Systematic Review of Diagnostic Tests for Vaginal Trichomoniasis

Sangnya R. Patel, Wilhelmine Wiese, Sanjay C. Patel, Christopher Ohl, James C. Byrd, and Carlos A. Estrada*
Sections of General Internal Medicine and Infectious Diseases, Brody School of Medicine, East Carolina University, Greenville, NC

ABSTRACT

Objective: To review critically and to summarize the evidence of diagnostic tests and culture media for the diagnosis of Trichomonas vaginitis.

Methods: We performed a systematic review of literature indexed in MEDLINE of studies that used Trichomonas culture as the reference standard (9,882 patients, 35 studies). Level I studies (5,047 patients, 13 studies) fulfilled at least two of three criteria: 1) consecutive patients were evaluated prospectively, 2) decision to culture was not influenced by test results, and 3) there was independent and blind comparison to culture.

Results: The sensitivity of the polymerase chain reaction technique (PCR) was 95% (95% CI 91% to 99%), and the specificity was 98% (95% CI 96% to 100%). One study was classified as Level I evidence (52 patients). The sensitivity of the enzyme-linked immunosorbent assay was 82% (95% CI 74% to 90%), and the specificity was 73% (95% CI 35% to 100%). The sensitivity of the direct fluorescence antibody was 85% (95% CI 79% to 90%), and the specificity was 99% (95% CI 98% to 100%). Sensitivities of culture media were 95% for Diamond’s, 96% for Hollander, and 95% for CPLM.

Conclusions: The sensitivity and specificity of tests to diagnose trichomoniasis vary widely. Infect. Dis. Obstet. Gynecol. 8:248–257, 2000. © 2000 Wiley-Liss, Inc.

KEY WORDS

diagnosis; evidence-based medicine; meta-analysis; sensitivity and specificity; Trichomonas

Trichomonas vaginitis is one of the most common sexually transmitted disease, with 167 million new cases each year worldwide, 8 million of which occur in the United States.1–3 Trichomonas vaginalis infection leads to symptomatic vaginitis and contributes to preterm labor, perinatal morbidity, and possible cervical dysplasia.4–7 Moreover, trichomoniasis increases the risk of transmission of the human immunodeficiency virus by twofold.8 Accurate, reliable, convenient, and inexpensive diagnostic tests are essential to reduce the incidence and impact of this important pathogen. Currently, the most convenient and widely used diagnostic test for trichomoniasis is the wet mount.6,9,10 A positive wet mount is diagnostic because of its high specificity, whereas a negative test cannot exclude trichomoniasis because of its low sensitivity.9,11,12

Vaginal culture is considered the best test for the diagnosis of trichomoniasis and is the current reference standard.6,10,13–15 The swab of the sample is immersed in culture broth and incubated at 37°C to maximize growth. Specimens are observed microscopically for presence of motile organisms; if no growth is observed, usually by 7 days, the culture is said to be negative. Unfortu-
nately, culture media are not widely available to the practicing physician, requiring 2–7 days to obtain results. The InPouch TV, a technique that has recently received attention, is a commercially available medium consisting of a two-chambered bag that allows culture and microscopic examination of the specimen. Other tests to identify Trichomonas include polymerase chain reaction (PCR), enzyme-linked immunoassay (ELISA), direct fluorescence antibody assay (DFA), enzyme immunoassay (EIA), dot-immunobinding (DIBA) assay, indirect fluorescent antibody (IFA) assay, agglutination test (AT), and stained smear techniques (Pappenheim stain, Papanicolaou smear). The latter tests were not mentioned in the 1998 Center of Disease Control and Prevention (CDC) guidelines for the treatment of sexually transmitted diseases; currently, no guideline regarding the diagnosis of trichomoniasis is available.

Clinical investigations may result in inaccurate estimates of sensitivity and specificity if: 1) no reference standard is used, 2) patients are not evaluated prospectively, 3) the test result or reference standard influences the decision to perform the comparison test, or 4) the tests are not examined blindly and independently. In a recent meta-analysis of the wet mount and Papanicolaou smear for the diagnosis of trichomoniasis, Wiese et al. found that 74 of 104 studies did not use a reference standard. Although several investigations have suggested the utility of other diagnostic tests for trichomoniasis, their methodologic validity has not been critically examined. We conducted a systematic review of other diagnostic tests for Trichomonas vaginitis in order to obtain overall estimates of test sensitivity and specificity. In addition, we reviewed the accuracy of various culture media. Our systematic review of the evidence may help with development of guidelines for the diagnosis of trichomoniasis.

