

Advances in Diagnosing Vaginitis: Development of a New Algorithm

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The current approach to diagnosing vulvovaginal symptoms is both flawed and inadequate. Mistakes occur at the level of the patient herself, her provider, and the sensitivity of office-based tests. Often, the differential diagnosis is so broad that providers may overlook some of the possibilities. A diagnostic algorithm which separates women into either a normal or elevated vaginal pH can successfully classify most women with vaginitis. Based on the amine test, vaginal leukocytes, and vaginal parabasal cells, those with an elevated pH can be placed into further diagnostic categories. Such an algorithm helps to prioritize different diagnoses and suggest appropriate ancillary tests.

Introduction

Vaginal complaints are very common in the general population and are one of the most frequent reasons for patient visits to obstetricians/gynecologists [1]. Vaginitis is loosely defined as the spectrum of conditions that cause vulvovaginal symptoms. Although vaginitis is seldom life-threatening, it may have important morbidities in terms of discomfort and pain, days lost from school or work, and sexual functioning and self-image. With the publication of studies associating trichomoniasis and bacterial vaginosis (BV) with sexually transmitted and other infections of the female genital tract, as well as adverse reproductive outcomes in pregnant and non-pregnant women [2], vaginitis can no longer be viewed as just a trivial problem. Although many health care providers consider only the triad of BV, trichomoniasis, and vulvovaginal candidiasis (VVC) when diagnosing a woman with vulvovaginal symptoms, there is, in reality, a much wider range of causative conditions [3••]. Current approaches to evaluating vaginitis often fail to take into account this broader differential diagnosis. In this review, we discuss the current pitfalls in diagnosing vaginitis and propose a diagnostic algorithm centered on vaginal pH testing to facilitate the classification of the most common causes of vaginal symptoms.

Current Approach to Treating Vaginitis

Figure 1 presents the current approach to evaluating women with vaginitis. In general, a woman with vaginitis may complain of symptoms of itching, burning, irritation, dyspareunia, an abnormal discharge, or some combination thereof. When she comes in for evaluation of those symptoms, the health care provider will usually obtain a problem-focused history, followed by an examination which should include a careful inspection of the vulva, vagina, and cervix. During speculum examination, samples should be obtained for vaginal pH, amine (whiff) test, saline (wet mount), and 10% potassium hydroxide microscopy. The pH and amine testing can be performed either through direct measurement or colorimetric testing. Often, at this point, an accurate diagnosis can be determined, and treatment can be initiated. However, in selected patients, cultures or polymerase chain reaction (PCR) for trichomonas or yeast may be helpful to establish a diagnosis. Furthermore, depending on her risk factors and the results of microscopy, DNA amplification tests may need to be obtained for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in selected patients. However, as indicated by the rectangles to the right of Figure 1, the current treatment approach is affected by a variety of factors which greatly influence the accuracy of each woman's evaluation.

In the past decade, with the approval of topical antifungal medications for the over-the-counter (OTC) treatment of VVC, women with vaginitis have increasingly come to rely on self-diagnosis and self-treatment; this approach relies almost entirely on her symptoms. In theory, self-treatment offers convenience and the ability to initiate therapy rapidly. Furthermore, it has been estimated that OTC treatment has resulted in annual savings of up to 45 million dollars in direct costs and 18.75 million dollars in indirect costs [1]. However, in the United States, a market where OTC antifungal-use was estimated at over 250 million dollars in 2002 [4], there are questions about whether there is frequent misuse of these products. In a study of 601 women recruited from a variety of medical and community sites in Augusta, Georgia, Ferris and colleagues [5] asked subjects to assign a diagnosis to a variety of common infections of the genitourinary system, including BV, VVC, urinary tract infections, and pelvic inflammatory disease. They found that only 11% of women with no prior diagnosis of VVC could accurately recognize the scenario for VVC. Although only 35% of women with a prior diagnosis of

