REVIEW

AMELIA CLEVELAND, MD
Women's Health Professionals, Akron, Ohio

Vaginitis: Finding the cause prevents treatment failure

ABSTRACT

Even though vaginitis has a limited number of causes, many physicians find it difficult to diagnose accurately and manage effectively. Before vaginitis is treated, the cause must be ascertained, but this is often not done, and treatment failure results. The physical evaluation and a simple office microscopic analysis are key to pinpointing the cause and tailoring treatment.

KEY POINTS

Of the three major causes of vaginitis, bacterial vaginosis (ie, nonspecific vaginitis or infection with *Gardnerella vaginalis* or *Haemophilus vaginalis*) accounts for 40% to 50% of cases, candidiasis for 20% to 30%, and trichomoniasis for 20% to 30%.

Avoid diagnosing and treating vaginitis on the basis of a telephone conversation with the patient. This often leads to misdiagnosis and treatment failure.

Encourage patients to refrain from using vaginal preparations or douches for 72 hours before the office evaluation.

THE PROBLEM WITH VAGINITIS is not that it is difficult to treat, but that physicians and patients too often attempt to treat it without first identifying the causative organism, often resulting in treatment failure.

Perhaps because the cause of vaginitis is most likely to be bacterial vaginosis, trichomoniasis, or candidiasis, physicians often diagnose and treat it on the basis of a cursory office evaluation or a telephone conversation with the patient. Furthermore, distress and discomfort often lead women to self-diagnose vaginitis and to use over-the-counter vaginal preparations improperly.[1]

Office-based physicians can follow a simple but methodical strategy for accurate diagnosis and effective treatment of inflammation of the vaginal mucosa, with or without abnormal vaginal discharge.

INCIDENCE

Vaginitis is exceptionally common. Although the exact incidence is not known, most women experience at least one episode in their lifetime, and more than half have multiple episodes.[1]

LACTOBACILLI NORMALLY PREDOMINATE

Vaginal discharge is made up of water, electrolytes, microorganisms, epithelial cells, and organic compounds such as fatty acids, proteins, and carbohydrates. It is derived from serum transudate in vaginal capillary beds. Normal vaginal pH is 4.5 or lower, which favors acidophilic organisms.

Lactobacilli, which are large, gram-positive rods, account for nearly 95% of the bacte-

TABLE 1

Causes of vaginitis

Common infective causes
- Bacterial vaginosis
- Vulvovaginal candidiasis
- Trichomoniasis

Less common infective causes
- Atrophic vaginitis with secondary bacterial infection
- Foreign body with secondary infection
- Desquamative inflammatory vaginitis (clindamycin-responsive)
- Streptococcal vaginitis (group A)
- Ulcerative vaginitis associated with *Staphylococcus aureus* and toxic shock syndrome
- Idiopathic vulvovaginal ulceration associated with human immunodeficiency virus infection

Noninfectious causes
- Chemicals or other irritants
- Allergy, hypersensitivity, and contact dermatitis (lichen simplex)
- Trauma
- Atrophic vaginitis
- Postpuerperal atrophic vaginitis
- Desquamative inflammatory vaginitis (steroid-responsive)
- Erosive lichen planus
- Collagen vascular disease, Behçet syndrome, pemphigus syndromes
- Idiopathic vaginitis

ADAPTED FROM SOBEL JD. VAGINITIS. N ENGL J MED 1997; 337:1896–1903.

ria normally present in the vagina. Lactobacilli are good: they produce lactic acid and hydrogen peroxide, keep the vagina acidic, and inhibit the growth of most other bacteria.

Other organisms are also present, however: 5 to 10 species on the average, including some we consider harmful but which are kept in check by lactobacilli.

Corynebacteria, streptococci, *Staphylococcus epidermidis*, and *Gardnerella vaginalis* are present in 40% to 80% of women. *Escherichia coli*, present in approximately 20% of women, is the most common of the virulent coliform microorganisms. Group B streptococci are present in about 15% to 20% of women.

The most prevalent anaerobic microorganisms in the vagina are *Peptostreptococcus*, *Bacteroides* species, anaerobic lactobacilli, and eubacteria. *Candida albicans*, present in 5% to 10% of women, is the most common yeast. *Mycoplasma hominis* is present in 20% to 50% and *Ureaplasma urealyticum* is present in 50% to 70% of sexually active women without symptoms.

