Clinical Presentation of *Mycoplasma genitalium* Infection versus *Neisseria gonorrhoeae* Infection among Women with Pelvic Inflammatory Disease

Vanessa L. Short,[1] Patricia A. Totten,[2] Roberta B. Ness,[1] Sabina G. Astete,[2] Sheryl F. Kelsey,[1] and Catherine L. Haggerty[1]

[1]Department of Epidemiology, University of Pittsburgh, Pittsburgh, Pennsylvania; and [2]Department of Medicine, Division of Infectious Diseases, University of Washington, Seattle

Background. Women with pelvic inflammatory disease (PID) often present with a spectrum of symptoms. The characteristics of nongonococcal, nonchlamydial PID have not been well described. Our objective was to examine the characteristics of *Mycoplasma genitalium* infection among women with clinically suspected PID.

Methods. We evaluated 722 women who were enrolled in the PID Evaluation and Clinical Health study. Women with *M. genitalium* monoinfection were compared with women with *Neisseria gonorrhoeae* monoinfection or *Chlamydia trachomatis* monoinfection.

Results. Compared with women with gonococcal PID, women with *M. genitalium* infection were less likely to have elevated systemic inflammatory markers, including an erythrocyte sedimentation rate >15 mm/h (5 [22.7%] of 22 patients vs. 45 [60.8%] of 74 patients; $P = .002$), a white blood cell count >10,000 cells/mL (4 [28.6%] of 14 patients vs. 42 [64.6%] of 65 patients; $P = .018$), and an oral temperature ⩾38.3°C (0 [0.0%] of 22 patients vs. 10 [13.9%] of 72 patients; $P = .085$). In addition, they were less likely to present with mucopurulent cervicitis (9 [47.4%] of 19 patients vs. 60 [83.3%] of 72 patients; $P = .001$), elevated vaginal pH ($P = .018$), and high pelvic pain score ($P = .014$). In contrast, women with chlamydial PID had signs and symptoms that were similar to those in women with *M. genitalium* infection.

Conclusions. Because symptoms might be mild, women with *M. genitalium* infection might not seek PID treatment. Further studies are needed to assess the potential reproductive tract sequelae of *M. genitalium* infection of the upper genital tract.

Pelvic inflammatory disease (PID), which is an inflammation of the female upper genital tract that is caused by the ascension of organisms from the lower genital tract, affects ~8% of reproductive-age women in the United States at some time in their lives [1]. Serious sequelae, including recurrent PID, tubal factor infertility, ectopic pregnancy, and chronic pelvic pain, are common sequelae of PID [2]. The sexually transmitted pathogens *Chlamydia trachomatis* and *Neisseria gonorrhoeae* cause 30%–50% of PID cases [3–5]. Although the etiology of PID is unknown in the majority of cases, it has been epidemiologically linked to bacterial vaginosis [6].

Mycoplasma genitalium has been identified as a possible etiologic agent of nongonococcal, nonchlamydial PID [7–9]. It has also been detected in cervical and salpingeal samples obtained from women with laparoscopically confirmed salpingitis [10] and in cervical and endometrial specimens obtained from women with endometritis [7]. Because *M. genitalium* is extremely difficult to culture, epidemiologic studies that assess the role of this organism in reproductive diseases among women are dependent on the development and application of PCR-based assays. Although little is known about the clinical characteristics of *M. genitalium* PID, evidence suggests that, as is the case in women with chlamydia, lower genital tract infections tend to be asymptomatic [11, 12].

At presentation, the characteristics of women with

Received 9 June 2008; accepted 17 September 2008; electronically published 24 November 2008.

Reprints or correspondence: Ms. Vanessa Short, University of Pittsburgh, Dept. of Epidemiology, 519 Parran Hall, 130 DeSoto St., Pittsburgh, PA 15261 (shortv@edc.pitt.edu).

Clinical Infectious Diseases 2009; 48:41–7

1058-4838/2009/4801-0007$15.00
DOI: 10.1086/594123

PID vary, and they may include pelvic pain, abnormal vaginal discharge, bleeding, itching, and/or odor. Although the most common symptom of PID is pelvic pain, many women with PID may have mild pain or no pain, despite evidence of infection and inflammation [13, 14]. The presence and severity of PID symptoms vary by microbiologic etiology, with women who have chlamydial PID being more likely than women who have gonococcal PID to be asymptomatic [15–18].

The purpose of our study was to describe the clinical features of women with lower and/or upper genital tract infection due to *M. genitalium* in a population of women who presented with clinically suspected PID. We hypothesized that clinical characteristics, symptoms, and pelvic pain at presentation would be less frequent and less severe among women with *M. genitalium* or *C. trachomatis* infection than they would be among women with gonococcal PID.