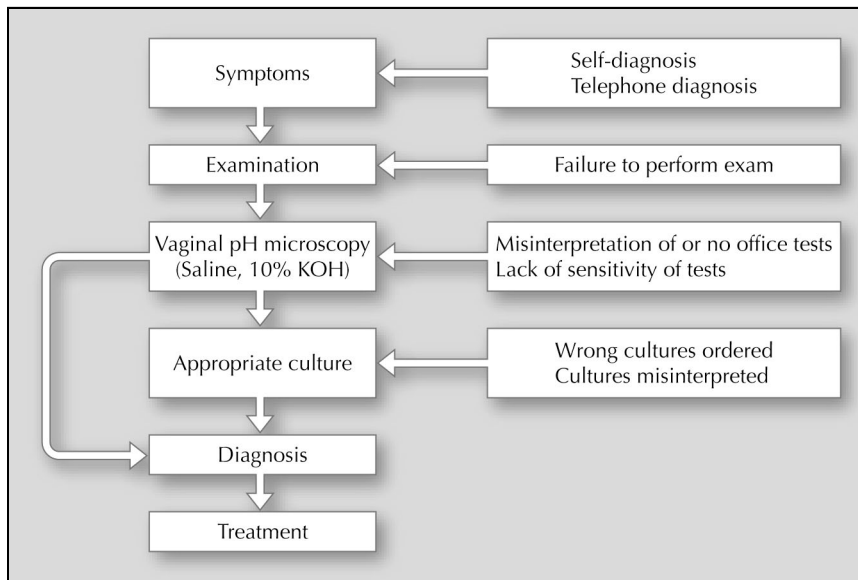


Figure 1. The traditional approach to diagnosing vaginitis is shown. KOH—potassium hydroxide.

VVC could accurately recognize the classic scenario for VVC, they were much more likely to say that they would self-treat themselves if they thought they had VVC. In a subsequent prospective study of 95 symptomatic women purchasing OTC antifungal products [6•], only 34% had pure VVC, and self-treatment with a topical antifungal agent would have been inappropriate or inadequate therapy in the rest; many of these women had BV. Clearly, a diagnosis based solely on a patient's interpretation of her symptoms will often be inaccurate.

Theoretically, having patients call in to a health care provider with a description of their symptoms should lead to greater diagnostic accuracy and still maintains the convenience of self-treatment. However, in practice, telephone diagnosis seems to fall short. In a study of women in the Denver area, women who were diagnosed over the phone by a nurse were then offered an immediate evaluation in the office [7]. Of the 485 who called in, 253 (54%) were subsequently evaluated; the authors found poor correlation beyond chance between the telephone and actual diagnosis.

It should also be noted that provider-based diagnoses, considered the cornerstone of effective therapy, may also be inadequate more often than we care to admit. In a review of 52 medical records of patients who were later referred to a tertiary care vaginitis center, Wiesenfeld and Macio [8] found that vaginal pH testing had been performed at only 3% of office visits and that 42% of referring physicians had not used microscopy as part of their evaluation. As demonstrated by Ledger and colleagues [9], even if microscopy is performed, it is often inaccurate. In a study of 61 women who were diagnosed as having VVC on the basis of clinical examination and microscopy in a university-based outpatient gynecology clinic, they found that 49% had a negative yeast culture and PCR test [9]. Finally, we have observed that many health care providers, though failing to obtain cultures which aid in diagnosing vaginal infections, will frequently and unnecessarily treat results of

bacterial cultures which are positive for *Escherichia coli*, Group B streptococci, or other normal flora which are not causing the patient's symptoms.