INFECTION: UPSETTING THE BALANCE

Vaginal infection is thought to arise when the complex balance of organisms changes and one organism (eg, G *vaginalis*, M *hominis*, *Mobiluncus*, gram-negative rods, or C *albicans*) increases in concentration enough to cause symptoms. Antibiotics, hormones, contraceptive preparations, vaginal douching, sexual intercourse, sexually transmitted diseases, stress, poor hygiene, and a change in sex partners are all suspected of playing a role in upsetting the balance of organisms.[2]

Bacterial infection causes 40% to 50% of vaginitis cases

THREE COMMON CAUSES OF VAGINITIS

Most cases of vaginitis arise from one of three causes:

Bacterial vaginosis (formerly known as nonspecific vaginitis), usually due to G *vaginalis* or *Haemophilus vaginalis*—40% to 50% of cases.

***Candida* species**—20% to 30%.

Trichomonas vaginalis—20% to 30%.[3]

Less-common infectious and noninfectious causes are listed in **TABLE 1**.

TABLE 2

Diagnostic clues in suspected vaginitis

CONDITION	SYMPTOMS REPORTED	VAGINAL DISCHARGE CHARACTERISTICS	VAGINAL PH	AMINE (FISHY) ODOR	MICROSCOPIC FINDINGS
Normal	None	White or clear Clumpy Flocculent	3.8–4.2	No	Lactobacilli Epithelial cells
Bacterial vaginosis	Discharge Bad odor Perhaps itching	Thin Homogeneous White-gray Adherent Often increased	> 4.5	Yes	Clue cells with adherent coccoid bacteria No white blood cells (WBCs)
Trichomoniasis	Frothy discharge Bad odor Vulvar itching Dysuria	Yellow-green Frothy Adherent Increased	> 4.5	Sometimes	Trichomonads > 10 WBCs per high-powered field
Candidiasis	Itching Burning Discharge	White Curdy Sometimes increased	≤ 4.5	No	On KOH slide preparation: Budding yeast Hyphae Pseudohyphae

HOW TO DIAGNOSE VAGINITIS

Many physicians do not go through the proper diagnostic steps

Despite the limited number of causes, many physicians find vaginitis difficult to diagnose accurately and manage effectively because they do not go through the proper steps.

Symptoms are unreliable

Most women with vaginitis complain of vaginal discharge, with or without itching, odor, burning, or discomfort. Although these symptoms are important, the diagnosis of vaginitis should not be based solely on the presence or absence of symptoms. Microscopic analysis for specific criteria greatly improves diagnostic accuracy.

Physical findings

Begin the physical examination with a thorough inspection of the vulva. Look for:

- Fissures or erythema, which may indicate candidiasis.
- White or "onion skin" epithelium, which may indicate lichen sclerosis.
- An unusual amount of vulvar tenderness, which may indicate vestibulitis.
- Vaginal discharge at the introitus, which may indicate bacterial vaginosis or trichomoniasis.

During the speculum exam, note:

- The amount, color, and texture of the discharge. Normal vaginal discharge is white and clumpy and tends to pool in the vagina. In bacterial vaginosis, however, the discharge may resemble skim milk—gray, homogeneous, and watery—and is often found on the anterior and lateral vaginal walls (TABLE 2).
- The appearance of the cervix, including the cervical mucus. During the estrogen-dominant phase of the menstrual cycle, cervical mucus is likely to be clear. During the progesterone-dominant phase of the cycle, cervical mucus is thick, scant, or invisible. Wipe any vaginal discharge off the ectocervix to make sure there is no purulent discharge from the endocervix, which could indicate cervicitis due to gonorrhea or a *Chlamydia* infection.

How to analyze the vaginal discharge

Check the pH. Place a drop of the vaginal discharge on a pH strip. A pH higher than 4.5 is found in patients with trichomoniasis,

bacterial vaginosis, or an inflammatory normal vaginal discharge. However, the pH is usually normal in candidiasis.

Prepare and examine slides.

