Vaginal pH as a marker for bacterial pathogens and menopausal status

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OBJECTIVES: Our purpose was to confirm the elevation of vaginal pH expected in patients with bacterial pathogens in premenopausal women and to examine the relationship of serum follicle-stimulating hormone and estradiol levels to vaginal pH in menopausal patients without and with hormone replacement therapy.

STUDY DESIGN: Vaginal pH was determined by phenaphthazine (Nitrazine) pH paper in 253 patients seen in a solo private practice for routine speculum examination. None of the patients were pregnant. Measurements were made of serum levels of follicle-stimulating hormone and estradiol for 172 patients and vaginal cultures were taken from 82 patients. Vaginal pH was correlated with vaginal cultures and serum follicle-stimulating hormone and estradiol levels by use of statistical analysis.

RESULTS: Vaginal pH was elevated in all premenopausal patients with documented bacterial pathogens. Serum estradiol levels showed an inverse and serum follicle-stimulating hormone levels a direct statistical correlation with vaginal pH in menopausal patients.

CONCLUSIONS: Measurement of vaginal pH is useful, effective, and inexpensive for screening purposes. A vaginal pH of 4.5 is consistent with a premenopausal serum estradiol level and the absence of bacterial pathogens. An elevated vaginal pH in the 5.0 to 6.5 range suggests a diagnosis of either bacterial pathogens or decreased serum estradiol. In patients with an elevated pH, vaginal culture should establish the diagnosis. In the absence of bacterial pathogens, a vaginal pH of 6.0 to 7.5 is strongly suggestive of menopause. Titration of estradiol level by vaginal pH during estrogen replacement therapy may help menopausal women avoid side effects or cessation of therapy. (Am J Obstet Gynecol 1997;176:1270-7.)

Key words: Vaginal pH, bacterial pathogenic organisms, serum estradiol level

In an era of increasingly managed care, physicians are continually urged to curb the use of expensive, "high-tech" diagnostic tools. In response, we must develop new "low-tech" diagnostic tools that are also cost effective. This article describes preliminary studies of a cost-effective "low-tech" diagnostic tool, the vaginal pH, as applied to two conditions: vaginitis and menopause.

Vaginitis is the most prevalent disorder for which women seek medical assistance.[1, 2] Although the diagnosis of trichomonal vaginalis and yeast or candidal infections is fairly straightforward, the diagnosis of bacterial infections of the vagina has undergone an erratic course. The most widely reported such disorder is bacterial vaginosis.[1, 2] Recent publications on bacterial vaginosis have stressed its association with pregnancy- and non-pregnancy-related infections of the upper genital tract.[3, 4] The use of vaginal pH, amine whiff testing, wet mount, and Gram's stain examination of the vaginal discharge in some combination are among at least seven diagnostic sets of criteria that have been used for diagnosis. However, an elevated vaginal pH (5.0 to 6.5) in a normally estrogenized patient is almost always associated with bacterial vaginosis.[1, 2, 5-7] These indirect measures reflect an attempt at cost containment and speeding diagnosis by eliminating culture, which otherwise would be the gold standard for the diagnosis of vaginitis or vaginosis. Although anaerobic organisms are considered the most prevalent in bacterial vaginosis, the presence of *Gardnerella vaginalis* is not currently considered to be pathognomonic for this disorder because *G. vaginalis* has been reported to be present in high percentages in the vaginas of asymptomatic individuals.[8] Although hydrogen peroxide–producing lactobacilli are reduced in number, *G. vaginalis* seemingly antecedes the increased numbers of anaerobic organisms in the development of bacterial vaginosis.[9] Furthermore, therapy directed at the anaerobic organisms is not always effective.[10] No one has reported on the presence of *G. vaginalis* or other aerobic pathogenic organisms associated with or independent of

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bacterial vaginosis as influencing vaginal pH. Most clinical laboratories available to the practicing obstetrician-gynecologist routinely culture only aerobically. Thus only aerobic vaginal cultures were obtained in this investigation.

