DIAGNOSIS OF VAGINITIS
OB401.016

COVERAGE:

DNA based identification of Trichomonas, Candida, and Gardnerella may be eligible for coverage in patients with symptoms of vaginitis.

DNA based screening for Trichomonas, Candida, and Gardnerella may be eligible for coverage in asymptomatic pregnant patients at high risk for premature labor.

High risk factors for premature labor include the following:

- Prior history of preterm labor in previous pregnancy
- Maternal weight of <50kg

DESCRIPTION:

Vaginitis is a common medical complaint, characterized by a vaginal discharge with or without accompanying pruritus. The most common causes of vaginitis are Candida infection, Trichomonas infection, and bacterial vaginosis (BV). BV is the clinical syndrome related to an alteration in the normal vaginal flora. While the normally occurring lactobacilli decline in numbers, there is an increase in the population of Gardnerella vaginalis, Mycoplasma hominis, Peptostreptococcus species, and anaerobic gram-negative rods.

Diagnosis of vaginitis is based on clinical symptoms, pH of the vaginal fluid, and microscopic examination of the discharge. Diagnosis of BV is typically based on the presence of 3 of 4 of the Amsel criteria—homogenous discharge, amine odor when potassium hydroxide (KOH) is applied to the vaginal discharge (called the whiff test), pH>4.5 and presence of the typical "clue" cells on a wet mount microscopic specimen. Microscopic examination may also reveal motile Trichomonads or Candida Hyphae. Culture is of no value in diagnosing BV, since the organisms associated with BV are present in the normal vaginal flora. Culture of trichomonas and candida may be helpful if clinical symptoms are suggestive and microscopy is negative. Mixed infections are also common, with Trichomonas, Candida, or both coexisting with BV.

While BV is the most common cause of vaginal discharge and malodor, approximately half of patients who meet clinical diagnostic criteria are asymptomatic. There has been intense research interest in the role of asymptomatic BV in the pathophysiology of preterm labor, with a corollary interest in routine testing of pregnant women.

Physicians have become interested in alternative, office-based methods of diagnosing vaginitis. Office microscopy to detect clue cells, Trichomonas, or Candida may be perceived as cumbersome and inaccurate. For example, the sensitivity of microscopy in diagnosing trichomonas is estimated at 60% to 70%. It is also estimated that only half of practicing physicians can correctly diagnose routine cases of vaginal
candidiasis. While the presence of clue cells to diagnose BV is considered a sensitive test, many physicians may not be adequately trained in microscopic techniques. Finally, several aspects of the diagnosis are subjective, i.e., the visual examination of the discharge, reading the pH paper, and evaluation of the odor as part of the whiff test.

Recently, DNA probes have been developed to directly detect the presence of Candida, Trichomonas, and Gardnerella, thus providing a more objective diagnosis. Since Gardnerella is a normal part of the vaginal flora, the DNA probe test is designed to be relatively insensitive, with detection only of pathogenic levels of Gardnerella. The Affirm VP III Microbial Identification System is a commercially DNA probe office-based test kit that simultaneously detects the presence of Gardnerella, Trichomonas, and Candida.

Other options include the use of test cards that contain pH indicators and an amine test system that can be evaluated visually, as opposed to evaluating the presence of amines by odor. The FemExam is an example of such a commercially available test system. Also available is pH paper developed specifically for evaluating vaginal secretions.

RATIONALE:

The following discussion focuses on the use of DNA probe tests for the diagnosis of vaginitis. Testing for amines and pH testing is a well-established practice. In contrast, the use of DNA probe tests may be used as an alternative or a complement to microscopic techniques.

Ferris and colleagues performed a study of the performance of the Affirm VP III test kit compared to the clinical diagnosis (based on microscopy, pH, and presence of amines) made by clinicians and experienced medical technicians. The diagnoses made by the medical technicians were considered the gold standard. The study included 499 symptomatic women, with an age range of 14 to 67 years. The following results were reported.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Candidiasis</th>
<th>Trichomonas</th>
<th>Bacterial Vaginosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Clinician DNA Test</td>
<td>80.2</td>
<td>91.6</td>
<td>95.0</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>39.6</td>
<td>75.0</td>
<td>*</td>
</tr>
<tr>
<td>Specificity</td>
<td>90.4</td>
<td>95.7</td>
<td>96.6</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>50.7</td>
<td>81.5</td>
<td>64.3</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>85.7</td>
<td>93.9</td>
<td>98.0</td>
</tr>
</tbody>
</table>

