Differentiation Of The Vaginoses-Bacterial Vaginosis, Lactobacillosis, And Cytolytic Vaginosis

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Citation


Abstract

Vaginosis occurs primarily from an imbalance of the normal healthy vaginal flora and should be carefully differentiated from vaginitis (1). Vaginal complaints are responsible for more than 10 million office visits per year (2,3). The most common vaginal complaint results from Bacterial Vaginosis (4-6). Accurate diagnosis is necessary for successful treatment and resolution of frustrating vaginal symptoms. This article discusses specifics regarding the history of vaginal diagnoses and treatment, differentiation and treatment of the Vaginoses: Bacterial Vaginosis--and the much less commonly known yeast mimics, Lactobacillosis, and Cytolytic Vaginosis. Emphasis is given to vaginal wet smear analysis and a chart was developed to help the advanced practice clinician discriminate between these vaginal flora disruptions.

INTRODUCTION

A 29-year-old woman comes in with a chief complaint of a white vaginal discharge off and on for the last 2 months. She notices that the discharge “smells really fishy after intercourse.” She reports that she has tried Monistat 3 vaginal suppositories with no relief. “I don’t feel clean unless I douche on a regular basis.” Another woman, 33 years old, complains of monthly vaginal infections. She reports that she has vaginal itching, no noticeable discharge, and “the outside of my vagina burns” particularly with urination. She states the symptoms disappear during her menses and then get worse again in the middle of her cycle. “I can’t have intercourse during this time because it is too painful... I have tried to use over-the-counter [OTC] lubricants and nothing eases the pain.” A third woman, a 44 year old, reports symptoms of vaginal itching, burning, and irritation with a thick, white, curdy vaginal discharge. She reports the symptoms appear about a week and a half before her menses. She has tried many OTC products initially and finally called her “OB/GYN” who did not see her but did call in prescriptions for Flagyl and Diflucan. However, the symptoms continued even after this treatment.

In each of these situations, clinical history and symptoms alone are inadequate to diagnose vaginal discharge problems (1). Vaginal complaints are responsible for more than 10 million office visits per year (2,3). Bacterial vaginosis is the most common vaginal complaint, followed by candidal vaginitis as the second and trichomonial vaginitis as the third (4-6). Women with chronic vaginal symptoms often use OTC and alternative medicines that add to health care costs and are unlikely to be of benefit (7). Vaginosis occurs primarily from an imbalance of the normal healthy vaginal flora (1). Many clinicians have noted the absence of tissue inflammation associated with vaginosis and only surface involvement of the mucosa (1). These findings led to the development of the concept of Vaginosis, and can be further differentiated to include specific subtypes of Bacterial Vaginosis (BV), Lactobacillosis (LB), and Cytolytic Vaginosis (CV). The purpose of this article is to assist the practitioner in the differentiation of vaginoses, thereby enhancing the quality of life of their female clients.

OVERVIEW

To understand the basics of vaginosis differentiation, an understanding of normal vaginal flora/environment is important. The normal vaginal ecosystem is a complex environment with dynamic interrelationships among endogenous microflora and their metabolic products, host metabolic products, estrogen, and pH (8). Normal vaginal discharge is composed of white blood cells, red blood cells, epithelial cells, and bacteria. (See Figure 1, Normal Vaginal Flora.) Lactobacilli acidophilus (straight, variable-length, rod-like organisms) are the dominant bacteria in a healthy vaginal ecosystem (8). As many as 80 different species of lactobacillus have been identified (9). Lactobacilli are a
pleomorphic, gram-positive, aerobic or a facultative anaerobic, non-spore forming organism (1). Lactobacilli decrease the vaginal pH through production of acidic products, thereby making the vagina inhospitable to some bacterial species (1). In a cohort study, Hawes et al. found lactobacillus organisms producing hydrogen peroxide (LB+) were twice as protective as those that did not (LB-) against development of BV (10).

Lactobacilli help to maintain the normal vaginal pH (3.8 to 4.2) by producing lactic acid, which balances the vaginal ecosystem, and hydrogen peroxide, which suppresses the growth of gram-negative and gram-positive facultative and obligate anaerobes (1, 4, 11). Throughout a woman's life, physiologic hormonal changes alter the vaginal flora (1). During childbearing years, a pH of 4.5 or less indicates vaginal health, whereas a pH of 5 or higher is usually a sign of vaginal disruption (1). Estrogen influences the health of the vagina by stimulating an increase in the glycogen level, cervical mucus, and epithelium thickness (1).