Prepubertal and postmenopausal vaginal mucous membranes possess an atrophic epithelium with a surface pH of 6.0 to 8.0. At puberty, circulating estrogens increase, resulting in a proliferation of vaginal epithelial cells. Glycogen is deposited in the intermediate and superficial epithelial cells of the vagina, and lactobacilli proliferate, causing the enzymatic breakdown of cellular glycogen. Lactic acid and hydrogen peroxide are produced, which lowers the vaginal pH to 3.5 to 4.5. This is considered an indicator for a normal, properly estrogenized vagina.[11] Vaginal pH can be elevated by bacterial vaginosis, blood, cervical mucus, semen, vaginal medications, and douches.

This article presents the results of vaginal pH testing on consecutive premenopausal and postmenopausal patients attending a private gynecologist' office, none with complaints of vaginitis. This study suggests that the presence of important aerobic pathogens is likely to be associated with pH values >4.5 in premenopausal women and also offers preliminary data supporting the hypothesis that pH values >4.5 in the absence of vaginitis are associated with a low estrogen level as in menopause.[11, 12]

Material and methods

Patients in a private gynecologic practice who appeared for a routine visit on a random day of their cycle were tested for vaginal pH during routine speculum examinations. None of these patients were pregnant and none were using vaginal medication. Consecutive premenopausal or menopausal patients categorized according to menstrual patterns and subsequent hormonal values (see below) were studied: 55 premenopausal patients had vaginal pH and aerobic and yeast cultures obtained and 152 consecutive postmenopausal patients were tested for vaginal pH and serum follicle-stimulating hormone (FSH) and serum estradiol levels. Of these 152 patients, 88 were receiving estrogen replacement therapy and 64 patients were receiving no hormonal treatment with 16 and 11, respectively, having vaginal cultures obtained. A unique opportunity to assess the changes in estrogen treatment was provided by 13 menopausal patients on two separate occasions. Six of these patients were tested before and after starting the use of estrogen and 7 were tested before and after a change in estrogen dose. Twenty-five patients were deemed premenopausal (see below) but did not have vaginal cultures obtained, 8 patients were receiving oral contraceptives, and 1 patient was using yam cream. All these patients had pH, FSH, and estradiol measurements. Therefore a total of 254 patients were studied.

Phenaphthazine (Nitrazine) pH indicator paper (supplied by Apothecon, Bristol-Myers Squibb, Princeton, N.J., and Micro Essential Laboratory, Brooklyn, N.Y.) was used for vaginal pH testing. The pH range is 4.5 to 7.5. It has been used in obstetrics since 1938.[14] Phenaphthazine pH indicator paper proved to be easy to read and served well for both bacterial vaginosis-vaginitis and serum estradiol level screening.

The pH paper was applied directly to the lateral vaginal wall at the outer third of the vagina.[15] Care was taken to avoid cervical mucus, blood, or other substances, such as semen and lubricating jelly, known to affect vaginal pH. All samples were interpreted in incandescent light for accuracy.

All vaginal specimens were collected with use of the Star Swab Starplex Transport System and were sent to Unilab Corporation (Tarzana, Calif.), where aerobic cultures were grown. When the predominant organism recovered was β-hemolytic streptococci, *G. vaginalis,* or yeast, it has been listed as such. If a combination of such organisms (excluding yeast), including gram-negative aerobic organisms such as *Escherichia coli* were grown, then the patient was deemed as having a "mixed" infection.

Venipuncture for all blood samples was obtained within 1 hour of the vaginal pH test and all were sent to Huntington Memorial Hospital Laboratory (Pasadena, Calif.). Serum FSH levels were determined with the Dade/Baxter Stratus II automated instrument and reported as milli–International Units per milliliter. Normal ranges for women are as follows: follicular phase, 3.6 to 16.0 mIU/ml; midcycle peak, 8.1 to 28.9 mIU/ml; luteal phase, 1.8 to 11.7 mIU/ml; and postmenopausal, 22.9 to 167.0 mIU/ml. Serum estradiol levels were determined by radioimmunoassay with Diagnostics Products Corporation's Coat-A-Count and reported as picograms per milliliter. The Huntington Hospital Laboratory serum estradiol range for ovulating females by cycle day relative to luteinizing hormone peak is follicular phase –12 (10 to 50 pg/ml), –4 (60 to 120 pg/ml), midcycle –1 (120 to 375 pg/ml), luteal phase +2 (50 to 155 pg/ml), +6 (60 to 260 pg/ml), and +12 (15 to 115 pg/ml).

