

# Management of Vaginitis

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Common infectious forms of vaginitis include bacterial vaginosis, vulvovaginal candidiasis, and trichomoniasis. Vaginitis also can occur because of atrophic changes. Bacterial vaginosis is caused by proliferation of *Gardnerella vaginalis*, *Mycoplasma hominis*, and anaerobes. The diagnosis is based primarily on the Amsel criteria (milky discharge, pH greater than 4.5, positive whiff test, clue cells in a wet-mount preparation). The standard treatment is oral metronidazole in a dosage of 500 mg twice daily for seven days. Vulvovaginal candidiasis can be difficult to diagnose because characteristic signs and symptoms (thick, white discharge, dysuria, vulvovaginal pruritus and swelling) are not specific for the infection. Diagnosis should rely on microscopic examination of a sample from the lateral vaginal wall (10 to 20 percent potassium hydroxide preparation). Cultures are helpful in women with recurrent or complicated vulvovaginal candidiasis, because species other than *Candida albicans* (e.g., *Candida glabrata*, *Candida tropicalis*) may be present. Topical azole and oral fluconazole are equally efficacious in the management of uncomplicated vulvovaginal candidiasis, but a more extensive regimen may be required for complicated infections. Trichomoniasis may cause a foul-smelling, frothy discharge and, in most affected women, vaginal inflammatory changes. Culture and DNA probe testing are useful in diagnosing the infection; examinations of wet-mount preparations have a high false-negative rate. The standard treatment for trichomoniasis is a single 2-g oral dose of metronidazole. Atrophic vaginitis results from estrogen deficiency. Treatment with topical estrogen is effective. (*Am Fam Physician* 2004;70:2125-32,2139-40. Copyright© 2004 American Academy of Family Physicians.)

► **Patient information:** A handout on vaginitis, written by the authors of this article, is provided on page 2139.

See page 2131 for definitions of strength-of-recommendation labels.

**Although it is tempting to treat vaginal complaints empirically based on the patient's history alone, studies have demonstrated poor correlation between symptoms and the final diagnosis.**

Vaginitis is among the most common conditions for which women seek medical care, with vaginal discharge accounting for approximately 10 million office visits each year.<sup>1</sup> Although vaginitis can have a variety of causes (*Table 1*), it most often is associated with infection or atrophic changes. Common infectious forms of vaginitis include bacterial vaginosis, vulvovaginal candidiasis, and trichomoniasis. Although these infections generally respond to treatment, misdiagnosis and, rarely, pharmacologic resistance may occur.

In almost all patients with vaginitis, it is important to perform a thorough assessment that includes speculum examination, pH testing, wet-mount and potassium hydroxide (KOH) preparations, and cultures when indicated. This article reviews the diagnosis and management

of bacterial vaginosis, vulvovaginal candidiasis, trichomoniasis, and vaginal atrophy.

## Diagnosis

Although it is tempting to treat vaginal complaints empirically based on the patient's history alone, studies<sup>2,3</sup> have demonstrated poor correlation between symptoms and the final diagnosis. Bacterial vaginosis often is identified based on the vaginal pH and the presence of clue cells on light microscopy (two of the Amsel criteria<sup>4</sup>). A recent analysis<sup>3</sup> found that examination of wet-mount preparations is neither highly sensitive nor specific for vulvovaginal candidiasis. Culture of the vagina is costly, but may be the only way to ensure diagnosis of vulvovaginal candidiasis in equivocal cases. A reasonable alternative is to use a wet-mount and KOH preparation or Gram stain of the vagina in conjunction with the findings of the physical examination, and to reserve culture for cases of treatment failure.<sup>5</sup> DNA-based diagnostic tools with varying degrees