The unhealthy vaginal environment can be described as an imbalance in the vaginal bacterial ecosystem. In BV, the hydrogen peroxide-producing lactobacilli are diminished, and Gardnerella vaginalis, anaerobes, and mycoplasmas are abundant (12,13,14). Hillier, Krohn, Nugent, and Gibbs studied 7,918 pregnant women and characterized vaginal smears as normal (predominant lactobacilli), intermediate (reduced lactobacilli), or positive for BV (15). The women with normal flora were least likely to have elevated pH, amine odor, milky discharge or colonization by Gardnerella, Bacteroides, or genital mycoplasmas. Lactobacilli-induced cytolytic vaginosis results from Lactobacillus overgrowth (11). LB is characterized by a transformation in the length of lactobacilli (1). The delicate balance of the vaginal ecosystem is challenged constantly by several factors such as hormonal changes, medications, intercourse, stress, infection, douching, and hygiene.

HISTORICAL PERSPECTIVES

In 1892, Doderlein first identified the presence or absence of gram-positive rods in normal vaginal flora (16). He named these organisms Doderlein's bacilli. The health of the vagina was dependent on the number of Doderlein's bacilli. The vaginal ailment was referred to as Doderlein's Cytolysis, and symptoms were similar to candidiasis (16).

Many early studies confirmed that the vagina is rich in glycogen, with some strains of Lactobacillus capable of directly fermenting glycogen, and increasing the vaginal acidity (17,18). Gardner and Dukes (19) defined a new entity that they felt accounted for almost all cases of what was then called nonspecific vaginitis. The single facultative organism isolated was named Hemophilus vaginalis. Until 1980 the term Hemophilus was popular until Greenwood and Pickett summarized all the bacteriologic evidence and showed that it belonged to neither genus but in fact represented a new genus not previously described (20). In honor of its principle discoverer Herman L. Gardner, they officially titled the organism Gardnerella vaginalis.

Amsel, Totten, Spiegel, Chen, Eschenbach, and Holmes proposed criteria for diagnosis of nonspecific vaginitis and confirmed the existence of nonspecific vaginitis as a clinical entity (21). In 1984, Mardh showed that neither Gardnerella nor Mobiluncus alone, inoculated into the vagina, were capable of producing the clinical disease (1). Only when both organisms were present did the classic group of findings result. This subsequently led to the development of the concept of vaginosis. In 1984, Westrom, Evaldson, Holmes, Meijden, Rylander, and Fredriksson suggested the current term bacterial vaginosis and defined it as "a replacement of the lactobacilli of the vagina by characteristic groups of bacteria accompanied by changed properties of the vaginal fluid" (22, p. 260). Cibley and Cibley reported that the clinical entity known as Doderlein's cytolysis was actually a misnomer because it referred only to the Doderlein species of lactobacillus, and over 80 different species of the lactobacillus species had been described (11). They felt that Cytolytic Vaginosis was a more accurate term for the condition.

Few reports regarding Leptothrix (Lactobacillosis) have appeared in the literature. Kaufmann and Faro (1994) described the organisms as gram-positive anaerobic rods that are longer than lactobacilli yet shorter than the filaments of Candida (1). They are also nonbranching, segmented, filamentous bacteria. Feo and Dellette placed them in the genus of Lactobacillus primarily because of their cultural and biochemical properties (23). Horowitz, Mardh, Nagy, and Rank published a study that suggested long serpiginous rods detected in their patients were anaerobic lactobacilli (24). In healthy women, vaginal lactobacilli are between 5 and 15 microns in length, whereas the lactobacilli in the Horowitz et al.'s study ranged between 40 and 75 microns in length (25). The cause of this morphologic transformation is unknown but it is known to cause vaginal discharge and possibly discomfort.
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BACTERIAL VAGINOSIS

Bacterial Vaginosis is the most common abnormal vaginal condition in women of reproductive age (1). Of 101 fertile women (15-50 years of age) with the chief complaint of vaginal discharge and/or genital malodor, BV was diagnosed in 34% (2). In a recent study in Denmark reported by Peterson, Danielson, and Renneberg, of 124 female patients attending an STD clinic, 54 (44%) were diagnosed with BV using wet smear diagnostic criterion (3). BV is the most prevalent cause of vaginal discharge or malodor; however, up to 50% of women with BV may not report the typical symptoms (29,30).