PATIENTS, MATERIALS, AND METHODS

Study population. We used data from the baseline interview of the PID Evaluation and Clinical Health (PEACH) study, which is described in detail elsewhere [19]. In brief, the PEACH study evaluated the effectiveness of inpatient versus outpatient treatment of PID in preventing infertility. From March 1996 through February 1999, nonpregnant women 14–36 years of age were recruited from emergency departments and outpatient facilities (obstetrics and gynecology clinics, sexually transmitted disease clinics, and private practices) from 7 primary sites (Atlanta, GA; Birmingham, AL; Charleston, SC; Detroit, MI; Philadelphia, PA; Pittsburgh, PA; and Providence, RI) and 6 secondary sites in the United States. Women were eligible to participate if they had clinically suspected PID, as defined by the following characteristics: (1) complaints of acute pain (<30 days in duration); (2) a clinical finding of pelvic tenderness; and (3) evidence of lower genital tract inflammation. Women were excluded from the study if they had severe disease that required inpatient management; could not tolerate an outpatient regimen because of vomiting; had an allergy to antibiotics; experienced a delivery, abortion, or gynecologic surgical procedure within the previous 45 days; had a previous hysterectomy, bilateral salpingectomy, or bilateral tubal ligation; had a tuboovarian abscess documented by ultrasound or laparoscope; and/or had appendicitis, hemorrhagic ovarian cyst, or another condition requiring surgery documented by ultrasound or laparoscopy. Informed consent was obtained from eligible women, and 831 participants were enrolled into the PEACH study. Institutional review board approval was obtained for the parent PEACH study, as well as for subsequent PCR testing of stored specimens for *M. genitalium.* For this analysis, stored cervical and endometrial specimens and *M. genitalium* PCR assay results were available for a subset of 722 women. The demographic, behavioral, and clinical characteristics of the 111 women who did not have *M. genitalium* PCR assays performed did not differ significantly from those of the women who were included in our analyses.

Data collection. Baseline data were collected by trained research staff at each study center using standardized interview, examination, and specimen collection techniques. Information was collected on demographic characteristics; medical, gynecologic, and sexual histories; presenting complaints; substance use; current medications; and contraception. Cervical and vaginal swab samples, endometrial biopsy samples, and serum and urine samples were obtained from the participants.

***Detection of* M. genitalium.** Previously collected cervical and endometrial samples that had been stored at −70°C were tested for *M. genitalium* with use of the MgPa-IMW PCR assay targeting the MgPa gene [20]. This assay has an analytical sensitivity of 15 genomes [20] and a high clinical sensitivity and specificity relative to transcription-mediated amplification, another *M. genitalium* nucleic acid amplification assay [21]. For all samples with positive test results, a second MgPa PCR assay [20] was performed using another aliquot of the sample to rule out PCR product contamination or cross contamination; all of the samples with initial positive test results were verified to be *M. genitalium* positive by this confirmatory test.

***Detection of* N. gonorrhoeae *and* C. trachomatis.** Baseline cervical and endometrial samples were assessed at a central laboratory for *N. gonorrhoeae* by culture and for *C. trachomatis* by PCR, as described elsewhere [4].

Clinical characteristics. The following baseline signs and symptoms were evaluated as potential characteristics of *M. genitalium* infection: elevated oral temperature (≥38.3°C), elevated WBC count (>10,000 cells/mL), elevated erythrocyte sedimentation rate (>15 mm/h), elevated C-reactive protein level (≥5 mg/dL), bilateral adnexal tenderness, mucopurulent cervicitis, and bacterial vaginosis (BV), defined using Gram stain [22] and Amsel's criteria [23]. Mucopurulent cervicitis was defined as the presence of a grossly yellow or green exudate observed on a swab specimen obtained from the cervix. Symptoms at presentation that were evaluated as potential characteristics of *M. genitalium* infection included the following: nausea or vomiting, nonmenstrual vaginal bleeding or spotting, more-prolonged or heavier menstrual bleeding than usual, vaginal bleeding during or after sex, abnormal vaginal discharge, increased frequency of urination, and overall self-rated pelvic pain. A pelvic pain score was calculated as the mean of scores for pain at worst, on average, and within the previous 24 h, measured on a Likert scale and multiplied by 10 (range, 0–100).

