75% metronidazole vaginal gel to prevent recurrent bacterial vaginosis. *Am J Obstet Gynecol*;194:1283–9.)

Allergy or Intolerance to the Recommended Therapy

Intravaginal clindamycin cream is preferred in case of allergy or intolerance to metronidazole. Intravaginal metronidazole gel can be considered for patients who do not tolerate systemic metronidazole, but patients allergic to oral metronidazole should not be administered intravaginal metronidazole.

Multiple studies and meta-analyses have not demonstrated a consistent plan for treatment in pregnancy.

Recommended Regimens Pregnancy

Recommended Regimens for Pregnant Women

Metronidazole 500 mg orally twice a day for 7 days

OR

Metronidazole 250 mg orally three times a day for 7 days

OR

Clindamycin 300 mg orally twice a day for 7 days

30% of patients have BV recurrence within 3 months.

Treatment Guidelines for Recurrent/Resistant Bacterial Vaginosis

Management of acute BV symptoms during relapse may require a longer treatment period of 10-14 days. Switch the agent. There is debate about treatment of partners. Most clinicians do not treat the partners.

Long term success with twice weekly suppression with intravaginal metronidazole has been reported (yeast infections did occur however).

www.baylorcme.org/vaginosis/pres_pres.html

Probiotics for bacterial vaginosis have been recommended. Studies are currently being performed to investigate their effectiveness. Many have not found them to be helpful.

Trichomoniasis

Trichomoniasis typically presents with a copious discharge which may be foul smelling. The classic cervical appearance is known as the "strawberry appearance". The patient may complain of vaginal discomfort which may be characterized as a soreness or burning and dyspareunia. However, the patient may be asymptomatic.

The diagnosis is made by identifying trichomonads on microscopic examination of vaginal discharge. White blood cells are usually present as trichomonas typically causes an inflammatory reaction. The vaginal pH is markedly elevated, almost always above 5.0 and not infrequently above 6.0. Several culture-medium methods are available and probably equivalent. They should be incubated anaerobically, and growth is detected within 48 hours (95% sensitivity). It should be considered in patients with vaginitis in whom there is a markedly elevated pH, PMN excess, absence of motile trichomonads, and clue cells. Polymerase chain reaction methods are also used to aid in the diagnosis of trichomoniasis (90% sensitivity, 99.8% specificity).

Treatment

The 5-nitroimidazole group of drugs (metronidazole, tinidazole, and ornidazole) are the cornerstone of therapy. Metronidazole and Tinidazole are agents of choice in the United States currently. Oral therapy should be utilized to ensure adequate treatment of the urethra, periurethral glands (Skene's glands), and Bartholin's glands.

Treatment options (from 2006 CDC STD Treatment Guidelines):

Recommended Regimens

Metronidazole 2 g orally in a single dose

OR

Tinidazole 2 g orally in a single dose

Alternative Regimen

Metronidazole 500 mg orally twice a day for 7 days.

Follow-Up

Follow-up is unnecessary for men and women who become asymptomatic after treatment or who are initially asymptomatic. Some strains of *T. vaginalis* can have diminished susceptibility to metronidazole; however, infections caused by the majority of these organisms respond to tinidazole or higher doses of metronidazole. Low-level metronidazole resistance has been identified in 2%–5% of cases of vaginal trichomoniasis. High-level resistance is rare. Tinidazole has a longer serum half-life and reaches higher levels in genitourinary tissues than metronidazole. In addition, many *T. vaginalis* isolates have lower minimum inhibitory concentrations (MICs) to tinidazole than metronidazole.

If treatment failure occurs with metronidazole 2 g single dose and reinfection is excluded, the patient can be treated with metronidazole 500 mg orally twice daily for 7 days or tinidazole 2 g single dose. For patients failing either of these regimens, clinicians should consider treatment with tinidazole or metronidazole at 2 g orally for 5 days. If these therapies are not effective, further management should be discussed with a specialist. The consultation should ideally include determination of the susceptibility of *T. vaginalis* to metronidazole and tinidazole. Consultation and *T. vaginalis* susceptibility testing is available from CDC (telephone: 770-488-4115; website: <http://www.cdc.gov/std>).

Management of Sex Partners

Sex partners of patients with *T. vaginalis* should be treated. Patients should be instructed to avoid sex until they and their sex partners are cured (i.e., when therapy has been completed and patient and partner(s) are asymptomatic).

It is important to rule out an allergy to metronidazole prior to treatment.

