

CHLAMYDIA TRACHOMATIS INFECTIONS IN FEMALE MILITARY RECRUITS

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ABSTRACT

Background Asymptomatic genital *Chlamydia trachomatis* infections in women can lead to pelvic inflammatory disease, infertility, and ectopic pregnancy. To design a chlamydia-control program, we conducted a large survey of women in the U.S. military.

Methods From January 1996 through December 1997, urine samples from 13,204 new female U.S. Army recruits from 50 states were screened by ligase chain reaction for *C. trachomatis* infection. Information on potential risk factors was obtained by questionnaire. With multivariate analysis, we identified criteria for a screening program.

Results The overall prevalence of chlamydial infection was 9.2 percent, with a peak of 12.2 percent among the 17-year-old recruits. The prevalence was 15 percent or more among the recruits from five southern states. The following risk factors were independently associated with chlamydial infection: having ever had vaginal sex (odds ratio for infection, 5.9), being 25 years of age or less (odds ratio, 3.0), being black (odds ratio, 3.4), having had more than one sex partner in the previous 90 days (odds ratio, 1.4), having had a new partner in the previous 90 days (odds ratio, 1.3), having had a partner in the previous 90 days who did not always use condoms (odds ratio, 1.4), and having ever had a sexually transmitted disease (odds ratio, 1.2). A screening program for subjects 25 years of age or less (87.9 percent of our sample) would have identified 95.3 percent of the infected women.

Conclusions Among female military recruits, the prevalence of chlamydial infection is high. A control program that screens female recruits who are 25 years old or younger with urine DNA-amplification assays has the potential to reduce infection, transmission, and the sequelae of chlamydial infection. (N Engl J Med 1998;339:739-44.)

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MORE than 4 million urogenital *Chlamydia trachomatis* infections occur in the United States annually.^{1,2} They occur in young, sexually active persons from all socioeconomic groups, with prevalence ranging from 5 percent to 20 percent.^{3,4} Women, especially, bear the burden of disease, with consequences of genital infections ranging from pelvic inflammatory disease to ectopic pregnancy and infertility.^{1,5} These sequelae are associated with a large economic burden.^{6,7} Because up to 80 percent of infected women are asymptomatic and therefore do not seek

medical care, screening of young, sexually active women has been recommended.^{1,8} In the past, screening for *C. trachomatis* infections in women has been limited by the need for access to a medical clinic and a pelvic examination. However, *C. trachomatis* infections can now be detected with high sensitivity (85 to 95 percent) and specificity with DNA-amplification assays performed on urine specimens,⁹⁻¹⁴ allowing cost-effective screening of large numbers of women in nonclinic settings.¹⁵

Few studies of the prevalence of chlamydial infection in U.S. military populations have been published, and there have been no studies using DNA-amplification techniques among women not seeking health care.¹⁶⁻²⁰ Because adolescents have the highest prevalence of disease and most military recruits are young, we conducted a large prevalence study and risk-factor analysis of female recruits from throughout the United States who began basic training at Fort Jackson, South Carolina. We performed this study to determine the extent of infection, assess the feasibility of screening urine specimens for *C. trachomatis* by the ligase chain reaction, and assess which epidemiologic correlates would be useful for implementing an effective chlamydia-control program for female recruits.

METHODS

Population and Specimens

All female Army recruits who were present on Sundays between January 1996 and December 1997 at the Physical Examination Section, Reception Battalion, Fort Jackson, South Carolina, were invited to participate in this study. The study was approved by the institutional review boards of Johns Hopkins University and Fort Jackson (Eisenhower Army Medical Center, Fort Gordon, Ga.), as well as the Human Subjects Research Review Board of the U.S. Army Surgeon General. Of the 16,593 recruits approached, 13,223 (79.7 percent) volunteered to participate in the study and were given a briefing about the study as well as an educational briefing about chlamydial infections by the civilian research nurse.

All subjects signed an informed-consent form and completed a questionnaire regarding demographic information, home state,

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and sexual history. The data instrument was a two-sided scannable form (Scantron, Tustin, Calif.). To determine the similarity of the study subjects and those who chose not to participate in the study with regard to demographic characteristics and sexual history, 823 of the 3370 women who did not volunteer were invited to fill out an anonymous questionnaire. Nonvolunteers were asked to fill out a questionnaire only during the first week of each month.