Statistical methods. The χ^2 test, Fisher's exact test, and analysis of variance were used to evaluate baseline characteristics and symptoms at presentation. Women with *M. genitalium* identified in the cervix and/or endometrium who had test results that were negative for both *N. gonorrhoeae* and *C. tra-*

chomatis were compared with women who had test results that were positive only for *N. gonorrhoeae* in the cervix and/or endometrium and with women who had test results that were positive only for *C. trachomatis* in the cervix and/or endometrium. Women who had test results that were positive only for *N. gonorrhoeae* were also compared with women with *M. genitalium* and *N. gonorrhoeae* coinfection. Similarly, women with test results that were positive only for *C. trachomatis* were compared with women with *M. genitalium* and *C. trachomatis* coinfection. We also examined the differences between women with gonococcal PID and women with chlamydial PID. All data were analyzed using SAS, version 9.1 (SAS). *P* values <.05 were considered to be statistically significant.

RESULTS

Compared with women with gonococcal PID, women with *M. genitalium* infection were generally less likely to have elevated systemic inflammatory markers, including erythrocyte sedimentation rates >15 mm/h (5 [22.7%] of 22 patients vs. 45 [60.8%] of 74 patients; $P = .002$), WBC counts >10,000 cells/mL (4 [28.6%] of 14 patients vs. 42 [64.6%] of 65 patients; $P = .018$), and oral temperatures ≥38.3°C (0 [0.0%] of 22 patients vs. 10 [13.9%] of 72 patients; $P = .085$) (table 1). Women with *M. genitalium* infection were also significantly less likely to present with mucopurulent cervicitis (9 [47.4%] of 19 patients vs. 60 [83.3%] of 72 patients; $P = .001$). In addition, they had significantly lower mean composite pain scores at baseline ($P = .014$). The clinical characteristics of women with test results positive for only *N. gonorrhoeae* did not differ from those of women with test results positive for *N. gonorrhoeae* and *M. genitalium.* After adjustment for BV status (normal or intermediate vs. BV flora), all results remained the same (data not shown).

In contrast with women with *N. gonorrhoeae* infection, women who had test results that were positive only for *M. genitalium* had clinical features that were similar to those of women who had test results that were positive only for *C. trachomatis.* The clinical characteristics of women who had test results that were positive only for *C. trachomatis* did not differ from those of women who had test results that were positive for both *C. trachomatis* and *M. genitalium* (table 2). The results remained the same after adjustment for BV (data not shown).

Compared with women with gonococcal PID, women with PID due to *C. trachomatis* were generally less symptomatic and less likely to have elevated systemic inflammatory markers, including elevated oral temperature (0 [0%] of 45 patients vs. 10 [13.9%] of 72 patients; $P = .013$) or elevated WBC count (9 [22.5%] of 40 patients vs. 42 [64.6%] of 65 patients; $P < .001$). They were less likely to present with cervicitis (22 [52.4%] of 42 patients vs. 60 [83.3%] of 72 patients; $P < .001$) or bilateral adnexal tenderness (35 [77.8%] of 45 patients vs. 61 [82.4%] of 74 patients; $P = .049$) and had statistically significantly lower mean composite pain scores ($P = .020$).

DISCUSSION

To our knowledge, this is the first study to compare the clinical characteristics of women with clinically suspected PID who had genital tract infection due to *M. genitalium, N. gonorrhoeae,* and/or *C. trachomatis.* Our study suggests that, as in chlamydial PID, upper genital tract infection due to *M. genitalium* is less symptomatic than gonococcal PID. However, it should be noted that all women in the PEACH study had clinically suspected PID; therefore, they all presented with some signs or symptoms. Because the inclusion criteria minimized the selection of asymptomatic patients, differences in the clinical characteristics between women with and women without *M. genitalium* infection may be minimized. It would be important to repeat these analyses in a population that includes women with symptomatic PID and women with subclinical or "silent" PID.

Mucopurulent cervicitis and numerous systemic markers of inflammation, including an elevated oral temperature, elevated WBC count, and elevated erythrocyte sedimentation rate, were more prevalent in women with *N. gonorrhoeae* infection than in women with only *M. genitalium* infection. In addition, pelvic pain scores were higher among women with *N. gonorrhoeae* infection. Women with only *N. gonorrhoeae* infection had clinical features that were similar to those of women with test results that were positive for both *N. gonorrhoeae* and *M. genitalium.* This suggests that, in patients with coinfection, the clinical signs and symptoms of *N. gonorrhoeae* infection dominate.

