Diagnosis And Management Of Infectious Vaginitis

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***Abstract*: Vaginitis is an important gynecologic disorder that accounts for nearly 5 million office visits to physicians each year. Infectious vaginitis is the most common cause for an abnormal vaginal discharge; other possible causes include cervicitis, atrophic vaginitis, physiologic discharge, physicochemical vaginitis, and psychosomatic vaginitis. Although the history and physical examination may suggest the diagnosis, laboratory confirmation is required. The vaginal pool wet mount remains the cornerstone in the office diagnosis of vaginitis, with the "sniff" test, vaginal pH determination, and the "swab" test all playing important adjunctive roles. Metronidazole is the only effective treatment for trichomoniasis in the United States. The vaginal administration of an imidazole antifungal agent is the mainstay of treatment of vaginal candidiasis. Despite a search for alternative drug regimens, a 7-day course of metronidazole therapy remains the treatment of choice for bacterial vaginosis. (J Am Board Fam Pract 1990; 3:195-205.)**

Vaginitis is an important and often challenging problem in office gynecology. Generally regarded as a mundane, benign disorder, vaginitis is nevertheless the source of physical discomfort and psychosocial embarrassment. In an ambulatory setting, nearly 1 percent of antibiotics are prescribed for women with this diagnosis.[1] Although "shotgun" therapy based on an "eyeball" diagnosis was a common practice in the past, modern management of vaginitis demands that a specific diagnosis be made. This article reviews the clinical aspects of vaginitis and focuses on the diagnosis and management of infectious vaginitis.

Frequency

Although exact figures are unavailable, vaginitis is thought to be the most common gynecologic disorder seen in clinical practice. Gardner estimated that vaginal infections were likely to develop in one-third of all menstruating females.[2] A national ambulatory medical care survey found that vaginal complaints were responsible for nearly 5 million physician visits per year.[3]

Causes

When vaginitis is the suspected diagnosis, it is important to appreciate that the presence of a vaginal discharge is not necessarily synonymous with a vaginal infection. In a study of more than 20,000 women with an "abnormal" discharge, Fleury found that etiologies other than infectious vaginitis accounted for more than one-third of cases.[4] The differential diagnosis of vaginitis is listed in Table 1.

Physiologic Vaginal Discharge

Because 10 percent of patients complaining of vaginitis may have a physiologic discharge,[4] it is important to understand what constitutes a normal discharge. The normal vaginal discharge consists primarily of exfoliated vaginal squamous and cervical columnar cells suspended in a fluid medium. The vaginal fluid is derived from cervical mucus; vulvar secretions from sebaceous, sweat, and Bartholin and Skene glands; and serum transudate from capillaries in the vaginal wall.[5]

Clinically, a normal vaginal discharge is a clear or opaque white, nonhomogenous, highly viscous suspension that is unassociated with pruritus, burning, or malodor.[6] It is normal for secretions to increase in volume at the time of ovulation, following menstruation, during pregnancy, and following intercourse.[7] In addition, increased volumes of vaginal secretions may also arise from anxiety, the use of oral contraceptives, cervical ectopy, and frequent vaginal douching.[8]

The indigenous vaginal flora is an ecological system comprising both anaerobic and aerobic organisms, with the former outnumbering the latter by a factor of approximately 10. Lactobacilli (or Döderlein bacilli) dominate the facul-

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Table 1. Differential Diagnosis of Vaginal Discharge.

Physiologic vaginal discharge
Infectious vaginitis
Bacterial vaginosis
Trichomonas vaginitis
Candida vaginitis
Atrophic vaginitis
Cervicitis
Physicochemical vaginitis
Allergic-irritant vaginitis
Foreign body vaginitis
Psychosomatic vaginitis
Miscellaneous
Cervical polyps-neoplasms
Condyloma acuminatum
Rectovaginal fistula
Vulvar or vaginal neoplasms

tative flora, which also includes *Staphylococcus epidermidis*, diphtheroid bacilli, Group D streptococci, and *Escherichia coli*. Important anaerobic organisms include *Peptococcus*, *Peptostreptococcus*, anaerobic lactobacilli, and *Bacteroides* species.[9,10] Despite their pathogenic potential, *Gardnerella vaginalis* and *Candida albicans* are part of the normal flora in up to 50 percent[11] and 20 percent[12] of women, respectively.

