

Sexual Behaviors and Other Risk Factors for *Candida* Vulvovaginitis

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ABSTRACT

Sexual behaviors are associated with many genital infections, but the role of sexual variables as risk factors for *Candida* vulvovaginitis has not been clearly determined. To assess the association between sexual behaviors and other risk factors with the presence of *Candida* vulvovaginitis, we performed a case-control study comparing these potential risk factors in women with and without culture-documented *Candida* vulvovaginitis in two Midwestern community-based medical offices. Participants included 156 women with *Candida* vulvovaginitis and 92 controls, ages 18–60. Risk factors for *Candida* vulvovaginitis, including sexual and partnership behaviors, demographic data, past genital infections, exposures, and diet, were investigated using logistic regression. The presence of *Candida* vulvovaginitis was positively associated with recent cunnilingus (odds ratio [OR] = 2.22 for five times a month compared with no times, 95% confidence interval [CI] 1.36, 3.84), but was less likely in women who masturbated with saliva in the previous month (OR = 0.30 if masturbated five times vs. no times, 95% CI 0.09, 0.99). Other independent risk factors included knowing the sexual partner a shorter period of time (OR = 1.56 for 1 year vs. 5 years, 95% CI 1.16, 2.13) and lower milk ingestion (OR = 3.57 for no servings vs. two servings per day, 95% CI 2.00, 6.67). Increased number of sexual partners, early age at first intercourse, and increased frequency of intercourse are not related to risk.

INTRODUCTION

CANDIDA VULVOVAGINITIS (CVV) is a common vaginal disorder, characterized classically by vaginal itching and discharge, with *Candida* species identified on potassium hydroxide microscopic preparation or culture. CVV causes discomfort, temporary disability, loss of time at work, significant expense (medical care, laboratory testing, and medications), and loss of productivity for millions of women each year. For

many women, CVV occurs repeatedly. Although several risk factors for acute CVV have been reported, no reason has been found for the majority of cases.^{1,2}

Many genital infections are related to sexual contact with infected partners. For CVV, previous reports suggest an association with sexual behaviors and partnership characteristics, although results are inconclusive. Specific sexual activities, such as oral sex to the female partner (cunnilingus), have been reported to increase the risk of

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CVV.³⁻⁷ *Candida* may be harbored in the male oral cavity, and male colonization is associated with female vaginal colonization, often with the same strain.^{2,8-10} In addition, contact with semen via intercourse not only exposes the woman to the organisms present, but also may expose her to numerous antigens, antibodies, or cytokines secreted in the seminal fluid that might influence her immune reaction to the *Candida* present.¹¹⁻¹⁹ Hence, sexual behaviors that expose the genital region to other sources of the organism (e.g., tongue, rectum) and to potential sources of immune modifiers (cytokines, antibodies) may be expected to increase the risk of current CVV.

Other risk factors for infection or recurrence have been suggested, such as the recent use of oral contraceptives (OC) or antibiotics, the presence of diabetes, dietary factors, wearing tight clothing, and gastrointestinal carriage of *Candida*.¹ Disparate findings exist, however, suggesting there are other unrecognized risk factors. We hypothesized that sexual behaviors associated with exposure of the female genitalia to other sources of *Candida* or immune mediators and those associated with microtrauma to the genital region (such as increased frequency of intercourse) would be associated with having CVV. We further hypothesized that these risk factors, if associated with CVV, may modify the apparent effect of previously described risk factors. Assessment of and controlling for previously described factors will avoid erroneous attribution of risk to confounding variables.

Using a case-control design, we evaluated the association between sexual behaviors and other risk factors in symptomatic women who had culture-proven CVV compared with women without vaginal complaints who reported no history of CVV in the previous year.

SUBJECTS AND METHODS

The University of Michigan Vaginitis Study was a case-control study of patients with CVV compared with clinic control women without CVV. The project was approved by the University of Michigan Investigational Review Board. Patient enrollment occurred in two family practice offices in the Ann Arbor, Michigan area—at the University of Michigan Family Practice offices in Chelsea (a small town 17 miles west of Ann Arbor) and in the Briarwood office in Ann Arbor.