The clinical features of women who present with upper genital tract *M. genitalium* infection have not been extensively examined. In a study involving 115 women with histologically confirmed endometritis, 100% of women with *M. genitalium* infection reported mild abdominal pain, compared with 68% of women without *M. genitalium* infection ($P = .06$) [24]. The association of *M. genitalium* with diseases of the lower genital tract in women has not been consistently reported, which possibly reflects differences in the population studied and criteria used to assess signs and symptoms at this site. Although some studies have shown an association between *M. genitalium* and cervicitis [9, 25–27], several PCR studies have failed to find a strong association between symptoms and *M. genitalium* lower genital tract infection [11, 28, 29]. Tosh et al. [11] conducted a study involving 383 adolescent females who attended a primary care clinic, and they found that women with *M. genitalium* identified in the lower genital tract were no more symptomatic than were uninfected women. In a group of women with test results that were negative for both *C. trachomatis* and *N. gonorrhoeae,* those who had test results that were positive for *M. genitalium* were not more likely to have signs (i.e., pres-

Table 1. Clinical characteristics of women with *Mycoplasma genitalium* monoinfection, *Neisseria gonorrhoeae* monoinfection, or *M. genitalium* and *N. gonorrhoeae* coinfection.

Variable	*M. genitalium* monoinfection ($n = 22$)	*N. gonorrhoeae* monoinfection ($n = 74$)	P[a]	*M. genitalium* and *N. gonorrhoeae* coinfection ($n = 16$)	P[b]
Sign or symptom at presentation					
Nausea and/or vomiting	10 (45.5)	30 (40.5)	.682	8 (50.0)	.487
Nonmenstrual vaginal bleeding	9 (40.9)	28 (37.8)	.795	3 (18.8)	.245
Heavier than usual menstrual bleeding	10 (45.5)	26 (35.1)	.380	5 (31.3)	.767
Bleeding during or after sex	4 (18.2)	6 (8.1)	.230	2 (12.5)	.629
Abnormal vaginal discharge	14 (63.6)	50 (67.6)	.731	8 (50.0)	.183
Increased frequency of urination	11 (50.0)	31 (41.9)	.501	10 (62.5)	.170
Marker of inflammation					
Temperature ≥38.3°C	0 (0.0)	10/72 (13.9)	.085	1 (6.67)	.681
WBC count >10,000 cells/mL	4/14 (28.6)	42/65 (64.6)	.018	5/12 (41.7)	.134
Erythrocyte sedimentation rate >15 mm/h	5 (22.7)	45 (60.8)	.002	8 (50.0)	.426
C-reactive protein level >5 mg/dL	1 (4.5)	9 (12.2)	.305	2 (12.5)	.970
Bilateral adnexal tenderness	17 (77.3)	61 (82.4)	.586	15 (93.8)	.257
Mucopurulent cervicitis	9 (47.4)	60/72 (83.3)	.001	9/16 (56.3)	.017
Bacterial vaginosis					
Confirmed by Gram stain[c]	13 (59.1)	50/65 (76.9)	.106	11/13 (84.6)	.540
Confirmed by Amsel's criteria	7 (38.9)	16/38 (42.1)	.819	4/9 (44.4)	>.999
Pelvic pain,[d] mean composite pain score ± SD	58.0 ± 21.9	72.3 ± 23.9	.014	75.2 ± 20.7	.658

NOTE. Data are no. (%) of patients, unless otherwise indicated. All patients had test results that were negative for *Chlamydia trachomatis*.

[a] Comparison with the *M. genitalium* monoinfection group.

[b] Comparison with the *N. gonorrhoeae* monoinfection group.

[c] Normal or intermediate vs. bacterial vaginosis flora.

[d] Mean composite pain score was calculated as the mean of the current pelvic pain score, the average pelvic pain score, and the worst pelvic pain score × 10.

ence of vaginal erythema, vulvar erythema, or vaginal discharge; $P = .33$) or symptoms (i.e., vaginal itching, vaginal burning, and dyspareunia; $P = .35$) than were women with test results that were negative for *M. genitalium* [11]. Manhart et al. [29] also found that lower genital tract *M. genitalium* infection was not associated with symptoms. PCR was used to test urine samples obtained from 1714 women who were enrolled in a population-based study, and *M. genitalium* infections were not associated with symptoms, because none of the participants who had test results that were positive for *M. genitalium* reported experiencing symptoms of vaginal discharge. Conversely, vaginal discharge was more common among women with lower genital tract *M. genitalium* infection than it was among women without *M. genitalium* infection in a study involving 390 minority women with an active sexually transmitted infection who attended a public health clinic [30]. The results were similar after controlling for coinfection with other sexually transmitted diseases. However, vaginal discharge was the only genitourinary sign or symptom that was statistically significantly different between women with positive test results and women who were not infected. Casin et al. [28] found no association between the identification of *M. genitalium* in the lower genital tract and urinary symptoms (OR, 1.34; 95% CI, 0.72–2.50) or pelvic pain (OR, 0.93; 95% CI, 0.50–1.73) among women attending a sexually transmitted disease clinic. These PCR studies indicate that *M. genitalium* does not produce stronger symptoms in women with lower genital tract infections, compared with symptoms in women without *M. genitalium* infection. The limited symptoms induced by *M. genitalium* infection are similar to those seen in *C. trachomatis* infection [31].