Each volunteer was instructed to collect 20 to 30 ml of first-catch urine (the first part of the urine stream). A unique study number was assigned to each volunteer. All urine specimens, consent forms, and questionnaires were shipped to the Johns Hopkins University chlamydia laboratory. Urine specimens were kept at 4°C until processed, within 48 hours.

Laboratory Procedures and Treatment

Urine specimens were processed and tested by the ligase chain reaction (Abbott Laboratories, Abbott Park, Ill.) for chlamydial DNA according to the manufacturer's directions. Each week a list of infected subjects was sent to the research nurse. The infected subjects were contacted and treated at the Troop Medical Clinic at Fort Jackson by directly observed therapy with a single 1-g dose of azithromycin. The subjects were also tested for coexisting sexually transmitted diseases. The sensitivity and specificity of the ligase chain reaction in urine specimens as compared with cervical culture for chlamydia had been previously determined to be 88.6 percent and 99.7 percent, respectively, in another military population.¹⁴

Statistical Analysis

Questionnaire forms were scanned into a data base (dBASE III Plus, Borland International, Spring Valley, Calif.). The results of the ligase chain reaction, demographic information, and risk-factor information were analyzed as dichotomous variables with the chi-square test. Univariate and multivariate logistic-regression analysis for factors associated with chlamydial infection was performed with Intercooled Stata software (version 4.0, Stata, College Station, Tex.). All independent variables were entered into the model, and a two-sided P value of less than 0.05 was considered to indicate statistical significance. The 95 percent confidence interval for the prevalence value for recruits from each state was calculated with Stata software. A one-way analysis of variance was performed to assess the degree of significance of differences in prevalence between states.

RESULTS

Characteristics of the Subjects

Of 13,223 subjects presenting at the Physical Examination Section on Sundays from January 1996 through December 1997, 19 could not be evaluated because of missing data or insufficient urine. The median age of the 13,204 who could be evaluated was 21 years (range, 17 to 39); 87.9 percent (11,603) were 25 years old or younger (Table 1). Fifty-one percent of the women were white, 35.9 percent were black, and 13.1 percent were of other races. For the entire population, the prevalence of *C. trachomatis* infection according to the urine ligase chain reaction was 9.2 percent.

On the questionnaire, 93.1 percent of the subjects reported having ever had vaginal sex, 26.7 percent having had more than one sex partner in the previous 90 days, and 31.4 percent having had a new sex partner in the previous 90 days. Only 16.9 percent reported that their partners always used condoms. A history of chlamydial infection was reported by 9.1

TABLE 1. CHARACTERISTICS OF 13,204 FEMALE ARMY RECRUITS SCREENED FOR *CHLAMYDIA TRACHOMATIS*.

CHARACTERISTIC	VALUE
Age — yr	
Median	21
Range	17–39
Race — no. (%)*	
White	6,715 (51.0)
Black	4,733 (35.9)
Other	1,726 (13.1)
Ever had vaginal sex — no. (%)†	12,281 (93.1)
Sexual history in previous 90 days — no. (%)	
More than one partner‡	3,478 (26.7)
New partner§	4,076 (31.4)
Partner always used condoms¶	2,115 (16.9)
Previous diagnosis of sexually transmitted disease — no. (%)	
<i>Chlamydia trachomatis</i>	1,206 (9.1)
<i>Neisseria gonorrhoeae</i>	430 (3.3)
Syphilis	74 (0.6)
Trichomonas	611 (4.6)
None	11,372 (86.1)
Chlamydia-positive — no. (%)	1,219 (9.2)

*Data were missing for 30 subjects.

†Data were missing for 9 subjects.

‡For 168 subjects, data were missing or subject did not know answer.

§For 225 subjects, data were missing or subject did not know answer.

¶For 684 subjects, data were missing or subject did not know answer.

percent of the subjects, gonorrhea by 3.3 percent, syphilis by 0.6 percent, and trichomonas infection by 4.6 percent. Of the volunteers who reported having had no vaginal sex, 1.4 percent (13 of 914) were chlamydia-positive, and of those who reported that their partners always used condoms, 8.4 percent (177 of 2115) were chlamydia-positive.