Women eligible for the study (1) were age 18–60 years, (2) were currently sexually active, (3) had a steady partner who would potentially participate in the study, and (4) were willing to give informed consent and follow-up for four additional visits over a period of 1 year. Women were primarily enrolled at the time they appeared with symptoms of vulvovaginitis at one of the study offices (cases) or at the time of a routine gynecological examination for a cervical cytology smear or contraception (controls). We used a consecutive sampling technique on days enrollment was scheduled. However, after over-the-counter antifungal medication became available, newspaper advertisements designed to recruit women with symptoms of CVV were included in the protocol to improve enrollment.

Informed consent was obtained, and each participant was given a comprehensive self-administered questionnaire to complete at the time of the visit. The questionnaire included items on risk factors for CVV, including questions on demographic variables, symptoms, past medical history, past vulvovaginitis history, medication usage, current and past birth control methods, sexual history and practices, clothing history, and dietary history.

The participating physician performed a pelvic examination and recorded examination data. Specimens of vaginal and cervical discharge and vaginal washings were collected for the following tests: in-office testing for KOH and normal saline preparations, pH of vaginal secretions, and “whiff” test for aromatic amines; bacterial culture of vaginal and cervical specimens; fungal culture of vaginal, vulvar, tongue, and rectal specimens; and cell culture of cervical scrapings for *Chlamydia trachomatis*. In addition, blood was drawn for glycosylated hemoglobin determination. The data from the initial visit were used for this report.

Laboratory testing

Microbiological testing was performed at the University of Michigan Clinical Laboratories, as previously described.^{20,21} *Candida* species isolation and identification were performed using Mycosel-Sabouraud's dextrose agar with chloramphenicol and cycloheximide, and all yeast were evaluated for germ tube production, with germ tube-negative yeasts being further identified using the API (Analytical Profile Index, Biomerieux Vitek, Inc., Hazelwood, MO) yeast identification test.

Data analysis

Cases included women with genital symptoms (itching or discharge) and a positive vaginal culture for *Candida* species. Control women included women who did not have vaginal symptoms and who denied having CVV in the previous year. Data analysis was conducted using SPSS and SAS software. The data were initially explored using frequency distributions for categorical variables and histograms and summary statistics for continuous variables. Univariate comparisons of potential risk factors among women with CVV compared with controls were performed using *t*-tests and chi-square tests. The available sample size gave adequate power (>80%) to detect effect sizes of 0.4 between cases and controls for continuous variables, and differences of 15% in the case/control prevalence of dichotomous variables of small prevalences (<30%) and differences of 20% or greater for dichotomous variables of higher prevalence.

To assess the effects of several risk factors simultaneously, logistic regression was performed using the presence or absence of CVV (case/control status) as the outcome measure. Continuous predictors were evaluated for correct functional form prior to use in the logistic model, with transformation required in some cases. Model residuals and diagnostics were assessed. Regression models were performed in a nonautomated stepwise fashion to carefully assess each model. In cases of collinearity, models were monitored for stability of coefficients. Odds ratios (OR) and 95% confidence intervals (CI) were reported indicating the odds of each exposure in the diseased vs. the nondiseased groups. Two-way interaction terms were included in the model with their component main effects and were assessed for statistical significance.

RESULTS

Between January 11, 1990, and July 29, 1993, 455 women were enrolled in the University of Michigan Vaginitis Study, 336 women with vaginal symptoms and 119 asymptomatic controls. Of those with vaginal symptoms suggestive of *Candida* infection, 156 (46.4%) had CVV diagnosed using office laboratory procedures and *Candida* culture. Of the controls, 92 (77.3%) reported no CVV in the previous year and were included in

the analysis. Of the women evaluated, 78% (190 of 246) were patients at the practices where they were enrolled. This included 65.4% of the women with CVV (102 of 156), and 97.8% of the controls (90 of 92, $p < 0.00001$). The remaining women were enrolled after responding to the published advertisement.