Our study is unique, in that we compared the clinical characteristics of lower and/or upper genital tract *M. genitalium* infection with infections caused by other known bacterial sexually transmitted diseases. In our study, although women with *M. genitalium* infection tended to be less symptomatic than women with gonococcal PID, their symptoms were similar to those of women with chlamydial PID. There were no statistically significant differences between women with *M. genitalium* infection and women with *C. trachomatis* infection with respect to demographic or clinical characteristics. Although no other study has, to our knowledge, compared the clinical characteristics of women with clinically suspected PID, our results are similar to those of a study [25] conducted among 465 women either attending a sexually transmitted disease clinic or enrolled in a cervical cancer screening program in Sweden that com-

Table 2. Clinical characteristics of women with *Mycoplasma genitalium* monoinfection, *Chlamydia trachomatis* monoinfection, or *M. genitalium* and *C. trachomatis* coinfection.

Variable	*M. genitalium* monoinfection (n = 22)	*C. trachomatis* monoinfection (n = 45)	P[a]	*M. genitalium* and *C. trachomatis* coinfection (n = 9)	P[b]
Sign or symptom at presentation					
Nausea and/or vomiting	10 (45.5)	21 (46.7)	.926	4 (44.4)	>.999
Nonmenstrual vaginal bleeding	9 (40.9)	26 (57.8)	.194	4 (44.4)	.489
Heavier than usual menstrual bleeding	10 (45.5)	17 (37.8)	.547	1 (11.1)	.244
Bleeding during or after sex	4 (18.2)	12 (26.7)	.444	1 (11.1)	.428
Abnormal vaginal discharge	14 (63.6)	32 (71.1)	.536	7 (77.8)	.684
Increased frequency of urination	11 (50.0)	21 (46.7)	.798	5 (55.6)	.626
Marker of inflammation					
Temperature ≥38.3°C	0 (0.0)	0 (0.0)	…	1/7 (14.3)	.137
WBC count >10,000 cells/mL	4/14 (28.6)	9/40 (22.5)	.722	2 (22.2)	.986
Erythrocyte sedimentation rate >15 mm/h	5 (22.7)	19 (42.2)	.118	6 (66.7)	.179
C-reactive protein level >5 mg/dL	1 (4.5)	6 (13.3)	.269	3 (33.3)	.161
Bilateral adnexal tenderness	17 (77.3)	35 (77.8)	.963	7 (77.8)	>.999
Mucopurulent cervicitis	9/19 (47.4)	22/42 (52.4)	.717	6 (66.7)	.434
Bacterial vaginosis					
Confirmed by Gram stain[c]	13 (59.1)	28/43 (65.1)	.634	4/8 (50.0)	.450
Confirmed by Amsel's criteria	7/18 (38.9)	15/32 (46.9)	.585	2/6 (33.3)	.672
Pelvic pain,[d] mean composite pain score ± SD	58.0 ± 21.9	61.8 ± 22.9	.517	64.4 ± 26.8	.764

NOTE. Data are no. (%) of patients, unless otherwise indicated. All patients had test results that were negative for *Neisseria gonorrhoeae*.

[a] Comparison with the *M. genitalium* monoinfection group.

[b] Comparison with the *C. trachomatis* monoinfection group.

[c] Normal or intermediate vs. bacterial vaginosis flora.

[d] Mean composite pain score was calculated as the mean of the current pelvic pain score, the average pelvic pain score, and the worst pelvic pain score × 10.

pared the symptoms of *C. trachomatis* infection with those of *M. genitalium* infection of the lower genital tract. In that study [25], no statistically significant differences between women with test results positive for *C. trachomatis* and those with test results positive for *M. genitalium* in the lower genital tract were reported with respect to the presence of symptoms (32% vs. 23%; relative risk, 1.4; 95% CI, 0.6–3.4) or signs (71% vs. 50%; relative risk, 1.4; 95% CI, 0.9–2.3).

Although women with *M. genitalium* infection present with fewer clinical signs and symptoms than do women with *N. gonorrhoeae* infection, there is evidence from animal and human studies that supports a pathogenic role of *M. genitalium* in female upper genital tract infection. *M. genitalium* has been found to induce salpingitis in experiments involving monkeys [32], and it adheres to human fallopian tube epithelial cells in organ culture, resulting in damage to the ciliated cells [33]. This bacterium can adhere to human spermatozoa, potentially allowing it to be carried to the female upper genital tract on motile sperm [34].