The 2002 Centers of Disease Control (CDC) STD Treatment Guidelines recommend that high-risk pregnant women (i.e., those who previously delivered a premature infant) who have asymptomatic BV should be evaluated for treatment (29). Studies have linked BV to various complications of pregnancy including spontaneous abortion, preterm labor, premature rupture of membranes, preterm birth, amniotic fluid infection, postpartum endometritis, and post cesarean wound infections (31, 32,33). Hillebrand, Harmanli, Whitman, and Khandelwal concluded that pregnant women with BV are more likely to have urinary tract infections (13.6% vs. 6.6%) (34). Ralph, Rutherford, and Wilson studied the influence of BV on conception and miscarriage in the first trimester and found no affect on conception, but an increased risk of miscarriage during the first trimester in women undergoing in vitro fertilization was noted (35). The 2002 U.S. Preventive Services Task Force concluded the evidence is insufficient to recommend for or against routinely screening high-risk pregnant women for BV (36).

Symptoms of BV include increased vaginal discharge, itching, and fishy odor, particularly after intercourse (4,21). Women with symptomatic BV usually present with a thin, gray-white, homogeneous discharge that tends to adhere to the vaginal wall (8,10,37). Vulvar pruritis and/or irritation is not common with BV; however, it may occur (4,21). The characteristic fishy odor results primarily from metabolic by-products of anaerobic bacteria (1,36,39). The odor is usually more noticeable after menses and intercourse due to the alkalinity of blood and semen (4).

The exact mechanism by which BV infection occurs is not known. An understanding of the risk factors for developing BV has been accumulated largely through convenience samples of women in selected clinical settings rather than from population-based studies. Many of the women studied included those attending family planning/obstetric and STD clinics. When groups of women in the U.S. were compared in regards to BV prevalence, it was highest among African American women and lowest among Asian American women (6,32). Stevens-Simon, Jamison, McGregor, and Douglas studied the pH of 273 sexually active adolescent females and several conclusions were reached (6). The pathophysiology mechanisms underlying racial differences remained unknown and the vaginal pH of Black adolescents was significantly more alkaline than that of other races, which may contribute to the apparently increased susceptibility of Black women to acquire BV (6).

Hawes et al. published the first account regarding the effect of douching on the acquisition of BV (10). They found that those women who douch for the purpose of hygiene had a hazard ratio more than twice that of all other women, including those few who douch because of symptoms. In a recent study of 1,200 women at high risk for sexually transmitted infections, Ness and associates concluded that douching at least once per month was associated with an increased frequency of BV by 1.4-fold (6). Alterations in the vaginal pH from douching can disrupt the vaginal environment and be less protective against pathogenic organisms (6).

It is commonly thought that the high pH of semen may lead to overgrowth of characteristic BV organisms (6). Amsel et al. found that none of the 18 virgins in their study had BV (6). Bump and Buesching studied 68 sexually active and 52 virginal adolescent girls and found 12% of the virgins and 15% of the sexually active had BV; thus, they concluded BV should not be considered a sexually transmitted disease (6). Skinner, Stokes, Kirlaw, Kavunagh, and Forster found in their study of 241 lesbians and 241 heterosexual controls that BV occurred in 33% of the lesbians and 13% of the heterosexuals (6). BV has been correlated with increased numbers of sex partners and use of an intrauterine device (IUD) (6). Among women using any form of contraception, IUD use was still more common among patients with BV (13 of 51) than among normal women (13 of 177, p<0.001) (6). Steinhandler, Peipert, Heber, Montagno, and Crickshank, in their study of 598 high-risk women, found that the presence of both BV and leukorrhea was associated with an increased risk of gonorrhea or chlamydia (6).

Clinical features necessary for diagnosis of BV include three of the four following clinical criteria (8):

1. Vaginal pH above 4.5.
2. Characteristic vaginal discharge that is thin, homogeneous, and milk-like consistency. The amount of discharge may be scant, moderate, or profuse.