In addition to sexual behavior variables, risk factors for CVV previously suggested in the literature were evaluated in both the univariate and the multivariate analysis. These behaviors included recent use of OCs or antibiotics, history of diabetes, wearing of tight clothing, several dietary components (milk, alcohol, breads, sugars), and history of CVV previously. Other factors potentially confounding relationships between sexual behavior variables and the presence of CVV were also evaluated, such as history of other genital infections and smoking history.

Demographic characteristics of women with CVV compared with controls are shown in Table 1. Differences identified between these two groups remained after controlling for whether the women were patients in our practices or had responded to the advertisement. Women with CVV were more likely than controls to report a history of CVV, bacterial vaginosis, *Trichomonas* vaginitis, and *Neisseria gonorrhoeae* infection (Table 2), but when controlled for whether patients were recruited via an advertisement or via clinic attendance, the history of *Trichomonas* vaginitis and of *N. gonorrhoeae* infection were no longer associated with current CVV. Histories of infections with *C. trachomatis*, genital herpes, pelvic inflammatory disease (PID), genital warts, urinary tract infections (UTI), and abnormal Papanicolaou smears did not differ significantly between the two groups.

Contraception, antibiotics, diet, diabetes, medications, allergies, and the wearing of tight clothing were evaluated as potential risk factors, and those associated with CVV are listed in Table 3. Although 31% had taken OCs during the 2 months prior to study enrollment, the women with CVV were not more likely to have been on OCs during the 2 months prior to study enrollment compared with controls ($p = 0.06$). The prevalence of each other type of contraception used, including barrier methods, vasectomy, or bilateral tubal ligation, did not differ significantly between the two groups. Although reported milk ingestion was significantly less among those with CVV compared with controls, no differences

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF WOMEN ENROLLED WITH AND WITHOUT CVV

Factor	CVV (n = 156)	Controls (n = 92)	OR (95% CI) or difference in means (95% CI)	p value
Mean age (years)	31.8	32.1	-0.3 (-2.2, 1.6)	0.77
African American vs. other ethnic groups (%)	14.9	5.5	3.0 (1.1, 8.2)	0.02
Mean education (years)	14.7	14.8	-0.1 (-.7, 0.6)	0.90
Household income ≤\$35,000 (%)	47.7	34.1	1.8 (1.0, 3.0)	0.04
Married or living as married (%)	60.6	79.3	0.4 (0.2, 0.7)	0.002
Currently pregnant (%)	2.6	14.1	0.2 (0.1, 0.5)	<0.001

were seen in dietary intake of sweets, carbonated beverages (regular or sugar free), vitamin supplements, alcohol, or breads. Smoking exposure (active or passive), glycosylated hemoglobin levels, and history of diabetes mellitus did not differ significantly between cases and controls. No patients were on immunosuppressants, and none reported chronic illnesses associated with immunosuppression.

We evaluated traditionally reported sexual behavior risk factors (such as age at first intercourse and number of lifetime partners) as well as detailed histories of various specific sexual behaviors that may be associated with genital exposure to other sources of *Candida* organisms or to other products that may effect *Candida* proliferation or viability. We found the length of time having

known the current partner and practicing cunnilingus in the past month differed significantly between women with CVV compared with control women (Table 4). Other sexual behaviors, including number of sexual partners ever, age at first intercourse, and frequency of intercourse, were remarkably similar when comparing cases and controls in the univariate analysis.

Multivariate analysis

Factors initially evaluated in the logistic regression model included those listed in the preceding tables that were associated with CVV status at the $p < 0.10$ level, factors suggested in the literature to be associated with CVV, and other factors hypothesized to potentially confound or

