

Abnormal vaginal discharge: Using office diagnostic testing more effectively

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Practice recommendations

- Accurate differential diagnosis for women complaining of abnormal vaginal discharge requires in-office diagnostic testing at minimum, and laboratory testing in selected cases.
- Test for *Chlamydia trachomatis* and *Neisseria gonorrhoea* when signs of purulent cervicitis are present (SOR: **B**).
- In suspected vulvovaginal candidiasis, culture is recommended for patients with recurrent or persistent symptoms and a negative wet mount result (SOR: **B**); rapid slide latex agglutination testing is not better than microscopy for diagnosing VVC (SOR: **B**).

In primary care practice, abnormal vaginal discharge is a common complaint. Signs and symptoms of vaginitis—the most common gynecologic diagnosis in primary care¹—are not specific for any single underlying cause.² Office-based diagnostic testing, which is underused,³ must be employed to ensure accurate diagnosis

and effective treatment. (An article on treatment by the same authors will appear in next month's issue of THE JOURNAL OF FAMILY PRACTICE.)

In a primary-care study,⁴ vulvovaginal symptoms including vaginal discharge were due to vulvovaginal candidiasis (VVC) in 27% of patients, bacterial vaginosis (BV) in 21%, trichomoniasis in 8%, *Chlamydia trachomatis* in 2%, *Neisseria gonorrhoea* (GC) in 1%, and no infection in 34%. Several pathogens may coexist.² VVC, BV, and trichomoniasis account for at least 90% of infectious vaginitis.⁵ This review will therefore focus heavily on these causes of vaginal discharge among women of reproductive age, including pregnant women.

■ CERVICITIS AND PHYSIOLOGIC CERVICAL DISCHARGE

Some women may interpret a physiologic increase in cervical mucous production as abnormal. It occurs cyclically prior to ovulation, is typically transparent and colorless, and may be more pronounced in women with an everted cervix.

Chlamydial infection

In the clinical examination of the cervix, 3 characteristics have been associated with chlamydial infection: yellow endocervical discharge, easily induced cervical bleeding, and opaque cervical discharge.⁶ All 3 findings are statistically significant and independently associated with

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How to perform a wet mount

To perform a wet-mount preparation correctly, dilute the vaginal discharge with 1 or 2 drops of 0.9% saline and place it on a slide. Examine the slide under low- and high-powered fields for vaginal squamous cells, white blood cells (WBCs), lactobacilli, clue cells, and trichomonads. An increased number of WBCs can be defined as >5–10 WBC/HPF or WBCs exceeding the number vaginal epithelial cells.

To prepare the potassium hydroxide (KOH) slide, place a generous amount of vaginal discharge on a slide with 10% KOH solution. Air- or flame-drying before examination under low-power microscopy may improve sensitivity. A positive KOH preparation will have hyphae, mycelial tangles, or spores.

chlamydial infection (odds ratios 2.8, 2.3, and 2.9, respectively). In the primary care study cited above, purulent cervical discharge was found in 6% of women, most commonly testing positive for Chlamydia, less often for GC.⁴

Trichomonas vaginalis may cause cervicitis as well as vaginitis. *Mycoplasma genitalium* has been proposed as an additional possible pathogen. It was identified in 7% of more than 700 women with mucopurulent cervical discharge seen in a STD clinic with otherwise negative cultures.⁷ With cervical discharge that appears to be purulent, testing is warranted as a minimum for Chlamydia and GC (SOR: **B**). Screening of asymptomatic women less than 26 years of age for Chlamydia is recommended by the US Preventive Services Task Force (SOR: **A**).