TABLE 1  
Causes of Vaginitis

Type of vaginitis	Causes and comments
Vulvovaginal candidiasis	<i>Candida albicans</i> , <i>Candida glabrata</i> , <i>Candida tropicalis</i>
Bacterial vaginosis	<i>Gardnerella vaginalis</i> , <i>Mycoplasma hominis</i> , <i>Mobiluncus</i> species, <i>Bacteroides</i> species (other than <i>Bacteroides fragilis</i> )
Trichomoniasis	<i>Trichomonas vaginalis</i>
Atrophic vaginitis	Estrogen deficiency
Chemical irritation	Soaps, hygiene products (tampons, sanitary napkins, latex condoms)
Lichen planus (desquamative type)	Flat, hyperkeratotic lesions that are pruritic or painful; associated vulvar and oral lesions
Allergic vaginitis	Sperm, douching, hygiene products (tampons, sanitary napkins, latex condoms or diaphragms), dyes, inhaled allergens, occupational exposures
Foreign body with or without infection or trauma	Tampons, contraceptive devices, pessary, others

of sensitivity and specificity also are available. Finally, a recent study<sup>6</sup> showed that in adolescents, vaginal swabs for wet-mount and KOH preparations may be performed reliably without speculum examination.

### Bacterial Vaginosis

Bacterial vaginosis accounts for 10 to 30 percent of the cases of infectious vaginitis in women of childbearing age.<sup>7</sup> In bacterial vaginosis, there is a decrease in normal lactobacilli and a proliferation of *Gardnerella*

*vaginalis*, *Mycoplasma hominis*, and anaerobes, including *Mobiluncus*, *Bacteroides*, and *Peptostreptococcus* species.

The Amsel criteria are considered to be the standard diagnostic approach to bacterial vaginosis and continue to be generally reliable.<sup>7,8</sup> The criteria are as follows: milky, homogeneous, adherent discharge; vaginal pH greater than 4.5; positive whiff test (the discharge typically has a fishy smell); and presence of clue cells in the vaginal fluid on light microscopy.<sup>4</sup> If three of the four criteria are met, there is a 90 percent likelihood of bacterial vaginosis.

The presence of small gram-negative rods or gram-variable rods and the absence of longer lactobacilli on a Gram stain of the vaginal discharge also is highly predictive of bacterial vaginosis.<sup>9</sup> However, this method of diagnosis is impractical in most family physicians' offices. Because *G. vaginalis* commonly is found in asymptomatic women, culture is not useful.

According to guidelines from the Centers for Disease Control and Prevention (CDC),<sup>10</sup> treatment of bacterial vaginosis is indicated to reduce symptoms and prevent infectious complications associated with pregnancy termination and hysterectomy. Treatment also may reduce the risk of human immunodeficiency virus (HIV) transmission.<sup>10</sup> Thus, it is reasonable to treat asymptomatic patients who are scheduled for hysterectomy or pregnancy termination or who are at increased risk for HIV infection;<sup>10</sup> other asymptomatic patients need not be treated.

### Treatment

The standard treatment for bacterial vaginosis is metronidazole (Flagyl) in a dosage of 500 mg orally twice daily for seven days (Table 2).<sup>10</sup> Although other treatments have been shown to have approximately equivalent efficacy,<sup>11-16</sup> they are associated with higher recurrence rates. These agents include 0.75 percent metronidazole gel (MetroGel-Vaginal) and 2 percent clindamycin cream (Cleocin). Less effective alternatives include metronidazole in a single 2-g oral dose, oral clindamycin, and intravaginal clindamycin ovules.

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**BACTERIAL VAGINOSIS IN PREGNANCY**

Bacterial vaginosis has been shown to be a risk factor for premature labor and perinatal infection.<sup>17</sup> Although evidence supports treatment of high-risk pregnant women with bacterial vaginosis<sup>5</sup> (defined as women who previously delivered a premature infant),<sup>7</sup> the benefits of treating asymptomatic, low-risk pregnant women is less clear.<sup>18-20</sup>

A Cochrane review<sup>21</sup> concluded that no evidence supports screening all pregnant women for bacterial vaginosis. Guidelines from the American College of Obstetricians and Gynecologists<sup>22</sup> and the Agency for Healthcare Research and Quality<sup>23</sup> do not recommend screening in low-risk patients (i.e., those without symptoms). However, family physicians should be aware that one recent study<sup>24</sup> demonstrated a significant reduction in spontaneous preterm birth and late miscarriage after treatment with oral clindamycin, 300 mg twice daily for five days, in women with asymptomatic bacterial vaginosis who were at 12 to 20 weeks of gestation. Therefore, the current recommendations against screening and treating asymptomatic pregnant women may be reevaluated.