KOH slide. Place a drop of vaginal discharge on a slide and add a drop of 10% potassium hydroxide (KOH). When you add the KOH, note the odor. A "fishy" amine odor indicates bacterial vaginosis or, possibly, trichomoniasis. The odor is a consequence of volatilization of amines (putrescine, cadaverine, and trimethylamine), the by-products of anaerobic metabolism.

Examine the KOH slide under the microscope, looking for the branching hyphae of *C albicans*. These may be clumped, so the entire slide must be scanned.

Saline slide. Place a drop of vaginal discharge on a slide and add a drop of normal saline. Examine the slide under the microscope—this should be done within minutes of preparing the slide. Look for:

- Large rods (lactobacillus). This is the predominant organism seen in patients with normal vaginal discharge, but also in candidiasis. Also note if lactobacilli are absent—an abnormal finding.
- White blood cells. If a large number of white blood cells is seen, then the cause of the vaginal discharge is likely trichomoniasis, cervicitis, or candidiasis. However, a few patients may have inflammatory vaginitis, which is characterized by a large number of white blood cells and absence of lactobacilli, a pH higher than 4.5, red vaginal spots, purulent discharge, other small rod or cocci morphotypes, and parabasal cells.
- Trichomonads. These are slightly larger than white blood cells, and white blood cells can actually inhibit their movement.
- Clue cells, which are vaginal epithelial cells with adherent bacteria that obscure the cellular border. In bacterial vaginosis, between 5% and 50% of epithelial cells seen are clue cells.

Alternatively, do a Gram's stain instead of a saline slide to look for white blood cells, predominant flora, and yeast (but not trichomonads). If this technique is used, small gram-negative bacilli represent *Gardnerella* species and anaerobic bacteria. Lactobacilli appear as large gram-positive rods.

Vaginal cultures are of limited benefit in vaginitis

If the diagnosis is uncertain

In patients with symptoms or abnormal physical findings, the finding of trichomonads, clue cells, or hyphae on simple microscopic analysis is 100% specific for vaginitis. However, even in ideal circumstances, these findings carry a sensitivity of only 80%.[3] If the microscopic diagnosis is unclear, then:

Repeat the evaluation in about 3 days.

Refer the patient to a specialist if the diagnosis remains unclear after microscopic analysis and physical examination, or if the response to therapy is inadequate. Lichen sclerosis and other dysplastic or neoplastic processes require a tissue biopsy to establish the diagnosis. These conditions are generally limited to the vulva. Vulvar vestibulitis, on the other hand, is a diagnosis of exclusion and is often rather difficult to manage.

When to perform cultures

Vaginal cultures are of limited benefit in the diagnosis of vaginitis because they lack specificity—"abnormal" organisms are often present, but not in clinically significant numbers. However, do perform cervical cultures whenever a purulent cervical exudate is seen. In addition, cultures for *Candida* may be useful when candidiasis is suspected but the KOH preparation is negative. A culture for *Candida* is also useful in women with pruritus, vulvar fissures, or erythema whose condition is unresponsive to antifungal therapy.

VAGINAL DISCHARGE CAN BE NORMAL

Vaginal discharge, although the most common symptom reported by women with vaginitis, is also a normal physiological occurrence. In fact, in approximately 10% of women who complain of increased vaginal discharge, the increase is actually physiologic, and the cervical mucus and vaginal fluid are normal. In these cases the only microscopic finding pertinent to the diagnosis of vaginitis is an abundance of vaginal epithelial cells and large rods. All other microscopic features indicative of infection are absent.

If a patient has vaginal discharge but otherwise normal findings:

- Reassure her
- Do not prescribe antimicrobials
- Reevaluate in 1 to 2 weeks if symptoms are present.

Discourage patients from douching, as it increases the risk of salpingitis and may also increase the amount of vaginal discharge.

BACTERIAL VAGINOSIS: TREATMENT RECOMMENDATIONS

Bacterial vaginosis results from an overgrowth of both anaerobic bacteria and G *vaginalis*. The latter is present in an estimated 40% of women without symptoms and in 95% of women with symptoms.[3] In infection, the most common anaerobic bacteria present are *Bacteroides*, *Peptostreptococcus*, and *Mobiluncus* species, and the number of lactobacilli is decreased.

