

Clinical Comparison of Microscopic and Culture Techniques in the Diagnosis of Candida Vaginitis

James J. Bergman, MD, Alfred O. Berg, MD, MPH,
Ronald Schneeweiss, MB, and Fred E. Heidrich, MD, MPH
Seattle, Washington

This study compares potassium hydroxide (KOH), Microstix-Candida, and Nickerson's medium with Sabouraud agar in the isolation of *Candida*. Of 204 symptomatic and asymptomatic women, 36 had Sabouraud cultures positive for *Candida*. The KOH preparation demonstrated both poor sensitivity and poor predictive value in the isolation of *Candida*, while Microstix-Candida and Nickerson's medium were statistically indistinguishable from Sabouraud agar. The use of either Microstix-Candida or Nickerson's medium is recommended in the evaluation of *Candida* vaginitis when the KOH preparation is negative.

Vulvovaginitis associated with *Candida albicans* is a common problem in ambulatory care. Reported prevalence rates from diverse populations vary from 5 to 17 percent.¹⁻³

Current clinical strategies suggest that classic symptoms (eg, vaginal discharge, vulvar pruritus) and microscopic identification of yeast organisms are sufficient to complete the diagnosis of *Candida* vaginitis. Even without microscopic verification, symptoms are often used to justify the initiation of therapy. Previous research, however, has indicated that there are probably few, if any, symptoms that accurately predict *Candida* infection.³⁻⁷ Moreover, with costs of medical therapy increasing, the economic implications of the therapeutic trial without microscopic or culture diagnosis must be addressed.

Several vaginal smear preparations and staining techniques are available, including potassium hydroxide, Gram stain, and India ink, each requiring

five to ten minutes for completion. The three commonly available culture techniques for *Candida* isolation are Nickerson's medium, Microstix-Candida (a modification of Nickerson's medium), and Sabouraud agar, the laboratory standard for fungal culture.

This study evaluates the sensitivity, specificity, and predictive value of the KOH preparation, Microstix-Candida, and Nickerson's medium in the isolation of *Candida* using Sabouraud agar as the reference standard. Based on the results, a strategy for using cultures in the diagnosis and management of *Candida* vaginitis will be proposed.

Methods

The study population was a representative sample of all nonpregnant female adult patients visiting the Family Medical Center at the University of Washington during a 12-month study period (September 1, 1980, through September 20, 1981).⁸ The study subjects were chosen among female patients who were expected to require a pelvic examination either as part of a health maintenance routine or for a variety of symptoms. A nurse

From the Department of Family Medicine, University of Washington, School of Medicine, Seattle, Washington. Requests for reprints should be addressed to Dr. James J. Bergman, Group Health Cooperative Primary Care Center, 2701 NE 156th Avenue, Redmond, WA 98052.

practitioner administered a questionnaire assessing demographic and historical information, completed a pelvic examination, and obtained and read laboratory specimens on all subjects. The study nurse practitioner was not unaware of clinical findings, but the investigators were able to verify KOH and culture reading accuracy through cross-reader reliability testing. During the pelvic examination a sterile cotton swab was applied to the left lateral vaginal wall or to the area of apparent symptom involvement. The single swab was plated on a slide for KOH preparation, a Microstix-Candida strip, a Nickerson's medium slant, and a Sabouraud agar preparation, in that order, rotating the swab 90° after each plating. The KOH preparation was read immediately, and the Microstix-Candida and Nickerson's medium preparation were read at 24 and 48 hours. The Sabouraud culture was read at 48 hours by a mycology laboratory consultant who was able to confirm *Candida albicans* by germ tube appearance.

KOH

A 20 percent solution of KOH is applied to the specimen, and the slide warmed briefly by flame prior to microscopic examination. The KOH dissolves the cellular elements on a wet smear, leaving behind hyphae of the *Candida albicans* organism, which are identified microscopically. The cost of the test materials is minimal.

Nickerson's Medium

Nickerson's medium is bacteriostatic agar containing a bismuth derivative that is affixed to a slant in a glass tube. When in contact with *Candida albicans*, the bismuth is reduced, leaving a brown or black deposit on the otherwise clear medium.⁹ The medium costs about 75 cents and requires a 24-hour and a 48-hour incubation at 37° C for final reading. Unused media must be refrigerated.

Microstix-Candida

Microstix-Candida is a plastic test strip modification of Nickerson's medium stabilized on a 1-cm² dehydrated surface. When hydrated, the square of medium is plated with the specimen, incubated at 37° C, and read at 24 and 48 hours. The cost per test strip is approximately \$1.40. No refrigeration is necessary, and the shelf life is three years.^{10,11}

Sabouraud Agar

Sabouraud agar is the clinical reference laboratory fungal isolation medium evaluated at 48 hours and thereafter for the presence of a variety of fungal organisms. Germ tube analysis confirms suspected *Candida* isolations.