■ BACTERIAL VAGINOSIS

Bacterial vaginosis (BV) is neither an inflammatory condition nor an STD, but is a shift in vaginal flora from the normal condition in which lactobacilli predominate, to a polymicrobial flora in which gram-positive anaerobes predominate. In addition to annoying vaginal symptoms, BV is associated with increased risks of more serious

conditions such as pelvic inflammatory disease (PID), postoperative infections, and pregnancy-related complications including prematurity. It also increases the likelihood of acquiring HIV in women exposed to the virus.^{8,9}

Two principal factors put women at risk for acquiring BV: douching and exposure to a new sexual partner, both of which are thought to disrupt the vaginal ecosystem.¹⁰

Relative benefits of diagnostic tests

A gold standard test has not been established for BV. In about 50% of asymptomatic women, culture results are positive for flora such as *Gardnerella vaginalis*.⁵ While Amsel's criteria are often used as a reference and generally suffice for the evaluation of symptomatic women, the best candidate for a gold standard test is probably Gram stain assessment using Nugent's criteria (described in this section).¹¹ Lack of leukocytes in the vaginal fluid supports a diagnosis of BV. A finding of white blood cells in excess of the number of vaginal epithelial cells suggests an inflammatory process (SOR: **C**).¹²

Amsel's criteria with wet mount. The diagnostic approach most commonly used in the office is Amsel's criteria—homogenous discharge, positive whiff-amine test, pH >4.5, and clue cells found on wet-mount microscopy (see **How to perform a wet mount**).¹³ Three of 4 criteria deemed positive is considered diagnostic. If Gram stain is used as the reference standard, then Amsel's criteria have 70% sensitivity and 94% specificity for diagnosing BV.¹⁴ An analysis of the individual criteria follows. The positive and negative predictive values of each compared with the whole group as reference standard is displayed in **Table 1**.

Homogenous discharge. A thin, homogenous, grayish discharge is traditionally associated with BV. However, it is not specific to BV, being found commonly also in women with culture results positive for VVC or no diagnosis of vaginitis.^{2,15} It is the criterion least likely to be consistent with the whole group, seen in about half of women BV-positive and over one third of women BV-negative

using Amsel's criteria as the reference standard.¹⁵

Whiff test. The whiff test is performed by adding drops of 10% potassium hydroxide solution to the vaginal fluid. A positive result is a "fishy" amine odor. In a study¹⁶ of 100 women complaining of malodorous discharge, a positive whiff test was predictive of positive culture results for anaerobic flora such as *Bacteroides* sp. with sensitivity 67%, specificity 94%, and a positive predictive value of 95%. The whiff test was not positive in any of the 5 cases with positive culture results for *G vaginalis* in the absence of anaerobes. There were also 12 cases positive for anaerobes without *G vaginalis*.

pH >4.5. Since the abnormal flora of BV is consistently associated with a vaginal pH >4.5, a normal pH excludes a diagnosis of BV.^{17,18} The determination of pH in the narrow range around 4.5 is not accurate using standard nitrazine paper. Narrower-range test paper is available and more accurate. Examples include pH paper for 4.5 to 5.5 (Micro Essential Laboratory), FemExam pH and Amines Test Card (Litmus Concepts), pHem-ALERT: pH paper on a stick (Imagyn Gynecology). Cervical mucous, semen, and blood are alkaline and can interfere with pH testing. Estrogen production is also necessary to maintain an acidic environment. A pH of 3.8 to 4.5 is consistent with normal vaginal flora in premenopausal women with normal estrogen production.¹⁷

Clue cells. Clue cells are vaginal epithelial cells coated with coccobacilli giving an appearance as if coated with ground black pepper. Clue cells on wet mount preparation is considered the most accurate of Amsel's diagnostic criteria for BV.¹⁹ On the other hand, office evaluation of the wet mount is considered by some authors to be unreliable due to dependence on the clinician's microscopy skills and lack of a durable record of the patient sample.

Gram stain a more objective test. A Gram stain evaluation using Nugent's criteria has been adopted as the gold standard test for research purposes, including studies of prematurity. The Gram-stained vaginal specimen is scored from

TABLE 1

Predictive values of Amsel's criteria (using 3 of 4 positive as diagnostic reference standard)

Diagnostic criterion	Predictive value (%)	
	Positive	Negative
Homogeneous thin discharge seen at introitus	42	89
pH >4.5	53	94
Odor on alkalization	94	93
Clue cells on wet mount	90	99

Source: Thomason et al 1990.¹⁵

0 to 10 based on semi-quantitative assessment of 3 classes of morphotypes (**Table 2**): large gram-positive rods (*Lactobacilli*), small gram-negative rods (*Gardnerella* and *Bacteroides* spp.), and small curved gram-variable rods (*Mobiluncus* spp.).¹¹

Diagnosis of BV is typically made when the Nugent score is 7 or more, which appears qualitatively as dominant morphotypes other than *Lactobacilli*. Gram staining is more objective and reproducible compared with wet-mount examination, with a sensitivity of 93% and specificity of 70% if Amsel's criteria are used as the gold standard.¹⁴ It is useful for the evaluation of asymptomatic women. It also provides a durable record of the patient specimen. Compared with Gram stain, Amsel's criteria tend to underdiagnose cases. We can expect that if screening for BV in pregnancy becomes a recommendation, Gram staining in a clinical laboratory will be the recommended method of diagnosis.

