Prevalence and Prediction of Chlamydial Cervical Infection in a Rural Area: An UPRNet Project*

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Background. Though many studies have described the prevalence of genital *Chlamydia trachomatis* infections in urban and suburban populations, no data on a rural general practice population have been published. Knowledge of the prevalence of infection is necessary to develop screening strategies.

Methods. The Upper Peninsula Research Network (UPRNet) is a rural primary care research group composed of five family practice offices. Cervical cultures for *C trachomatis* were taken on all women under the age of 36 years who presented to UPRNet physicians for a pelvic examination for any reason between August 15 and November 10, 1989. Demographic and clinical variables were analyzed for correlation with infection, and the best predictors of infection were identified by logistic regression. Previously published screening protocols were then tested on our data to develop the best predictive model for our rural population.

Results. *C trachomatis* was cultured from 25 (4.7%, 95% CI 2.9% to 6.5%) of 530 consecutive women. Infection was significantly more common among younger and single women, women with a new sex partner, and women with mucopurulent cervical discharge or increased cervical friability. No symptoms were predictive of an increased risk of infection. Based on the clinical presentation alone, the physicians correctly predicted only 28% of the infections. Using a modified Rosenthal protocol, we would have identified 80% of the infections while testing only 31% of the women. The protocols of Magder and Handsfield and their respective colleagues performed reasonably well, too. Other published screening protocols were less useful.

Conclusions. The prevalence of *C trachomatis* cervical infection in our rural primary care office population is relatively low. In rural primary care we recommend testing all high-risk women using a modification of Rosenthal's protocol instead of relying on symptoms or clinical suspicion.

Key words. Chlamydia trachomatis; rural population; clinical protocols. *J Fam Pract 1991; 33:369-374.*

There have been many attempts to characterize the distribution of *Chlamydia trachomatis* genital infections in women. Prevalence estimates range from 3.6% to 30%, depending on the population sampled.[1–20] Most of these studies were done with high-risk groups in adolescent and family planning clinics,[1–7] student health centers,[8–10] or Native American and Alaskan Eskimo clinics.[15,19,20] Four reports from family practice offices found prevalence rates ranging from 4% in asymptomatic women to 30% in women with dysuria, frequency of urination, or vaginal discharge.[11–14] These data come from urban and suburban family practice offices. No prevalence data from a rural family practice office population have been published.

Several different screening protocols based on the history and physical examination have been proposed. These protocols attempt to select the population most at risk of infection for whom laboratory testing would be indicated. Some studies emphasize the importance of symptoms to predict infection,[3,4] some find that symptoms are of limited use,[1,2,13,18] and others find no association between symptoms and infection.[3,9,15,16] These varied screening recommendations have not been tested in a rural population where prevalence of infection and risk factors for infection may differ from urban and suburban populations. Therefore, selective screening in a rural family practice office has no firm empirical basis.

The goals of this study were to determine the prev-

*UPRNet stands for the Upper Peninsula Research Network.

Submitted, revised, July 29, 1991.

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ISSN 0094-3509

alence of infection in patients visiting a group of rural family practice offices, to determine the factors that are related to a woman's risk of infection, to assess the ability of physicians to predict infection by clinical finding, and to test the effectiveness of different proposed screening protocols on our rural population data.

Methods

The five participating practices are located in four towns in the rural Upper Peninsula of Michigan. The towns' populations range from 700 to 15,000. The practices include 14 family practice physicians, 2 nurse practitioners, and 5 physician assistants. All but two of the family physicians provide routine obstetric care, and all are board certified. One of the offices is a teaching site for third-year medical students from Michigan State University, and that practice contributed 10% of the patients. One is a National Health Services Corps site that contributed 6% of the patients. The other offices are traditional, private, fee-for-service practices.

Between August 15 and November 10, 1989, all women 35 years of age or younger presenting for a pelvic examination for any reason were invited to participate in the study, which involved filling out a questionnaire and having a free cervical *C trachomatis* culture taken. The confidential questionnaire inquired about demographics, current symptoms, contraception, sexual partners, and history of sexually transmitted diseases. After completing the examination but before test results were available, the physicians completed a separate form on which they reported pertinent history and physical examination findings and estimated the likelihood that the patient had *C trachomatis* infection. The physicians described their view of that likelihood as "highly suspicious," "somewhat suspicious," "unlikely," or "definitely not."