New Algorithm for Diagnosing Vaginitis

Even when done in the best of circumstances by personnel whose focus is the diagnosis of vaginal symptoms, current office-based tests each have relatively low sensitivity relative to their gold standards: 92% for BV, 62% for trichomoniasis, and a mere 22% for yeast [10]. Thus, as discussed earlier, ancillary tests and cultures are frequently indicated to establish a correct diagnosis. However, it may not be practical to administer a broad battery of ancillary tests to every woman who is left undiagnosed with simple office tests. Furthermore, depending on the patient population, the number of patients who do not have BV, VVC, or trichomoniasis can range from 7% to 72% [3••]. In these women, possible diagnoses may include infections (such as genital herpes), vulvar conditions (such as an irritant dermatitis or lichen sclerosus), or vaginal problems (such as atrophic vaginitis or desquamative inflammatory vaginitis [DIV]). Depending on the cause, the diagnosis may rest on a variety of factors, such as a more careful history, vulvar or vaginal biopsy, or a viral culture. For the health care provider who is weighing a broad differential diagnosis and a battery of potential tests at his or her disposal, it may be quite daunting to determine which tests are the most likely to be of use. A diagnostic algorithm which uses vaginal pH to separate out diagnostic categories may help to streamline the clinical decision making process.

Essential to an understanding of the normal vagina is the concept that in a woman in her reproductive years, the vaginal pH is a measure of overall balance of the bacterial flora. In the prepubertal and postmenopausal states, the vagina is thinned, and the pH is usually elevated (> 4.7). A routine bacterial culture will demonstrate a broad variety

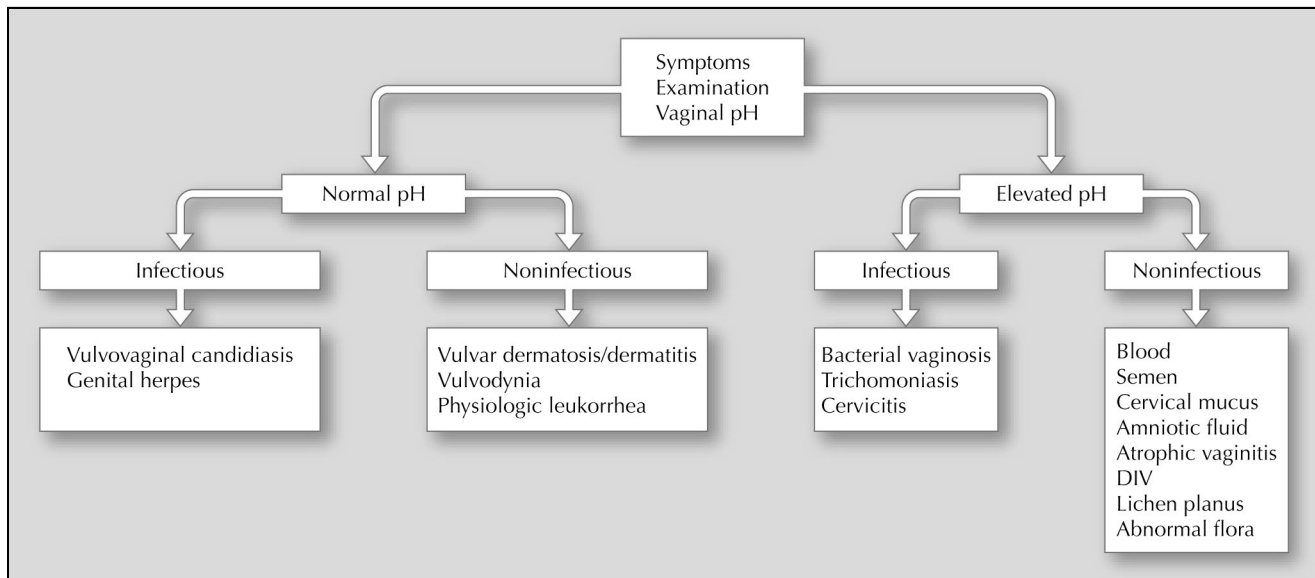


Figure 2. A pH-based framework for the most common causes of vaginitis is shown. DIV—desquamative inflammatory vaginitis.

of organisms, including skin and fecal flora. Under the stimulation of estrogen, vaginal epithelial cells have increased glycogen content, which in turn, encourages colonization of the vagina by lactobacilli. This increased level of colonization then leads to lactic acid production and to a decrease in the vaginal pH to less than 4.7. Thus, a normal pH is a marker for adequate amounts of lactobacilli. As discussed earlier, women with vulvovaginal symptoms have a relatively broad differential diagnosis; some, but not all, of the conditions will disrupt lactobacilli and alter pH. In Figure 2, this differential is subdivided on the basis of normal or elevated vaginal pH.