Other diagnostic tests for BV. DNA testing for *Gardnerella* is accurate for detection, but it is not synonymous with a diagnosis of BV, as described.²⁰ DNA testing is further described under "Differential Diagnosis." Gram staining is more reliable than gas-liquid chromatography²¹

TABLE 2

How to use Nugent's Gram stain criteria to diagnose bacterial vaginosis

<i>Lactobacillus</i> morphophytes	<i>Gardnerella</i> and <i>Bacteroides</i> spp. morphophytes	Curved gram-variable rods	Points
4+	0	0	0
3+	1+	1+ or 2+	1
2+	2+	3+ or 4+	2
1+	3+		3
0	4+		4

Review each of the first 3 columns in turn, assigning points at far right according to your exam findings. Add the points for all 3 columns for a final sum. A score of 7 or higher indicates bacterial vaginosis. Source: Nugent et al 1991.¹¹

and an assay for proline aminopeptidase (a metabolic product of some of the bacteria associated with BV).²² Latex agglutination testing for vaginal lactoferrin is a nonspecific marker for leukocytes, and thus inflammation. It is of little clinical utility in the diagnosis of vaginal discharge.²³

■ VULVOVAGINAL CANDIDIASIS

Candidiasis is the second most commonly diagnosed vaginitis in the United States. Some experts estimate that 75% of women will have a yeast infection at some point in life and 5% will have recurrent infections.²⁴ However, 10% to 30% of asymptomatic women with normal flora have positive culture results for *Candida*.²⁵⁻²⁹ The proportion of symptomatic women with positive culture results is 20% to 40%.^{4,30,31} Complications of VVC are rare,³² though vulvar vestibulitis³³ and chorioamnionitis in pregnancy³² have been reported.

Risk factors. Symptomatic yeast vaginitis has been associated with condom and diaphragm use, recent antibiotic use, receptive oral sex, oral contraceptive use, spermicide use, diabetes, and immunosuppression including AIDS.^{31,34-37} The associations with antibiotic use and oral contraceptives are not consistent.^{30,38} Although pregnan-

cy has been postulated as a risk factor for symptomatic VVC, prevalence of yeast on culture in pregnant women is similar to that of nonpregnant women.³⁰

Suggestive symptoms. Among women with a culture result positive for *Candida*, the most common symptom is pruritus or burning.²⁸ Abnormal discharge is a complaint for most symptomatic women with VVC confirmed by culture.² In addition, women may complain of a thick, odorless, cottage cheese-like discharge.³⁹ A thick, curdled-appearing discharge points to a diagnosis of *Candida* because it is rarely present with BV or trichomoniasis. In one study,²⁸ a thick curdled discharge had a positive predictive value of 84% for diagnosis of VVC by culture (SOR: **B**). However, a thin discharge does not rule out VVC; in another study, clinicians described discharge as thin in about half of women ultimately diagnosed with VVC by culture in another study (SOR: **B**).² On exam, vulvar and vaginal erythema are often present but are not specific findings. The accuracy of the clinical exam for VVC is poor compared with culture (SOR: **A**).^{2,30}

Pathogens. *Candida albicans* is present in 80% to 90% of patients with VVC.^{5,40} The

remainder have non-*albicans* species, including *C glabrata* and others.²⁸ An increase to almost 20% of non-*Candida* species in a vaginitis clinic by the mid-1990's may be related to increased use of imidazoles available over-the-counter.^{40,41} Wet mount results are typically negative in the presence of non-*Candida* VVC.²⁸