SUBJECTS AND METHODS

We searched the MEDLINE database in all languages for articles published between January, 1976, and November, 1998, describing diagnostic tests for vaginal trichomoniasis in humans (Ovid 7.05; Ovid, Technologies Inc., New York, NY). The key words to identify trichomoniasis were: explode (exp) Trichomonas, exp Trichomonas infections, Trichomonas vaginalis, and Trichomonas vagi-
### TABLE 1. Summary of studies included in the meta-analysis

| Reference                        | Year  | Setting          | Quality criteria satisfied | Disease prevalence (%) | Sample size (n) | Reference standard                          |
|----------------------------------|-------|------------------|----------------------------|------------------------|----------------|---------------------------------------------|
| **Level I**                      |       |                  |                            |                        |                |                                             |
| Boeke et al. (26)                | 1993  | 1, 2 General clinic | 1, 2                      | 6                      | 667            | CPLM (cysteine-peptide-liver medium)        |
| Sharma et al. (27)               | 1991  | 1, 2 Specialty clinic | 1, 2                     | 7                      | 1,000          | Diamond, wet mount                         |
| Beal et al. (28)                 | 1992  | 1, 2 Specialty clinic | 1, 2                     | 9                      | 710            | Oxoid, Hollander, wet mount                 |
| Briselden et al. (29)           | 1994  | 1, 2, 3 STD clinic | 1, 2, 3                   | 9                      | 170            | Diamond, wet mount                         |
| Levi et al. (16)                 | 1997  | 1, 2 STD clinic   | 1, 2                      | 10                     | 715            | Diamond, InPouch TV (protease-peptone-medium) |
| Jeremias et al. (30)             | 1994  | 1, 2 General clinic | 1, 2                      | 12                     | 52             | Diamond                                    |
| Krieger et al. (31)              | 1988  | 2, 3 STD clinic   | 2, 3                      | 15                     | 600            | Diamond, Feinberg Wittington               |
| Schmid et al. (32)               | 1989  | 1, 2 STD clinic   | 1, 2                      | 27                     | 375            | Diamond, Kupferger-Trichosel,               |
|                                 |       |                  |                            |                        |                | Kupferger-STS, Difco-Kupferger, Lash       |
| Bickley et al. (11)              | 1989  | 1, 2, 3 STD clinic | 1, 2, 3                   | 37                     | 104            | Diamond, wet mount                         |
| de Carli et al. (33)             | 1987  | 1, 2 STD clinic   | 1, 2                      | 38                     | 200            | Diamond, wet mount                         |
| Watt et al. (34)                 | 1986  | 1, 2 STD clinic   | 1, 2                      | 47                     | 177            | Diamond                                    |
| Philip et al. (35)               | 1987  | 1, 2 STD clinic   | 1, 2                      | 49                     | 177            | Diamond, wet mount                         |
| Spence et al. (36)               | 1980  | 1, 2, 3 STD clinic | 1, 2, 3                   | 50                     | 100            | Hollander, wet mount                       |
|                                 |       |                  |                            |                        |                |                                             |
| **Subtotal**                     |       |                  |                            |                        | 16             | 5,047                                      |
| **Level II**                     |       |                  |                            |                        |                |                                             |
| Madico et al. (37)               | 1988  | 2 General clinic  | 2                         | 7                      | 350            | InPouch TV (protease-peptone-medium)        |
| Shaio et al. (38)                | 1997  | 2 Specialty clinic | 2                         | 8                      | 378            | Agar                                       |
| Yule et al. (39)                 | 1987  | 2 STD clinic      | 2                         | 9                      | 482            | Diamond                                    |
| Lin et al. (40)                  | 1997  | 2 Specialty clinic | 2                         | 10                     | 165            | Agar                                       |
| Carney et al. (41)               | 1988  | 2 Specialty clinic | 2                         | 11                     | 395            | Oxoid, wet mount                           |
| Draper et al. (42)               | 1993  | 2 Specialty clinic | 2                         | 15                     | 232            | Diamond, InPouch TV (protease-peptone-medium) |
| DeFleo et al. (43)               | 1996  | 2 General clinic  | 2                         | 15                     | 615            | Diamond, wet mount                         |
| Heine et al. (44)                | 1997  | 2 STD clinic      | 2                         | 16                     | 300            | Trichosel broth, wet mount                  |
| Schweikle et al. (45)            | 1997  | 2 Specialty clinic | 2                         | 26                     | 100            | InPouch TV (protease-peptone-medium)        |
| Smith et al. (46)                | 1986  | 2 STD clinic      | 2                         | 30                     | 105            | Hollander                                  |
| Imandel et al. (47)              | 1985  | 2 Specialty clinic | 2                         | 30                     | 125            | Oxoid, diaphasic egg, Merck, wet mount      |
| Gelbart et al. (48)              | 1989  | 2 Specialty clinic | 2                         | 32                     | 163            | Diamond, Kupferger, wet mount               |
| Garber et al. (49)               | 1987  | 2 STD clinic      | 2                         | 41                     | 227            | Diamond, McCoy cell                        |
| Thomason et al. (50)             | 1988  | 2 General clinic  | 2                         | 42                     | 88             | Kupferger, Hirsh, wet mount                |
| Gombosova et al. (51)            | 1990  | 2 Not described   | 2                         | 78                     | 245            | Diamond                                    |
|                                 |       |                  |                            |                        | 20             | 3,970                                      |
| **Subtotal**                     |       |                  |                            |                        |                |                                             |
| **Level III**                    |       |                  |                            |                        | 20             | 9,882                                      |
| Oliemeyer et al. (52)            | 1998  | — General clinic  | —                         | 13                     | 268            | Diamond                                    |
| Mason (53)                       | 1979  | — Specialty clinic | —                         | 26                     | 200            | Agar                                       |
| Su (54)                          | 1982  | — STD clinic      | —                         | 44                     | 54             | Diamond                                    |
| Lisi et al. (55)                 | 1988  | — General clinic  | —                         | 55                     | 66             | Feinberg Wittington, wet mount             |
| Bosner et al. (56)               | 1992  | — General clinic  | —                         | 57                     | 49             | Diamond                                    |
| Weinberger et al. (57)           | 1993  | — Specialty clinic | —                         | 73                     | 60             | Diamond, wet mount                         |
| Romia et al. (58)                | 1991  | — Specialty clinic | —                         | 79                     | 118            | Diamond, wet mount                         |
| Sharma et al. (27)               | 1991  | — Specialty clinic | —                         | 98                     | 50             | Diamond                                    |
|                                                                                             | 42             | 865   |                                             |
| **Subtotal**                     |       |                  |                            |                        | 20             | 3,970                                      |
| **Total**                        |       |                  |                            |                        | 20             | 9,882                                      |