Patients were considered to be menopausal if they had not had a menstrual period in 1 year or if the FSH value was >22.9 mIU/ml or the estradiol value was <40 pg/ml. A lower limit for estradiol of 40 pg/ml was selected as adequate replacement therapy because patients with this value usually have withdrawal periods when challenged with progesterone. Patients were considered to be premenopausal if their cycles were regular. Additionally, because patients arrived for their visit on a random day, some patients were found to have high FSH and estradiol levels and were considered to be premenopausal. The estradiol values for patients ingesting oral contraceptives was deemed unreliable because ethinyl estradiol is not

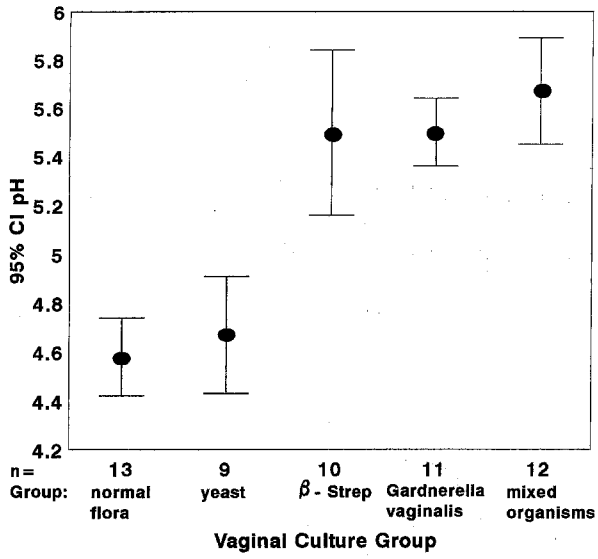

Fig. 1. Fifty-five premenopausal patients who had vaginal pH determinations and vaginal cultures to confirm relationship of vaginal pH to bacterial pathogens. *CI,* Confidence interval.

measured by this assay; therefore these patients are separately reported.

Statistical analysis was performed by use of the computer program Statistical Package for Social Sciences (SPSS, Chicago). Treated and untreated groups were compared for variables with *t* tests and analysis of variance with Duncan multiple comparisons. Paired *t* tests were used to compare the difference in means resulting from initiation or change of estrogen therapy.

Predictive value tables were generated by standard techniques.[16] Two issues are involved in the assessment of any diagnostic test: disease present or absent and diagnostic test result positive or negative (Table I). It is customary to define certain rates as applied to data categorized in this manner. The predictive value of a positive or negative test result is defined as the number of true-positive or true-negative tests divided by all positive or negative tests, respectively. False-positive or false-negative rates are calculated by subtracting the respective predictive value of positive or negative test results from 100%. The sensitivity of a test is defined as the number of true-positive test results divided by all who had the disease or condition. The specificity of a test is defined as the number of true negative test results divided by all who did not have the disease or condition. The efficiency of a test result is defined as the sum of all true-positive and true-negative results divided by all who had the test.

Results

Of 55 premenopausal patients who had vaginal cultures, 13 cultures grew normal flora and 9 yeast. Ten cultures grew β-hemolytic streptococci, 11 *G. vaginalis,* and 12 mixed aerobic pathogens. The results of pH testing in each of these subgroups is depicted in Fig. 1. The mean pH of three subgroups with growth of aerobic bacterial organisms was significantly higher than that obtained in patients with either normal flora or yeast infection (one-way analysis of variance, $p < 0.05$). There was no significant difference in the vaginal pH among the three subgroups with bacterial pathogens, and there was no significant difference between the pH in patients with yeast infection and those with normal flora. All 42 patients with positive culture results were asymptomatic. Thirteen of these patients returned after appropriate antibiotic treatment and all had a normal vaginal pH after therapy. Three of the patients had β-hemolytic streptococci, 6 had *G. vaginalis,* and 4 had mixed aerobic organisms.