Diagnosis

The most common symptom of bacterial vaginosis is a fishy vaginal odor that occurs either spontaneously or after intercourse.

The diagnosis requires three of the following four characteristics:

- A thin vaginal discharge
- A pH greater than 4.5
- An amine odor when a drop of 10% KOH is added to the vaginal discharge on a microscope slide
- Clue cells seen on microscopy.

Treatments

For patients with confirmed bacterial vaginosis, the following regimens can achieve cure rates of 85% to 95%:

- Metronidazole 500 mg orally twice daily for 7 days
- Metronidazole 750 mg orally once daily for 7 days
- Clindamycin 300 mg orally twice daily for 7 days
- Metronidazole 0.75% gel intravaginally daily for 5 days
- Clindamycin 2% cream intravaginally nightly for 7 days.

Other options. Metronidazole 2 g orally as a one-time dose provides a cure rate of 80% to 85%. This is also true of amoxicillin/clavulanic acid 500 mg three times daily for 7 days.

Do not use ciprofloxacin, erythromycin, tetracycline, doxycycline, triple sulfa cream (sulfabenzamide, sulfacetamide, sulfathiazole), and povidone-iodine douches. These all either have unacceptably low cure rates or are completely ineffective.

Treatment failure

Most treatment failures are due to incorrect diagnosis of bacterial vaginosis in patients who actually have normal lactobacillus-dominant flora associated with either an excessive discharge or odor, cervicitis, or other lower genital tract infection.

Treatment in pregnancy and genital surgery

Women with bacterial vaginosis have higher rates of endometritis and wound infection after cesarean delivery, premature rupture of membranes and premature delivery, and cuff cellulitis after hysterectomy. Therefore, patients with symptoms who are pregnant or candidates for invasive genital surgery should be treated.

Is bacterial vaginosis sexually transmitted?

There is no proof that bacterial vaginosis is sexually transmitted, though it often recurs. Treatment of male partners has not been shown to be useful in preventing recurrence in women.[4] If infection recurs rapidly, the prescribed antimicrobial should be changed. If symptoms recur after sex, then consider prescribing oral metronidazole 500 mg prophylactically after coitus. However, this is rarely necessary if the patient completes a week's therapy using metronidazole 500 mg twice daily.

In bacterial vaginosis, treating the male partner has not proved useful

CANDIDIASIS: TREATMENT RECOMMENDATIONS

C albicans causes 80% to 90% of all cases of vaginitis due to yeast infection. The remainder are caused by other *Candida* species, particularly *C torulopsis* and *C glabrata*.

Treatments

Yeast medications are available both over the counter and by prescription (TABLE 3). Over-

TABLE 3

FDA-approved antifungal medications for candidal vaginitis

MEDICATION	TRADE NAME	HOW SUPPLIED	DOSAGE
Butoconazole	Femstat	2% vaginal cream	Nonpregnant: 1 applicator at bedtime for 3 days Pregnant: 1 applicator at bedtime for 6 days in second or third trimester only
Clotrimazole	Gyne-Lotrimin, Mycelex	100-mg tablets 500-mg tablets 1% vaginal cream	1 tablet vaginally at bedtime for 7 days 1 tablet vaginally (one dose) 1 applicator at bedtime for 7 days
Fluconazole*	Diflucan	150-mg tablets	1 tablet orally (one dose)
Itraconazole*	Sporanox	200-mg tablets	1 tablet orally twice a day for 1 day 1 tablet orally once a day for 3 days
Ketoconazole*	Nizoral	400-mg tablets	1 tablet orally twice a day for 5 days
Miconazole	Monistat	200-mg vaginal suppository	1 suppository at bedtime for 3 days
Nystatin	Mycostatin	100,000-U vaginal tablets	1 tablet vaginally daily for 14 days
Terconazole*	Terazol	0.4% cream (5 g) 0.8% cream (5 g) 80-mg vaginal suppository	1 applicator vaginally at bedtime for 7 days 1 applicator vaginally at bedtime for 3 days 1 suppository vaginally at bedtime for 3 days
Tioconazole	Vagistat	6.5% ointment (4.6 g)	1 applicator vaginally once

*Requires a prescription

ADAPTED FROM SOBEL JD. VAGINITIS. N ENGL J MED 1997; 337:1896–1903.

the-counter preparations can be used appropriately after an office evaluation has confirmed that vaginitis is due to yeast. However, to use these preparations in any other way often leads to therapeutic failure.