1 Criteria: 1, prospective evaluation of consecutive patients; 2, test results did not influence the decision to perform trichomonas culture; 3, test and trichomonas culture were examined independently and blindly.

2 Speciality clinic, urology, obstetrics, gynecology, parasitology, STD, sexually transmitted diseases.

3 Same article which used two study designs.

4 CPLM (cysteine-peptide-liver medium).

5 InPouch TV (protease-peptone-medium).

from Bio Med Diagnostics Inc., Santa Clara, CA; Trichosel broth from Becton-Dickinson Microbiology Systems, Cockeysville, MD).

Studies were classified as Level I when they explicitly fulfilled at least two of three validity criteria: 1) consecutive patients were evaluated prospectively, 2) the test result did not influence the decision to perform the reference standard, and 3) the test of interest and reference standard were blinded and independently examined (Table 2). Studies that fulfill these methodologic criteria are more likely to provide accurate estimates of sensi-
**TABLE 2. Level of Evidence**

| Methodologic criteria                      | Evidence Level |
|-------------------------------------------|----------------|
| A reference standard is used              | Level I        |
| Consecutive patients are evaluated prospectively | Level II       |
| Test result does not influence the decision to perform the reference standard | Level III      |
| Test and reference standard are examined blindly and independently | Level II or III |

Activity and specificity. Studies were classified as Level II or III, respectively, when any one, or none, of the criteria was fulfilled.

The articles were randomly distributed among raters with expertise in evidence-based medicine. Two raters independently abstracted validity criteria and data from 2 × 2 contingency tables. Disagreement was resolved by consensus among four raters examining the full article. The kappa interrater agreement for the three study validity criteria were 0.48 for consecutive patient evaluation, 0.17 for influence to perform the reference standard, and 0.61 for test and reference standard independent evaluation.

**Statistical Analysis**

Prevalence, sensitivity, specificity, positive and negative predictive values, and likelihood ratios were calculated. Homogeneity of sensitivity and specificity between studies was explored with the χ² test. Studies were considered homogeneous when the result of an individual study was mathematically compatible with the results of any of the others. We used a random-effects model to pool estimates of sensitivity and specificity. Statistical methods are not available to pool likelihood ratios, so a weighted likelihood ratio could not be calculated.

We calculated an overall likelihood ratio positive (LR⁺) by using pooled estimates of sensitivity and specificity, LR⁺ = sensitivity/(1 – specificity). SPSS 8.0 software was used to perform statistical analyses (SPSS Inc., Chicago, IL).

**RESULTS**

Overall, 31% of diagnostic test studies utilized a reference standard (35/112 studies; Table 1). The validity criteria were reported in 33% of studies for consecutive patients and were evaluated prospectively; 78% of studies for the test result did not influence the decision to perform trichomonas culture as a reference standard; and 11% of studies for the cultures were examined independently and blindly. Table 1 shows the characteristics of the 35 articles (9,882 patients); one publication used two study designs. Thirteen studies (36%) were classified as Level I (5,047 patients), 15 (42%) as Level II (3,970 patients), and eight (22%) as Level III (865 patients). No consistent details of patient information across studies were available from the original papers. Asymptomatic patients accounted for 11% of the reports, patients with/without symptoms 64% (no breakdown of estimates among groups provided), and the remainder of the reports did not specify whether patients were symptomatic or not.

**PCRT Technique**

Six studies examined the test characteristics of the PCR (1,973 patients; Table 3). The pooled sensitivity was 95% (95% CI 91% to 99%), the pooled specificity was 98% (95% CI 96% to 100%), and the LR⁺ was 48. One study was classified as Level I (52 patients), five as Level II (1,921 patients), and none as Level III. The overall estimates of sensitivity were homogeneous. The overall estimates of specificity were heterogeneous.

**ELISA**

Five studies examined the test characteristics of the ELISA technique (806 patients; Table 3). The pooled sensitivity was 82% (95% CI 74% to 90%), the pooled specificity was 73% (95% CI 35% to 100%), and the LR⁺ was 3. One study was classified as Level I (177 patients), one as Level II (395 patients), and three as Level III (234 patients). The overall estimates of sensitivity and specificity were heterogeneous.