Diagnosis of VVC

The gold standard test for diagnosis of VVC is culture. The potassium hydroxide (KOH) wet mount is only 40% to 75% sensitive.^{28,29,42,43} False-positive results are also observed with variable frequency.⁴⁴ The pH of the discharge is usually not more than 5.0 with *Candida albicans*, but may be higher with non-*albicans* species such as *C glabrata*.⁴⁵ Culture is recommended for patients with recurrent or persistent symptoms and a negative wet mount result (SOR: **B**).^{5,28,46} Rapid slide latex agglutination testing is not better than microscopy (SOR: **B**).⁴²

■ TRICHOMONIASIS

Trichomonas, a motile protozoan with 4 flagella, causes the third most common form of vaginitis in the United States and is more common in some developing countries. Trichomoniasis accounts for no more than 10% of all cases of vaginitis, and it appears to be decreasing since the introduction of metronidazole.^{47,48} It is classified as an STD, although transmission is possible by other means if the organism is protected from desiccation—for example, in dirty washcloths or towels and contaminated water. Nonsexual transmission is thought to be uncommon.

Trichomoniasis is associated with GC and Chlamydia infections, and, like them, has been associated with seroconversion to HIV-positive status.⁴⁹ Trichomonads are identified in 30% to 80% of male sexual partners of infected women. In men, trichomoniasis most often is an asymptomatic carrier state.⁵⁰ However, it is the cause of about 10% of cases of nongonococcal urethritis in men.⁵¹

Limited epidemiologic knowledge

Our knowledge of the epidemiology of abnormal vaginal discharge is limited. Studies of vaginitis may exclude patients with vaginal discharge due to cervicitis; studies performed in sexually transmitted disease clinics are not representative of primary care practice; women who do not complain of abnormal vaginal discharge may have positive cultures for *Gardnerella vaginalis* and *Candida albicans*; and self-treatment of presumed yeast vaginitis with antifungals available over-the-counter further limits our knowledge of the prevalence and causes of vaginal discharge.

Clinical presentations. Women with trichomoniasis have variable presentations ranging from an asymptomatic carrier state to a malodorous, purulent discharge with vulvovaginal erythema. Punctate hemorrhagic cervical lesions are considered pathognomonic of trichomoniasis, but are seen in only about 2% of cases (SOR: **B**).⁵²

Diagnosis. Culture for trichomoniasis is the gold standard. Several culture media have been used, most commonly the Diamond medium. Recently introduced is a transport and culture medium for detection of Trichomonas (InPouch TV), which performs as well as Diamond medium (SOR: **A**).⁵³⁻⁵⁵ A DNA probe is also available and accurate (SOR: **A**).

Motile trichomonads are seen on wet preparation in only 50% to 80% of culture-positive cases (SOR: **B**).^{50,54,56} Polymorphonuclear leukocytes can be dominant on wet mount, making visualization of trichomonads more difficult. The pH of the vaginal fluid is usually basic.

Trichomonas reported with cervical cytology

Trichomonas may also be reported on Pap smears. A meta-analysis⁵⁷ comparing the pooled sensitivities and specificities of wet mounts and cytology

TABLE 3

Comparative findings among causes of vaginitis

Cause	Physical exam findings*	Gold standard test	pH	Leukocytes	Wet mount	Alternative test
Bacterial vaginosis	Variable	Gram stain	>4.5	No	Clue cells	Amsel's criteria
Aerobic vaginitis	Abundant purulent discharge	Culture	>4.5	Yes	Cocci or coarse rods	
<i>Candida</i> vaginitis	Adherent white disch. (thrush)	Culture	3.8–4.5	±	Pseudohyphae or budding yeast	DNA testing
Non- <i>Candida</i> yeast vaginitis	Variable	Culture	Any	±	Usually negative	
Trichomoniasis	Variable, occ. strawberry spots on cervix	Culture	>4.5	±	Motile trichomonads	DNA testing
Cytolytic vaginitis	Profuse discharge, often cheesy	Cytology and negative culture	3.5–5.5	±	Overgrowth of lactobacilli and squamous cell fragments	
Desquamative inflammatory vaginitis	Abundant purulent discharge	Parabasal epithelial cells and negative culture	>4.5	Yes		
Irritant and allergic vaginitis	Variable, often erythema	None	Any	±		

* Helpful when present.

demonstrated low sensitivities of 68% and 58%, respectively, and high specificities, 99.9% and 97%, respectively (SOR: **A**).