Testing for *C trachomatis* was done by cell culture. The physicians were instructed to clean the cervix carefully with a large swab, then use a Dacron-tipped plastic endocervical swab for their own purposes, such as a Papanicolaou smear. Next, a second endocervical Dacron swab was used for culture. Samples were transported in Bartel's chlamydia transport media at 4°C. Within 24 hours of collection, two cultures per specimen were done on cyclohexamide-treated McCoy cells on coverslips in 1 dram vials. After culturing 72 hours at 37°C, one specimen was stained with Syva's fluorescein isothiocyanate conjugate (Syva Co, Palo Alto, Calif) and read under a fluorescence microscope. The second vial was blind-passed to another vial and incubated for another 72 hours before a final reading was performed as above. If gross contamination with yeast made the sample unreadable, the specimen was treated with anisomycin and recultured. Despite such treatment, one sample was toxic and unreadable. Laboratory personnel were blinded to all clinical data. Four technologists were involved. An effort was made to get different technologists to read the preliminary and the final passages and to determine the final readings without knowledge of preliminary culture results. During one of the study weeks, 27 of the cultures did not have a blind pass done because of a shortage of tubes.

Factors associated with infection were identified initially by chi-square testing. An alpha level of .05 was assigned for significance testing. Logistic regression analysis was used to confirm which factors identified by univariate analysis contributed independently to the risk of the culture being positive for *C trachomatis*. The probability of infection by age for women with zero, one, or two risk factors was calculated by logistic regression.

Finally, we tested the utility of seven different screening protocols proposed in the literature. We applied the protocols, with modifications as described in the Results section, to our data set. We used the following criteria to arrive at our judgment of the best screening protocol for a rural family practice office: (1) only data obtained easily during the history and physical examination should be included, (2) the protocol should include no more than four risk factors so a physician can easily remember it, and (3) the protocol should identify at least 80% of patients with infections while testing the lowest number of patients possible.

Results

Infection Rates and Risk Factors

During the study period, 593 eligible women presented for a pelvic examination at the five offices. Only 12 refused to give consent to participate. Thirty-eight women had pelvic examinations more than once, so only the first visit was counted. Eight women had had a hysterectomy and were excluded from analysis. In four cases, the provider forgot to take the culture. One culture was unreadable. This left 530 patients for analysis. All of the patients were white, other than a few Native Americans (less than 2%).

Twenty-five women had a positive culture, for an overall prevalence of 4.7% (95% CI 2.9% to 6.5%). The infection rates by age, marital status, source of payment, education, pregnancy status, and "new sex partner" are given in Table 1. Infection rates were significantly higher in single women and in those with a new sexual partner

Table 1. Culture Results of 530 Women Screened for Chlamydial Infection, by Demographic Characteristics

Characteristic	*n*	Positive Culture No. (%)	χ^2	*P* Value
Age (y)				
14–20	111	13 (11.7)	17.06	.0007
21–25	140	8 (5.7)		
26–30	156	3 (1.9)		
31–35	123	1 (0.8)		
Married or previously married	350	8 (2.3)	13.55	.0002
Single	180	17 (9.4)		
Insured	313	11 (3.5)	2.31	NS
Medicaid	149	10 (6.7)		
Uninsured	68	4 (5.8)		
Education				
High school or less	282	15 (5.3)	.44	NS
Some college or more	248	10 (4.0)		
Pregnant or postpartum	146	6 (4.1)	.15	NS
Nonpregnant	384	19 (4.9)		
New sex partner*	55	10 (18.2)	20.26	.0001
No new sex partner*	475	15 (3.2)		

**Within the past 2 months.*
NS denotes not significant.

in the past 2 months. The infection rate significantly decreased with age.

Two physical findings on pelvic examination, cervical mucopurulent exudate and friability (cervical bleeding when swabbed with a Dacron swab), were significantly correlated with risk of infection, but vaginal discharge and pain on examination were not (Table 2).