**DFA Technique**

Three studies examined the test characteristics of the DFA technique (809 patients; Table 3). The pooled sensitivity was 85% (95% CI 79% to 90%), the pooled specificity was 99% (95% CI 98% to 100%), and the LR⁺ was 85. Two studies were classified as Level I (704 patients), one as Level II (105 patients), and none as Level III. The overall esti-
**TABLE 3. Accuracy of tests to diagnose Trichomonas Vaginitis**

| Test/reference | Level | Prevalence (%) | Sensitivity (n/n) | Specificity (n/n) | Likelihood ratio positive | Likelihood ratio negative | Positive predictive value (%) | Negative predictive value (%) |
|----------------|-------|----------------|-------------------|-------------------|-------------------------|--------------------------|----------------------------|-----------------------------|
| PCR            |       |                |                   |                   |                         |                          |                            |                             |
| Jeremias et al. | I     | 12             | 100 (6/6)         | 98 (45/46)        | 46                      | 0.00                     | 86                         | 100                         |
| Madico et al. (37) | II    | 7              | 96 (22/23)        | 95 (310/327)      | 18                      | 0.05                     | 56                         | 100                         |
| Shaio et al. (38) | II    | 8              | 100 (31/31)       | 100 (347/347)     | ∞                       | 0.00                     | 100                        | 100                         |
| Shaio et al. (38) | II    | 8              | 100 (9/9)         | 100 (104/104)     | ∞                       | 0.00                     | 100                        | 100                         |
| Lin et al. (40) | II    | 10             | 100 (16/16)       | 100 (149/149)     | ∞                       | 0.00                     | 100                        | 100                         |
| DePreo et al. (43) | II    | 15             | 89 (85/95)        | 100 (519/520)     | 465                     | 0.11                     | 99                         | 98                          |
| Heine et al. (44) | II    | 16             | 90 (44/49)        | 95 (239/251)      | 19                      | 0.11                     | 79                         | 98                          |
| **Pooled total** |       |                |                    |                   |                         |                          |                            |                             |
| PCR             |       | 95             | 98*               | 95% CI 91 to 99    | 96 to 100               | 19 to ∞                  | 0 to 0.11                  | 79 to 100 98 to 100          |
| ELISA          |       |                |                   |                   |                         |                          |                            |                             |
| Watt et al. (34) | I     | 47             | 77 (65/84)        | 100 (93/93)       | ∞                       | 0.23                     | 100                        | 83                          |
| Carney et al. (41) | II    | 11             | 95 (40/42)        | 99 (351/353)      | 168                     | 0.05                     | 95                         | 99                          |
| Lisi et al. (55) | III   | 55             | 89 (32/36)        | 97 (29/30)        | 27                      | 0.11                     | 97                         | 88                          |
| Romia et al. (58) | III   | 79             | 75 (70/93)        | 60 (15/25)        | 2                       | 0.41                     | 88                         | 39                          |
| Sharma et al. (27) | III  | 98             | 76 (37/49)        | 0 (0/1)           | 1                       | 97                       | 0                          |                             |
| **Pooled total** |       |                |                    |                   |                         |                          |                            |                             |
| ELISA          |       | 82*            | 73*               | 95% CI 74 to 90    | 35 to 100               |                         |                            |                             |
| DIA            |       |                |                   |                   |                         |                          |                            |                             |
| Krieger et al. |       |                |                   |                   |                         |                          |                            |                             |
| (31)           | I     | 15             | 86 (76/88)        | 99 (509/512)      | 147                     | 0.14                     | 96                         | 98                          |
| Bickley et al. (11) | I    | 37             | 84 (22/38)        | 98 (65/66)        | 56                      | 0.16                     | 97                         | 92                          |
| Smith et al. (46) | II    | 30             | 81 (23/31)        | 99 (73/74)        | 60                      | 0.20                     | 96                         | 92                          |
| **Pooled total** |       |                |                    |                   |                         |                          |                            |                             |
| DIA            |       | 85             | 99                | 95% CI 79 to 90    | 98 to 100               |                         |                            |                             |
| EIA; Yule et al. (39) | II  | 15             | 93 (41/44)        | 98 (429/438)      | 45                      | 0.07                     | 82                         | 99                          |
| Pappenheim stain; |       |                |                   |                   |                         |                          |                            |                             |
| Garber et al. (49) | II    | 41             | 83 (77/93)        | 99 (132/134)      | 55                      | 0.17                     | 97                         | 89                          |
| DIBA; Gombosova et al. (51) | II | 78             | 92 (175/191)     | 93 (50/54)        | 12                      | 0.09                     | 98                         | 76                          |
| IFA; Mason (53) | III   | 26             | 92 (48/52)        | 62 (92/148)       | 2                       | 0.12                     | 46                         | 96                          |
| IFA; Romia et al. (58) | III | 79             | 87 (81/93)        | 80 (20/25)        | 4                       | 0.16                     | 94                         | 63                          |
| IFA, IgA; Su (54) | III   | 44             | 8 (2/24)          | 100 (30/30)       | ∞                       | 0.92                     | 100                        | 58                          |
| IFA, IgE; Su (54) | III   | 44             | 13 (3/24)         | 100 (30/30)       | ∞                       | 0.88                     | 100                        | 59                          |
| IFA, IgG; Su (54) | III   | 44             | 71 (17/24)        | 77 (23/30)        | 3                       | 0.38                     | 71                         | 77                          |
| IFA, IgM; Su (54) | III   | 44             | 4 (1/24)          | 100 (30/30)       | ∞                       | 0.96                     | 100                        | 57                          |
| AT; Romia et al. (58) | III | 79             | 65 (60/93)        | 96 (24/25)        | 16                      | 0.37                     | 98                         | 42                          |

*Symptomatic patients.
*Asymptomatic patients.
*Denotes heterogeneity of data (P < 0.05).

mates of sensitivity and specificity were homogeneous.