TABLE 2. HISTORY OF CVV AND OTHER UROGENITAL INFECTIONS IN WOMEN WITH AND WITHOUT CVV

Factor	CVV (n = 156)	Controls (n = 92)	OR (95% CI) or difference in means (95% CI)	p value
CVV in the past				
Ever told had CVV (%)	90.4	64.1	5.3 (2.7, 10.4)	<0.001
Mean number episodes ever	7.3	2.4	4.6 (2.8, 7.1)	<0.001
Reported CVV in past year (%)	76.7	NA ^a	NA	NA
Bacterial vaginosis				
History of bacterial vaginosis (%)	54.7	21.7	4.4 (2.3, 8.1)	<0.001
Bacterial vaginosis diagnosed in past 6 months (%)	29.3	0.0	^b	<0.001 ^c
Bacterial vaginosis diagnosed in past 6 months (including controls who had been excluded because of having had CVV in past year)	29.3	2.0	20.5 (4.8, 87.6)	<0.001
History of <i>Trichomonas</i> vaginitis (%)	21.2	10.8	2.2 (1.0, 4.9)	0.05 ^d
History of <i>Chlamydia</i> infection (%)	17.4	9.3	1.9 (0.8, 4.5)	0.13
History of gonorrhea infection (%)	4.8	0.0	^b	0.05 ^{c,d}

^aControls included only women who did not report a history of CVV in the past year, unless otherwise stated. Of potential controls, 22.7% were excluded because of this history.

^bEstimated OR is infinite.

^cUsing Fisher's exact test.

^dNo longer significant when controlled for whether the women were enrolled in the practice or recruited by an advertisement.

TABLE 3. EXPOSURES ASSOCIATED WITH CVV

Factor	CVV (n = 156)	Controls (n = 92)	OR (95% CI) or difference in means (95% CI)	p value
OC use				
OCs taken ever (%)	87.8	89.9	0.8 (0.4, 1.9)	0.63
Mean time on OC (months)	38.5	47.5	-9.0 (-22.3, 4.4)	0.19
OCs taken in past 2 months (%) ^a	36.4	25.0	1.6 (1.0, 3.0)	0.06 ^b
Antibiotic use				
Antibiotics used in past month (%)	23.8	11.0	2.5 (1.2, 5.4)	0.01
Average number of days since last took antibiotic	11.0	8.9	2.1 (-5.4, 9.6)	0.58
Diet				
Average number of servings of milk per day	1.8	2.5	-0.7 (-0.9, -0.3)	<0.001
Two or less servings per day (%)	73.9	57.1	2.1 (1.2, 3.7)	0.007

^aOR and CI on contraceptive methods by case/control status were calculated by comparing each method to no contraception. Percentages do not add to 100% because some women used more than one type of contraception.

^bIf pregnant women (who are unlikely to be on OCs) are excluded ($n = 17$), 35.8% of cases of CVV and 29.1% of controls had used OCs during the past 2 months (OR = 1.4, CI 0.8, 2.4, $p = 0.31$).

explain the previous associations reported. Demographic variables included age, ethnicity, education, income, and marital status. Potential risk factors suggested by the literature included types of contraceptives used, antibiotic use, dietary components, presence of diabetes, and clothing characteristics. Sexual behavior frequencies and partnership formation characteristics (Table 4) were included in the initial model, with sequential removal of individual variables until the final model was obtained.

The resulting logistic regression model contained four variables that predicted CVV with a sensitivity of 86.4% (108 of 125), a specificity of 45.0% (36 of 80), and 70.2% correct classification. The variables independently associated with the CVV status—cunnilingus, masturbation with saliva, partnership duration, and milk ingestion—are shown in Table 5. Increasing frequency of cunnilingus was positively associated with the presence of CVV, and increased masturbation with saliva, duration of the relationship with the partner, and milk ingestion were associated with a lower prevalence of infection. Other factors that were significant in the univariate analysis (such as marital status, ethnic group, household income, and antibiotic use) were no longer significant in the multivariate analysis. Because the mode of recruiting patients may have resulted in cases being more likely than controls to respond to advertisements and controls to be more likely than cases to be pregnant, we recalculated the resulting logistic regression model after excluding

women recruited from the ads ($n = 56$) and those who were pregnant ($n = 17$). We found the final model to be unchanged after these exclusions.

We further evaluated potential confounders that may explain the association observed between sexual behavior variables and the presence of CVV. Although cunnilingus was found to be associated with other sexual behaviors, such as frequency of intercourse, masturbation with saliva, and frequency of orgasms, these relationships did not explain the association between the behavior and the presence of CVV.