When examined in the predictive value format (Table II), an elevated pH >4.5 was 100% sensitive, 92% specific, and 98% efficient for the presence of aerobic pathogens (excluding yeast) in premenopausal women. In menopausal women (Table III), although sensitivity was 100%, specificity and efficiency was low regardless of whether patients were receiving hormone replacement therapy. The latter group had only slightly better results. In menopausal women, when pH was assessed as a predictor for estradiol status (Table IV), those not receiving hormone replacement therapy had a sensitivity of 88%, a specificity of only 50%, and an efficiency of 86%, whereas those receiving hormone replacement therapy had values of 28%, 96%, and 82%, respectively. These findings demonstrate a positive predictive value of 96% in the group with no hormone replacement therapy and a negative predictive value of 84% in the group receiving hormone replacement therapy. Use of vaginal pH only missed identifying 4% of those individuals who needed estrogen therapy (false-positive rate: 100% –96% = 4%). Only 16% of those receiving hormone replacement therapy who had a normal vaginal pH had an estradiol value <40 pg/ml (false-negative rate: 100% – 84% = 16%). The corresponding estradiol values are shown (Table V) with a format similar to that of Table IV. Of the 25 premenopausal patients in whom estradiol levels but not vaginal cultures were obtained, all had pH values <4.5, 3 had estradiol values <40 pg/ml, and the remainder had estradiol values >40 pg/ml. Thus only a few of the predictive value terms could be calculated. The predictive value of a negative test result (pH <4.5) was 88% and the false-negative rate was 12%.

Table VI shows the characteristics of the 13-patient "couplet group" studied both before and after initiation or change of estrogen replacement therapy. Serum estradiol levels increased and pH and FSH levels decreased significantly after initiation or change of estrogen dose.

All eight patients using oral contraceptive pills had a vaginal pH <4.5, as did the 52-year-old patient using yam cream in spite of having an estradiol value of 19 pg/ml.

Table I. Predictive value table

	Test result positive	*Test result negative*	*Total*	
Disease positive	TP	FN	TP+FN	Sensitivity = TP/(TP + FN)
Disease negative	FP	TN	FP+TN	Specificity = TN/(FP + TN)
TOTAL	TP + FP	FN + TN	All	

TP, True positive; *FN*, false negative; *FP*, false positive; *TN*, true negative. Positive predictive value = TP/(TP + FP); False-positive rate = (100% − Positive predictive value); Negative predictive value = TN/(FN + TN); False-negative rate = (100% − Negative predictive value); Efficiency = (TP + TN)/All.

Table II. pH as predictor for positive β-hemolytic streptococci, *G. vaginalis* or mixed aerobic organisms in premenopausal women

	Test + (pH >4.5)	*Test − (pH ≤4.5)*	*Total*	
Disease +	33	0	33	Sensitivity = 100%
Disease −	1	12	13	Specificity = 92%
TOTAL	34	12	46	

+, Positive; −, negative. Positive predictive value 97%, false-positive rate 3%, negative predictive value 100%, false-negative rate 0%, efficiency 98%.

Table III. pH as a predictor for positive β-hemolytic streptococci, *G. vaginalis*, or mixed aerobic organisms in menopausal women

	Test + (pH >4.5)	*Test − (pH ≤4.5)*	*Total*	
No HRT*				
Disease +	3	0	3	Sensitivity 100%
Disease −	5	2	7	Specificity 29%
TOTAL	8	2	10	
With HRT†				
Disease +	7	0	7	Sensitivity 100%
Disease −	4	2	6	Specificity 33%
TOTAL	11	2	13	

+, Positive; −, negative; *HRT*, hormone replacement therapy.

* Positive predictive value 38%, false-positive rate 62%, negative predictive value 100%, false-negative rate 0%, efficiency 50%.

† Positive predictive value 64%, false-positive rate 36%, negative predictive value 100%, false-negative rate 0%, efficiency 69%.