Special Considerations

Pregnancy

Vaginal trichomoniasis has been associated with adverse pregnancy outcomes, particularly premature rupture of membranes, preterm delivery, and low birthweight. However, data do not suggest that metronidazole treatment results in a reduction in perinatal morbidity. Although some trials suggest the possibility of increased prematurity or low birthweight after metronidazole treatment, limitations of the studies prevent definitive conclusions regarding risks of treatment. Treatment of *T. vaginalis* might relieve symptoms of vaginal discharge in pregnant women and might prevent respiratory or genital infection of the newborn and further sexual transmission. Clinicians should counsel patients regarding the potential risks and benefits of treatment. Some specialists would defer therapy in asymptomatic pregnant women until after 37 weeks' gestation. In addition, these pregnant women should be provided careful counseling regarding condom use and the continued risk of sexual transmission.

Women may be treated with 2 g of metronidazole in a single dose. Metronidazole is pregnancy category B (animal studies have revealed no evidence of harm to the fetus, but no adequate, well-controlled studies among pregnant women have been conducted). Multiple studies and meta-analyses have not demonstrated a consistent association between metronidazole use during pregnancy and teratogenic or mutagenic effects in infants. Tinidazole is pregnancy category C (animal studies have demonstrated an adverse event, and no adequate, well-controlled studies in pregnant women have been conducted), and its safety in pregnant women has not been well-evaluated.

Refractory trichomoniasis

It is important to reconfirm the diagnosis in patients complaining of recurrent infection. The majority of patients who return with recurrence of symptoms are likely reinfections due to failure to treat all partners.

If treatment failure occurs with metronidazole 2 g single dose and reinfection is excluded, the patient can be treated with metronidazole 500 mg orally twice daily for 7 days or tinidazole 2 g single dose. For patients failing either of these regimens, clinicians should consider treatment with tinidazole or metronidazole at 2 g orally for 5 days. If these therapies are not effective, further management should be discussed with a specialist. The consultation should ideally include determination of the susceptibility of *T. vaginalis* to metronidazole and tinidazole. Consultation and *T. vaginalis* susceptibility testing is available from CDC (telephone: 770-488-4115; website: <http://www.cdc.gov/std>).

High-dose tinidazole for refractory Trichomoniasis has been utilized. Tinidazole is a 5-nitroimidazole used in other countries to treat *T. vaginalis* infections. There have been reports of patients allergic to metronidazole who are also allergic to tinidazole.

Dosage- Tinidazole (varies dependent on study regimen)-

Tinidazole- 500 mg po 4x/day plus 500 mg vaginally BID x 14 days

vs.

Tinidazole- 2g po bid x 14 days

vs.

Tinidazole- 500 mg po tid for 7 – 10 days

Reculture in 2 weeks

Side effects: malaise, metallic taste, anorexia, nausea and vomiting, abdominal pain, headache, dizziness, rash

Other drugs Another drug, furazolidone, a nitrofurantoin presently marketed in the United States for use against enteric bacteria and *Giardia lamblia*, has been investigated for effectiveness against *T. vaginalis* patient isolates. This drug was sold in the early 1950's under the trade name Tricofuran by Eaton laboratories. A recent study found furazolidone to be effective against several clinically metronidazole-resistant isolates. It may be a useful alternative therapy for metronidazole-resistant *T. vaginalis* infections and for patients allergic or sensitive to metronidazole. Finally, in patients who have an allergy to metronidazole an incremental dosing protocol (oral or intravenous) for women with severe vaginal Trichomoniasis and adverse reactions to metronidazole has been used.

- CDC susceptibility testing
- Division of STD Prevention

Vulvovaginal Candidiasis (VVC)

The incidence of mycotic vulvovaginitis is rising dramatically in the United States. There are over 13 million cases of vulvovaginal candidiasis annually in the United States. Seventy-five percent of all women will have at least one episode of vulvovaginal candidiasis. About half of those infected experience more than one episode, and some patients suffer relapse and recurrence over a period of many years. Five percent of women with vulvovaginal candidiasis will develop recurrent episodes. *Candida albicans* most often causes infections in the United States. It is a dimorphic fungus that forms both spores and mycelia. It is followed in infection rate by *C. glabrata* and *C. tropicalis*. Over the past two decades, an increasing trend in the number of vaginal infections attributable to yeasts other than *Candida albicans* has emerged. If the common

antifungal preparations used to treat yeast are ineffective, consideration should be given to culturing for a resistant strain of fungus. Recurrences are common. Predisposing factors include uncontrolled diabetes mellitus, steroid use, tight-fitting clothing/synthetic underwear, antibiotic use, increased frequency of coitus, "candy binges", and IUD use. Additionally, immune system alterations such as HIV/AIDS may be associated with a higher incidence and greater persistence of yeast infections. In patients with frequent yeast infections, consideration should be given to culturing specimens from sexual partners as well and giving appropriate antifungal therapy to them if positive cultures are obtained. Accurate diagnosis depends on culture techniques that will yield correct identification of the fungal pathogen(s).