*Statistically significant differences

As indicated by the above table, the diagnostic performance of the DNA based tests was better than that of the clinician, although the only statistically significant differences were recorded for the sensitivity of detecting candida and bacterial vaginosis. The only exception was the specificity of detecting bacterial vaginosis, where the clinician diagnosis outperformed the DNA test. This discrepancy
may be due to the fact that the DNA probe test may not be able make the distinction between the presence of normal vs. pathogenic levels of Gardnerella. A total of 14% of women in the study had mixed infections, consisting of bacterial vaginosis occurring with either Trichomonas, Candida or both. The diagnostic performance of the DNA probe test in this setting was more impressive. For example, the sensitivity of the clinical diagnosis of a mixed infection including Candida was only 14.5% compared to 54.8% with the DNA probe test. This difference in sensitivity may be related to the fact that some physicians may not consider the possibility of a mixed infection and do not pursue the diagnosis once an initial pathogen is recognized.

Bacterial Vaginosis and Preterm Birth:

The association of BV and preterm labor was initially investigated in epidemiologic studies. A causal role of BV has been investigated by comparing the incidence of preterm birth in patients with BV, either treated or untreated. The results of these studies have led both the American College of Obstetrics and Gynecology and the Centers for Disease Control and Prevention to issue recommendations regarding testing and treating pregnant women. These studies are reviewed below.

Epidemiologic Studies:

The largest epidemiologic study was reported by Hillier in 1995. This cohort study enrolled 10,397 women with no known medical risk factors for preterm delivery. All women underwent testing for BV at 23 to 26 weeks gestation. The diagnosis of BV was based on vaginal pH and results of Gram's staining. The principal outcome measure was delivery at less than 37 weeks of an infant with a birth weight below 2,500 g. BV was detected in 16% of the women and 4.8% of the women were delivered of a low birth weight infant. BV was found to be associated with low birth weight infants, independent of other factors. However, the association was relatively weak, with an odds ratio of 1.4. The odds ratio of other factors included:

Smoking: 1.4
Black Race: 1.4
Primigravidity: 1.7
Loss of earlier pregnancy: 1.7
Previous low birth weight baby: 6.2

Clinical Studies of Antibiotic Use in Pregnant Patients with BV:

Gibbs and Eschenbach have reviewed the studies focusing on the use of antibiotics to prevent preterm birth. Two randomized studies of high-risk pregnant patients with BV, either treated or untreated, have concluded that treatment results in improved pregnancy outcome. For example, in a study of 80 patients with BV plus a history of preterm birth or preterm premature rupture of membranes, the incidence of preterm birth was 18% in the treated group vs. 39% in the control group. Hauth and colleagues reported on a randomized study of 258 women with a history of previous preterm birth or low maternal weight. The incidence of preterm birth in those randomized to the treatment group was 31% compared to 49% in the control group. In a nonrandomized study, McGregor and colleagues reported on the results of screening and treating 1,260 women at an inner city hospital where the preterm birth rate was 15%. Treated patients had a 9.8% incidence
of preterm birth, compared to 18.8% in untreated patients. There are no controlled trials of BV screening and treatment in low-risk women.

In February of 1998, the American College of Obstetrics and Gynecology (ACOG) issued a Committee Opinion regarding BV screening for prevention of preterm delivery. The following strategies were recommended:

• Screening for BV may be considered in women at high risk for preterm labor.

• Women who have positive results or symptoms of BV should be treated with metronidazole administered orally on a daily basis.

• Current studies do not clarify whether women who test positive and are treated or those who test negative should be re-screened periodically during pregnancy. In addition the effect of re-treatment of persistent or recurrent BV is unclear.

• Routine BV screening of asymptomatic women at low risk for preterm delivery and the subsequent treatment of women with positive results cannot be endorsed based on current studies.

The above recommendations do not explicitly establish criteria for identifying women at high risk. However, one of the studies cited by the Committee Opinion suggests that high-risk women are those with a prior history of preterm birth or a weight less that 50kg.

In 1998 the Centers for Disease Control and Prevention (CDC) issued guidelines for the treatment of sexually transmitted disease, including BV. The following recommendation regarding pregnant women was made:

"Because treatment of BV in high-risk women (i.e., those who have previously delivered a premature infant) who are asymptomatic might reduce preterm delivery, such women may be screened, and those with BV can be treated. The screening and treatment should be conducted at the earliest part of the second trimester of pregnancy."

DISCLAIMER:

State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, takes precedence over Medical Policy and must be considered first in determining coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Any benefits are subject to the payment of premiums for the date on which services are rendered. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

HMO Blue Texas physicians who are contracted/affiliated with a capitated IPA/medical group must contact the IPA/medical group for information regarding HMO claims/reimbursement information and other general polices and procedures.