Infection rates did not differ significantly by reason for the woman's visit (pelvic complaint compared with routine examination), the presence or absence of pelvic symptoms, or the contraceptive method.

None of the 54 women with a history of sexually transmitted disease (STD) in the past had a culture positive for *C trachomatis*. Of the 14 women seen because of concern about exposure to a sexually transmitted disease, only one had a culture positive for *C trachomatis*. Having a history of an abnormal Papanicolaou smear was also not a predictor of infection, as these 93 women had an infection rate of 2.2%. None of the 75 women who had taken antibiotics in the preceding 4 weeks had a positive culture. The type of antibiotic that had been taken was not determined.

Table 2. Positive Culture Rates for *C trachomatis* in Women with Abnormal Physical Findings (N = 530)

Abnormal Finding	With Finding No. (%)	Culture Positive No. (%)	χ^2	*P* Value*
Cervical friability	55 (10.4)	8 (14.5)	11.09	.0009
Mucopurulent cervicitis	50 (9.4)	8 (16.0)	12.99	.0003
Vaginal discharge	89 (16.8)	7 (7.9)	2.10	NS
Painful examination	45 (8.5)	4 (8.9)	1.67	NS

**By χ^2 compared with those without the finding.*
NS denotes not significant.

Table 3. Probabilities of Chlamydial Infection in Women, by Age and Number of Risk Factors*

No. of Risk Factors	Age (y)				
	17	20	25	30	35
0	.05	.04	.01	.01	.004
1	.22	.16	.13	.04	.004
2	.54	.45	.29	.20	.12

**Calculated by logistic regression using age and the following risk factors: new sex partner in the past 2 months; mucopus on cervical examination; and abnormal bleeding on swabbing the cervix. (Only one patient had all three risk factors, so no analysis could be performed on a "three risk factor group.")*

Factors significantly associated with infection by univariate analysis (age, marital status, new sex partner, mucopurulent exudate on examination, and cervical friability on examination) were entered into the logistic regression model. All of the factors except age and marital status were found to be independent predictors of a positive culture for *C trachomatis* ($P < .05$). Since age was a better predictor than marital status, we dropped marital status from our predictive model. Therefore, our predictive model included the following risk factors: age, new sex partner, mucopurulent exudate on examination, and cervical friability on examination. The probability of infection by age and number of risk factors was calculated by logistic regression and ranged from .004 in a 35-year-old woman with no risk factors to .54 in a 17-year-old with two other risk factors (Table 3).

Physicians' Prediction of Infection

The physicians were "highly suspicious" of infection in nine cases and were correct in five (56%) of those. They were "somewhat suspicious" in 52 cases, and only two (4%) of these women had infection. Based on the physicians' presumptive diagnosis by history and physical examination, 31 women were treated empirically for *C trachomatis* at the initial encounter. Only five (16%) of the 31 cultures, however, were positive. Seventy-two percent of the infections were not predicted by the physicians, based on the presentation. The seven factors associated with physicians' prediction of infection are listed in Table 4. Of these, only marital status was actually significantly associated with infection.

Table 4. Factors Associated with Physicians' Prediction of Chlamydial Infection

Factors	No.	% Predicted Infected*	*P* Value†
Married	296	6.4	.0003
Single	234	17.9	
Insured	313	8.3	.0455
Medicaid	149	16.7	
Uninsured	68	14.7	
Routine visit‡	316	6.6	.0001
Nonroutine‡	144	27.8	
Examination			
Painful	45	60.0	.0001
Painless	485	7.0	
Genitourinary symptoms	197	23.0	.0001
No symptoms	333	4.5	
Pregnant	80	3.9	.0303
Nonpregnant	450	12.9	
STD exposure reported	53	24.5	.0079
No exposure reported	477	10.1	

**Combining "highly" and "somewhat" suspicious.*
†P values are by χ^2.
‡Total is less than 530 because not all patients answered this question.
STD denotes sexually transmitted disease.

Performance of Proposed Screening Protocols

The performance of seven screening protocols when applied to their own data and to our data set are summarized in Table 5.