Because of concerns about teratogenicity,

many physicians hesitate to use oral metronidazole in women who are in the first trimester of pregnancy. However, one meta-analysis<sup>25</sup> showed no increased risk of birth defect in infants exposed to metronidazole in utero. Vaginal clindamycin does not reduce the risk of preterm birth or peripartum infection.<sup>19</sup> In fact, the CDC<sup>10</sup> advises that topical clindamycin cream may increase the risk of prematurity and neonatal infections.

**RECURRENT BACTERIAL VAGINOSIS**

Recurrent bacterial vaginosis is common and requires longer treatment (10 to 14 days) with any of the recommended or alternative therapies<sup>9</sup> (Table 2).<sup>10</sup> Although lactobacillus suppositories<sup>26</sup> and oral lactobacillus<sup>27</sup> (without concurrent antibiotic treatment) have been shown to briefly resolve bacterial vaginosis, recurrence rates with these treatments have been high.<sup>26</sup>

**Vulvovaginal Candidiasis**

Reported risk factors for vulvovaginal candidiasis include recent antibiotic use, uncontrolled diabetes mellitus, and HIV infec-

Because *Gardnerella vaginalis* commonly is found in asymptomatic women, vaginal culture is not useful for diagnosing bacterial vaginosis.

TABLE 2

**Recommended Treatments for Bacterial Vaginosis**

Agents	Dosage	Use in pregnancy
<b>Recommended regimens</b>		
Metronidazole tablets (Flagyl)	500 mg orally twice daily for 7 days	250 mg three times daily for 7 days
Metronidazole 0.75% gel (MetroGel-Vaginal)	5 g intravaginally once daily for 5 days	No*
Clindamycin 2% vaginal cream (Cleocin)	5 g intravaginally once daily at bedtime for 7 days	No*
<b>Alternative regimens</b>		
Metronidazole tablets	2 g orally in a single dose	No†
Clindamycin tablets	300 mg orally twice daily for 7 days	300 mg twice daily for 7 days
Clindamycin ovules	100 g intravaginally once daily at bedtime for 3 days	No†

\*—Existing data do not support use of topical agents during pregnancy.

†—Data are insufficient to support use of these regimens during pregnancy.

Information from reference 10.

**Vaginal culture can be helpful in women with recurrent symptoms of vulvovaginal candidiasis or in women with typical symptoms but a negative potassium hydroxide preparation.**

tion/acquired immunodeficiency syndrome.<sup>28,29</sup> Although *Candida albicans* frequently is the cause of vaginal yeast infections, the organism can be present in asymptomatic women. Family physicians also must remember that vaginal yeast infections may be caused by species other than *C. albicans*, such as *Candida glabrata* and *Candida tropicalis*.

Infections with these species are less common than *C. albicans* infection and tend to be more resistant to treatment.

Patients with vulvovaginal candidiasis usually report one or more of the following: vulvovaginal pruritus (50 percent), vulvovaginal swelling (24 percent), and dysuria (33 percent).<sup>29</sup> The characteristic vaginal discharge,

when present, is usually thick and white. Because these symptoms are not specific for vulvovaginal candidiasis, family physicians also should consider other causes.