However, since cytology carries a 3% false-positive rate, its results are not diagnostic of trichomoniasis in low-risk, asymptomatic women.^{50,57} Treatment may be prescribed empirically based on positive cytology results. However, if an asymptomatic woman were concerned about whether she really has an STD, a positive wet prep would confirm the diagnosis.

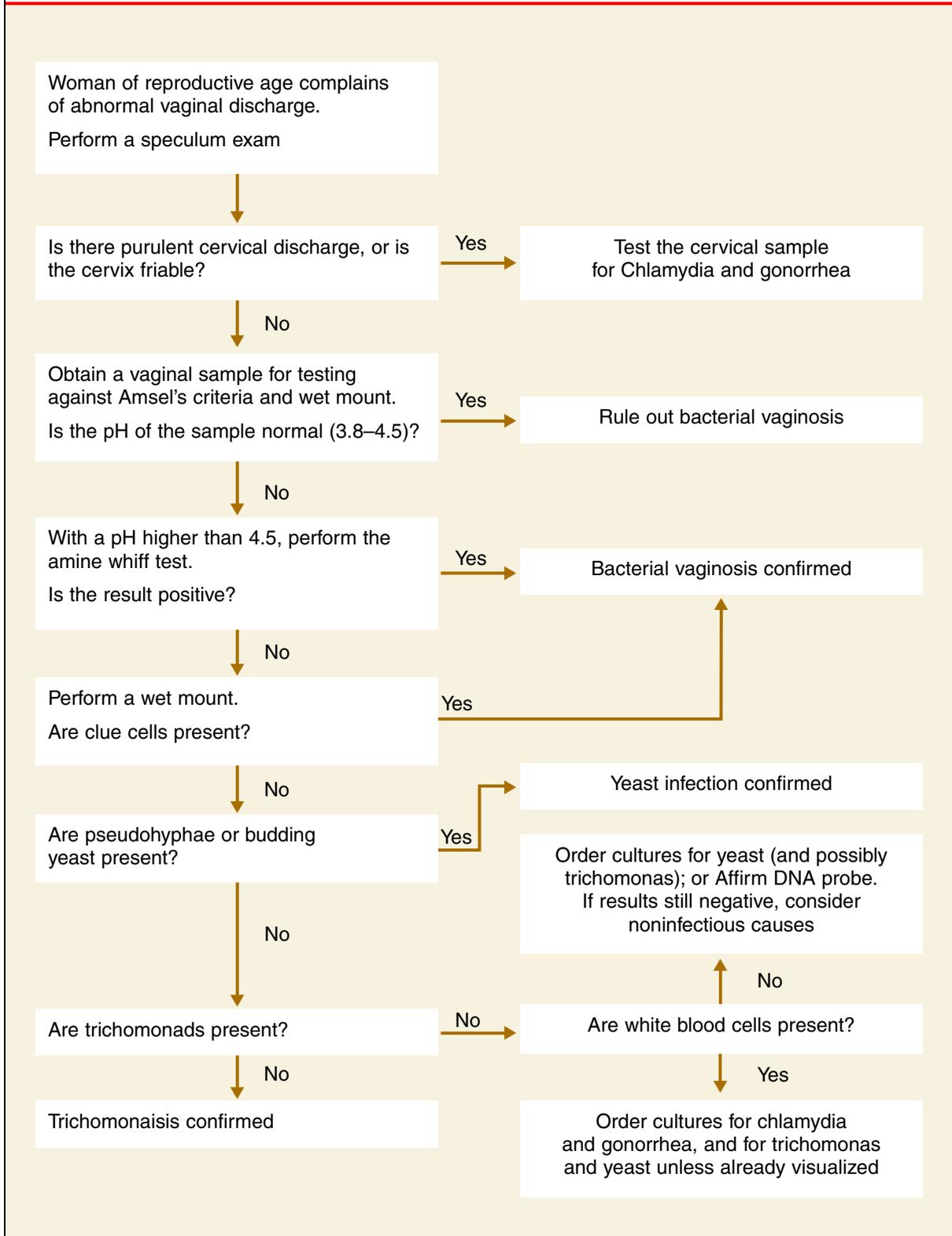
A negative wet prep should be followed up with culture to reliably rule out disease (SOR: **B**).