**Other Techniques**

Six studies examined nine other techniques (Table 3). The sensitivities ranged from 4% to 93%, and the specificities ranged from 62% to 100%. The LR* ranged from 2 to infinity. No studies were classified as Level I, three as Level II, and three as Level III.

**Culture Media**

Twenty studies examined the test characteristics of 11 culture media techniques (Table 4). The pooled
TABLE 4. Accuracy of culture media to diagnose trichomonas vaginitis

| Culture media/reference | Prevalence | Sensitivity |
|-------------------------|------------|-------------|
|                         | Level (%)  | Percent (n/n) |
| Diamond                 |            |             |
| Sharma et al. (27)      | I          | 7           | 99 (67/88) |
| Levi et al. (16)        | I          | 10          | 88 (65/74) |
| Schmid et al. (32)      | I          | 27          | 90 (92/102) |
| Schmid et al. (32)      | I          | 27          | 97 (99/102) |
| Bickley et al. (11)     | I          | 37          | 95 (36/38) |
| de Carli et al. (33)    | I          | 38          | 97 (73/75) |
| Philip et al. (35)      | I          | 49          | 98 (84/86) |
| Draper et al. (42)      | II         | 15          | 91 (31/34) |
| DeMee et al. (43)       | II         | 15          | 98 (93/95) |
| Garber et al. (49)      | II         | 60          | 98 (53/54) |
| Weinberger et al. (57)  | III        | 73          | 98 (43/44) |
|                        |            | Pooled total| 95% CI       |
|                        |            | 93 to 98    |
|                        |            | Range       | 7 to 73      |
|                        |            | 88 to 99    |
| Hollander              |            |             |
| Beal et al. (28)        | I          | 9           | 97 (60/62) |
| Spence et al. (36)      | I          | 50          | 96 (48/50) |
|                        |            | Pooled total| 96           |
|                        |            | 95% CI      | 93 to 100    |
|                        |            | Range       | 9 to 50      |
|                        |            | 96 to 97    |
| CPLM                    |            |             |
| Boeke et al. (26)       | I          | 6           | 92 (34/37) |
| Boeke et al. (26)       | I          | 6           | 97 (36/37) |
|                        |            | Pooled total| 95           |
|                        |            | 95% CI      | 80 to 100    |
|                        |            | Range       | 6            |
|                        |            | 92 to 97    |
| InPouch TV              |            |             |
| Levi et al. (16)        | I          | 10          | 82 (61/74) |
| Draper et al. (42)      | II         | 15          | 88 (30/34) |
| Schwebke et al. (45)    | II         | 26          | 85 (22/26) |
| Schwebke et al. (45)    | II         | 26          | 88 (23/26) |
| Ohlemeyer et al. (52)   | III        | 13          | 81 (29/36) |
|                        |            | Pooled total| 84           |
|                        |            | 95% CI      | 79 to 89     |
|                        |            | Range       | 7 to 26      |
|                        |            | 81 to 88    |
| Oxoid                   |            |             |
| Beal et al. (28)        | I          | 9           | 89 (55/62) |
| Carney et al. (41)      | II         | 11          | 76 (32/42) |
| Imandel et al. (47)     | II         | 30          | 81 (30/37) |
|                        |            | Pooled total| 83           |
|                        |            | 95% CI      | 76 to 90     |
|                        |            | Range       | 9 to 30      |
|                        |            | 76 to 89    |
| Kuperberg-Trichosel     |            |             |
| Schmid et al. (32)      | I          | 27          | 75 (77/102) |
| Gelbart et al. (48)     | II         | 32          | 77 (40/52) |
| Thomason et al. (50)    | II         | 42          | 86 (32/37) |
|                        |            | Pooled total| 78           |
|                        |            | 95% CI      | 72 to 85     |
|                        |            | Range       | 27 to 42     |
|                        |            | 75 to 86    |
| Other media             |            |             |
| Merck; Imandel et al. (47)| II     | 30          | 76 (28/37) |
| Diphasic egg; Imandel et al. (47)| II | 30 | 89 (33/37) |
| Hirsh; Thomason et al. (50)| II   | 42          | 81 (30/37) |
| McCoy cell; Garber, et al. (49)| II | 60 | 96 (52/54) |
| Feinberg Wittington; Lisi et al. (55)| III | 55 | 97 (35/36) |
|                        |            | Pooled, all cultures | 90 |
|                        |            | 95% CI      | 87 to 93     |
|                        |            | Range       | 75 to 99     |

1Diamond-modified. 2Cervix sampling. 3Self-collected sample. 4Collected by physician. *Denotes heterogeneity of data (P < 0.05).
sensitivity for all studies was 90% (95% CI 87% to 93%). The Diamond’s culture medium was examined in 10 studies (3,568 patients; Table 4). The pooled sensitivity was 95% (95% CI 93% to 98%). Six studies were classified as Level I (2,571 patients), three as Level II (937 patients), and one as Level III (60 patients). The overall estimates of sensitivity were heterogeneous.