Topical azoles remain the first choice for the treatment of infrequent acute candidiasis. Azoles inhibit ergosterol and membrane synthesis and are fungistatic, and *Candida* are killed by the host lymphocytes. Cure rates for 3-day and 7-day treatment courses are similar at 80% to 90%. If vaginal irritation increases with the use of a topical therapy, stop and change preparations immediately. Most irritations result from "inactive" compounds in the cream vehicle.

Fluconazole, an oral azole, provides effective therapy of candidiasis in patients with mild to moderate symptoms. A single dose of 150 mg is required. If the patient has severe symptoms, a repeat dose of fluconazole should be given in 4 or 5 days. Otherwise, failure rates will exceed that of local therapy.

Topical nystatin is less effective than azole therapy, with cure rates of 50% to 80%.

Boric acid capsules (600 mg or boric acid "0"-size gelatin capsules) intravaginally twice daily for 14 days give a clinical cure rate similar to that of topical azole therapy.[5] Boric acid capsules are inexpensive and well tolerated. Boron ions have not been detected in the blood. However, boric acid can cause esophageal ulcers if swallowed, so great care should be taken to keep it away from small children.

Adjunctive treatments

In one study,[6] eating 4 ounces of lactobacillus-containing yogurt twice daily significantly reduced recurrences of candidiasis. Other adjunctive treatments to consider in treating vulvovaginal candidiasis are:

- Sitz baths followed by superdrying (with a hair dryer)

- Direct vulvar application of antifungal creams
- Abandonment of tight or poorly ventilated clothing
- Dietary restriction of carbohydrates
- Cessation of chronic antibiotic use.

Resistance

Resistance of *C albicans* to antifungal medications is unusual. It is more common with fungi such as *C glabrata*, *C torulopsis*, *C tropicalis*, and other non-albicans species. Some experts theorize that recurrent vaginal candidiasis results from gastrointestinal tract *Candida*. However, most people carry *Candida* in their gastrointestinal tract without developing candidiasis, and no longitudinal study has related vaginal candidiasis to gastrointestinal *Candida*.

Treatment in pregnancy

Systemic absorption of either topical azoles or nystatin is limited. Therefore, either can be used safely during all trimesters of pregnancy.

Boric acid, fluconazole, and ketoconazole should not be used during pregnancy. Fluconazole, an oral azole, is to be avoided because of a lack of information about its effect on the human fetus. In animal studies using fluconazole, problems were seen with maternal weight gain, and the number of abortions increased. With ketoconazole, there are increased congenital abnormalities in rats. Further, these agents are not more effective than topical azoles or topical nystatin.

As candidiasis is more resistant to treatment during pregnancy, relapse is more likely. Better cure rates are obtained with prolonged therapy (7 to 14 days) than with abbreviated therapy.

How to manage recurrence

Noncompliance is a common reason for rapid recurrence of candidiasis. In general, recurrences are not related to drug resistance. Few of these patients are diabetic or on oral contraceptives, immunosuppressives, or antibiotics. When recurrence is rapid, change medications to eliminate the possibility of drug reactions. Also, consider other diagnoses, including neurodermatitis, lichen sclerosis, burning vulvar syndrome, and minor vestibular gland inflammation.

In patients with chronic or frequently recurrent episodes of vaginal candidiasis, a defective immunologic response is possible. Consider human immunodeficiency virus testing, though this virus is not a common cause.

In rare cases, such as in immunocompromised patients with HIV infection, suppressive therapy rather than curative therapy is in order. There are no established protocols for suppressive therapy. One approach is to give an initial therapeutic dose of a standard intravaginal medication followed by a maintenance dose of antifungal therapy for 6 to 12 months. A practical form of maintenance therapy is biweekly topical boric acid or azole administration.[3] I usually give terconazole 0.8% vaginal cream or 80-mg vaginal suppositories, which the patient can use once or twice weekly if needed. I avoid suppression with fluconazole primarily because of cost.