Caution should be exercised in basing treatment decisions on a patient's self-diagnosis of yeast infection. In one study,<sup>30</sup> the presence of vulvovaginal candidiasis was confirmed in only 33.7 percent of women who self-diagnosed yeast infection. Therefore, the diagnosis of vulvovaginal candidiasis should rely heavily on microscopic examination of a sample taken from the lateral vaginal wall (10 to 20 percent KOH preparation). Although vaginal culture is not routinely necessary for diagnosis, it can be helpful in women with recurrent symptoms or women with typical symptoms and a negative KOH preparation.<sup>7,28</sup>

**TABLE 3  
Treatments for Uncomplicated Candidiasis**

<i>Agent</i>	<i>Dosage</i>
Butoconazole 2 percent vaginal cream (Mycelex-3)*	5 g intravaginally per day for 3 days
Butoconazole 2 percent vaginal cream, sustained release (Gynezone-1)	5 g intravaginally one time
Clotrimazole 1 percent vaginal cream (Mycelex-7)*	5 g intravaginally per day for 7 to 14 days
Clotrimazole 100-mg vaginal tablet (Gyne-Lotrimin, Mycelex-7)	One tablet intravaginally per day for 7 days or Two tablets intravaginally per day for 3 days
Clotrimazole 500-mg vaginal tablet (Mycelex-G)	One tablet intravaginally one time
Fluconazole (Diflucan) <sup>31</sup> †	One 150-mg tablet orally one time
Miconazole 2 percent vaginal cream (Monistat)*	5 g intravaginally per day for 7 days
Miconazole 100-mg vaginal suppository (Monistat 7)*	One suppository intravaginally per day for 7 days
Miconazole 200-mg vaginal suppository (Monistat 3)*	One suppository intravaginally per day for 3 days
Nystatin 100,000-unit vaginal tablet*	One tablet intravaginally per day for 14 days
Tioconazole 6.5 percent ointment (Vagistat-1)*	5 g intravaginally one time
Terconazole 0.4 percent vaginal cream (Terazol 7)	5 g intravaginally per day for 7 days
Terconazole 0.8 percent vaginal cream (Terazol 3)	5 g intravaginally per day for 3 days
Terconazole 80-mg vaginal suppository (Terazol 3)	One suppository intravaginally per day for 3 days

\*—Available over the counter.

†—Not recommended for use during pregnancy.

Information from references 10 and 31.

## TREATMENT

All standard treatment regimens for uncomplicated vulvovaginal candidiasis are equally efficacious, resulting in a clinical cure rate of approximately 80 percent<sup>7</sup> (Table 3).<sup>10,31</sup> Various topical treatments are available without prescription. However, many women may prefer the simplicity of a single 150-mg oral dose of fluconazole (Diflucan). In women with candidal vaginitis, treatment with oral fluconazole has been shown to be safe and as effective as seven days of treatment with intravaginal clotrimazole.<sup>31</sup> It is important to remember that fluconazole is a pregnancy class C agent. In some patients, fluconazole may cause gastrointestinal upset, headache, dizziness, and rash, although these side effects typically are mild.

When therapy for vulvovaginal candidiasis is considered, it is helpful to classify the infection as uncomplicated or complicated (Table 4).<sup>10</sup> The practical importance of such classification is that the treatments differ. For example, in complicated vulvovaginal candidiasis, topical therapy has been shown to be more effective than single-dose oral therapy,<sup>28</sup> but treatment should be extended to 10 to 14 days.<sup>7</sup>

If oral therapy is preferred for severe vulvovaginal candidiasis, two sequential 150-mg doses of fluconazole, given three days apart, have been shown to be superior to a single 150-mg dose.<sup>32</sup> Although the optimal duration of extended oral fluconazole therapy has not been determined, one older study<sup>33</sup> comparing oral fluconazole with clotrimazole found that extended use of fluconazole was safe and well tolerated.