Infectious Vaginitis

Bacterial vaginosis is the most recent and perhaps most appropriate term for a clinical entity that has previously been known by a number of names including nonspecific vaginitis, *Hemophilus* vaginitis, *Corynebacterium vaginale* vaginitis, nonspecific vaginosis, and *Gardnerella* vaginitis. It has emerged as the number one cause of infectious vaginitis, accounting for nearly one-half of cases.[13] Bacterial vaginosis is a synergistic, polymicrobial, superficial vaginal infection characterized by a reduction in the concentration of lactobacilli and concomitant overgrowth of both anaerobic bacteria (particularly *Peptococcus*, *Bacteroides*, and *Mobiluncus* species) and *Gardnerella vaginalis* to a concentration 100 to 1000 times higher than normal.[11,14] Trimethylamine, putrescine, and cadaverine are among the amines elaborated in excess by the anaerobic overgrowth and probably are responsible for the fishy malodor, which is the hallmark of this infection.[15]

Vaginal candidiasis is a common problem that affects up to 75 percent of women at least once during their reproductive years.[16] Eighty to 90 percent of cases are caused by *Candida albicans*,[12] with the remainder caused by other *Candida* species such as *Candida glabrata* and *Candida tropicalis*.[17] *Candida albicans* is a dimorphic fungus that is frequently isolated as a commensal on mucocutaneous surfaces, including the vagina. It is an opportunistic pathogen that produces vaginitis when it overgrows the bacterial vaginal flora, a development that occasionally can be linked to factors altering its environmental milieu, compromising local host defenses, or both. Such predisposing factors include the reduction of the normal bacterial population stemming from broad-spectrum antibiotic use, increased vaginal epithelial glycogen as in pregnancy or uncontrolled diabetes, as well as excessive perineal heat and moisture associated with the wearing of tight, insulating clothing.[12]

Trichomonas vaginalis is a unicellular, flagellated protozoan that commonly inhabits the lower genitourinary tract. It is an anaerobic parasite that is the third leading cause of infectious vaginitis, accounting for 15 to 30 percent of cases.[4,6] Although trichomoniasis is sexually transmitted and acquired in almost all cases, rare nonvenereal transmission is theoretically possible because the organism has been isolated from toilet seats and can survive in tap water, soap water, bubble baths, chlorinated swimming pools, and hot tubs.[18,19]

Atrophic Vaginitis

Atrophic vaginitis is an inflammatory disorder of the vagina, a consequence of inadequate estrogen production. It is primarily a problem of postmenopausal women but may be seen in lactating and prepubertal patients as well. The hypoestrogenic state causes "thinning" of the vaginal epithelium, making it more susceptible to trauma and secondary bacterial invasion.

Cervicitis

Cervicitis is a common though oftentimes overlooked cause of an abnormal discharge. Fleury[4] reported that nearly one-fourth of women complaining of vaginal discharge had cervicitis instead. Herpes simplex virus, *Chlamydia trachomatis*, and *Neisseria gonorrhoeae* are the major infectious causes of cervicitis, with the latter two responsible for nearly one-half of cases of mucopurulent cervicitis.[20]

Physicochemical Vaginitis

Allergic-irritant vaginitis can arise from almost any agent that comes in contact with the vagina. Agents capable of eliciting vaginal inflammation include genital soaps, douche preparations, bubble baths, genital deodorants, spermicidal agents, and intravaginal medications.[21] Sexual transmission of IgE antibodies in semen has recently been implicated by Witken and coworkers as a possible cause of allergic vaginitis.[22]

Although more commonly seen in the preadolescent girl, foreign body vaginitis can occur in adult women as well. Wads of toilet tissue and cotton are commonly responsible in children, whereas forgotten tampons, contraceptive devices, pessaries, and sexual implements are commonly implicated in adults.