The histories of past diagnoses of CVV and of bacterial vaginosis, which were highly correlated with each other and with having CVV at the current visit, also were not included in the primary analysis. The history of CVV is not independent of having current CVV and was, therefore, not entered into the model assessing risk factors for CVV. The accuracy of the diagnosis of bacterial vaginosis in women with frequent genital symptoms may be low because of the tendency for these women to be treated for this entity when symptoms persist. This variable, therefore, was not evaluated until after the model was otherwise constructed. Adding the past diagnoses of CVV to the logistic regression model improved the specificity and accuracy of the model significantly (sensitivity = 83.7% and specificity = 62.7%, with accuracy of 75.5%), with masturbation with saliva and cunnilingus becoming no longer associated with the presence of CVV. For each additional episode of past CVV reported, the OR increased

TABLE 4. ASSOCIATIONS BETWEEN SEXUAL HISTORY VARIABLES AND CVV

Factor	CVV (n = 156)	Controls (n = 92)	OR (95% CI) or difference of means (95% CI)	p value
Partnering history				
Mean number of partners ever	6.4	5.6	0.8 (-1.1, 2.9)	0.39
Average age at first intercourse (years)	18.2	17.7	0.5 (-0.2, 1.3)	0.17
Mean number of years known this partner	8.2	11.1	-2.9 (-4.9, -1.0)	0.004
Proportion of women who have known this partner < 2 years (%)	24.7	6.7	4.6 (1.9, 11.4)	<0.001
Sexual activities				
Intercourse				
Any in past month (%)	93.4	92.9	1.1 (0.4, 3.2)	0.87
Mean number of times in past month	7.6	7.1	0.5 (-1.2, 2.2)	0.55
Fellatio (oral sex to partner)				
Ever (%)	89.0	88.8	1.0 (0.4, 2.4)	0.95
In past month (%)	67.1	58.4	1.5 (0.8, 2.5)	0.18
Mean number of times in past month ^a	3.2	2.8	0.4 (-0.8, 1.5)	0.51
Cunnilingus (oral sex to woman)				
Ever (%)	91.1	89.9	1.2 (0.5, 2.8)	0.76
In past month (%)	67.3	55.1	1.7 (1.0, 2.9)	0.06
Mean number of times in past month ^a	2.8	2.2	0.6 (-0.3, 1.6)	0.19
Anal intercourse				
Ever (%)	38.0	41.2	0.9 (0.5, 1.5)	0.64
In past month (%)	5.0	3.5	1.4 (0.4, 5.7)	0.61
Average number of times in past month ^a	0.1	0.1	0.0 (-0.2, 0.2)	0.99
Masturbation with saliva				
Ever (%)	39.7	39.8	1.0 (0.6, 1.7)	0.99
In past month (%)	13.7	13.6	1.0 (0.5, 2.2)	0.99
Average number of times in past month ^a	0.3	0.8	-0.5 (-1.0, 0.0)	0.07
Masturbation with other lubricant				
Ever (%)	44.8	41.9	1.1 (0.7, 1.9)	0.67
In past month (%)	18.2	16.3	1.1 (0.6, 2.3)	0.71
Average number of times in past month ^a	0.6	0.3	0.3 (-0.2, 0.6)	0.26

^aMean number includes those reporting none in the past month.

1.22-fold (95% CI, 1.11, 1.35). This finding was not altered by including the 27 controls who had been excluded because of their history of having had CVV in the past year. The addition of the number of times the woman had had bacterial vaginosis in the past to the model shown in Table 5 was statistically significant, with an OR of 1.46 for each episode of past bacterial vaginosis reported (95%, CI, 1.16, 1.84). However, if the number of times the woman had had CVV was added to this model, the episodes of past bacterial vaginosis were no longer associated with current CVV.