TRICHOMONIASIS: TREATMENT RECOMMENDATIONS

T vaginalis is a ubiquitous sexually transmitted anaerobic parasite. Only 50% of women infected with *T vaginalis* are symptomatic. *T vaginalis* can be recovered from the prostatic fluid in up to 70% of men who have had sexual intercourse with women with trichomoniasis. The organism can be carried for a long time.

Intravaginal metronidozole does not cure trichomonal vaginitis

Women with symptomatic trichomoniasis complain of a profuse, malodorous, uncomfortable vaginal discharge that may cause both internal and external dysuria. Vulvar and vaginal fullness and lower abdominal pain may also be present.

Treatment

Metronidazole is the only effective drug approved for the treatment of trichomoniasis in the United States. Abbreviated therapy with a one-time dose of 2 g of metronidazole by mouth is as effective as 500 mg of metronidazole taken twice daily for 7 days.[7] Cure rates of over 95% may be achieved when male sexual partners are treated concomitantly.

The most common side effects are nausea, a metallic taste, cephalgia, dizziness, and dark urine, and are experienced by 5% to 25% of

patients. Advise patients to avoid alcohol consumption for 24 hours after taking the last dose of metronidazole to avoid a disulfiram-like effect that produces significant nausea.

Treating male partners

Seventy-five percent of male sexual contacts of women with trichomoniasis acquire the microorganism.[8] Approximately one third of these men appear to have spontaneous cures. Concomitant treatment of male sexual partners increases the cure rates in women by 10% to 25%. Nonetheless, men are generally asymptomatic and may resist therapy because they do not believe they have an infection.

Reasons for treatment failure

Treatment failure is usually related to noncompliance or reinfection through sexual contact. Resistance has been reported in small numbers. Currently, no uniform treatment of resistance is known, though many gynecologists would prolong treatment and increase daily dosages of metronidazole.

Treatment during pregnancy

Treatment of trichomoniasis during pregnancy is controversial. With the exception of two very small studies, metronidazole has not been recognized as a teratogen or associated with other adverse pregnancy outcomes. Clotrimazole can temporarily reduce the symptoms of trichomoniasis. If the patient is asymptomatic or minimally symptomatic, 2 g of metronidazole can be given on the day of delivery. Many physicians will treat trichomoniasis any time after completion of the first trimester of pregnancy. Breast feeding should be delayed or withheld for 24 hours after taking metronidazole.

With trichomoniasis, treatment failure is usually due to noncompliance or reinfection

REFERENCES

1. Vulvovaginitis Causes and Therapies: An Update of the National Institute of Child Health and Human Development Roundtable Highlights. Clinical Courier 1997; 16:1–8.
2. American College of Obstetricians and Gynecologists (ACOG) Technical Bulletin, number 226, July 1996.
3. **Eschenbach DA.** Diagnosis and treatment of vaginitis. In: Stenchever MA. Office Gynecology. 2nd ed. St. Louis; Mosby-Year Book, 1996:317–342.
4. **Vejtorp M, Bollerup AC, Vejtorp L, et al.** Bacterial vaginosis: a double-blinded randomized trial of the effect of treatment of the sexual partner. Br J Obstet Gynaecol 1988; 95:920–926.
5. **Van Slyke KK, Michel VP, Rein MF.** Treatment of vulvovaginal candidiasis with boric acid powder. Am J Obstet Gynecol 1981; 141:145–148.
6. **Hilton E, Isenberg HD, Alperstein P, France K, Borenstein MT.** Ingestion of yogurt containing *Lactobacillus acidophilus* as prophylaxis for candidal vaginitis. Ann Intern Med 1992; 116:353–357.
7. **Hager WD, Brown ST, Kraus SJ, et al.** Metronidazole for vaginal trichomoniasis: seven-day vs single-dose regimens. JAMA 1980; 244:1219–1220.
8. **Krieger JN.** Trichomoniasis in men: old issues and new data. Sex Transm Dis 1995; 22:83–96.

ADDRESS: *Amelia Cleveland, MD, Turning Pointe, Women's Health Professionals, 789A White Pond Dr., Akron, OH 44087, e-mail ameliacleveland@msn.com.*