Trichomoniasis in pregnancy

Screening for asymptomatic trichomoniasis in pregnancy has not been recommended. In fact, some evidence suggests that treatment of trichomoniasis in pregnancy is associated with poorer pregnancy outcomes including lower birth weight and more prematurity (SOR: **B**).^{58,59}

FIGURE

Sequence of office tests to evaluate abnormal vaginal discharge



■ AEROBIC VAGINITIS

Aerobic vaginitis is a term proposed to describe purulent vaginal discharge with predominance of abnormal aerobic flora.⁶⁰ Aerobic vaginitis, which may be severe, has been reported as the cause of 5% of cases in a series from a specialty vaginitis clinic.⁶¹ The usual predominant microorganisms are group B streptococci, *Escherichia coli*, and *Staphylococcus aureus*. It is likely that less severe cases of aerobic vaginitis are not recognized in the primary care setting and are treated as BV or resolve spontaneously (SOR: C). The case series referred to above also reported good therapeutic response to 2% topical clindamycin (SOR: C).⁶¹

■ NONINFECTIOUS VAGINITIS

Noninfectious causes of vaginal discharge include physiologic, irritant and allergic, cytolytic vaginitis, desquamative inflammatory vaginitis, collagen vascular disease, and idiopathic vaginitis.

Irritant and allergic vaginitis may result from sensitivities to topical medications, the active or base ingredients of spermicidal products, douching solutions, and the latex of condoms or diaphragms. If a woman with persistent symptoms has been using such intravaginal products, she should stop (SOR: C).

Cytolytic vaginitis is characterized by overgrowth of lactobacilli and cytolysis of squamous cells, including presence of cytoplasmic fragments and intact cells with naked nuclei.⁶² The cause is uncertain but may include a reaction to intravaginal medications or other products such as tampons. It can be found in up to 5% of women with symptoms and signs of vaginitis.^{62,63} Symptoms often mimic VVC and may include a white, cheesy discharge. Vaginal pH ranges from 3.5 to 5.5. Recurrences during luteal phase of the menstrual cycle have been described.⁶⁴ Intravaginal antifungals should be discontinued. Baking soda sitz baths or douches are often used, but clinical trial data to support this practice are lacking (SOR: C).

Noninfectious desquamative inflammatory vaginitis (DIV) has also been described.⁶⁵ DIV is an uncommon vaginitis characterized by profuse purulent discharge with epithelial cell exfoliation. It may occur at any time during the reproductive years or after menopause. There is probably a heterogeneous group of causes of DIV. Some cases may correspond to a disorder within the spectrum of lichen planus.⁶⁶ Treatment is usually difficult, though there may be some response to local or systemic corticosteroid therapy (SOR: C).⁶⁵

■ DIFFERENTIAL DIAGNOSIS

A comparison of physical examination findings and diagnostic test results for various etiologies of vaginitis is summarized in **Table 3**. An algorithmic approach to the differential diagnosis of abnormal vaginal discharge is presented in the **Figure**. Diagnosis is complicated in that signs and symptoms do little to help differentiate among BV, VVC, and trichomoniasis. A study² of 22 genitourinary symptoms and signs showed that none differentiated among the 3 infections. This lack of clear-cut differences in symptoms also makes self-diagnosis and telephone triage inaccurate.^{67,68}

A DNA probe testing system (Affirm VP III Microbial ID Test) for differential diagnosis is available but expensive. It identifies *Gardnerella*, *Trichomonas*, and *Candida albicans* with a sensitivity of 90% to 95%.^{54,66} The analyzer costs approximately \$10,000 and would typically be purchased by a laboratory. Individual test kits cost about \$27.

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For more on bacterial vaginosis:

See “Should we screen for bacterial vaginosis in those at risk for preterm labor?” in this month’s **Clinical Inquiries, page 827.**

And next month’s Applied Evidence article:

Abnormal vaginal discharge: What does and does not work in treating underlying causes