M. genitalium PID may lead to subsequent reproductive morbidity, including infertility, recurrent PID, and pelvic pain. In a previous analysis of the PEACH data, Haggerty et al. [35] found that rates of short-term treatment failure (defined as persistent endometritis and pelvic pain after treatment with cefoxitin and doxycycline; found in 41% of patients), infertility (22%), recurrent PID (31%), and chronic pelvic pain (42%) were high among women with test results positive for endometrial *M. genitalium* at baseline. These results were similar to those in a subset of women with test results that were negative for *N. gonorrhoeae* and *C. trachomatis*. Although the association between *M. genitalium* and these sequelae did not reach statistical significance, the findings were similar to those previously reported by analyses of the PEACH data, which showed that chlamydial and gonococcal upper genital tract infection was not associated with subsequent morbidity [36]. This could be explained by the fact that women in the comparison groups who did not have test results positive for *M. genitalium, C. trachomatis,* or *N. gonorrhoeae* did have signs and symptoms of PID; thus, all women in the PEACH study were at high risk of sequelae, because they had clinically suspected PID.

Infertility after infection with *M. genitalium* could result from inflammation and scarring of the fallopian tubes because of frequent PID treatment failure, given that 44% of women with test results positive for *M. genitalium* at baseline had positive test results obtained again 30 days after completion of treatment [35]. A relationship between *M. genitalium* and tubal factor

infertility has also been identified in serological studies [37]. Specifically, *M. genitalium* antibodies were identified more frequently among women with tubal factor infertility than among women without tubal factor infertility (22% vs. 6%) [37]. In another serological study, 17% of women with tubal factor infertility had antibodies to *M. genitalium,* compared with only 4% of women with healthy fallopian tubes [38].

The ability to test for concomitant infections due to *C. trachomatis, N. gonorrhoeae,* and BV was a strength of our study. However, the unavailability of data on other pathogens may limit the interpretation of our findings. It may be possible that specific BV-associated bacteria, anaerobes, and other mycoplasmal bacteria confounded our analysis. However, adjustment for these bacteria was not possible in our current analysis, because only a subset of women in the PEACH study were tested for these bacteria.

In this study, we compared clinical characteristics and signs and symptoms at presentation by microbial etiology among a population of women with clinically suspected PID. As our study suggests, women with *M. genitalium* infection may have less symptomatic PID, which, if left untreated, can lead to serious reproductive morbidity, including tubal factor infertility, ectopic pregnancy, chronic pelvic pain, and recurrent PID [39]. Because the etiology of up to 70% of PID cases is unknown, and because *M. genitalium* has frequently been found in women with PID, detection of the pathogen may help to reduce the burden of untreated PID. However, because clinical symptoms may be mild, and because PID is typically diagnosed through clinical suspicion, women with *M. genitalium* infection might not seek PID treatment, and cases of *M. genitalium* PID might go undiagnosed. Additional studies are needed to determine a diagnostic approach for *M. genitalium* PID and to assess the potential reproductive tract sequelae of *M. genitalium* upper genital tract infection.

Acknowledgments

We thank the following investigators, who were involved in the PEACH study: Antonio Amortegui (University of Pittsburgh and Magee-Womens Hospital, Pittsburgh, PA), Susan L. Hendrix (Wayne State University, Detroit, MI), Sharon L. Hillier (University of Pittsburgh and Magee-Womens Hospital, Pittsburgh, PA), Robert L. Holley (University of Alabama School of Medicine, Birmingham, AL), Deborah B. Nelson (University of Pennsylvania, Philadelphia, PA), John Nichols, Jr., Jeffrey Peipert (Washington University, St. Louis, MO), Hugh Randall (Emory University, Atlanta, GA), Diane Schubeck (MetroHealth Medical Center, Cleveland, OH), Steven J. Sondheimer (University of Pennsylvania, Philadelphia, PA), David E. Soper (Medical University of South Carolina, Charleston, SC), Richard L. Sweet (University of Pittsburgh and Magee-Womens Hospital, Pittsburgh, PA), Wayne Trout (Ohio State University, Columbus, OH), Guiliana Trucco (University of Pittsburgh and Magee-Womens Hospital, Pittsburgh, PA), Harold C. Wiesenfeld (Magee-Womens Hospital, Pittsburgh, PA, and Brown University School of Medicine, Providence, RI), and Tamer Yalcinkaya. We thank and acknowledge the efforts of the following interviewers, who recruited and interviewed study participants: Susan Allen, Audrey Baum, Corina Becker, Hope Cohen-Webb, Amy Cooper, Peg Crowner, Leslie Curll, Jackie Faas, Amanda Farmer, Emily Hoffman, Anne Holdredge, Alice Howell, Susan Kay, Faye Leboeuf, Ingrid Macio, Kathy Martin, Margaret McNamee, Ann Meers, Kim Miller, Andrea Montagno, Joy Mowery, Jan Mitton, Cheryl Myers, Brenda Nobels, Tara Pealer, Anne Rideout, Georgia Rothstein, Carol Sams, Tara Schuda, Buffie Schiavoni, Marsha Scott, Kelly Timbers, Sam Whitaker, Lisa Williams, and Mirza Vincetic. We thank consultants Tom Songer, Judy Lave, and Sheryl Kelsey and technical assistant Debra Bass.