3. The release of a fishy amine odor on addition of potassium hydroxide to a drop of vaginal discharge.

4. Clue cells on saline wet mount of vaginal discharge.

Using these clinical criteria, more than 90% of women with BV can be correctly diagnosed, and the number of false-positive diagnoses will be less than 10% (21, 45). Thomason, Gelbart, Anderson, Walt, Osypowski, and Broekhuizen found that the identification of 5% to 20% clue cells on saline wet-mount examination accurately predicts 85% to 90% of women with clinical BV (45). (See Figure 2, Clue Cell.) Among the individual criteria used to diagnose BV, a raised pH is recognized as the most sensitive but least specific (13). The usual practice of collecting cervical and endocervical samples for cytologic screening does not provide an accurate identification of vaginal fluid clue cells. Because of decreased sensitivity and specificity, the characteristics of vaginal fluid should be used along with the other diagnostic criteria and not as the only indicator of BV. (See Table 1, Diagnostic Criteria.) Cervical pap tests have limited clinical utility for the diagnosis of BV because of low sensitivity (29). The best single diagnostic criterion of clue cells on wet mount examination produces a sensitivity of 98.2% and a specificity of 94.3% with positive and negative predictive values of 89.9% and 99.0%, respectively (45).

Based on the 2002 CDC guidelines, recommended treatment regimens for BV include Metronidazole 500 mg orally twice a day for 7 days; or Metronidazole gel 0.75%, one full applicator (5gm) intravaginally, once a day for 5 days; or Clindamycin cream 2%, one full applicator (5gm) intravaginally at bedtime for 7 days (45). In a study by Paavonen, Mangioni, Martin, and Wajszczuk, there was no significant difference in cumulative cure rates 5-10 days after completing treatment: 86% for oral metronidazole 500 mg twice daily for 7 days vs. 85% for clindamycin vaginal cream 5 gm at bedtime for 7 days vs. 81% for metronidazole vaginal gel 5 gm twice daily for 5 days (51). Cure rates post 4 weeks after treatment were 78% for oral metronidazole vs. 82% for clindamycin vaginal cream vs. 71% for metronidazole vaginal gel. Alternate and less efficacious regimens include Metronidazole 2 gm orally in a single dose, or Clindamycin 300 mg orally twice a day for 7 days, or Clindamycin ovules 100 gm intravaginally once at bedtime for 3 days. The CDC guidelines also recommended that all symptomatic pregnant women should be tested and treated. The 2002 CDC recommended regimens include Metronidazole 250 mg orally three times a day for 7 days or Clindamycin 300 mg orally twice a day for 7 days. CDC guidelines recommended a follow-up evaluation 1 month after completion of treatment for women who are at a high risk for preterm delivery to evaluate whether therapy was effective. Women who have BV and also have HIV should receive the same treatment regimen as those who are HIV-negative (7). Therapy of BV need not include routine treatment of the male sexual partner (29, 36, 46, 47).

Even before the availability of OTC antimycotic therapy, women used a variety of home or alternative medicines for symptom relief of BV. Unfortunately, these treatments usually result in a continuation of symptoms and increased frustration for the woman. In a study by Nyirjesy, 42% of women used alternative methods for the treatment of vaginal symptoms (7). The study also revealed that the most frequently used was acidophilus pills orally (50%) or vaginally (11.4%), yogurt orally (20.5%) or vaginally (18.2%), vinegar douches (13.6%), and boric acid (13.6%) (7). Many health care providers question the use of herbs in BV treatment primarily because of the lack of scientifically validated research in efficacy (7, 48).
LACTOBACILLOSIS

Few studies exist in regards to the prevalence rates of LB. In a study by Feo and Dellette, 500 pregnant women's vaginal discharge was examined and 15.2% had the filamentous bacillus present (23). Horowitz and his colleagues described symptoms as occurring cyclically confirmed by a study of 67 patients from a private practice (24). Thirty-seven had cyclical symptoms of vaginal itching, burning, and irritation occurring for an average of 22.2 months. Thirty women requesting annual exams and reporting no symptoms of genital disease were selected for comparison. Anaerobic lactobacilli were found in 36 of the 37 patients (97%) exhibiting symptoms, 40% from the controls. A healthy woman had vaginal lactobacilli between 5 and 15 microns in length, whereas the lactobacilli in the symptomatic patients ranged between 40 and 75 microns in length (24).