Psychosomatic Vaginitis

Psychosomatic vaginitis is an elusive diagnosis that accounts for up to 2 percent of patients with vaginitis. It is primarily a diagnosis of exclusion that should be considered in patients who have completely normal examinations and laboratory evaluations. Hallmarks of this disorder, first described by Dodson and Friedrich,[23] are: (1) persistent symptoms of longstanding duration, (2) lack of demonstrable pathology, (3) sexual inactivity as a direct result of symptoms, (4) unsuccessful consultations with multiple physicians, (5) "allergy" to many common vaginal preparations, (6) reluctance to accept the suggestion of a psychophysiologic cause, and (7) emotional lability and dependency.

Miscellaneous

Less common causes of an abnormal vaginal discharge include cervical polyps or neoplasms, macerated condyloma acuminatum, rectovaginal fistulas, and vulvar and vaginal neoplasms.

Clinical Evaluation

Patients with vaginitis generally have complaints of vaginal irritation, vaginal discharge, or both. Important historical information to elicit from such patients is presented in Table 2. Bacterial vaginosis typically produces a grayish, malodorous discharge, whereas a copious, frothy, yellow-green discharge is characteristically associated with vaginal trichomoniasis. Vaginal soreness and dyspareunia in association with a thin, grayish, occasionally bloody discharge in a postmenopausal woman should immediately arouse suspicion of atrophic vaginitis. Likewise, a pruritic, white, curdlike discharge in a woman with history of recent antibiotic or steroid use, pregnancy, or diabetes suggests vaginal candidiasis.

Following the history, a thorough gynecologic examination should be performed. This should include not only careful inspection of the discharge but the vulvovaginal and cervical areas. Vaginal erythema and edema are indicative of an inflammatory vaginal process, while a mucopurulent cervical discharge coupled with a friable, inflamed cervix is pathognomonic for cervicitis.

Although clinical findings may suggest a diagnosis, they generally lack the sensitivity and specificity to be used as the sole basis for diagnosis. For example, pruritus, usually a symptom of candidiasis, can be absent in 25 percent[24] and present in 48 percent of those with *Trichomonas* vaginitis and 13 percent of those with bacterial vaginosis.[25,26] Similarly, vaginal malodor, the hallmark of bacterial vaginosis, can be absent in one-third[27,28] and present in 50 percent of those with vaginal trichomoniasis.[29] Finally, the presence of a "strawberry cervix" (punctate subepithelial hemorrhages) is pathognomonic for trichomoniasis but seen in only 2 to 3 percent of cases.[30] It is evident that the laboratory must play a pivotal role in the diagnosis of suspected vaginitis.

Table 2. Information Useful in the Evaluation of Vaginitis.

Age
Menstrual status
Characteristics of discharge
Onset
Color
Texture
Viscosity
Odor
Associated symptoms
Vaginal irritation
Pruritis
Dysuria
Dyspareunia
History of diabetes mellitus, genitourinary infections
Medication use
Method of contraception
Sexual history
Marital status
Number of partners
Feminine hygienic practices

Laboratory Evaluation

Vaginal Pool Wet Mount

The vaginal pool wet mount is the most important tool in the office diagnosis of vaginitis. The optimal time for performing this examination is while the patient is experiencing symptoms. It is important that the patient abstain from douching for at least 2 days before the examination and not to insert an intravaginal medication or contraceptive for at least 5 days.[31] The test entails the microscopic examination of the vaginal discharge, first with the low-power (×100) objective and then with the high-power (×400) objective. Two vaginal slides are generally examined, one with saline and the other with potassium hydroxide (KOH).

The saline slide is prepared by mixing a small sample of the discharge with a few drops of fresh, physiologic saline and then covering the suspension with a coverslip. The microscopic examination of a normal vaginal discharge shows many vaginal epithelial cells with sharply defined cellular and nuclear borders (Figure 1), an abundance of large gram-positive rods (lactobacilli), and a few white cells (WCs). An excessive number of white cells (generally defined as either more than one per epithelial cell or more than ten per high-power field) is indicative of an inflammatory process (Figure 2) and suggestive of cervicitis or trichomoniasis.[32] A variable number of white cells are seen in patients with candidiasis, and a reduced number are generally seen in patients with bacterial vaginosis.