Brunham[4] noted that cervical mucopurulent exudate identified 91% of the infections found in testing 40% of the women in a sexually transmitted disease clinic. Brunham relied, however, on routine Gram stains from the cervix to count polymorphonuclear leukocytes for 35% of his case identifications, and this violates our selection protocols of using only clinical data easily obtained by history or physical examination.

The protocol of Addiss et al[3] performed better than that of Brunham and colleagues on our data, but it relied partly on inflammatory changes on the Papanicolaou smear. Again, this violates our criterion of incorporating only data easily obtained by history or physical examination. Nevertheless, having a history of an abnormal Papanicolaou smear was not a predictor of infection in our patients.

Saxer[11] recommended testing women who have been exposed to a man with urethritis, and testing anyone with signs or symptoms of infection. These include abdominal or pelvic tenderness and cervical or vaginal discharge. In Saxer's protocols many women were tested because of the presence of symptoms; this was not an indicator of infection in our population.

Phillips et al[16] recommended selectively testing women who have had no education beyond high school, whose sexual partner has had other sexual contacts in the last 3 months, or whose cervix had bled when swabbed. If we had used the protocols of Phillips et al, substituting "who has had a new partner in the last 2 months" for the second criterion, we would have found 84% of the infections through testing 61% of the women. This system seems less effective in our patients, as the criterion of educational level used by Phillips et al was not a useful predictor among our patients.

Table 5. Performance of Proposed Screening Criteria for Chlamydial Cervical Infection

		Data from Published Report		Data from Current Study	
	Prevalence of Infection	% Tested	% of Infections Detected	% Tested	% of Infections Detected
Current study	4.7	—	—	—	—
Brunham et al[4]	22	40	91	9.3	32
Addiss et al[3]	11	36	72	36	64
Saxer[11]	12	49	79	47	64
Phillips et al[16]	2.8	55	88	61	84
Magder et al[5]*	17	68	98	61	92
Handsfield et al[1]*	9.3	65	90	34	76
Rosenthal et al[9]*	3–6	44	83	30	80

**These protocols were modified as described in the Results section when testing the data from the current study.*

Magder and colleagues[5] found that risk factors included: being younger than 26 years of age; being unmarried; having an abnormal cervix; having pelvic inflammatory disease; having used no antibiotics recently, and having had contact with gonorrhea. None of the women who used diaphragms were infected. Unlike us, Magder et al found that, by cell culture, 5% of the women who had recently used antibiotics were infected. As with our study, symptoms were not predictive of infection. Magder and co-workers suggested not culturing women who use diaphragms or who have a zero or one risk factor, culturing those who have two or three risk factors, and presumptively treating women who have four or more risk factors. Following their recommendations, we would have cultured 61% of the women we saw, treated 92% of the infections, and incorrectly treated 6.5% of the women.

Handsfield and co-workers[1] recommended testing women with at least two of the following five risk factors: aged 24 years or younger; having had a new sex partner within the last 2 months; having a purulent cervical exudate; cervical bleeding when swabbed; and the absence of a barrier contraceptive. If we had followed these recommendations by modifying only "absence of a barrier contraceptive" criterion to "single and absence of a barrier contraceptive," then we would have found 76% of the infections through testing only 34% of the women seen.

Rosenthal et al[9] identified three independent predictors of cervical infection with *C trachomatis* and/or gonorrhea, and weighted these to produce a risk-scoring system: age (two points if less than 20 years of age and one point if between age 20 and 29 years); a new sex partner or one suspected of having a genital infection (one point); and purulent vaginal discharge (one point). Using a "modified Rosenthal index," that is, the Rosenthal age index with our own other risk factors (new sex partner in the past 2 months, cervical mucopurulent exudate, and cervical friability), we obtained the results in Table 6. If all of our patients with two or more risk points had been tested, 164 of 530 (31%) would have been tested, and 80% of those with positive test results would have been identified.