Comment

Faro[5] has stated that in assessing the status of the vaginal ecosystem the hydrogen ion concentration (pH) of the vagina is perhaps the most significant predictor of its status and that "three simple procedures can be performed in the office to characterize the vaginal ecosystem: pH determination, whiff test and microscopic examination of unstained or Gram-stained vaginal discharge."[5] The American College of Obstetricians and Gynecologists Technical Bulletin on vaginitis states that three of the following four criteria are needed for the diagnosis of bacterial vaginosis: pH >4.5, clue cells, positive potassium hydroxide, and homogeneous discharge.[1] Platz-Christensen et al.[17] have stated: "the occurrence of clue cells and an increased pH of the vaginal fluid were utilized as indications of BV."[17]

The clinical consequences of an elevated vaginal pH have been recently amplified. Hillier et al.[6] reported that bacterial vaginosis is associated with preterm delivery of low-birth-weight infants, independent of other recognized risk factors. Women with a vaginal pH >4.5 and a Gram stain score ≥7 on a scale of 0 to 10 were considered to have bacterial vaginosis. Ernest et al.[18] reported that among 115 women at high risk for a low-birth-weight infant those with a mean vaginal pH >4.5 had a threefold increased risk of premature rupture of the membranes compared with those with a mean pH ≤4.5. These articles, along with a study by Krohn et al.[7] and the current American College of Obstetricians and Gynecologists Technical Bulletin[1] on vaginitis, all stress the pivotal importance of the vaginal pH level for the diagnosis of bacterial vaginosis.

This study supports the fact that recovering potentially pathogenic bacteria from the vagina results in an elevated vaginal pH (5.0 to 6.5).[1, 2, 5, 7, 18] In menopausal women two factors may influence vaginal pH, menopausal status and the presence of potentially pathogenic organisms. There were too few patients in whom cultures were obtained to adjust for estradiol status and culture results. Therefore it is not surprising that the false-positive rates were high, especially in those patients not receiving hormone replacement therapy; however, the false-negative rates were 0% in both groups, demonstrating that vaginal pH is still useful. The observation that the presence of *G. vaginalis* precedes the development of bacterial vaginosis warrants consideration of its treatment even in asymptomatic individuals. If *G. vaginalis* were eradicated, perhaps the numbers of individuals who have bacterial vaginosis and its associated disorders could be reduced. For this reason alone vaginal pH should become a routine test during most speculum examinations.

The patients studied varied widely in their need for estrogen. Some menopausal patients maintained a vaginal pH of 4.5 and a normal serum estradiol level while

Table IV. pH as predictor for estradiol status in menopausal women

	Test + (pH >4.5)	*Test − (pH ≤4.5)*	*Total*	
No HRT*				
Disease + (E_2 <40 pg/ml)	53	7	60	Sensitivity 88%
Disease − (E_2 ≥40 pg/ml)	2	2	4	Specificity 50%
TOTAL	55	9	64	
On HRT†				
Disease + (E_2 <40 pg/ml)	5	13	18	Sensitivity 28%
Disease − (E_2 ≥40 pg/ml)	3	67	70	Specificity 96%
TOTAL	8	80	88	

+, Positive; −, negative; *HRT*, hormone replacement therapy; E_2, estradiol.

* Positive predictive value 96%, false-positive rate 4%, negative predictive value 22%, false-negative rate 78%, efficiency 86%.

† Positive predictive value 63%, false-positive rate 27%, negative predictive value 84%, false-negative rate 16%, efficiency 82%.

Table V. Mean estradiol ± SEM values corresponding to subsets of data shown in Table IV

	Test + (pH >4.5)	*Test − (pH ≤4.5)*
No HRT		
Disease + (E_2 <40 pg/ml)	13.9 ± 1.0	18.6 ± 3.3
Disease − (E_2 ≥40 pg/ml)	51.5 ± 11.5	61.0 ± 15.0
HRT		
Disease + (E_2 <40 pg/ml)	19.2 ± 5.1	24.8 ± 2.6
Disease − (E_2 ≥40 pg/ml)	56.0 ± 7.5	135.3 ± 12.8

+, Positive; −, negative; *HRT*, hormone replacement therapy; E_2, estradiol.