In patients with severe discomfort secondary to vulvitis, the combination of a low-potency steroid cream and a topical antifungal cream may be beneficial.<sup>34</sup>

## RECURRENT VULVOVAGINAL CANDIDIASIS

Recurrent vulvovaginal candidiasis is defined as four or more yeast infections in one year. The possibility of uncontrolled diabetes mellitus or immunodeficiency should be considered in women with recurrent vulvovaginal candidiasis. When it is certain that no reversible causes are present (e.g., antibiotic therapy,

TABLE 4

### Classification of Vulvovaginal Candidiasis

Uncomplicated	Complicated
Sporadic or infrequent infection	Recurrent infection
Mild-to-moderate infection	Severe infection
<i>Candida albicans</i> as likely cause	Infection with <i>Candida</i> species other than <i>C. albicans</i>
Woman without immunosuppression	Woman with uncontrolled diabetes mellitus, immunosuppression, or debilitation; pregnant woman

Adapted from Sexually transmitted diseases treatment guideline 2002. Centers for Disease Control and Prevention MMWR Recomm Rep 2000;51(RR-6):1-80. Accessed online June 28, 2004, at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5106a.htm>.

uncontrolled diabetes, oral contraceptive pill use) and initial therapy has been completed, maintenance therapy may be appropriate.<sup>35</sup> Selected long-term regimens are listed in Table 5.<sup>10</sup> The role of boric acid and lactobacillus therapy remains controversial.

Culture and sensitivity results should be used to guide therapy, because non-*C. albicans* species often are present in women with recurrent vulvovaginal candidiasis and these species are more likely to be resistant to standard azole therapy.<sup>35</sup>

## Trichomoniasis

*Trichomonas vaginalis* infection causes a foul-smelling, frothy discharge that usually is accompanied by vaginal irritation. Although the presence of motile trichomonads in a

TABLE 5

### Selected Regimens for Recurrent Vulvovaginal Candidiasis

Treatment	Initial dosage	Maintenance dosage
Clotrimazole 100-mg vaginal tablet (100 mg, Gyne-Lotrimin, Mycelex-7; 500 mg, Mycelex-G)	One 100-mg tablet intravaginally per day for 7 days	One 500-mg tablet intravaginally once per week
Fluconazole (Diflucan)	One 150-mg tablet orally; repeat after 3 days.	One 150-mg tablet orally once per week

Information from reference 10.



**Examination of the wet-mount preparation can be negative in up to 50 percent of women with culture-confirmed trichomoniasis.**

wet-mount preparation is diagnostic, the examination can be negative in up to 50 percent of women with culture-confirmed infection.<sup>36</sup> Therefore, when microscopic examination of a wet-mount preparation is negative but trichomoniasis still is suspected, a vaginal culture on specialized culture medium is appropriate to rule out *T. vaginalis* infection.<sup>37</sup> A DNA probe test (e.g., Affirm VPIII) also can be useful in detecting this organism.

Unlike women with asymptomatic *G. vaginalis* or *Candida* colonization, women with asymptomatic *T. vaginalis* infection should be treated. *T. vaginalis* is highly transmissible and is associated with other sexually transmitted diseases (STDs); asymptomatic infection may increase the risk of acquiring HIV.<sup>10,38</sup> Consequently, patients with vaginal trichomoniasis should be offered HIV and other STD screening.

Occasionally, *T. vaginalis* is found incidentally in a routine Papanicolaou (Pap) test. Detection by this method is reported to be 57 percent sensitive and 97 percent specific for trichomoniasis.<sup>39</sup>

When trichomoniasis is found during routine Pap testing, management should be based on the pretest probability of infection in the patient, which is determined by the prevalence of *T. vaginalis* infection in the community; information on prevalence usually can be obtained from the local health department. For example, if the pretest probability of *T. vaginalis* infection is 20 percent and the protozoan is found in a patient's Pap smear, the positive predictive value of the test is 83 percent, which warrants treatment. Alternatively, the patient can be offered the options of treatment or confirmatory culture followed by treatment if the culture is positive.<sup>39</sup>