In women with a normal pH, the infectious causes of vaginal symptoms consist primarily of VVC and genital herpes. If a potassium hydroxide smear demonstrates hyphae or blastospores, VVC is confirmed and treatment can be initiated. However, because microscopy is relatively insensitive, a yeast culture should be obtained in all symptomatic women with normal vaginal pH and with negative microscopy or simply to confirm the diagnosis if the provider is unsure of his or her skills with the microscope. Furthermore, in women with recurrent VVC, a positive culture will also help to guide therapy by determining the species of yeast causing the infection [11]. Because an episode of genital herpes may often present with just a minor fissure or break in the skin, patients with vulvar fissures should receive a viral culture and type-specific IgG antibody testing for herpes simplex virus. In women with a normal pH and no infectious cause, their symptoms may be due to a vulvar condition such as an irritant dermatitis, a nonneoplastic epithelial vulvar skin disorder (eg, lichen sclerosus or lichen simplex), or vulvodynia. Depending on the clinical examination, such women may require a biopsy to establish the diagnosis or may need appropriate treatment for their vulvar condition. Finally, if her only symptom is an abnormal discharge and the rest of the evalua-

tion is normal, she may simply have a physiologic leukorrhea. Thus, in a symptomatic woman with a normal pH, the cause of her symptoms will either be VVC, genital herpes, a vulvar condition, or a change in her physiologic discharge.

Significance of an Elevated Vaginal pH

As shown in Figure 2, women may have an elevated pH because of either infectious or noninfectious causes. Many of the noninfectious causes are actually normal: the presence of blood during menses, semen if she has had recent intercourse, profuse cervical mucus (especially if she is ovulatory), or amniotic fluid if she is pregnant and has ruptured membranes. Sometimes, a temporary decrease in lactobacilli, such as what occurs after antibiotic use, will elevate the vaginal pH. Other conditions, such as lichen planus, can be diagnosed on the basis of clinical examination and biopsy.

Fortunately, in women with an elevated pH, other markers which are visible with office tests may help to further refine the diagnosis. In our experience, the amine or whiff test, the presence of white blood cells, and the presence of immature epithelial or parabasal cells are particularly helpful and can be used to create a diagnostic algorithm for an elevated pH (Fig. 3). In general, a positive whiff test is associated with both BV and trichomoniasis [3••]. Because women with BV do not have white blood cells, most women who have a high pH, a positive whiff test, and no white blood cells on microscopy will have BV. Clue cells or a grossly altered vaginal flora will be seen on microscopy to confirm the diagnosis and fulfill Amsel's criteria; these criteria correlate quite well with gram-stain diagnosis [10]. On the other hand, the combination of a high pH, a positive whiff test, and white blood cells suggests either the presence of trichomoniasis or a mixed picture of BV in combination with cervicitis.