Symptoms/Signs

The main symptoms and signs of candidiasis are discharge, itching, burning/irritation, erythema, edema and excoriation. Rarely is vulvar candidiasis seen without concomitant vaginal candidiasis. Not all patients have symptoms of yeast infection. The incidence of asymptomatic fungal carriage in the vagina is quoted as 8-12 percent.

Diagnosis

The acidity of vaginal secretions in candidiasis is usually within the pH range of 4.0-4.7. A wet mount preparation reveals spores of *C. albicans* which are uniform in size, isolated and almost always associated with hyphal-filaments. The spores of *C. glabrata* are of variable size (2-8 micrometers), spherical or ovoid, and usually smaller than a red cell. They are often grouped in clusters, although they may appear alone. Potassium hydroxide (10%-20%) preparation is often used to evaluate for yeast when they are not seen on saline prep. In this solution, pus cells and red blood cells dissolve. The branching, budding, and hyphal cell walls of *C. albicans* are easily visualized. Stained smears may also be used to diagnose *Candida*. Spores of *Candida* are strongly gram positive. The filaments are uniformly gram positive or have large gram positive granules.

Cultures should be obtained when symptoms are not explained on the wet prep or a patient presents with recurrent candidiasis. Some yeast forms may require as long as a month of incubation for detection (particularly with a small inoculum). Sabouraud's dextrose agar on modified Sabouraud's Difco mycobiotic media and Nickerson's media are satisfactory for growing *Candida* in an incubator or at room temperature, although identification of the species is not permitted. The most reliable differentiation of the species is provided by sugar fermentation reactions.

Treatments

It is necessary to consider removal or improvement of predisposing factors in the treatment of candidiasis. Numerous antifungal preparations are available. If these are ineffective, then consideration should be given to culturing for a resistant strain of fungus. Such infections may require topical application of gentian violet solution or boric acid (per vagina). With failure of topical therapies, oral preparations should be considered.

Topical Agents (First-line Therapy) for the Primary Treatment of Candidiasis

Drug	Formulation	Dosage
Butoconazole (Gynazole-1®)	2% vaginal cream	1 applicator (5 gm) vaginally x 1 day
Butoconazole (Femstat 3®, Mycelex-3®)	2% vaginal cream	1 applicator vaginally (5 gm) x 3 days
Clotrimazole (Mycelex 7®, Gyne-Lotrimin 7)	1% vaginal cream	1 applicator vaginally (5 gm) x 7 days
Clotrimazole vaginal insert (Gyne-Lotrimin 7®, Mycelex-7®)	100 mg vaginal tablet	1 tablet vaginally daily for 7 days
Clotrimazole vaginal insert (Mycelex G®)	100 mg vaginal tablet	2 tablets vaginally daily for 3 days
Clotrimazole (Mycelex G®)	500 mg vaginal tablet	1 tablet vaginally, once
Clotrimazole (Gyne-Lotrimin 3®)	2% vaginal cream	1 applicator vaginally for 3 days
	1% cream	1 applicator vaginally for 7 days
Clotrimazole (Gyne-Lotrimin 7®, Mycelex-7®)	100 mg supp +2% topical cream	1 supp daily for 7 days. Use cream externally as needed
Clotrimazole (Gyne-Lotrimin 7® combination pack)		
Clotrimazole (Lotrisone®)	clotrimazole.1% cream with betamethasone 0.5% vaginal cream	apply cream topically BID (maximum use 2-4 wks)
Miconazole (Monistat 7®)	2% vaginal cream	1 app. (5 gm) vaginally x 7 days
Miconazole (Monistat 7®)	100 mg vaginal supp.	1 supp. vaginally x 7 days
Miconazole (Monistat 3®)	200 mg vaginal supp.	1 supp. vaginally x 3 days
Miconazole (Monistat 7®)	Combination pack: 100 mg vaginal supp. and 2% topical cream	1 supp. vaginally x 7 days; apply cream twice daily (maximum use 2-4 wks)
Miconazole (Monistat 7®)	Combination pack: 2% cream. and 2% topical cream	1 app. of 2% cream for 7 days; apply cream twice daily (maximum use 2-4 wks)
Miconazole (Monistat 3®)	Combination pack: 200 mg vaginal supp. and 2% topical cream	1 supp. vaginally x 3 days; apply cream twice daily (maximum use 2-4 wks)
Miconazole (Monistat 3®)	Combination pack: 4% cream and 2% topical cream	1 app. of 4% cream for 3 nights; 2% cream bid topically (maximum use 2-4 wks)
Miconazole (Monistat 1®)	6.5% vaginal ointment	1 app. (4.6 gm) vaginally, once
Monistat 1 Combination Pack®	Ovule insert (miconazole nitrate 1200 mg) for vagina plus miconazole nitrate cream 2% for vulva	1 combination pack- use as directed
Tioconazole (Vagistat-1®)	6.5% vaginal ointment	1 app. (4.6 gm) vaginally, once
Terconazole (Terazol 7®)	0.4% cream	1 app. (5 gm) x 7 days
Terconazole (Terazol 3®)	0.8% cream	1 app. (5 gm) x 3 days
Terconazole (Terazol 3®)	80 mg vaginal supp	1 supp x 3 days
Econazole Nitrate (Spectazole®)	1% topical cream	Apply cream twice daily
Polyene Nystatin	100,000 -unit vaginal tablet	100,000 units a daily for 14 days (best choice for 1 st trimester of pregnancy)
Nystatin powder	100,000 units/gram	apply to vulva bid x 14 days