Table 6. Screening Results on Study Population Using a Modified Rosenthal Index*

	No. Tested	No. Positive	Percent Positive
Risk points			
0	110	1	0.9
1	256	4	1.6
2	116	7	6
3–4	48	13	27
Total	530	25	4.7

NOTE: If women with 2, 3, or 4 risk points had been tested, 164 of 530 (31%) would have been tested, and 80% of positives would have been discovered.
**Risk points: 2 points for age under 20 years, 1 point each for age 20 to 29 years, new sex partner in the past 2 months, mucopurulent cervical exudate, and cervical friability.*

Discussion

C trachomatis pelvic infection is about as common in our northern, rural, white, private-practice population as it is in a suburban population. Infection is more likely in women who are single, young, have new partners, or have mucopurulent exudate or increased cervical friability on examination. We found no association between infection and symptoms, payment source, education level, a history of abnormal Papanicolaou smears, or a history of venereal disease. Our sample size was too small to detect small effects in some of these variables, but such a missed effect would probably have been clinically insignificant. Because our population was almost entirely white, our results may not apply to other rural populations that are predominately black, Hispanic, or Native American. Infection rates among Native Americans and Alaskan Eskimos have been found to be very high, ranging from 23% to 30%.[15,19,20]

That *C trachomatis* is often an asymptomatic infection in women accounts for its ability to be transmitted widely while remaining undetected and untreated. As others have noted, we found that patients' symptoms, while strongly influencing our preliminary diagnosis of infection, were not an accurate predictor of infection. We found that a "clinical suspicion" approach to screening was very inadequate, as all of the published screening protocols would have been more successful at identifying patients who had infections than we were by using our clinical intuition. We recommend that testing be done on all women at risk based on one of the screening systems. The protocols of Magder, Handsfield, and Rosenthal and their respective co-workers all performed reasonably well on our patient population. Because of its simplicity, we recommend the Rosenthal index or our "modified Rosenthal index" to identify women for whom a culture is indicated. Testing the modified Rosenthal index on another rural population would be helpful to validate this protocol.

In addition to those we have discussed, other *C trachomatis* screening protocols have been published.[8,13,17] Buhaug et al[17] studied cost-effectiveness of screening but did not do a risk-factor analysis. Bro and Juul[13] analyzed risk factors, but did not recommend a

specific protocol. Johnson et al[8] developed an elegant model but relied partly on two microscopic examinations, and we believe this is unlikely to be adopted by busy, rural family physicians.

Regarding the cost-effectiveness of *C trachomatis* screening, Phillips and colleagues[21] recommended a prevalence threshold of 7% for routine screening by direct fluorescent assay or enzyme immunoassay, and a prevalence threshold of 14% for cell culture. Using the modified Rosenthal index, the testing prevalence of our sample is the rate of positive cultures in women with two or more risk points. From Table 6, 20 positive cultures in the 164 women with two or more risk points gives a test prevalence of 12%, well above the Phillips cost-effective screening threshold for enzyme immunoassay, and close to the threshold for screening by culture. (Cultures are more expensive than enzyme immunoassay; hence, the higher threshold.)

Because cell culture is the reference standard, we chose to use it for this research study. *C trachomatis* cultures are not 100% sensitive, however, so we have probably underestimated the prevalence slightly.[22] In rural practice without a sophisticated microbiology laboratory nearby, one might be inclined to use one of the newer office enzyme immunoassay test kits for identifying *C trachomatis* infection. A recent analysis of the Abbott TestPack Chlamydia kit (Abbott Laboratories, North Chicago, Ill) and of the Kodak Surecell Chlamydia kit (Eastman Kodak Co, Rochester, NY) suggests that these methods may not be sensitive enough in population prevalences of 5% or less.[6] By screening selectively using our modified Rosenthal index, one would expect a testing prevalence in rural family practice offices of about 12%, making these test kits a reasonable choice.

Acknowledgments

We gratefully acknowledge the American Academy of Family Physicians for financial support of this project; Steven Dosh, MD, Raymond Hockstad, MD, Raymond Koivunen, MD, Elizabeth Wilson, DO, and their partners and office staffs in the Upper Peninsula Research Network (UPRNet) for their participation in data gathering; at Saint Francis Hospital, Susan Koski, James Dehlin, Jr, and Jeanne M. Korpi for their generous help processing the cultures; Dr Blake Smith for his assistance with statistical analysis; Dr John Dyke for his technical advice, and the Syva Company for supplying reagents.

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