The diagnosis of vaginal trichomoniasis is made in 50 to 90 percent of affected women by

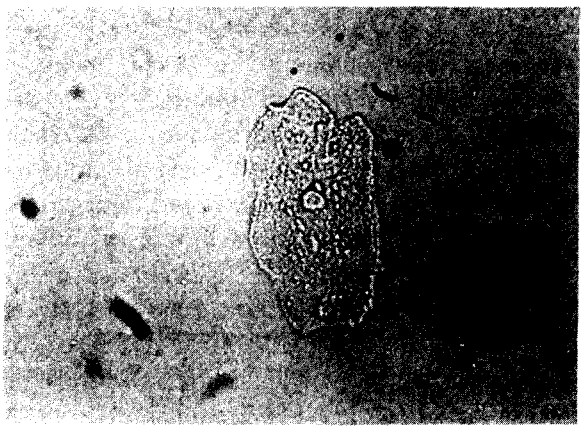

Figure 1. Photomicrograph of a saline wet mount preparation demonstrating a normal vaginal epithelial cell. Note the distinct cell border and the discernable nuclear outline.

Figure 2. Photomicrograph of a saline wet mount showing an excessive number of white cells.

identification of this extracellular parasite on saline wet mount (Figure 3).[33] *Trichomonas vaginalis* is a pear-shaped organism slightly larger than a white cell that is readily identified by its jerky, flagellate motility and undulating membrane. Because trichomonads become round when they die and are indistinguishable from white cells, it is important that the saline is fresh and that the slide is examined as soon after preparation as possible.[34]

A "clue cell" is an exfoliated vaginal epithelial cell that appears under light microscopy to be heavily stippled or granular in appearance because of the adherence of gram-negative coccobacilli to its surface. An obscure cellular outline is an important diagnostic feature of a clue cell, distinguishing it from a normal vaginal epithelial cell (Figure 4). The presence of "clue cells" substantiates the diagnosis of bacterial vaginosis and is found in 90 percent of cases.[27]

The KOH slide is prepared by mixing a sample of the discharge with a few drops of 10 percent KOH. The KOH dissolves the epithelial elements on the slide (a process accelerated by gently heating the slide), facilitating the identification of fungal elements. The identification of pseudohyphae and budding yeast forms (spores) confirms the presence of *Candida albicans* (Figure 5), whereas the finding of only spores with the absence of pseudohyphae (mycelia) suggests the presence of *Candida glabrata*. The reported sensitivities of the KOH slide for detecting vaginal candidiasis range from 21 to 94 percent.[35-37]

Figure 3. Photomicrograph of a saline wet mount showing *Trichomonas vaginalis*.

"Sniff" Test

The "sniff" test (or "whiff" test) is a simple test that detects the presence of certain amines arising from abnormal vaginal anaerobic metabolism. A positive test, defined as the production of a "fishy," aminelike odor when 10 percent KOH is added to the vaginal discharge sample, occurs as the result of increased volatility of the odoriferous amines with elevation of the pH. A positive result substantiates the diagnosis of bacterial vaginosis and is found in 67 to 76 percent of cases.[27,28] However, this test is not specific for this infection and can be positive in other anaerobic states, such as vaginal trichomoniasis.[38]

Vaginal pH

Determination of the vaginal pH is a simple though often overlooked diagnostic aid that is a valuable adjunct to the wet mount preparation. It is performed by placing a drop of the discharge onto commercial pH paper and interpreting the resultant color. The vaginal sample should be obtained from the lateral or posterior fornix of the vagina, taking special care to avoid sampling the cervical mucus.[11]

In the menstrual woman, the normal vaginal pH is slightly acidic (pH 3.5 to 4.5) as a result of lactic acid production by lactobacilli. Ninety-two percent of normal women have been found to have a vaginal pH of less than 4.7.[13] A pH greater than 4.5 is considered abnormal and is present in 81 to 97 percent of patients with bacterial vaginosis[27,39] and more than 60 percent of patients with *Trichomonas* vaginitis.[30] An abnormally alkaline pH, however, is a relatively nonspecific finding; Eschenbach and colleagues[39] reported a vaginal pH greater than 4.7 in nearly 50 percent of patients attending a sexually transmitted diseases clinic, excluding those with bacterial vaginosis and trichomoniasis. The diagnostic value of this test is invalidated if the sample is contaminated with blood, cervical mucus, semen, amniotic fluid, or a douche preparation.