The cause of LB is unknown. Kaufman and Faro wrote that "among American women, the organism behaves commensally, lacking evidence to the contrary, it may safely be ignored; its chief significance lies in the possibility of confusion with the candida species" (8, p. 380). Clinical characteristics described in 1952 by Feo and Dellette included a white discharge varying from slight to moderate in amount, vulvar itching, and a burning sensation over the introital area following urination (23). Horowitz and group reported 83.3% of patients had a thick, white, creamy, or curdy vaginal discharge; 86.7% vaginal itching; and 63.3% had vaginal burning (24). In the Horowitz et al.'s study, the symptoms appeared cyclically: symptoms occurred in the second half of the menstrual cycle, reaching a peak shortly before menses, and recurred approximately 7 to 10 days before the next menses (24). There was no difference in the appearance of the vulva, vagina, and cervix of symptomatic patients and the controls. The pH in both the symptomatic patients and controls was approximately 4.5. In two studies, wet mount examination revealed long chains of slender bacilli ranging from 38 to 60 microns in length (23, 24).

The most effective treatment of LB consists of Augmentin 500 mg orally three times a day for one week. Horowitz et al. found that 86.3% of patients reported absence of symptoms after treatment with Augmentin. Six of the patients who were penicillin sensitive were selected for Doxycycline of 100 mg twice daily for 10 days. All six obtained relief from symptoms. Seven patients were initially treated with bicarbonate douches, and three-reported relief from symptoms. The other four were treated with either Augmentin (n = 3) or Doxycycline (n = 1) and successfully had resolution of symptoms. Eighteen months later, patients were symptom free and reexamination of wet mount slides revealed an absence of long serpiginous rods (24).

CYTOLYTIC VAGINOSIS

Similar to LB, the prevalence and incidence of CV is unknown. In the experience of Cibley and Cibley, Lactobacillus overgrowth and candidiasis are frequently confused; therefore, many women are incorrectly diagnosed with chronic yeast infections (11). Many times women have tried many OTC antifungal medications with no relief. The women presenting with cytolytic vaginosis complain of a thick or thin white cheesy vaginal discharge, pruritus, dyspareunia, vulvar dysuria, and a cyclic increase in symptoms that are more pronounced in the luteal phase (11, 37, 49). There is very little data on predictors or variables associated with CV although numerous clinicians have reported empirically high incidence with increased levels of stress (Personal communication, R. Britt, RN, EdD, 2002).

Clinical features include a normal appearing vulva or slight erythema and edema of the vulva (49). The vaginal discharge pH is between 3.5 and 4.5. Wet mount slide reveals a paucity of white blood cells, evidence of cytolysis, and an increased number of lactobacilli (11). False clue cells may be present resulting from the large number of lactobacilli adhering to the cell edges (11). Vaginal cultures will reveal normal
vaginal flora or heavy growth of lactobacilli and will not grow candida (8, 49).

The treatment goal is to increase the vaginal pH with sodium bicarbonate douching or sitz baths (1, 37, 49). Cytophagic vaginitis is an easily diagnosed and treated condition. Kaufman and Faro as well as Goldman recommended 1 teaspoon of sodium bicarbonate in 1 pint warm water, 1-2 times weekly as needed (49). Paavonen recommended women discontinue tampon use until they are symptom-free for at least 6 months (52). Hatcher and associates recommended sitz baths since douching may introduce pathogens and increase the risk of Pelvic Inflammatory Disease (PID) (49). The woman is instructed to sit for 15 minutes in a sitz bath of approximately 2-4 tablespoons of sodium bicarbonate added to 2 inches of warm bath water 2-3 times in the first week, then 1-2 times weekly as needed to prevent recurrences. The woman who experiences recurrent symptoms is encouraged to start bicarbonate douching or sitz baths 24 to 48 hours before the anticipated onset of symptoms (49, 37, 49).