Results

Of 204 women who completed the study, 37 had no elicitable genitourinary symptoms, while the remainder complained of a variety of symptoms, including dysmenorrhea, pruritus, vaginal discharge, dysuria, and pelvic pain. Vaginal symptoms were reported by 132 (65 percent) of the participants. Microbiologic results are summarized in Table 1. Using Sabouraud medium as the reference standard, sensitivity of comparison tests ranged from a low of 19 percent (KOH) to a high of 83 percent (Microstix-Candida). Sensitivities of Microstix-Candida cultures and Nickerson's medium were highest at 48 hours' incubation, suggesting that negative cultures at 24 hours be re-evaluated at 48 hours. Specificity proved to be greater than 95 percent for all of the comparison tests. Using McNemar's chi-square test for paired data, the results of Microstix-Candida and Nickerson's medium read at 48 hours are statistically similar to those of Sabouraud agar. Nickerson's medium and Microstix-Candida were compared with each other and found to be statistically similar in their ability to detect the presence or absence of *Candida*.

Discussion

Vulvovaginitis associated with *Candida* infection is a benign problem; however, the symptoms are uncomfortable and most office visits are characterized by a sense of urgency in diagnosis and treatment. The classic symptoms of infection alone are not sufficiently reliable to permit correct diagnosis and treatment.¹²⁻¹⁶ Indeed, Odds,³ in a chapter on the diagnosis of *Candida*, states:

Acute pruritus and discharge are the commonest presenting complaints but neither symptom is invariably associated with the disease. The classic sign is the presence of white curd-like particles, although intense erythema and edema of the labia minora, introitus, and lower third of the vaginal mucosa with or without thrush particles are a more consistent finding. The accurate diagnosis of vaginal thrush requires both clinical and laboratory information.

Table 1. Comparison of Diagnostic Tests With Results on Sabouraud Agar

Diagnostic Test	No.	Positive Sabouraud Cultures	Positive Diagnostic Test	Sensitivity of Diagnostic Test (%)	Specificity of Diagnostic Test (%)	McNemar* Chi-Square
KOH (20% solution)	199	36	7	19	98	19.53 P < .001
Microstix-Candida (24 h)	200	35	18	51	97	5.5 P < .025
Microstix-Candida (48 h)	193	35	29	83	96	0 NS
Nickerson's medium (24 h)	200	35	11	31	99	19.36 P < .001
Nickerson's medium (48 h)	199	36	26	72	97	1.067 NS

*Note: Significant difference indicates that comparison test result differs statistically from Sabouraud culture result

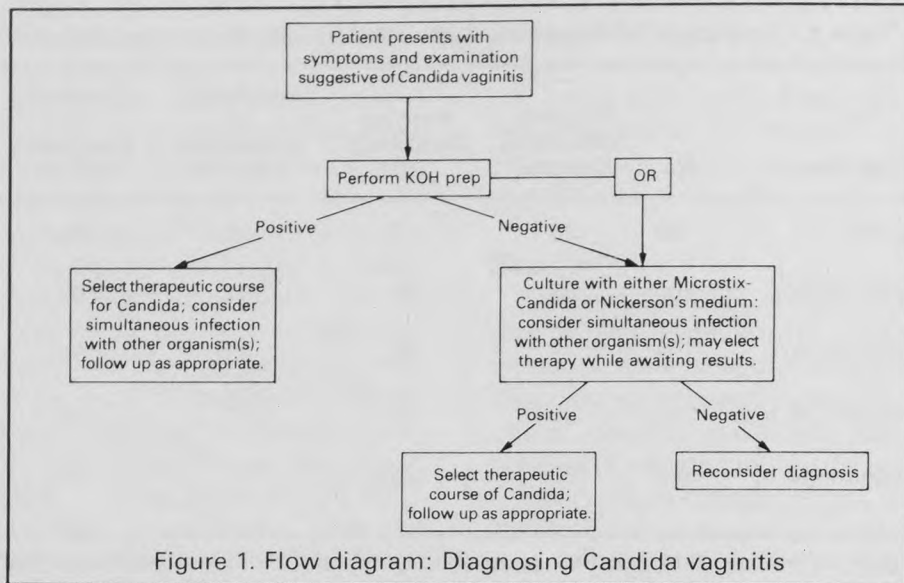
McLennan et al add, "Symptoms alone are unreliable for diagnosis; swabs made directly from the lesion should be cultured for yeasts. Detection of yeasts or pseudohyphae by microscopic examination of smears of a discharge are occasionally useful, but the isolation of *Candida* in culture is the sensitive and necessary finding to confirm the diagnosis."¹²

It must be recognized that although the isolation of *Candida* does not prove disease, it offers adjunctive evidence to be considered with the clinical presentation in making a diagnosis. This study does not address different strategies combining clinical and laboratory findings, but documents the value of several tests in the isolation of *Candida*. The results of this study support the assertion that the KOH preparation is only occasionally useful, having demonstrated poor sensitivity and predictive value. Furthermore, two simple and inexpensive office culture techniques, Microstix-Candida and Nickerson's medium, yield results that are statistically indistinguishable from the reference standard, Sabouraud culture.