"Swab" Test

The "swab" test was first proposed in 1984 by Brunham and coworkers[40] as a means of confirming the diagnosis of mucopurulent cervicitis. It is a simple test that is performed by collecting endocervical mucus on a white-tipped swab (taking care to avoid contamination by vaginal secretions) after wiping the ectocervix clean with a large cotton swab. A positive result is indicated by either a "yellow" appearance of the cervical mucus on the swab or the presence of 10 or more polymorphonuclear leukocytes in five nonadjacent fields on Gram stain of the endocervical mucus.

Vaginal Stained Smears

Stained smears of vaginal secretions are not routinely performed in the evaluation of vaginitis but can be of value in certain patients. For example, a Hansel stain can detect and quantitate the presence of eosinophils in the vaginal secretions.[21] Eosinophilia in the vaginal discharge, greater than 25 percent, has been found by Ricer to indicate allergic vaginitis.[41]

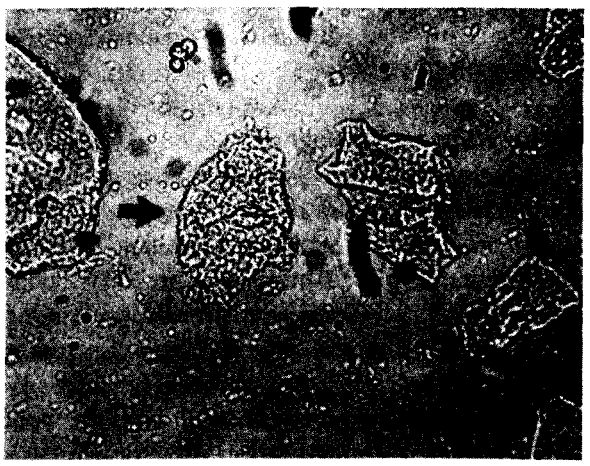

Figure 4. Photomicrograph of a saline wet mount showing a clue cell (arrow). Note how the cell border and nuclear outline are obscured by the adherent coccobacilli.

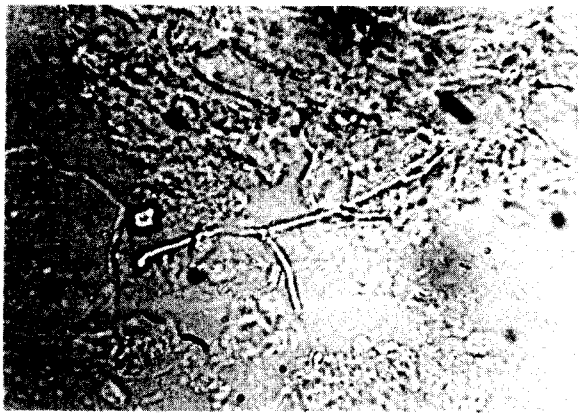

Figure 5. Photomicrograph of a potassium hydroxide wet mount showing pseudohyphae characteristic of *Candida albicans*.

Several investigators have found the vaginal Gram stain smear to be an accurate means of diagnosing bacterial vaginosis.[11,39,42] Gram stain criteria for bacterial vaginosis are *Gardnerella* morphotypes (small, gram-variable bacilli) and at least one other morphotype (gram-positive cocci, curved rods, gram-negative rods, or fusiforms) in amounts of five or more per oil immersion field with fewer than five lactobacillus morphotypes (large gram-positive bacilli) per oil immersion field. A vaginal Gram stain is classified as normal if lactobacillus morphotypes are present in amounts greater than five or more per oil immersion field, alone or in combination only with *Gardnerella* morphotypes. Although found by Spiegel, et al.[42] to possess excellent sensitivity and specificity for bacterial vaginosis, the diagnostic accuracy of the vaginal Gram stain is likely to vary with the skill and experience of the microscopist.