Table VI. Couplet data: Changes in pH, FSH, and estradiol in patients with start or change of therapy

	Pretherapy (mean ± SEM)	*Therapy (mean ± SEM)*	*Significance*
No therapy to on HRT (n = 6)			
pH	6.0 ± 0.3	4.7 ± 0.2	p = 0.021
FSH (mIU/ml)	72.2 ± 12.8	30.9 ± 5.5	p = 0.012
Estradiol (pg/ml)	16.0 ± 3.5	137.8 ± 45.5	p = 0.036
On therapy to increase in HRT (n = 6)*			
pH	4.9 ± 0.2	4.5 ± 0.0	p = 0.093
FSH (mIU/ml)	50.8 ± 10.2	28.7 ± 6.3	p = 0.004
Estradiol (pg/ml)	46.2 ± 10.0	131.2 ± 23.0	p = 0.021

HRT, Hormone replacement therapy.

* One patient had reduction in dosage because of symptoms and was excluded from this analysis.

taking estradiol 0.5 mg on Monday, Wednesday, and Friday each week. How often have we had patients bleed irregularly or have breast tenderness, cramps, or genital swelling while taking estrogen replacement therapy daily or cyclicly and become noncompliant as a result? Wouldn't it be better to encourage women's health care practitioners to provide estrogen replacement therapy in such a way as to discover which dose is ideal for each patient? In a retrospective study of 301 postmenopausal women who were prescribed various forms of estrogen replacement therapy and a similar number of untreated control subjects, Ravnikar[19] reported that the overall rate of compliance was only 30%.

Patients during serum estradiol transition or menopause and patients who have become noncompliant as a result of side effects could do self-testing for vaginal pH. This could become as routine as self-testing of urine and blood for diabetes, breast self-examinations, or self-testing of blood pressure for hypertension. The goal is to achieve patient cooperation and compliance, resulting in a vaginal pH of 4.5, with relief of menopausal symptoms and side effects.

With an increase in the number of menopausal women, the need for estrogen replacement therapy will escalate. With this increase comes the need to better manage estrogen replacement therapy. In spite of better understanding of menopause, many physicians have a "one size fits all" attitude toward estrogen dosing, using 0.625 mg of conjugated estrogens (Premarin) as a gold standard. While obtaining a vaginal pH on all patients, the authors confirmed that estrogen depletion results in a vaginal pH of 6.0 to 7.5. As serum estradiol increases

with estrogen replacement, there is a decrease in vaginal pH.[11]

Vaginal pH as a marker for the serum estradiol level demands further investigation. The numbers of menopausal women in this report are too small a number to draw definite conclusions. Should this proposition be validated by larger studies, a powerful screening tool will have been established. This tool could assist the physician or clinical assistant in checking the vaginal estradiol effect and, as a result, establish proper estrogen dosing.

In summary, a vaginal pH of 6.0 to 7.5, in the absence of potentially pathogenic aerobic bacteria, appears to be a reasonable marker of estradiol status for most menopausal patients. A vaginal pH of 5.0 to 6.5 in a well-estrogenized patient (premenopausal or menopausal) appears to be a reasonable marker for the presence of potentially pathogenic aerobic bacteria. Further investigations will be required to delineate the appropriate algorithms for selection of patients for culture and antibiotic therapy or hormonal therapy adjustments. In consideration of all that has been said, vaginal pH testing appears to be that cost-effective, "low-tech" diagnostic tool.

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Editors' note: This manuscript was revised after these discussions were presented.

Discussion

Dr. E. Paul Kirk, Portland, Oregon. Dr. Caillouette offers us today the intriguing and to me novel idea that vaginal pH could be used as a cheap, accessible test for assessing the estrogen status of a postmenopausal patient and thus a means of titrating the effect of hormone replacement therapy, as he sates it, to produce the proper dose for individual patients.

The study had two objectives: (1) to confirm the elevations of vaginal pH expected in patients with bacterial vaginosis and (2) to examine the relationship of serum FSH and estradiol levels to vaginal pH in normal patients without bacterial vaginosis.

Vaginal pH was determined in 2038 patients seen in a solo private practice for routine pelvic examinations. A total of 42 patients had documented bacterial vaginosis, although I am unclear as to how these cases were documented because Dr. Caillouette, while referencing a variety of sources defining criteria for the diagnosis of bacterial vaginosis, does not list the particular criteria used in his study other than to say that 42 had cultures compatible with a diagnosis of bacterial vaginosis. Was a positive culture the criterion? If so, is it not inconsistent with the current criteria, which include homogeneous discharge, pH >4.5, clue cells, the presence of amine odor, and a Gram stain score ≥ 7. Positive cultures are not included in any of the current criteria lists.