Financial support. Agency for Healthcare Research and Quality Development (HS08358-05) and the National Institute of Allergy and Infectious Diseases (1 R01 AI067661-01A2).

Potential conflicts of interest. All authors: no conflicts.

References

1. Public Health Service, Center for Health Statistics. National survey of family growth. Hyattsville, MD: US Department of Health and Human Services, **1995**.
2. Westrom L. Effect of acute pelvic inflammatory disease on fertility. Am J Obstet Gynecol **1975**; 121:707–13.
3. Kiviat NB, Wolner-Hanssen P, Eschenbach DA, et al. Endometrial histopathology in patients with culture-proved upper genital tract infection and laparoscopically diagnosed acute salpingitis. Am J Surg Pathol **1990**; 14:167–75.
4. Ness RB, Soper DE, Holley RL, et al. Effectiveness of inpatient and outpatient treatment strategies for women with pelvic inflammatory disease: results from the Pelvic Inflammatory Disease Evaluation and Clinical Health (PEACH) randomized trial. Am J Obstet Gynecol **2002**; 186:929–37.
5. Simms I, Stephenson JM, Mallinson H, et al. Risk factors associated with pelvic inflammatory disease: a UK study. Sex Transm Infect **2006**; 82:452–7.
6. Haggerty CL, Hillier SL, Bass DC, Ness RB. Bacterial vaginosis and anaerobic bacteria are associated with endometritis. Clin Infect Dis **2004**; 39:990–5.
7. Cohen CR, Manhart LE, Bukusi EA, et al. Association between *Mycoplasma genitalium* and acute endometritis. Lancet **2002**; 359:765–6.
8. Simms I, Eastick K, Mallinson H, et al. Associations between *Mycoplasma genitalium, Chlamydia trachomatis* and pelvic inflammatory disease. J Clin Pathol **2003**; 56:616–8.
9. Uno M, Deguchi T, Komeda H, Hayasaki M, Iida M, Nagatani M. *Mycoplasma genitalium* in cervices of Japanese women. Sex Transm Dis **1997**; 24:284–86.
10. Cohen CR, Mugo NR, Astete SG, et al. Detection of *Mycoplasma genitalium* in women with laparoscopically diagnosed acute salpingitis. Sex Transm Infect **2005**; 81:463–6.
11. Tosh AK, Van Der Pol B, Fortenberry JD, et al. *Mycoplasma genitalium* among adolescent women and their partners. J Adolesc Health **2007**; 40:412–7.
12. Williams J, VanDerPol B, Batteiger B, et al. *Mycoplasma genitalium* symptoms and concordance in sexual dyads [abstract O-034]. In: International Society for STD Research book of abstracts. **2007**.
13. Eckert L, Thwin S, Hillier S, Kiviat N, Eschenbach D. The antimicrobial treatment of sub-acute endometritis: a proof of concept study. Am J Obstet Gynecol **2004**; 190:305–13.
14. Wiesenfeld H, Hillier S, Krohn M, et al. Lower genital tract infection and endometritis: insight into subclinical pelvic inflammatory disease. Obstet Gynecol **2002**; 100:456–63.
15. Henry-Suchet J, Utzmann C, De Brux J, Ardoin P, Catalan F. Microbiologic study of chronic inflammation associated with tubal factor infertility: role of *Chlamydia trachomatis.* Fertil Steril **1987**; 47:274–7.
16. Moore DE, Spadoni LR, Foy HM, et al. Increased frequency of serum antibodies to *Chlamydia trachomatis* in infertility due to distal tubal disease. Lancet **1982**; 2:574–7.
17. Sellors JW, Mahony JB, Chernesky MA, Rath DJ. Tubal factor infertility: an association with prior chlamydial infection and asymptomatic salpingitis. Fertil Steril **1988**; 49:451–7.
18. Haggerty CL, Peipert JF, Weitzen S, et al. Predictors of chronic pelvic