Weissberg¹ found a nearly perfect correlation between Microstix-Candida and Sabouraud agar. Schurz et al¹⁷ noted that Nickerson's medium detected 10 percent fewer mycoses, and Microstix-Candida detected 20 percent fewer compared with Sabouraud agar. Weissberg¹ found that the KOH preparation detected 70 percent of isolations identified by culture. Davies and Savage¹⁸ demon-

strated similar Microstix-Candida sensitivity (89 percent), while finding a higher KOH sensitivity (78 percent) than did all comparable studies. Rindt and Weigerding¹⁹ noted that Nickerson's medium correlated almost perfectly with Microstix-Candida (425 cases). It is difficult to explain the poor results of the KOH preparation in this study. This test is complex, however, and could produce variable results because of a number of factors, eg, sample taken, time spent in the slide examination, and skill required to identify yeast. In this study, the use of vaginal medications or douching in the weeks prior to examination was less than 15 percent and was not related to yeast identification on KOH smear. Diagnostically similar, Microstix-Candida and Nickerson's medium both require 24 to 48 hours to demonstrate growth. Microstix-Candida requires less storage space and does not require refrigeration, but it costs more than Nickerson's medium. The cost of an empirical trial of a therapeutic medication ranges from \$8 to \$15, representing a several-fold increase over the cost of either culture. It is suggested that when the KOH preparation is negative, the practitioner consider the use of Microstix-Candida or Nickerson's medium culture technique, selecting the one more convenient for the particular office setting.

Further study will be necessary to clarify the relationships between historical factors, symptoms, signs, and laboratory results in making the diagnosis of *Candida* vaginitis. As an interim step,



however, a proposed clinical strategy is illustrated in Figure 1. If the history, symptoms, and physical findings suggest the presence of Candida, a KOH preparation should be examined. If the KOH preparation is negative (or not elected), a specimen should be cultured for Candida using either Nickerson's medium or Microstix-Candida. A positive culture adds to the clinical suspicion of Candida infection, whereas a negative culture directs the physician to reconsider the diagnosis. The clinician may or may not elect to initiate therapy while awaiting the culture result, based on the urgency of the situation and the results of other laboratory tests.

Conclusions

The literature suggests that the typical symptoms alone are poor predictors of Candida identification in the diagnosis of vulvovaginitis. This study concludes that KOH preparations have low sensitivity in detecting Candida, and that Microstix-Candida and Nickerson's medium are comparable to the reference medium, Sabouraud agar. Microstix-Candida and Nickerson's medium are recommended as adjuncts in the evaluation of Candida vaginitis when the KOH preparation is negative.

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References

1. Weissberg SM: Evaluation of a dipstick for Candida. *Obstet Gynecol* 52:506, 1978
2. De Costa EJ: Infections of the vagina and vulva. *Clin Obstet Gynecol* 12:198, 1969
3. Odds FC: *Candida and Candidosis*. Baltimore, University Park Press, 1979
4. Green TH: *Gynecology*, ed 2. Boston, Little, Brown, 1971
5. Jeffcoate NJ: *Principles of Gynaecology*. Boston, Butterworths, 1975
6. Greenhill JP: *Office Gynecology*, ed 9. Chicago, Year Book Medical, 1971
7. Willson JR, Beecham CT, Carrington ER: *Obstetrics and Gynecology*. St. Louis, CV Mosby, 1975
8. Berg AO, Heidrich FE, Fihn SD, et al: Establishing the etiology of genitourinary symptoms in women in a family practice: Comparison of clinical examination and comprehensive microbiology. *JAMA* 251:620, 1984
9. Nickerson WJ: Reduction of inorganic substance by yeast. *J Infect Dis* 93:43, 1953
10. Package Insert: Microstix^R-Candida. Ames, Elkhart, Ind, 1975
11. Corcoran L, Kenney J, Tilton RC: Detection of Candida vaginitis by a dipstick method. *Health Lab Sci* 12:100, 1975
12. McLennan M, Smith J, McLennan C: Diagnosis of vaginal mycosis and trichomonas. *Obstet Gynecol* 40:231, 1972
13. Eddie DAS: The laboratory diagnosis of vaginitis infection caused by Trichomonas and Candida species. *J Med Microbiol* 1:153, 1978
14. Carroll CJ, Hurley R: Criteria for diagnosis of Candida vaginitis in pregnant females. *J Obstet Gynaecol Br Comm* 80:258, 1973
15. O'Brien J: Nickerson's medium in the diagnosis of vaginal monilia. *Can Med Assoc J* 90:1073, 1964
16. Bergman JJ, Berg AO: How useful are symptoms in the diagnosis of Candida vaginitis? *J Fam Pract* 16:509, 1983
17. Schurz AR, Breitfellner G, Keisler J: Die diagnostik vulvovaginaler mykosen. *Geburtshilfe Frauenheilkd* 39: 413, 1979
18. Davies RR, Savage MA: Evaluation of a dehydrated test strip for the detection of yeasts. *J Clin Pathol* 28:750, 1975
19. Rindt W, Weigerding A: Zur diagnostik der Soor-kolpitis mittels Microstix^R-Candida. *Med Klin* 72: 598, 1977