Although the association between the recent use of OCs and the presence of CVV was not statistically significant in the univariate or multivariate models, this potential relationship is of great research and clinical interest. Reasons for past divergent results were therefore assessed. Those on OCs within the past 2 months had significantly shorter partnership lengths than did those not taking OCs (78.4 months vs. 125.7 months, $p < 0.001$). Evaluation of a possible in-

teraction between OC use and partnership length on CVV risk indicated an elevated odds of OC use in those with CVV compared with those without infection in the partnerships of short duration, with the odds decreasing toward 1 as the lengths of the relationships increased ($p = 0.07$). The OR for OC use among those with CVV compared with those without CVV were 4.7 at 1 year duration of the relationship, 2.4 at 5 years, and 1.5 at 10 years, with the excess risk disappearing by 15 years duration of the relationship. Addition of this interaction term and the recent use of OCs in the logistic regression analysis did not change the classification accuracy.

DISCUSSION

CVV occurs frequently, yet the associated risk factors are poorly understood. Women with CVV receive varied advice from physicians and other healthcare providers and, in addition to pharma-

TABLE 5. RESULTS OF LOGISTIC REGRESSION ANALYSIS OF RISK FACTORS ASSOCIATED WITH HAVING CVV COMPARED WITH CONTROLS

Variable ^a	OR	95% CI	p value
Diet			
Milk ingestion (servings/day)			<0.001
0	1.00	Referent	
1	0.53	0.39, 0.71	
2	0.28	0.15, 0.50	
Sexual activities			
Cunnilingus (oral sex to woman) ^b			0.03
None	1.00	Referent	
One time in month	1.36	1.03, 1.79	
Five times in month	2.22	1.09, 4.51	
Masturbation with saliva ^b			0.04
None	1.00	Referent	
One time in month	0.63	0.40, 0.99	
Five times in month	0.30	0.09, 0.99	
Partnership characteristics			
Years known partner ^c			0.003
1 year	1.00	Referent	
5 years	0.64	0.47, 0.86	
10 years	0.45	0.26, 0.76	

^aEach variable was entered as a continuous variable.

^bLogarithmic transformation of variable used.

^cSquare root transformation of variable used.

ceutical remedies, often try a number of lifestyle modifications, such as dietary, medication, and clothing modifications, in an attempt to gain control over these infections. Yet data suggest the impacts of these changes are inconsistent. Further understanding of the pathogenesis of CVV infections is needed to better advise women on factors associated with this disease.

The association of sexual behaviors with the presence or recurrence of CVV has been suggested by several investigators, but consistency in findings has been lacking. Early studies concentrated on the impact of testing and treating sexual partners of women with CVV for *Candida* carriage or infection. The majority of these studies suggested little impact of treatment of the partner on recurrences, although controversy exists.^{8,22} Other sexual behavior risks reported include a history of cunnilingus,^{4-6,23-25} increased frequency of intercourse,²⁶ and younger age at initiation of sexual activity.^{7,24} We report on a broader selection of potential sexual risk factors and used a multivariate analysis approach to control for previously described risk factors.

Cunnilingus as risk

Our data indicate cunnilingus is associated with risk of CVV independent of other known risk

factors. Early reports in the 1970s suggested that cunnilingus was related to vulvar inflammation²³ and to CVV.^{4,6} More recently, Markos et al.²⁵ reported a retrospective evaluation of 27 women with a history of three or more cases of CVV in the past year and 27 controls and found a strong association between oral sex and recurrent CVV (OR = 29.68, $p < 0.001$), but culture documentation of CVV was not required for diagnosis.

Two culture-documented epidemiological evaluations also reported an association between receptive oral sex and risk for CVV. Geiger and Foxman⁵ used multivariate analysis to compare female college students who had culture-documented symptomatic CVV with population controls without culture documentation of status and with culture-negative clinic controls. They found CVV was associated with the practice of receptive oral sex. Hellberg et al.²⁴ evaluated women with a history of six or more episodes of CVV who had a current infection documented compared with women without current CVV or such a history and found sexual risk factors of not only frequent oral sex but also younger age at first intercourse, casual sex partners during the previous month, and anal intercourse ever. However, one third of the cases included had a positive KOH preparation but a negative culture. Because misclassification of the presence of CVV using the

KOH-based diagnosis may be differential (differing across exposure categories), the association may have been overestimated.