The Hollander culture medium was examined in two studies (810 patients; Table 4). The pooled sensitivity was 96% (95% CI 93% to 100%). Both studies were classified as Level I. The overall estimates of sensitivity were homogeneous.

The CPLM culture medium was examined in one study (667 patients; Table 4). The pooled sensitivity was 95% (95% CI 80% to 100%). Both studies were classified as Level I. The overall estimates of sensitivity were homogeneous.

The InPouch TV technique was examined in four studies (1,315 patients; Table 4). The pooled sensitivity was 84% (95% CI 79% to 89%). One study was classified as Level I (715 patients), two as Level II (332 patients), and one as Level III (268 patients). The overall estimates of sensitivity were homogeneous.

**DISCUSSION**

We performed a systematic review of tests comparing to a reference standard to help with the development of guidelines for the diagnosis of trichomoniasis. Ideally a test should have high sensitivity and specificity and be easily available, simple to perform, and inexpensive. Currently, for the diagnosis of trichomoniasis, the wet mount is the least costly to perform, yet its sensitivity is poor. In the latest guidelines for the treatment of sexually transmitted diseases, the CDC reports that “The motile *T. vaginalis* is identified easily in the saline specimen [and] culture for *T. vaginalis* is more sensitive than microscopic examination.” However, no guidance was provided regarding other diagnostic tests.

This systematic review shows that PCR for the diagnosis of trichomoniasis has high sensitivity, specificity, and LR+. The narrow confidence intervals indicate consistent results between studies. However, most of the data were derived from Level II studies. Self-collection of the specimen and rapid results are some of the advantages of this technique. Women with asymptomatic trichomoniasis serve as a reservoir for continuing disease transmission. Therefore, perhaps PCR would be most useful in mass screening of trichomoniasis, similarly to its use in the detection of *Chlamydia trachomatis*. Detection of nonviable organisms in patients previously treated and unavailability in most institutions are presently some of the limitations of the PCR technique. In the future, PCR may be superior to culture. Other techniques such as ELISA and DFA have lower sensitivities compared to PCR or culture.

Our study raises an important issue: What should the culture reference standard be for the diagnosis of vaginal trichomoniasis? Our systematic review shows that the Diamond, Hollander, and CPLM culture media seem to be the most accurate, with sensitivities over 95%. Therefore, they could be used as reference standards. Among these, Diamond’s medium produces the maximal *Trichomonas* growth in vitro. Other culture media have lower sensitivities and so probably should not be used as reference standards. Some authors have recommended selective media (Diamond’s, Trichosel, Hollanders, InPouch TV) as superior for culture of *Trichomonas*, whereas others have not. All of the Level I studies included in this study utilized one of the culture media with the highest sensitivities (Diamond, Hollander, CPLM). Although the cost of these culture media is not high, most practicing physicians are not aware of their existence, and few hospitals have them available. Cultures could detect trichomonads at 48–72 hr, but it may take up to 7 days to obtain the final result. A delay in therapy while waiting for results is undesirable. *Trichomonas* culture should be used when the wet mount is negative and the clinical suspicion is still present. Culture should also be obtained to confirm a positive Papanicolaou smear in settings of low to intermediate prevalence. The estimates of sensitivity for culture should be interpreted cautiously. The reference standard in some studies was the culture medium itself with the wet mount, which may yield higher estimates of sensitivity for the culture, whereas in other studies the reference standard was multiple culture media with/without the wet mount, which may yield lower estimates of sensitivity. As an example, the sensitivity of the Diamond’s medium ranged from 95% to 99% for the former scenario and 88% to 97% for the latter.
Our systematic review has several strengths. We used a systematic approach in the evidence-based framework, including studies that utilized a reference standard. Studies without a reference standard when one exists are uninterpretable. We also used explicit validity criteria to assess the level of the evidence.18,19 Finally, multiple raters abstracted data to avoid observation bias. Our study has certain limitations. The methodologic quality criteria in the studies were not always explicitly described, resulting in less-than-ideal interrater agreements. We address this by discussing the criteria among four authors but acknowledge that other reviewers might reach different decisions. The study design was not uniform among reports, and not all estimates were homogeneous. We used a random-effect model to attempt to correct for heterogeneity among such studies, but we caution the reader to examine the primary data instead of the pooled estimates.

In summary, PCR is a promising technique with sensitivity equal to or better than that of culture. However, more Level I studies are needed. The CDC should make a uniform recommendation with the appropriate reference standard for the diagnosis of trichomoniasis. In the meantime, it seems prudent to use only the culture media with the highest sensitivity as a reference standard (Diamond, Hollander, or CPLM).

ACKNOWLEDGMENTS

We thank Ms. Amy Jackson and Ms. Laurin Gibson for technical assistance and Dr. Harry Adams for suggestions.