Vaginal Hormone Cytology

Vaginal hormone cytology has been used for many years to evaluate the estrogen status of postmenopausal women. It is a cytological technique that samples a minimum of 200 vaginal epithelial cells obtained from the lateral wall of the midportion of the vagina, classifying them into one of three cell types: parabasal, intermediate, and superficial. An increased proportion of parabasal cells (i.e., maturation value of less than 40 percent or parabasal cells exceeding 20 percent) characterizes a hypoestrogenic state and substantiates the presence of atrophic vaginitis.[43]

Genital Cultures

Vaginal cultures have a limited role in the diagnosis of vaginitis and are best used on a selective basis. Vaginal cultures should be strongly considered in patients with persistent or recurrent vaginitis, particularly when a definitive diagnosis could not be made on the basis of the previously described tests. When trichomoniasis is suspected clinically, but the wet mounts are repeatedly negative, confirmation of this diagnosis can be made by culturing the discharge on either Kupferberg medium or Diamond Medium Modified™.[33] Similarly, the Sabouraud or Nickerson medium can be used to identify Candida infection. Because *Gardnerella vaginalis* can be recovered from normal women and is but one component of a polymicrobial infection, isolation of this organism adds little to the clinical picture and is rarely, if ever, helpful for making a diagnosis.

Patients with suspected cervicitis, a purulent vaginal discharge, or both, warrant evaluation for the presence of *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. The diagnosis of gonorrhea is best made on culture, using a modified Thayer-Martin medium. Although cultures remain the most sensitive and accurate method for detecting *Chlamydia*, antigen detection systems (e.g., direct immunofluorescent test, enzyme immunoassay test) have been developed that are not only more convenient but have a reported sensitivity ranging from 70 to 98 percent and specificity exceeding 90 percent.[44]

Management of Infectious Vaginitis

Trichomonas Vaginalis

A definitive diagnosis of *Trichomonas* vaginitis can be made by either identifying motile trichomonads on the wet mount preparation or by a positive culture. If trichomonads are absent on the wet mount and cultures are unavailable, a presumptive diagnosis can be made in patients with a compatible clinical picture (abnormal vaginal discharge, elevated pH, and excessive number of white cells) provided the possibility of cervicitis is adequately excluded.[45]

Metronidazole, a 5-nitroimidazole derivative first introduced in 1960, remains the only effective treatment for trichomoniasis in the United States. The single 2-gram dose is effective in 86 to 97 percent of cases[25,46,47] and is favored by most clinicians because of easy administration,

better compliance, and lower cost. However, nausea and vomiting can be a problem with this regimen, affecting 4 to 16 percent of treated patients.[25,47] Alternatively, the traditional 7-day regimen of 250 mg three times daily can be considered, particularly in those intolerant of or who fail the single 2-gram treatment. Cure rates reported for the 7-day treatment range from 81 to 98 percent.[25]

Metronidazole-resistant strains of *Trichomonas vaginalis* are rare but must be considered in patients refractory to standard treatment. After excluding noncompliance and reinfection from an untreated partner, *Trichomonas* cultures and susceptibility testing to metronidazole can be done. The treatment options in patients with resistant trichomoniasis include prescribing a higher dose of metronidazole (i.e., 500 mg three times daily for 10 to 14 days), combined oral and intravaginal metronidazole therapy, and intravenous metronidazole.[48,49]

Adverse reactions to metronidazole include nausea, dysgeusia, headache, dizziness, peripheral neuropathy, and reversible neutropenia. Metronidazole can produce a disulfiramlike reaction when alcohol is consumed during therapy; thus, patients need to abstain from alcoholic beverages for at least 24 hours following the last dose.