Markos et al.²⁵ postulated that organism transmission from the sexual partner's oral cavity mediated this risk. In fact, the species of *Candida* isolated from the oral cavity of male partners of women with CVV are typically the same as those from the woman's vagina.^{3,27} However, whether this oral *Candida* in the male is associated with oral sex or is secondary to transmission from the infection in the female and whether it plays a causative role in symptomatic recurrences in the female partner are unclear. Clinical data suggest that attempts to eradicate the *Candida* organism from the male partner do not improve the symptomatic recurrence rates in the female partners significantly,²² although controversy exists.^{3,8} Components of semen or of saliva other than the *Candida* organism, such as allergens, nutrients, and acidity characteristics, may play a role in this association. In addition, the potential of mild abrasion or desiccation of the mucosa associated with oral-genital interaction may be contributory.

Our study indicates cunnilingus is associated with increased risk of CVV when evaluated in a multivariate manner requiring culture documentation for diagnosis.

Masturbation with saliva

The finding of a protective effect of masturbating with saliva was unexpected and has not been reported previously. Masturbation was not associated with painful intercourse, suggesting this was not a substitute for intercourse in women with CVV. Saliva constituents are many, including, but not limited to, sugars, microorganisms, and immunological components, such as antibodies, T cells, and cytokines.^{28,29} Some salivary components are known to be fungicidal or fungistatic,^{30,31} and oral bacteria are associated with decreased growth of *Candida* in saliva via competition for nutrients.³²

Although both cunnilingus and masturbation with saliva result in genital contact with oral fluids, these exposures were associated with contrasting findings—an increased risk with cunnilingus and a protective effect of masturbation with saliva. The difference may be related to immunological components present in saliva that recognize self-antigens and past exposures vs. others in the partner's saliva that may react dif-

ferently with vaginal antigens or organisms. Further investigation of these relationships is needed.

Partnership duration

The longer a woman had known her current partner, the less likely she was to have CVV. This finding was not confounded by other sexual partnership characteristics, such as the number of past sexual partners, the frequency of intercourse, or the patient's age. This factor has not previously been reported with CVV but has been implicated with other genital infections, such as human papillomavirus (HPV)²⁰ and urinary tract infections.³³ The demonstrated interaction between partnership duration and the use of OCs and the effect of this interaction on the presence of CVV may explain past discrepant reported results about the risk of OC use for the presence of CVV.

Milk ingestion

In our study, milk ingestion was protective against the presence of CVV infection, rather than being a risk factor, and was not altered by the inclusion of other variables. A previous study suggested dairy products as a risk factor for CVV.³⁴ A small study reported that ingestion of *Lactobacillus*-positive yogurt decreased the recurrence rate of CVV,³⁵ although no association was seen in a study in which participants were randomized to ingest either *Lactobacillus*-positive yogurt or pasteurized yogurt.³⁶ Milk and yogurt may share properties that decrease the risk of CVV that are independent of the presence of *Lactobacillus*. Further study is needed to clarify this risk factor.

OC use

Controversy over whether the use of OCs confers risk of CVV has continued over the years, with some indicating increased risk^{5,37-43} and others refuting this.⁴⁴⁻⁵² We found no statistically significant association between OCs use and the presence of CVV in either the univariate or the multivariate analysis. There was a suggestive interaction ($p = 0.07$) between the length of time the woman had known her partner and the use of OCs on the presence of CVV. At very short times of knowing the partner, OC use was a very strong predictor of infection (OR approximately 8), but no increased risk remained at prolonged partnership durations. This interaction may explain some of the vari-

ability noted in studies addressing OC use as a risk factor. Some studied women in relatively new relationships⁵ (with an expected higher association with OC use) compared with others in which the women were often in longer-term relationships, in which the OC relationship may be noncontributory.⁵³

Increased frequency of intercourse

A study on recurrent UTI by Foxman²⁶ found women given the diagnosis of CVV at the University Health Service were more likely than women not given this diagnosis to have had more frequent intercourse in the past 4 weeks. We did not find such an association with CVV in our study. However, the women Foxman studied had intercourse less frequently than did those in our population. In addition, the diagnostic categorization in her study was based on physician diagnosis, not culture. When we analyzed our data using physician opinion regarding the presence of CVV as opposed to the diagnosis given after the culture returned, we saw a similar association between frequency of intercourse with assumed CVV that was not present when culture data were used.

