Making the diagnosis: Vaginal infections

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Most women experience at least one vaginal infection characterized by vaginal discharge, itching, and/or odor during their lives. In women who present with these vaginal symptoms, the three most common conditions are bacterial vaginosis, vulvovaginal candidiasis, and trichomoniasis. In some cases, more than one vaginal infection is present. A problem-focused history, physical examination, and laboratory evaluation are necessary for accurate diagnosis. The author describes characteristic findings for these vaginal infections and discusses currently available diagnostic tests.

Although a health history by itself is unreliable for making a vaginal infection diagnosis, it can provide valuable information to guide physical examination and laboratory test decisions. The focused health history includes a description of the characteristics of the vaginal discharge, a sexual history, vaginal hygiene practices (e.g., douching), and previous history of vaginal infections and sexually transmitted infections (STIs). Healthcare providers (HCPs) should ask the patient whether she has used any medication or other products to treat her current symptoms, as well as the outcome of the treatment. In addition, HCPs should inquire about the date of the patient’s last normal menses and the presence of any spotting or bleeding between menses. A sexually active patient should be asked about postcoital spotting or bleeding, dyspareunia, and use of contraception. HCPs should review current medications and allergies.

The physical exam includes inspection of the vulva, vagina, and cervix. HCPs should evaluate the vulva and vagina for erythema, edema, and lesions. The cervix is inspected for signs of cervicitis that may be the source of abnormal discharge. HCPs should note vaginal discharge characteristics such as color, viscosity, adherence to vaginal walls, and presence of odor, and should collect a specimen from the lateral wall of the vagina for evaluation under a microscope. If the patient has risk factors for an STI or signs of cervicitis (e.g., mucopurulent discharge, friability), HCPs should collect a specimen from the endocervix for chlamydia and gonorrhea testing. In-office diagnostic tests include measurement of vaginal pH, wet mount microscopy, and an amine odor test (whiff test). In addition, point-of-care and laboratory-based diagnostic tests are available. Table 1 lists signs, symptoms, and various in-office test results for the differential diagnosis of vaginal discharge.1-3

Review of diagnostic tests
The most common in-office tests used to aid in the diagnosis of vaginal infections are a pH test of the vaginal discharge, wet mount microscopic inspection, and a whiff test. Also available are organism-specific point-of-care tests, which have higher sensitivity and equal or higher specificity than those of the wet mount. In some cases, laboratory tests may be indicated for diagnosis.
The pH of vaginal fluid can be determined by placing a strip of pH litmus paper directly on the wall of the vagina or placing discharge from a collection swab on the strip. As an alternative, HCPs can dip the strip into discharge pooled on the upper blade of the speculum. HCPs should avoid using discharge from the posterior vaginal fornix, which might be mixed with cervical secretions and could possibly affect the pH.1-3

The normal pH of the vagina is between 3.8 and 4.5. A vaginal pH less than 4.5 is consistent with physiologic discharge or vulvovaginal candidiasis (VVC). A vaginal pH greater than 4.5 predicts a diagnosis of bacterial vaginosis (BV) or Trichomonas vaginalis infection. When VVC and a concomitant BV or T. vaginalis infection occur, the vaginal pH may be above 4.5. Other factors that can cause an elevated pH include atrophic vaginitis or contamination of the specimen with blood, semen, or urine. A woman who is immediate postpartum, lactating, or menopausal may have an elevated vaginal pH due to reduced systemic estrogen levels. Because vaginal pH testing is not highly specific, the results must be interpreted within the context of a patient’s symptoms, physical exam findings, and wet mount findings.1-4

### Table 1. Differential diagnosis of vaginal discharge1-3

<table>
<thead>
<tr>
<th>Condition</th>
<th>Symptoms</th>
<th>Physical examination findings</th>
<th>In-office diagnostic test findings</th>
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| Bacterial vaginosis        | Thin, white vaginal discharge with a fishy odor that may worsen after sexual intercourse; itching and irritation are not common; up to half of women with bacterial vaginosis have no symptoms | Milky gray-white malodorous vaginal discharge, mildly adherent to the vaginal walls; no inflammation | - Vaginal pH >4.5  
- Whiff test result is positive  
- Wet mount: >20% of epithelial cells are clue cells, 0-1 WBCs per epithelial cell, lactobacilli reduced or absent  
- Point-of-care vaginal fluid sialidase test result is positive |
| Trichomoniasis             | Profuse yellow vaginal discharge; may have unpleasant odor; vulvar itching; dysuria may be present; may have postcoital spotting; many women are asymptomatic | Yellow or green, frothy vaginal discharge; erythema and edema of vulva and vagina; cervical petechiae (strawberry cervix) may be present | - Vaginal pH >4.5  
- Whiff test result negative or positive  
- Wet mount: motile trichomonads, >1 WBC per epithelial cell, lactobacilli reduced or absent  
- Point-of-care rapid antigen test result is positive |
| Vulvovaginal candidiasis   | Pruritus is predominant symptom; thick, white, clumpy vaginal discharge; depending on degree of vulvar skin involvement, may have external dysuria and dyspareunia | Erythema, edema, and excoriation of vulva may be present; cottage cheese-type discharge may be adherent to vaginal walls | - Vaginal pH <4.5  
- Whiff test result is negative  
- Wet mount: hyphae/spores (best seen after KOH applied), >1 WBC per epithelial cell, lactobacilli present |

KOH, potassium hydroxide; WBC, white blood cell.