Be that as it may, the discussion of pH measurement as an important tool in our routine practice serves as a useful introduction to the meat of this study. A total of 201 patients were studied, 93 untreated patients, mean age 54.6 $\pm$ 14.5 years, and 108 estrogen treated, mean age 56.6 $\pm$ 11.5. Higher pH values (mean 5.73) were associated with lower estradiol levels (mean 47.4 pg/ml). In 9 patients treated sequentially there appeared to be a trend toward a lower vaginal pH as serum estradiol levels rose.

This idea is intriguing. Dr. Caillouette does not give us any clinical data as to how symptomatic either group was nor what sort of side effects, such as breakthrough bleeding, occurred in the treated group. A much larger study will be required to see whether there is any sort of linear relationship between vaginal pH and estradiol levels. If such a relationship is established, how useful

might it be? We know that there are end-organ differences in response to hormonal therapy, and we also appreciate that there are two phases to hormone replacement therapy—initial symptom control and subsequent health maintenance.

Most important, Dr. Caillouette raises the important concept of the proper dose. Will this test help us find the dose in individual patients? What do we mean by the proper dose? In general terms, we usually mean the lowest dose that is most effective and that is associated with the fewest side effects. We have all, in our clinical practices, had experience with wide individual variations both of menopausal symptoms and symptomatic response or lack of response to increasing doses. Estradiol levels are often used to demonstrate the adequacy of hormone replacement in individual cases, and if a reliable relationship between vaginal pH and estradiol levels can be established, then Dr. Caillouette may have hit on a most simple device.

More difficult is knowing what "the proper dose" should be for health maintenance. It has been shown that estradiol levels need to be maintained at 40 to 50 pg/ml to have a positive effect against osteoporosis, but no figures are available for cardiovascular disease. Williams et al.[1] demonstrated that short-term administration of estrogen produced an endothelium-mediated dilation on the coronary arteries of 13 cynomolgus monkeys at levels of 300 pg/ml. But this was an acute animal model demonstrating the mechanism of effect of estrogen but giving no guidance as to the optimal levels to be sought in the chronic replacement.

Finally, the frustrations that occur with side effects such as breakthrough bleeding could be minimized if a relationship between estradiol levels and side effects could be established. To my knowledge, such a relationship has not been demonstrated except in the broadest terms; however, a study comparing vaginal pH and specific side effects could easily be done.

I have already asked these questions. (1) A much larger study will be required to see whether there is any sort of linear relationship between vaginal pH and estradiol levels. If such a relationship is established, how useful might it be? (2) Most important, Dr. Caillouette raises the important concept of the proper dose. Will this test help us find the dose in individual patients? (3) Where does his vision take him next? I would welcome his opinion as to what studies should be planned to pursue this idea to the point of clinical applicability.

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Dr. Michael T. Medchill, Phoenix, Arizona. In women who have an elevated pH, even if they are asymptomatic, will it be necessary to identify whether they have bacterial vaginosis, adding more cost to the workup, to find out what the appropriate dose for hormone replacement therapy might be in these women?

Dr. Martin L. Schwartz, Portland, Oregon. I have a concern with the use of Nitrazine paper to adjust the estrogen dose when the desired value is at one end of the test scale. If a pH of 4.5 is ideal, Nitrazine paper can indicate by an elevated pH that the patient may be estrogen deficient. However, if the pH is normal, we may have an excessive dose of estrogen and cannot tell it by the test used. Unless a test of pH that will go below 4.5 is used, Nitrazine paper to monitor systemic estrogen levels will have limitations.

Dr. Enrique C.M. deCastro, Portland, Oregon. If I understood you correctly, you mentioned that you found β-hemolytic streptococci in almost the same number of patients that you found vaginosis or gardnerella. Many patients are asymptomatic and, yet, have gardnerella. I wonder if the added streptococci is a factor in causing symptoms of vaginosis? How significant is finding β-hemolytic streptococci in these patients?