Among the azoles, tioconazole and terconazole appear to be the most active in vitro, with tioconazole demonstrating activity against *C. albicans* as well as *C. glabrata*, *C. tropicalis*, *C. krusei*, *C. kefyr*, and *C. parapsilosis*. By contrast, clotrimazole, miconazole, and butoconazole do not seem to be as active against *C. glabrata* and *C. tropicalis* as against *C. albicans*.

Oral agents are convenient, but confer some risk of side effects and drug interactions.

Oral azoles used for short term treatment

Drug	Dosage
Fluconazole (Diflucan®)	150 mg po x 1 dose
Ketoconazole (Nizoral®)	400 mg po qd x 5 days
Itraconazole (Sporanox®)	200 mg bid x 1 day vs 200 mg po qd x 3 days

***of the above medications, fluconazole is approved for vaginal/vulvar candida treatment

Management of chronic and recurrent VVC

Recurrent vulvovaginal candidiasis is defined as 4 or more episodes of symptomatic *Candida* vaginitis in a 12-month period.

Risk Factors for Recurrent Vulvovaginal Candidiasis

Antibiotic use	Receptive oral genital sex
Estrogen excess (OCP's , hormone replacement, local estrogens)	Sponge for contraception
Immune suppression (Lupus, HIV, corticosteroids)	Glucose excess (uncontrolled diabetes; refined sugar excess)
IUD use	Vulvar dermatoses (lichen sclerosus, eczema, atopic dermatitis)

Adapted from Sobel JD. Pathogenesis of recurrent vulvovaginal candidiasis. *Current Infectious Disease Reports.* 2002;4:514-9.

Complicated Vulvovaginal Candidiasis

Recurrent Vulvovaginal Candidiasis (RVVC) (adapted from the 2006 CDC STD Treatment Guidelines)

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. Most patients with recurrent yeast prefer the oral antifungals. Side effects occur infrequently. Hepatotoxicity, such as is seen with ketoconazole, occurs less often with fluconazole, but is a known complication. In a patient with no known liver function abnormalities, consider checking liver function tests after 6 months of treatment with fluconazole.

Maintenance Regimens

Oral fluconazole (i.e., 100-mg, 150-mg, or 200-mg dose) weekly for 6 months is the first line of treatment. If this regimen is not feasible, some specialists recommend topical clotrimazole, 200 mg twice a week, or clotrimazole (500-mg dose vaginal suppositories once weekly), or other topical treatments used intermittently.

Suppressive maintenance antifungal therapies are effective in reducing RVVC. However, 30%–50% of women will have recurrent disease after maintenance therapy is discontinued. Routine treatment of sex partners is controversial. *C. albicans* azole resistance is rare in vaginal isolates, and susceptibility testing is usually not warranted for individual treatment guidance.