Metronidazole has been shown to be mutagenic in bacteria and carcinogenic and tumorigenic in mice and rats receiving long-term, high doses of the drug.[48] Studies in humans have not shown metronidazole to be a significant carcinogen but have been deemed inadequate to exclude the possibility of delayed oncogenic potential.[48,50] Because human teratogenicity remains uncertain, metronidazole should be avoided during pregnancy and is absolutely contraindicated in the first trimester. In pregnant patients, intravaginal clotrimazole (100 mg daily for 7 days) can provide symptomatic relief and may effect a cure in 48 to 66 percent of patients.[33] When metronidazole is required in a lactating woman, it should be administered as a single 2-gram oral dose, and breast-feeding should be withheld for 24 hours after the dose to permit adequate maternal excretion of the drug.[51]

Because trichomoniasis is a sexually transmitted disease (STD), examination and simultaneous treatment with either the single dose or 7-day regimen is recommended for the patient's sexual contacts. Although empiric treatment of the man partner is generally favored,[2,10,12,33] the diagnosis of trichomoniasis in the man can be confirmed on microscopic examination of the sediment of a first-void morning urine specimen or of a urethral discharge obtained spontaneously or following prostatic massage. Because studies have shown concomitant infection with gonorrhea in 20 to 50 percent of women with trichomoniasis,[45] both the patient and her sexual consort(s) warrant examination for gonorrhea and other STDs.

Vaginal Candidiasis

Management of symptomatic vaginal candidiasis in the United States has generally relied on topical polyene and imidazole antifungal agents. In the past, candidiasis called for nystatin, a polyene antibiotic, at a dose of 100,000 units intravaginally twice daily for 14 days. During the past decade, the imidazoles replaced nystatin as the mainstay of treatment, producing cure rates of 85 to 95 percent.[10,32] Effective vaginal regimens employing imidazoles include: (1) butoconazole nitrate – 100 mg daily for 3 days; (2) miconazole nitrate – 100 mg daily for 7 days or 200 mg daily for 3 days; (3) clotrimazole – 100 mg daily for 7 days, 200 mg daily for 3 days, or 500 mg immediately; and (4) terconazole – 20 mg daily for 7 days or 80 mg daily for 3 days.[24,52-54] In addition to the local adverse effects (e.g., vaginal itching, burning) occurring infrequently with all these agents, flulike symptoms (e.g., transient headache, chills, fever, and hypotension) have been reported in some patients treated with terconazole.[55]

Less commonly used agents for the treatment of vaginal candidiasis include boric acid powder and gentian violet. In a study by Van Slyke, et al.,[37] the daily intravaginal administration of 600 mg boric acid powder in a gelatin capsule for 14 days yielded a cure rate of 92 percent 7 to 10 days after treatment and 72 percent 30 days after treatment. Although messy and occasionally irritating, the topical application of 1 percent aqueous solution of gentian violet to the vulvovaginal area is also considered an effective form of treatment.[19]

For patients with persistent or recurrent *Candida* vaginitis, predisposing factors should be identified and, if possible, eliminated. Such pre-

disposing factors include unrecognized or poorly controlled diabetes mellitus, antibiotic or corticosteroid use, a *Candida* genital infection in the patient's sex partner, and the wearing of tight, restrictive, synthetic underclothing. When these factors have been adequately excluded, fungal cultures may be of value by detection of a *Candida* species likely to be resistant to the usual antifungal agents.[17] For example, effective management of *Candida glabrata* may require the use of gentian violet,[2,19] and *Candida tropicalis* may require topical treatment with 5-flucytosine.[56]

Repeated courses of topical anticandidal agents are commonly employed for patients with recurrent candidiasis. These agents can be administered either at the first sign of infection or on an intermittent, prophylactic basis. Davidson and Mould[57] concluded that a once-a-month, 7-day course of intravaginal clotrimazole was effective in alleviating symptoms associated with recurrent candidiasis. In a recent study, Sobel, et al.[58] reported a one-third reduction in recurrence rates in patients treated with an intravaginal 500-mg clotrimazole tablet administered once a month.

In patients who fail to respond to topical therapy, prophylactic therapy with oral ketoconazole is the final therapeutic option. In a prospective study of 74 women with recurrent vulvovaginal candidiasis, Sobel[16] found that cyclic ketoconazole (400 mg daily for 5 days beginning with the onset of menses for six menstrual cycles) prevented recurrences in more than 70 percent of patients and that continuous low-dose therapy (100 mg daily for 6 months) was successful in 95 percent of patients. Although clearly the most effective treatment available, enthusiasm for ketoconazole is tempered by the cost, as well as hepatotoxicity (seen primarily in patients more than 50 years) associated with its prolonged use.[16,59]