### Vaginal pH

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### Wet mount

Healthcare providers use a cotton swab to obtain the specimen for a wet mount from the lateral vaginal wall—avoiding contamination with cervical secretions. The wet mount slide can be made by placing a drop of warn 0.9% saline and a drop of the vaginal discharge specimen directly onto it. As an alternative, the swab used to collect the specimen can be placed into a test tube containing less than 1 mL of saline and stirred gently, with a drop of the mixture placed onto a slide. HCPs then place a cover slip over the solution on the slide, followed by immediate examination under a microscope at both low (10x) and high (40x) power. The slide is thoroughly scanned for clue cells and motile trichomonads. Delays of more than 10 minutes in viewing the wet mount significantly reduce the chance of visualizing motile trichomonads required for diagnosis.3

Healthcare providers then place a second sample of the vaginal dis-
charge specimen on a slide and add a drop of 10% potassium hydroxide (KOH) solution. After mixing the sample with the wooden end of the cotton swab or a spatula, HCPs can bring the slide near the nose to perform the whiff test; the presence of a strong amine or fishy odor is considered a positive result. A positive whiff test is consistent with a diagnosis of BV, although it may also be present with *T. vaginalis* infection. After performing the whiff test, HCPs place a cover slip over the preparation on the slide, followed by examination under the microscope. KOH destroys most of the cells and bacteria, but it does not significantly affect any fungal organisms, thereby making it much easier to visualize pseudohyphae and spores. Pseudohyphae seen on the wet mount confirm the presence of *Candida albicans*. *C. glabrata* strains may form spores, but not pseudohyphae, making wet mount detection more difficult.

Readers can view an excellent video on wet mount microscopy developed by the Seattle STI/HIV Prevention Training Center [here](http://www.womenshealthcare.com). Figures 1, 2, and 3 show microscopic images of clue cells, trichomonads, and pseudohyphae/spores, respectively.

### Amsel criteria

Amsel criteria for the diagnosis of BV combine findings from vaginal pH, wet mount microscopy, the whiff test, and characteristics of the vaginal discharge seen on speculum exam. Presence of three of these four criteria provides sufficient evidence for a clinical diagnosis of BV:

- vaginal pH >4.5;
- positive KOH whiff test result;
- clue cells (must constitute ≥20% of vaginal epithelial cells viewed on saline wet mount microscopy); and
- homogeneous, milky-white discharge adherent to vaginal walls.¹

### Point-of-care tests

FDA-approved point-of-care tests offer the convenience of prompt diagnosis of vaginal infections, along with sensitivity superior to and specificity equal to or better than those of wet mount evaluation. Some tests provide the option for self-collection or clinician collection of vaginal specimens. Point-of-care tests are more expensive than the combination of pH testing, whiff testing, and vaginal microscopy. Therefore, some HCPs may choose to use point-of-care tests only if the traditional in-office tests do not reveal the most likely cause of a patient’s symptoms or a microscope is not available. The OSOM® Trichomonas Rapid Test detects *T. vaginalis* antigens; live organisms are not necessary to make the diagnosis.²,³ The OSOM® BVBlue® Test detects elevated activity of vaginal fluid sialidase, an enzyme produced by BV-associated organisms such as *Gardnerella vaginalis*, *Bacteroides* species (spp), *Prevotella* spp, and *Mobiluncus* spp.⁴ The vaginal discharge sample for both of these tests can be self-collected or clinician collected. Results are available within 10 minutes.

The BD Affirm™ VPIII Microbial Identification Test is a non-amplified molecular test that detects *T. vaginalis*, various *Candida* spp, and high concentrations of *G. vaginalis*.⁵ This DNA probe-based test requires only one specimen obtained with a sterile swab for all three organisms. To conduct this point-of-care test, HCPs must purchase an automated processor that can run six specimens simultaneously in about 45 minutes. Unless the clinical site does high-volume testing, the expense overrides the convenience.

### Nucleic acid amplification tests (NAATs)

Laboratory testing technology for both vaginal and cervical infections has shifted from cultures to NAATs that use molecular-based techniques. These tests are designed to amplify nucleic acid sequences (DNA or RNA).
that are specific for the organism being detected. NAATs can detect live or nonviable organisms. Several different NAAT-based methods are available, including transcription-mediated amplification (TMA) and polymerase chain reaction (PCR).