#### TREATMENT

The standard treatment for trichomoniasis is a single 2-g oral dose of metronidazole.<sup>10</sup> An alternative treatment is oral metronidazole in a dosage of 500 mg twice daily for seven days.<sup>10</sup> Because *T. vaginalis* can colonize the urethra and associated glands, topical ther-

apy is less effective.<sup>10</sup> However, topical agents have been shown to decrease symptoms and may be useful in patients with the rare problem of metronidazole resistance.<sup>40</sup>

Because metronidazole is the only agent that is used to treat *T. vaginalis* infection, potential management problems include hypersensitivity and drug resistance. A desensitization protocol is available for the management of documented trichomoniasis and frank allergy to metronidazole.<sup>41</sup>

Although evidence indicates that resistance of *T. vaginalis* to metronidazole can be overcome by increasing the dosage and duration of therapy, many patients cannot tolerate the regimens. If tolerance is a problem, the CDC<sup>10</sup> recommends repeating the 2-g dose of metronidazole orally and if the patient still is infected, giving oral metronidazole in a dosage of 2 g per day for three to five days.<sup>10</sup> If the infection does not respond to this regimen, consultation with the CDC is available by telephone (800-227-8922) or via the CDC Web site (<http://www.cdc.gov/std/>).

Several alternative regimens for trichomoniasis have been shown to be efficacious. Tinidazole (marketed as Fasigyn) is widely used in Europe and developing countries. This agent is effective and generally well tolerated,<sup>42</sup> but has not been approved by the U.S. Food and Drug Administration and, therefore, is not available in this country. Another treatment option is paromomycin (Humatin) in a dosage of 5 g intravaginally per day for 14 days. This treatment is reported to be effective in 58 percent of patients.<sup>43</sup> However, paromomycin must be used with caution because of its side effects, which include vulvitis and local ulceration.

#### TRICHOMONIASIS DURING PREGNANCY

*T. vaginalis* infection during pregnancy has been linked to preterm labor and low birth weight.<sup>10</sup> Unfortunately, treatment of asymptomatic trichomoniasis has not been shown to prevent these outcomes.<sup>44</sup> The decision to treat trichomoniasis during pregnancy is further complicated by the fact that physicians are reluctant to use metronidazole in pregnant women. As previously noted, however, the risk of teratogenicity appears to be

## Strength of Recommendations

Key clinical recommendation	Label	References
The etiology of a vaginal discharge should not be determined solely on the basis of a woman's symptoms.	C	2, 3, 30
Treating bacterial vaginosis in pregnancy reduces preterm birth and late miscarriage.	B	24
Complicated vulvovaginal candidiasis should be treated with topical antifungal agents for 10 to 14 days.	C	7, 28
Culture and sensitivity results should be used to guide therapy in women with recurrent vulvovaginal candidiasis (i.e., four or more yeast infections per year).	C	35

overstated.<sup>25</sup> Risks and benefits of treatment must be considered in formulating a treatment plan for pregnant patients who have *T. vaginalis* infection. The CDC<sup>10</sup> advises treatment of symptomatic pregnant women with a single 2-g oral dose of metronidazole but does not recommend treatment of asymptomatic pregnant women.

### Atrophic Vaginitis

The decrease in estrogen levels during perimenopause and after menopause can cause vaginal atrophy. One important physiologic change is thinning of the vaginal epithelium; another is loss of glycogen, which leads to changes in the vaginal pH and flora. Many women with these vaginal changes are minimally symptomatic and require only explanation and reassurance. In women with more severe changes, vaginal irritation, dyspareunia, and fragility may become problems. Atrophy is diagnosed by the presence of a thin, clear or bloody discharge, a vaginal pH of 5 to 7, loss of vaginal rugae, and the finding of parabasal epithelial cells on microscopic examination of a wet-mount preparation.<sup>18</sup>

Treatment with topical estrogen (cream, tablet, or ring) usually provides complete relief of symptoms within weeks. In the interim, patients may obtain relief through use of vaginal lubricants and moisturizers (e.g., Astroglide, Replens). Rarely, endometrial hyperplasia can be a side effect of vaginal estrogen treatment.<sup>45,46</sup>

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