Bacterial Vaginosis

The diagnosis of bacterial vaginosis can be made reliably if at least three of the following four criteria are met: (1) the presence of a thin and homogenous-appearing vaginal discharge, (2) a vaginal pH exceeding 4.5, (3) a positive "sniff" test, and (4) clue cells on saline wet mount examination.[8,27] The importance of effective treatment for this condition lies not only in the symptoms it can produce but also its implication as a risk factor for pelvic inflammatory disease and certain obstetric complications (e.g., preterm labor, postpartum endometritis, and post-Cesarean endometritis).[39,60,61] A 7-day course of metronidazole, 500 mg orally twice daily, remains the treatment of choice for bacterial vaginosis, with a cure rate exceeding 97 percent immediately after therapy and 86 to 94 percent 4 weeks after therapy.[28,62,63]

Cost, compliance, and drug safety have spurred a search for shorter though equally effective courses of metronidazole treatment. The most effective of these is the two-dose regimen reported by Jerve and associates.[63] In their multicenter Norwegian study, metronidazole given orally as a single 2-gram dose on days 1 and 3 produced a 94 percent cure rate determined 4 weeks from the start of therapy. Three- and 5-day regimens have also been studied and judged inferior to the standard 7-day regimen on the basis of clinical recurrence rates 29 days post-therapy.[64] Studies investigating the efficacy of a single 2-gram dose have yielded mixed results,[65] with most investigators reporting a higher failure rate for the single dose 3 to 4 weeks after treatment.[62,64,66] The use of vaginal metronidazole sponges in the treatment of bacterial vaginosis is currently under investigation, with a recent clinical trial reporting an 88 percent rate of cure 4 weeks after therapy.[67]

A number of alternative drugs have been studied in the treatment of bacterial vaginosis, but none has matched the efficacy of metronidazole. Intravaginal sulfonamide creams were commonly prescribed in the past but have since been shown to be effective in only 14 to 56 percent of patients. Doxycycline, 100 mg twice daily for 7 days, has produced equally mixed results, with rates of cure ranging from 14 to 64 percent.[28,68] Ampicillin, 500 mg four times daily for 7 days, effectively treats 34 to 46 percent of patients and is considered the drug of choice in pregnant patients. In a recent double-blind study by Greaves, et al.,[69] 7 days of clindamycin, 300 mg twice daily, yielded a cure rate (94 percent) 7 to 10 days after treatment that was comparable with the standard 7-day metronidazole regimen; however, whether clindamycin is as effective in reducing recurrence (or relapse) rates during the month following completion of therapy still remains to be determined.

Controversy continues to exist whether the man consort(s) of the patient with bacterial vaginosis requires simultaneous treatment. Despite a study by Mengel, et al.,[65] which concluded that treatment of the man partner produced a short-term reduction in recurrence rate, other studies have failed to report a benefit from simultaneous treatment.[8,62,64] At the present time, it appears reasonable to reserve treatment of the man partner to instances of recurrent infections in the woman.

Summary

Vaginitis is a common outpatient problem that represents a diagnostic challenge. It is a disorder that is responsible for an estimated 5 million physician visits per year, accounting for nearly 1 percent of antibiotics prescribed in the ambulatory setting. Infectious vaginitis is the most common diagnosis made in patients seeking care for an "abnormal" discharge, with most of the remaining cases caused by cervicitis, physiologic discharge, atrophic vaginitis, and physicochemical vaginitis. Although the history and physical examination may suggest a diagnosis, confirmation by simple office tests should be performed routinely. The vaginal pool wet mount is the most important diagnostic test, with adjunctive roles played by measurement of the vaginal pH, the "sniff" test, and the "swab" test. For patients with persistent or recurrent vaginitis in whom a definitive diagnosis cannot be made on the basis of these tests, vaginal stained smears and genital cultures should be performed. Effective management for vaginal trichomoniasis continues to be metronidazole, prescribed either in a single-dose regimen or an extended 7-day course. The imidazole antifungal agents have emerged as the treatment of choice for vaginal candidiasis. A 7-day course of metronidazole is the gold standard of treatment for vaginosis.

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