Fluconazole: Adverse effects

- Nausea and vomiting in 3-4% (long term therapy)
- LFT monitoring consideration secondary to hepatotoxicity

>> chronic therapy

>> AIDS patients

Fluconazole: Drug-Drug Interaction

- Drug history important with long term/chronic fluconazole therapy
- Not as much of a clinical concern with single dose therapy

Drug interactions with long term fluconazole:

Drug	Interaction
•warfarin (Coumadin®)	may increase PT
•cimetidine (Tagamet®)	20% lower Fluconazole peak
•oral contraceptives	decreased estradiol levels; no effect on break through bleeding, efficacy
•phenytoin (Dilantin®)	increased phenytoin serum levels
•rifampin levels	increased Fluconazole metabolism
•cyclosporine	increased levels of cyclosporine
•oral hypoglycemics	Hypoglycemia
•theophylline	increased theophylline levels
•terfenadine	?cardiac arrhythmias

Ketoconazole

Ketoconazole traditionally has been used for long term therapy. Hepatotoxicity occurs and liver function tests need to be performed monthly.

Itraconazole

Itraconazole is an azole that has been labeled in the United States only for histoplasmosis and blastomycosis. Studies in other countries indicate that it is quite effective in candidal and dermatophyte infections. A study evaluating a one-day monthly, intermittent itraconazole prophylaxis (two doses of 200 mg itraconazole 12 hours apart during the fourth or fifth day of the menstrual cycle) found a reduced rate of recurrence of yeast, but the beneficial effects of itraconazole were lost within a few months after cessation of prophylaxis. Liver function studies will also need monitoring with itraconazole.

Serious cardiac arrhythmias have occurred in patients taking oral azoles together with non-sedating antihistamines (e.g. astemizole and terfenadine).

Other treatments for recurrent vulvovaginal candidiasis: Consider suppression with a weekly intravaginal antifungal, for example, clotrimazole (Mycelex-G®), or butoconazole (Gynezone-1®), or tioconazole (Vagistat-1®).

For irritation of yeast (like a diaper rash), triamcinolone acetonide ointment 0.1 % plus Nystatin 100,000 units per gram to vulva bid x 14 days.

Boric acid suppositories (per vagina) Fill 0 gel capsule halfway (600 mg). For the initial treatment a 600 mg capsule is inserted **per vagina** daily for 14 days. For long term maintenance, insert **into vagina** twice weekly. (Especially useful with *Torulopsis glabrata*)

Gentian violet 0.25% or 0.5% aqueous solution is applied at home daily or it may be given in the physician's office as a 1.0% solution (once weekly for up to three times). Permanent purple staining on clothing may occur. Some patients develop a vulvar irritation following application.

5-flucytosine This is a pyrimidine developed for use as an anticancer drug. Though not effective against cancer, it is fungicidal and is apparently deaminated within the yeast cell to 5-fluorouracil, which is incorporated into RNA and interferes with cell development. However, not all strains of *C. albicans* are susceptible, and drug resistance develops.

- 500 mg / 5 grams compounded in hydrophilic cream base
- Insert 5 gram per vagina qhs x 14 nights

Horowitz has shown that, when used in this manner by women infected by imidazole-resistant strains of *C. tropicalis*, the drug is highly effective.

Vaginal candidiasis and pregnancy

Many of the above agents are not to be used in pregnancy. Only topical azole therapies, applied for 7 days, are recommended for use among pregnant women. Young and Jewell searched the Cochrane Pregnancy and childbirth Group register and concluded that topical imidazole was more effective than nystatin for treating symptomatic vaginal candidiasis in pregnancy.

Treatments for seven days may be necessary.

Desquamative Inflammatory Vaginitis (DIV)

This condition is characterized by an alkaline vaginal pH and vestibular irritation. When the speculum is inserted, fine red "dots" may be present in the vagina. On wet prep, numerous inflammatory cells and parabasal cells are present. Vaginal lichen planus can present with this appearance, as can atrophy.

Rarely it can be seen with the chronic bullous diseases – cicatricial or classic Pemphigus.

This traditionally was treated with intravaginal clindamycin, but recently the use of a steroid/clindamycin vaginal compound has been beneficial to many patients.

Treatment of DIV

-For patients presenting with their first episode of DIV

2% clindamycin- i applicator per vagina qhs (or every other night if preferred) x 14.

-For recurrent DIV or resistant DIV

Combine 2% clindamycin (i applicator) with one Anusol HC suppository (25 mg) per vagina every other night (it is easier for patients to use these agents together rather than alternate days).

-For difficult DIV: Hydrocortisone 100 mg/gram in clindamycin 2% emollient cream base. Insert 5 gram (applicator full) q.o.d. (at night time) x 14 doses. This needs to be made at a compounding pharmacy.

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