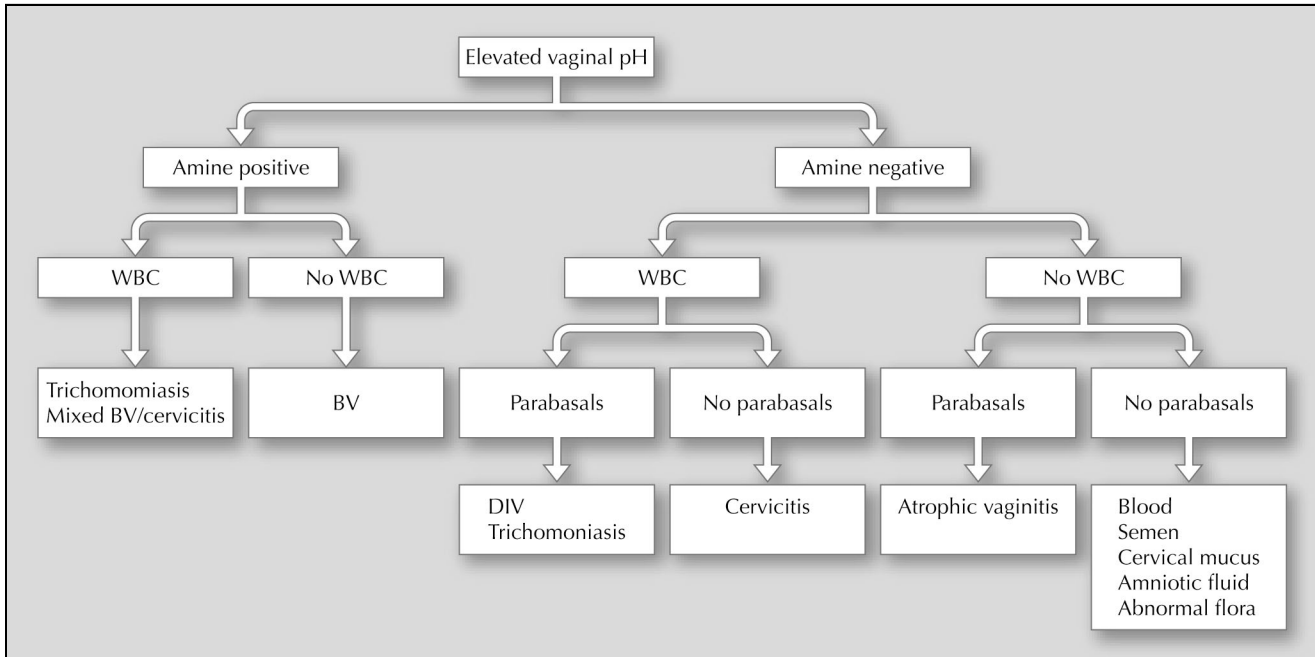


Figure 3. A diagnostic algorithm for patients with an elevated pH is shown. BV—bacterial vaginosis; DIV— desquamative inflammatory vaginitis; WBC—white blood cell.

Trichomoniasis appears in two different categories in Figure 3. Although it is often associated with a positive whiff test [3••], many women will have a negative whiff test. It is not clear whether the positive whiff test is a result of vaginal flora which has been altered by trichomoniasis or whether it represents concurrent infection with BV [12]. The presence of trichomonads on saline microscopy has a relatively low sensitivity and can easily miss infected women. In our experience, most of the women with negative microscopy will have white blood cells, either with or without parabasal cells. If trichomonads are not visualized on microscopy in a woman with an elevated pH, a culture for trichomonas should be obtained. If culture is not available, a trichomonas point-of-care rapid antigen test is more sensitive than microscopy and offers a sensitivity and specificity of approximately 95% [12].

In addition to trichomoniasis, a woman with a positive amine test and white blood cells may have a mixed picture of BV in combination with cervicitis [13]. In women with BV, Geisler and colleagues [13] found that almost 40% had elevated vaginal leukocyte counts. Women with BV who had vaginal leukocytes were more likely to have clinical evidence of cervicitis. On further evaluation, they had higher rates of concurrent trichomoniasis, gonorrhea, and chlamydia than BV patients who did not have leukocytes. Thus, in addition to cultures for trichomonas, testing for gonorrhea and chlamydia should be performed. If negative but there are signs consistent with cervicitis, therapy for both BV and cervicitis should be administered.