Previous episodes of CVV or bacterial vaginosis

Women with a history of CVV are more likely to have a current infection. Because risk factors for current and previous CVV would be expected to be similar, we did not include previous CVV in the initial model, to avoid obscuring the effects of other factors. Adding this variable to the final model in Table 5 did improve the predictive accuracy of the model as expected, but it also obscured the associations seen between current CVV and cunnilingus or masturbation with saliva. The diagnosis of CVV is not always accurate, with accuracy increasing with use of the in-office KOH preparation and *Candida* culture^{53,54} or DNA probe.⁵⁵ These tests are not routinely performed in many offices, and hence, the diagnosis of CVV, even in a physician's office, may be inaccurate. At a minimum, however, these data suggest that women with CVV are more likely to have had vaginal symptoms suggesting CVV in the past compared with those without such a history.

Similarly, the univariate analysis suggested that a history of bacterial vaginosis might be a risk factor for CVV, although the accuracy of this diagnosis as reported by patient recall of physi-

cian diagnosis is fraught with potential bias. Women with genital symptoms are more likely to be tested for infections that may have not otherwise come to their attention. Hence, the validity of comparing this historical information between women with a history of more frequent CVV (and, thus, genital evaluations) and controls with fewer evaluations is unclear. Physician diagnosis of bacterial vaginosis depends on performance of several in-office laboratory tests. Often, the diagnosis is made without such analyses, and even using these criteria, the diagnosis may be inaccurate.⁵⁵ Furthermore, women with recurrent vaginal symptoms may have been treated for bacterial vaginosis empirically, if treatment for CVV appeared to be unsuccessful, creating an increased association between CVV and bacterial vaginosis. Women treated for bacterial vaginosis are often treated with intravaginal metronidazole or clindamycin, both of which may be followed by an increased risk of CVV. Hence, whether a history of bacterial vaginosis is causally associated with CVV or the association is related to diagnostic bias or confounding cannot be determined from this study.

Limitations of the study

The women enrolled in this study reflect those seen in two primary care settings—for the complaint of vaginitis symptoms or for a routine gynecological examination. Because antifungal medications became available over-the-counter during the course of the study, those who came to the offices for evaluation of symptoms may reflect a group with a higher rate of resistance or recurrence compared with the general population, which consists of many who may be self-treating. Also, the women were predominantly well-educated, Caucasian, and in ongoing relationships. Although these characteristics apply to a large number of women in the United States, the applicability of these results to other populations has yet to be addressed. Finally, other, unrecognized risk factors may not be equally distributed between the case and controls groups; for example, unrecognized HIV infection may be a potential confounder. However, the rate of HIV is very low in the population studied (<1%), and no new diagnoses were found in this group of women over the 2 years after enrollment, making the role of HIV as a significant confounder in this study unlikely.

CONCLUSIONS

Women with CVV are likely to have had oral sex from a partner more frequently and have masturbated with saliva less frequently in the previous month compared with women without CVV. Similarly, the average duration of their relationship with their current partner was shorter than that observed among the controls. Additional studies of physiological alterations associated with these variables, such as immune response alterations with self/non-self saliva and changes over time in a relationship, as well as evaluation in women with recurrent infections, are needed to clarify the mechanisms by which risk is altered. Causality cannot be assumed from these cross-sectional data, and further research is needed to clarify the pathophysiology of these relationships. If a woman with CVV is counseled to avoid the risks described by this analysis, evaluation of the impact of behavioral change on her infection rate should be assessed so that unnecessary curtailing of activities can be avoided.

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