The FDA-approved Aptima® Trichomonas vaginalis Assay is an NAAT (TMA) that is highly specific and considerably more sensitive than wet mount, culture, or the Affirm VIIP point-of-care test.1,3 The CDC recommends NAAT as the preferred test for the diagnosis of trichomoniasis. The specimen for the test can be from a self- or clinician-collected vaginal swab, a urine sample, or an endocervical sample collected and placed in a specified liquid cytology medium.1,9

The BD MAX™ Vaginal Panel test, an FDA-approved NAAT (PCR), detects the microorganisms responsible for causing BV, trichomoniasis, and VVC. The panel identifies several Candida spp; the most common species, when present, are reported as a group, whereas C. glabrata and C. krusei are reported separately. The panel utilizes a BV algorithm that quantifies the ratio of organisms specific to BV infections to normal vaginal bacteria, including lactobacilli.10 A self- or clinician-collected vaginal swab is used to obtain a specimen for this test.

Several NAAT assays test for Neisseria gonorrhoeae, Chlamydia trachomatis, and T. vaginalis on the same sample.3

Cultures
Cultures can detect both Candida spp and T. vaginalis. Although a yeast culture is not usually necessary to make a diagnosis of VVC, it may be useful when a wet mount is negative for pseudohyphae or spores but a patient has symptoms and discharge or other signs suggestive of VVC on exam. When a woman has recurrent or persistent symptoms of VVC, a culture can help confirm the diagnosis and identify the species of yeast, if present. However, a culture is of no value if a woman has recently used antifungal treatment.2,4 Culture for T. vaginalis is more sensitive than wet mount but less sensitive and more expensive than NAAT.2,3

Culture for BV is not recommended because no bacteria are specific to BV. Although cultures for G. vaginalis are positive in almost all women with symptomatic BV, the organism is detected in up to 50%-60% of healthy asymptomatic women; therefore, its presence alone is not diagnostic of BV.2,3 An option for clinical settings that lack a microscope or point-of-care testing for BV is to send a vaginal discharge specimen to a laboratory for Gram stain diagnosis.3

Pap test
A Pap test may identify Candida spp in about 25% of patients with symptomatic VVC. Because cells evaluated on a Pap test are from the cervix and not as likely to be affected by VVC, the Pap test is not sensitive for this purpose.2 If Candida spp are found on a Pap test of an asymptomatic woman, treatment is not required. For T. vaginalis, the Pap test has a specificity of 96% with liquid-based tests and 92% with slide-based tests.5 However, it has a low sensitivity—similar to that of a wet mount (51%-65%).1,2 The Pap test should not be used as a diagnostic test for T. vaginalis because of the high possibility for false-negative results. In a symptomatic patient, treatment may be considered if the Pap test reveals trichomonas. If trichomonas is found on a Pap test in an asymptomatic patient, an NAAT should be performed to confirm the diagnosis before any treatment is initiated. The Pap test is an unreliable tool for diagnosing BV. If a Pap test suggests a shift in flora in a symptomatic patient, HCPs should perform a vaginal pH, an amine test, and a wet mount.

Asymptomatic women do not need further evaluation or treatment.2

Sensitivity and specificity of diagnostic tests
Sensitivities and specificities for the various vaginal infection diagnostic tests differ. Results must be considered in the context of patient symptoms and physical exam findings. Low sensitivity of a test can result in false-negative results. Low specificity can result in false-positive results. The range of documented sensitivity and specificity for a test may vary depending on the resource and the method of calculation. Table 2 provides the sensitivity and specificity of various vaginal infection diagnostic tests with reference citations.

Implications for clinical practice
When a patient presents with vaginal infection symptoms, making an accurate diagnosis is important so that appropriate treatment can be prescribed. In most cases, the combination of a problem-focused health history and physical exam, along with vaginal pH, wet mount microscopy, and whiff testing, provides sufficient information to pinpoint the cause of a patient’s symptoms. Point-of-care and laboratory tests are available if the diagnosis remains uncertain. When HCPs do not take the time to fully evaluate possible causes of a patient’s symptoms, the result may be persistent symptoms that adversely affect quality of life, repeat visits, overuse of unnecessary antimicrobial medications, and increased healthcare costs.

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NPs; and NPWH Director of Publications, Washington, DC. She states that she does not have a financial interest in or other relationship with any commercial product named in this article.

References
7. OSOM® BVBlue Test (sialidase activity) BV: 90.3 BV: 96.6 Results available in about 10 minutes
8. BD Affirm™ VPIII Microbial Identification Test BV: 90.5-90.7 BV: 84.5-85.8 G. vaginalis: 93.3-100 G. vaginalis: 96 T. vaginalis: 93.9-94.1 Candida spp: 96.6-99.7 NAAT recommended by CDC

Web resource
A. youtube.com/watch?v=8dgeOPGxoYI