REFERENCES

1. Gerbase AC, Rowley JT, Mertens TE. Global epidemiology of sexually transmitted diseases. Lancet 1998;351:2-4.
2. World Health Organization. Report on the global HIV/AIDS epidemic June 1998—HIV and AIDS: the global situation. 1998. Available from http://www.who.int/emc-hiv/global_report/Rep_Htm/report2.html.
3. Khan JO, Walker BD. Acute human immunodeficiency virus type I infection. N Engl J Med 1998;339:33-39.
4. La Vecchia C. The epidemiology of cervical neoplasia. Biomed Pharmacother 1985;39:426-433.
5. McGregor JA, French JJ, Parker R, et al. Prevention of premature birth by screening and treatment for common genital tract infections: results of a prospective controlled evaluation. Am J Obstet Gynecol 1995;173:157-167.
6. Petrin D, Delgaty K, Bhatt R, Garber G. Clinical and microbiological aspects of Trichomonas vaginalis. Clin Microbiol Rev 1998;11:300-317.
7. Gram IT, Macaluso M, Churchill J, Stalsberg H. Trichomonas vaginalis (TV) and human papillomavirus (HPV) infection and the incidence of cervical intraepithelial neoplasia (CIN) grade III. Cancer Causes Control 1992;3:231-236.
8. Laga M, Manoka A, Kivuvi M, et al. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. AIDS 1993;7:95-102.
9. Black ER, Bordley DR, Tape TG, Panzer RJ. Diagnostic Strategies for Common Medical Problems, 2nd Ed. Philadelphia: American College of Physicians-American Society of Internal Medicine; 1999. p 255-268.
10. Murray P (Editor-in-Chief). Manual of Clinical Microbiology, 7th ed. Washington, DC: American Society for Microbiology; 1999. p 1346-1347, 1401-1403.
11. Bickley LS, Krisher KK, Punsalang A Jr, Trupé MA, Reichman RC, Menegus MA. Comparison of direct fluorescent antibody, acridine orange, wet mount, and culture for detection of Trichomonas vaginalis in women attending a public sexually transmitted diseases clinic. Sex Transm Dis 1989;16:127-131.
12. Wiese WJ, Patel SR, Patel SC, Ohl G, Estrada CA. A meta-analysis of the Papanicolaou smear and wet mount for the diagnosis of vaginal trichomoniasis. Am J Med 2000;108:301-308.
13. Sobel JD. Vaginitis. N Engl J Med 1997;337:1896-1903.
14. Anonymous. 1989 Sexually Transmitted Diseases Treatment Guidelines. MMWR 1989;38(Suppl 8):1-43.
15. Henry JB. Clinical Diagnosis and Management by Laboratory Methods, 19th Ed. Philadelphia: W.B. Saunders Company; 1996. p 1278.
16. Levi MH, Torres J, Pina C, Klein RS. Comparison of the InPouch TV culture system and Diamond’s modified medium for detection of Trichomonas vaginalis. J Clin Microbiol 1997;35:3308-3310.
17. Centers for Disease Control and Prevention. 1998 Guidelines for treatment of sexually transmitted diseases. MMWR 1998;47(RR-1):70.
18. Irwig L, Tosteson AN, Gatsonis C, et al. Guidelines for meta-analyses evaluating diagnostic tests. Ann Intern Med 1994;120:667-676.
19. Cochrane Methods Working Group on Systematic Review of Screening and Diagnostic Tests: Recommended Methods. 1996. Available from http://som.flinnders.edu.au/fusa/cochrane/.
20. Jaeschke R, Guyatt G, Sackett DL. Users’ guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? Evidence-Based Medicine Working Group. JAMA 1994;271:389-391.
21. Reid MC, Lachs MS, Feinstein AR. Use of methodological standards in diagnostic test research. Getting better but still not good. JAMA 1995;274:645-651.
22. Haynes RB, Wilczynski N, McKibbon KA, Walker CJ, Sinclair JC. Developing optimal search strategies for de-
tecting clinically sound studies in MEDLINE. J Am Med Inform Assoc 1994;1:447–458.

23. McKibbon KA, Walker-Dilks CJ. Beyond ACP Journal Club: how to harness MEDLINE for diagnostic problems. ACP J Club 1994;121(Supp1 2):A10–A12.

24. Carr PL, Felsenstein D, Friedman RH. Evaluation and management of vaginitis. J Gen Intern Med 1998;13:335–346.

25. Sackett DL, Haynes RB, Guyatt GH, Tugwell P. Clinical epidemiology. A Basic Science for Clinical Medicine, 2nd Ed. Boston: Little, Brown and Company; 1991. p 30–31.

26. Boeke AJ, Dekker JH, Peerbooms PG. A comparison of wet mount, culture and enzymelinked immunosorbent assay for the diagnosis of trichomoniasis in women. Trop Geogr Med 1991;43:257–260.

27. Sharma P, Malla N, Gupta I, Ganguly NK, Mahajan RC. A comparison of wet mount, culture and enzyme linked immunosorbent assay for the diagnosis of trichomoniasis in women. Trop Geogr Med 1991;43:257–260.

28. Beal C, Goldsmith R, Kotby M, et al. The plastic envelope method, a simplified technique for culture diagnosis of trichomoniasis. J Clin Microbiol 1992;30:2265–2268.