VAGINAL MICROSCOPY

Basic microscopy skills are necessary for identification of organisms obtained in a vaginal wet mount sample. In addition to basic microscopy operation, the health care provider should properly obtain a vaginal pH. Cotton-tipped applicators are not recommended because they may contaminate the sample with fiber artifact, which can be confused with candida forms (53). With the unlubricated vaginal speculum in place, the spatula should be positioned to the side of the cervix and drawn forward along the lateral aspects of the vaginal wall. Kaufman and Faro found ordinary nitrazine paper to be unreliable for pH determination and recommended pH strips that change color at increments of 0.2 to 0.4 in the range of 4 to 7 (4). A pH of greater than 6 suggests contamination of the strip with a fishy whiff or amine test. Anaerobic bacteria present in bacterial vaginosis cause the release of amine gas (53). The 10% KOH solution destroys the cellular material except for epithelial cells and hyphal yeast forms. The epithelial cells appear enlarged and rounded. The hyphal yeast forms (mycelia, pseudohyphae) become more prominent and easier to identify (54). It is important to utilize high power to differentiate yeast from various similarly shaped forms such as fiber, long lactobacilli, and hair (4). Secor described hyphal forms as tubular, thin, and translucent segments that taper at various points with round, smooth yeast buds present (54). The results of the vaginal microscopy evaluation are documented on the patient chart and in the Clinical Laboratory Improvement Act (CLIA) log.

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PATIENT EDUCATION

Practitioners caring for women experiencing vaginosis must educate them about differentiating between normal and abnormal vaginal discharge. Emphasis should be placed on seeing a health care provider at the first sign of infection and avoiding self-treatment with OTC medications, folk remedies, and douching products. Education regarding appropriate genital hygiene includes:

1. Wiping genital area from front to back.
2. Washing with warm water only.
3. Avoiding scented soaps and feminine hygiene products.
4. Avoiding douching, tampons, steroid creams (unless prescribed).
5. Wearing cotton underwear.
6. Avoiding constricting, tight fitting clothing.
7. Performing monthly vulvar self-examination
8. Sleeping without underwear.

REFERRAL AND CONSULTATION

Of the three types of vaginoses, BV recurrence is the most common. Approximately 30% of treated women relapse at 4 weeks (6,59). Cook et al. studied recurrence of BV and found that even after successful treatment of symptomatic women indicated by resolution of fishy odor and discharge, residual vaginal abnormalities continued (60). These included mild elevation of pH, polyamine and fatty acid levels, and the presence of clue cells in small numbers. These residual abnormalities were quantified and recurrence predicted based on a severity code. This represented a relapse rather than a reinfection. Taylor-Robinson recommended that treatment of recurrent BV must be improved and that vaginal recolonization with exogenous lactobacilli is an approach to be studied (61). Secor recommended several strategies to reduce BV recurrence, which include post treatment vaginal microscopy, lengthening therapy, alternating first-line agents, utilizing prophylactic topical agents, and treatment of partner (37).

CONCLUSIONS

Expertise of the clinician in identifying Bacterial Vaginosis, Lactobacillosis, and Cytolytic Vaginosis is necessary to eliminate frustrating vaginal symptoms and prevent misdiagnosis. Each of the women described in the beginning of the article must be accurately diagnosed for therapy to be successful. (See Table 2 Treatment.) The first example of subjective data describes the symptoms of Bacterial Vaginosis. The subjective data in the second case indicates a probable diagnosis of Cytolytic Vaginosis. In the last case, the subjective data indicates probable Lactobacillosis. Differentiation of the vaginoses can occur by obtaining a thorough history regarding symptoms and a problem-focused physical exam. The collection, preparation, and identification of the vaginal specimen are all necessary components for successful treatment. Properly performed vaginal microscopy skills can achieve an 80% sensitivity rate in the diagnosis of vulvovaginal problems (4).

Figure 2

Table 2: Treatment as Extrapolated fromReviewed Literature

Researchers have shown that the specific mechanisms causing an imbalance of the vaginal ecosystem are complex. Differences obviously exist in women exhibiting symptoms and women not experiencing symptoms. More research is necessary to evaluate the causal factors related to the microflora imbalances. Vaginal pH seems to be a critical factor, and research directed toward maintaining it within the normal range would be valuable in the treatment and prevention of these conditions.

RECOMMENDED READING

“Vaginal Microscopy: Refining the Nurse Practitioner’s Technique” (4)

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