In patients with a negative amine test and with increased numbers of white blood cells, the presence or absence of parabasal cells will help to distinguish DIV

from cervicitis. Generally occurring in peri- or postmenopausal women, DIV causes burning, dyspareunia, and an abnormal yellow or green discharge. Although streptococcal species, including group B streptococci, are found in more than 90% of affected women, this does not mean that DIV is caused by streptococcal species. Some have argued that DIV may represent a vaginal expression of erosive lichen planus. Examination will reveal a purulent discharge with varying amounts of vestibular and vaginal erythema. The vaginal pH is elevated; the whiff test is negative. Microscopy will reveal large amounts of polymorphonuclear cells and parabasal cells. This condition is easily mistaken for trichomoniasis, but no motile trichomonads will be present and cultures for *T. vaginalis* will be negative. Selective bacterial cultures may help to detect the occasional patient with Group A streptococcal infection. Although no prospective randomized, controlled studies have been performed, a 14-day course with clindamycin 2% cream will often achieve a cure; relapse after therapy is fairly common [14••]. More sustained improvement and cure will follow a course of intravaginal hydrocortisone.

Mucopurulent cervicitis, which is sometimes caused by *N. gonorrhoeae* or *C. trachomatis* [13], may present as an abnormal yellow discharge, accompanied by signs of cervical friability or inflammation. Because of the profuse cervical discharge, affected women will often have an elevated pH but a negative amine test. Microscopy will usually be essentially normal except for increased numbers of leukocytes. As noted earlier, women with cervicitis should be tested for gonorrhea and chlamydia, although most will have neither.

The last group of women in Figure 3 will have a negative amine test and no increase in white blood cells. If

parabasal cells are noted on microscopy, the most common cause by far is atrophic vaginitis. Patients with atrophic vaginitis may complain of an abnormal vaginal discharge, dryness, itching, burning, or dyspareunia. Although more common in postmenopausal women, it can sometimes be observed in younger, premenopausal women. On saline microscopy, in contrast to healthy premenopausal women, lactobacilli are characteristically absent and the identified bacterial flora is scanty. A therapeutic trial of intravaginal estrogen rapidly reverses all the described abnormalities within 4 to 6 weeks. Finally, if there are no parabasal cells, the elevated pH may be secondary to nonpathologic causes in most women.

Advantages and Pitfalls to a pH-based Treatment Algorithm

There are many factors which affect the accuracy of diagnosis in women with vulvovaginal symptoms, and no algorithm will successfully address all of them. However, depending on when and where the pH is done, this algorithm can be helpful in a variety of settings. As noted earlier, Ferris and colleagues [6•] found that BV was the most common missed and unrecognized condition in women about to self-treat for VVC. With the availability of self-testing for vaginal pH, it has been estimated that 50% of inappropriate antifungal use could be avoided [15]. Although this approach is as yet unstudied, if a symptomatic patient were to call her health care provider and describe both her symptoms and her vaginal pH, one could assume that the provider would be more likely to decide whether she needed to be evaluated or could proceed with self-treatment. In a patient who describes symptoms of itching and in whom the pH is normal, VVC is probably the most likely diagnosis, and self-treatment with a course of antifungals would avoid the costs, direct and indirect, of an office evaluation. However, if the symptoms fail to respond or if they recur, the patient would need to be seen to obtain a more accurate evaluation. On the other hand, an elevated pH indicates that the patient does not have VVC and needs further evaluation. In the hands of the practitioner, the use of this new algorithm helps to rapidly rank the most likely diagnoses. If the other office-based tests do not provide a definitive diagnosis, the differential diagnoses in each subgroup suggest which ancillary tests should be ordered.

Although this approach to diagnosis may help clinicians to think about the myriad causes of vulvovaginal symptoms, one must recognize that there are pitfalls. For example, patients may have VVC in conjunction with conditions that cause a high pH (ie, mixed infections BV and VVC). Certain conditions, such as erosive lichen planus, vaginal presentations of pemphigus and other rare conditions, cannot be easily fit into one of the boxes in Figure 3.

Conclusions

The current system for diagnosing vaginal symptoms lends itself to inaccuracies at every level. A diagnostic algorithm based on vaginal pH can help to accurately categorize the cause of a woman's symptoms. Important questions remain about whether this algorithm should be implemented at home, in the provider's office, or both. Although our proposed algorithm still has some limitations, we believe that it represents a useful tool in the approach to women with vaginitis.

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