pain in an urban population of women with symptoms and signs of pelvic inflammatory disease. Sex Transm Dis **2005**; 32:293–9.
19. Ness RB, Soper DE, Peipert J, et al. Design of the PID Evaluation and Clinical Health (PEACH) study. Control Clin Trials **1998**; 19:499–514.
20. Dutro S, Hebb J, Garin C, Hughes J, Kenny G, Totten P. Development and performance of a microwell-plate–based polymerase chain reaction assay for *Mycoplasma genitalium.* Sex Transmi Dis **2003**; 30:756–63.
21. Wroblewski J, Manhart L, Dickey K, Hudspeth M, Totten P. Comparison of transcription-mediated amplification and PCR assay results for various genital specimen types for detection of *Mycoplasma genitalium.* J Clin Microbiol **2006**; 44:3306–12.
22. Nugent R, Krohn M, Hillier S. Reliability of diagnosing bacterial vaginosis is improved by a standardized Gram stain interpretation. J Clin Microbiol **1991**; 29:297–301.
23. Amsel R, Totten PA, Spiegel CA, Chen KC, Eschenbach D, Holmes KK. Nonspecific vaginitis: diagnostic criteria and microbial and epidemiologic associations. Am J Med **1983**; 74:14–22.
24. Cohen C, Manhart L, Bukusi E, Astete S, Brunham R, Holmes K. Association between *Mycoplasma genitalium* and acute endometritis. Lancet **2002**; 359:765–66.
25. Falk L, Fredlund H, Jensen JS. Signs and symptoms of urethritis and cervicitis among women with or without *Mycoplasma genitalium* or *Chlamydia trachomatis* infection. Sex Transm Infect **2005**; 81:73–8.
26. Manhart LE, Critchlow CW, Holmes KK, et al. Mucopurulent cervicitis and *Mycoplasma genitalium.* J Infect Dis **2003**; 187:650–7.
27. Pepin J, Labbe AC, Khonde N, et al. *Mycoplasma genitalium:* an organism commonly associated with cervicitis among West African sex workers. Sex Transm Infect **2005**; 81:67–72.
28. Casin I, Vexiau-Robert D, De La Salmonière P, Eche A, Grandry B, Janier M. High prevalence of *Mycoplasma genitalium* in the lower genitourinary tract of women attending a sexually transmitted disease clinic in Paris, France. Sex Transm Dis **2002**; 29:353–9.
29. Manhart LE, Holmes KK, Hughes JP, Houston LS, Totten PA. *Mycoplasma genitalium* among young adults in the United States: an emerging sexually transmitted infection. Am J Public Health **2007**; 97: 1118–25.
30. Korte J, Baseman J, Cagle M, et al. Cervicitis and genitourinary symptoms in women culture positive for *Mycoplasma genitalium.* Am J Reprod Immunol **2006**; 55:265–75.
31. Stamm W. *Chlamydia trachomatis* infections of the adult. In: Holmes K, Sparling P, Mardh P-A, et al., eds. Sexually transmitted diseases. New York: McGraw Hill, **1999**:407–22.
32. Moller BR, Taylor-Robinson D, Furr PM, Freundt EA. Acute upper genital tract disease in female monkeys provoked experimentally by *Mycoplasma genitalium.* Br J Exp Pathol **1985**; 66:417–26.
33. Baczynska A, Funch P, Fedder J, Knudsen HJ, Birkelund S, Christiansen G. Morphology of human fallopian tubes after infection with *Mycoplasma genitalium* and *Mycoplasma hominis:* in vitro organ culture study. Hum Reprod **2007**; 22:968–79.
34. Svenstrup HF, Fedder J, Abraham-Peskir J, Birkelund S, Christiansen G. *Mycoplasma genitalium* attaches to human spermatozoa. Hum Reprod **2003**; 18:2103–9.
35. Haggerty CL, Totten PA, Astete SG, et al. Failure of cefoxitin and doxycycline to eradicate endometrial *Mycoplasma genitalium* and the consequence for clinical cure of pelvic inflammatory disease. Sex Transm Infect **2008**; 84:338–42.
36. Haggerty C, Ness R, Amortegui A, et al. Endometritis does not predict reproductive morbidity after pelvic inflammatory disease. Am J Obstet Gynecol **2003**; 188:141–8.
37. Clausen H, Fedder J, Drasbek M, Nielsen P, Toft B, Ingerslev H. Serological investigation of *Mycoplasma genitalium* in infertile women. Hum Reprod **2001**; 16:1866–74.
38. Svenstrup HF, Fedder J, Kristoffersen SE, Trolle B, Birkelund S, Christiansen G. *Mycoplasma genitalium, Chlamydia trachomatis,* and tubal factor infertility: a prospective study. Fertil Steril **2008**; 90:513–20.
39. Westrom L, Joesoef R, Reynolds G, Hagdu A, Thompson SE. Pelvic inflammatory disease and fertility: a cohort study of 1,844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results. Sex Transm Dis **1992**; 19:185–92.