Dr. Subir Roy, Los Angeles, California. I was at a conference recently in New Orleans that had a section on bacterial vaginosis, and two of the speakers, Drs. Jack Sobel from Detroit and Sharon Hillier from Pittsburgh, mentioned but gave no exact information as to the relationship between bacterial vaginosis and pH as a screening tool. In part, Dr. Caillouette's study addresses that issue. The other fact raised in the New Orleans meeting was that bacterial vaginosis is the wrong term: it should be vaginal bacteriosis. As Sharon Hillier said, it was interesting to consider that all these bacteria had vaginosis! Should the descriptive phrase be kept or changed?

Dr. Frank R. Gamberdella, Santa Barbara, California. In terms of vaginal pH, did you notice any correlation in postmenopausal patients who used equine estrogen versus β-estradiol? Second, could you comment on the use of estrogen creams in treating patients with recurrent infections?

Dr. Caillouette (Closing). Dr. Kirk, because the literature is inconsistent on this subject, both as to definition and diagnosis, my study does interchange the terms vaginitis and vaginosis. Because the use of the term bacterial is consistent, I chose to use bacterial cultures. The new polymerase chain reaction test kit states "for bacterial vaginitis/BV." Clinicians remain confused. Most do not use potassium hydroxide, look for clue cells, or check vaginal pH.

To answer the first question, I have been told that a larger study on the relationship of vaginal pH to serum estradiol levels is being planned. If the relationship shown in my study is confirmed by larger studies, this simple cost-effective tool could have a positive effect on the stated 30% compliance rate for estrogen replacement therapy.

As for the second question, it is my hope that the larger studies will confirm my proposition that estrogen dose is as patient specific as are other endocrine replacement medications.

To answer the third and final question, I hope that this preliminary study will stimulate others to publish much

larger, well-controlled studies to challenge or confirm the propositions that this article has put forth. For example, are serum estradiol levels patient specific, or species specific, as they relate to the prevention of osteoporosis, cardiovascular disorders, or Alzheimer's disease? The use of 38 different combinations and doses of estrogen or hormone replacement therapy was necessary to address patient preference, compliance, and side effects. By doing self-testing for estradiol levels through the simple, cost-effective use of vaginal pH, patient compliance may be improved.

Dr. Mitchell, an elevated vaginal pH in my office causes me to consider bacterial vaginitis, bacterial vaginosis, or estradiol deficiency. My mental checklist includes the following: Is the patient pregnant, ovulatory, menopausal, or receiving insufficient or no estrogen replacement therapy?

Dr. Schwartz, you are correct. The lowest pH level for phenaphthazine pH testing paper (4.5) is not low enough. The pH paper should test from 3.0 to 7.0. Some patients have a vaginal pH of 3.5, which might suggest estradiol excess. A study to address this issue would be helpful.

Dr. deCastro, as to the significance of β-hemolytic streptococci and gardnerella and as to whether these findings should be treated, I fall back on my understanding of normal and pathologic vaginal physiologic features. A normal vaginal ecosystem has a predominance of *Lactobacillus acidophilus,* which produces lactic acid and hydrogen peroxide resulting in the normal vaginal pH of 4.5. If this normal ecosystem is upset by pathogenic bacteria, which can be eliminated by a common antibiotic, then I choose to treat and help the ecosystem return to its normal state.

Dr. Roy, as to whether the term bacterial vaginosis should be changed for the sixth time since 1955, if it should be changed again, it should not be changed by physicians or bacteriologists but rather by etymologists. I agree with Dr. Hilliar that the term bacterial vaginosis suggests that the bacteria have vaginosis. However, to change the term to "vaginal bacteriosis" would result in total confusion for physicians, and the subject seems sufficiently confused. I would choose to leave it alone.

Dr. Gamberdella, I regularly use conjugated equine estrogens, estradiol, estropipate, and estrogen vaginal cream. Each of these medications will increase serum estradiol and each will lower vaginal pH. In my experience estradiol and estropipate have a shorter half-life and are easier to adjust than conjugated estrogens. I have no data on the use of estrogen creams in treating patients with recurrent vaginal infections.