29. Briselden AM, Hillier SL. Evaluation of affim VP microbial identification test for Gardnerella vaginalis and Trichomonas vaginalis. J Clin Microbiol 1994;32:148–152.

30. Jeremias J, Draper D, Ziegert M, et al. Detection of Trichomonas vaginalis using the polymerase chain reaction in pregnant and nonpregnant women. Infect Dis Obstet Gynecol 1994;2:16–19.

31. Krieger JN, Tam MR, Stevens CE, et al. Diagnosis of trichomoniasis. Comparison of conventional wet-mount examination with cytologic studies, cultures, and monoclonal antibody staining of direct specimens. JAMA 1998;259:1223–1227.

32. Schwebke JR, Morgan SC, Pinson GB. Validity of self-obtained vaginal specimens for diagnosis of trichomoniasis. J Clin Microbiol 1997;35:1618–1619.

33. Smith RF. Detection of Trichomonas vaginalis in vaginal specimens by direct immunofluorescence assay. J Clin Microbiol 1986;24:1107–1108.

34. Imandel K, Aflatoni M, Behjatnia Y. Clinical manifestations of female trichomoniasis and comparison of direct microscopy and culture media in its diagnosis. Bull Soc Pathol Exot Filiæes 1985;78:360–367.

35. Gelbart SM, Thomason JL, Ospowski PJ, James JA, Hamilton PR. Comparison of Diamond’s medium modified and Kuperberg medium for detection of Trichomonas vaginalis. J Clin Microbiol 1989;27:1095–1096.

36. Garber GE, Shib L, Ma R, Proctor EM, Shaw CE, Bowie WR. Cell culture compared with broth for detection of Trichomonas vaginalis. J Clin Microbiol 1996;34:1275–1279.

37. Thomason JL, Gelbart SM, Sobun JF, Schulien MB, Hamilton PR. Comparison of four methods to detect Trichomonas vaginalis. J Clin Microbiol 1988;26:1869–1870.

38. Gombosova A, Valent M. Dot-immunobinding assay with monoclonal antibody for detection of Trichomonas vaginalis in clinical specimens. Genitourin Med 1990;66:447–450.

39. Ohlemeyer CL, Hornberger LL, Lynch DA, Swierkosz EM. Diagnosis of Trichomonas vaginalis in adolescent females: InPouch TV culture versus wet-mount microscopy. J Adolescent Health 1998;22:205–208.

40. Mason PR. Serodiagnosis of Trichomonas vaginalis infection by the indirect fluorescent antibody test. J Clin Pathol 1979;32:1211–1215.

41. Su KE. Antibody to Trichomonas vaginalis in human cervices vaginalis secretions. Infect Immun 1982;37:852–857.
55. Lisi PJ, Dondero RS, Kwiatkoski D, Spence MR, Rein MF, Alderete JF. Monoclonal-antibody-based enzyme-linked immunosorbent assay for *Trichomonas vaginalis*. J Clin Microbiol 1988;26:1684–1686.

56. Bozner P, Gombosova A, Valent M, Demes P, Alderete JF. Proteinases of *Trichomonas vaginalis*: antibody response in patients with urogenital trichomoniasis. Parasitolology 1992;105:387–391.

57. Weinberger MW, Harger JH. Accuracy of the Papanicolaou smear in the diagnosis of asymptomatic infection with *Trichomonas vaginalis*. Obstet Gynecol 1993;82:425–429.

58. Romia SA, Othman TA. Detection of antitrichomonal antibodies in sera and cervical secretions in trichomoniasis. J Egypt Soc Parasitol 1991;21:373–381.

59. Laird NM, Mosteller F. Some statistical methods for combining experimental results. Int J Technol Assess Health Care 1990;6:5–30.

60. Midgette AS, Stukel TA, Littenberg B. A meta-analytic method for summarizing diagnostic test performances: receiver-operating-characteristic-summary point estimates. Med Decision Making 1993;13:253–257.

61. Shapiro DE. Issues in combining independent estimates of the sensitivity and specificity of a diagnostic test. Acad Radiol 1995;2(Suppl 1):S37–S47.

62. Mosteller F, Golditz GA. Understanding research synthesis (meta-analysis). Annu Rev Public Health 1996;17:1–23.

63. Hasselblad V, Hedges LV. Meta-analysis of screening and diagnostic tests. Psychol Bull 1995;117:167–178.

64. Kardaun JW, Kardaun OJ. Comparative diagnostic performance of three radiological procedures for the detection of lumbar disk herniation. Methods Inf Med 1990;29:12–22.

65. Moses LE, Shapiro D, Littenberg B. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations. Stat Med 1993;12:1293–1316.

66. Tabrizi SN, Paterson B, Fairley CK, Bowden FJ, Garland SM. A self-administered technique for the detection of sexually transmitted diseases in remote communities. J Infect Dis 1997;176:289–292.

67. Gaydos CA, Howell MR, Pare B, et al. *Chlamydia trachomatis* infections in female military recruits. N Engl J Med 1998;339:739–744.

68. Garcia-de-Lomas M, Nogueira JM, Garcia-de-Lomas J, Buesa FJ. In vitro growth of *Trichomonas vaginalis*: a comparative study of six culture media. Eur J Sex Transm Dis 1984;1:195–199.