Of the 823 nonvolunteer recruits who filled out a questionnaire anonymously, 203 (24.7 percent) did not provide their ages and were dropped from the analysis. The mean age of the remaining nonvolunteer recruits was 21 years (range, 17 to 36); 51.3 percent were white, and 31.9 percent were black. The mean age and the racial distribution of these recruits were not significantly different from those of the volunteers. Only 66.9 percent reported having had vaginal sex, as compared with 93.1 percent of the volunteers ($P < 0.001$). This group differed significantly from the volunteers in four variables, even after adjustment for whether the women reported having had vaginal sex: only 4.0 percent reported prior chlamydial infections ($P = 0.013$), 18.2 percent had had a new sex partner in the previous 90 days ($P = 0.002$), 20.1 percent had partners who consistently used condoms ($P < 0.001$), and 90.7 percent reported no previous diagnosis of a sexually transmitted disease ($P = 0.001$). Of the nonvolunteers, 17.7 percent had had more than one sex partner in the previous 90 days; the proportion of the volunteers who had had more than

one sex partner in the previous 90 days was similar after adjustment for vaginal sex (P=0.189).

Prevalence of Infection

The age-specific prevalence of *C. trachomatis* infection among the 13,204 volunteers is shown in Figure 1. The highest prevalence of chlamydial infection (12.2 percent) was among 17-year-olds. The prevalence declined sharply with increasing age, to below 5 percent for women over 25 years of age. For further analysis, the youngest age groups (17 to 25 years) were combined into a category called "young." The prevalence in this group was 10.0 percent (1162 of 11,603). In the older-age category (26 to 39 years), the prevalence was 3.6 percent (57 of 1601). The prevalence was 5.5 percent (369 of 6715) for whites, 14.9 percent (707 of 4733) for blacks, and 8.1 percent (143 of 1756) for other races.

Univariate Analysis

Univariate analysis identified 10 variables significantly associated with chlamydial infection: young age (17 to 25 years), black race, race other than white or black, ever having had vaginal sex, having had more than one sex partner in the previous 90 days, having had a new sex partner in the previous 90 days, having had a partner who did not always use condoms in the previous 90 days, a prior diagnosis of gonorrhea, a prior diagnosis of trichomonas, and a history of any sexually transmitted disease (Table 2). A prior diagnosis of chlamydia or syphilis was not significantly associated with being positive for chlamydial infection.

Multivariate Analysis

In the complete multivariate model, having had vaginal sex, an age of 25 years or less, black race, hav-

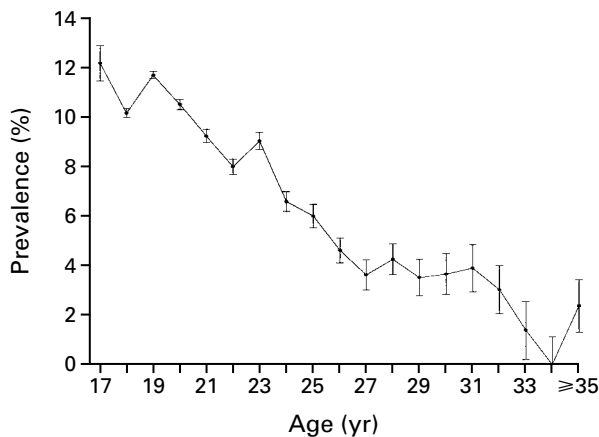


Figure 1. Mean (±SE) Age-Specific Prevalence of Chlamydial Infection among 13,204 Female Army Recruits, According to Ligase-Chain-Reaction Assays of Urine Specimens.

ing had more than one sex partner in the previous 90 days, having had a new sex partner in the previous 90 days, having had a partner who did not always use condoms in the previous 90 days, and a history of any sexually transmitted disease were independent predictors of chlamydial infection (Table 3).

Strategies for Selective Screening

A screening strategy involving all variables identified as independent predictors would require that 100 percent of the population be tested and would detect 100 percent of the positive subjects. In this model, the magnitude of risk associated with having had a new sex partner might vary according to race. For the purpose of a screening program, this would not alter the proportion of the population tested or the percentage of positive subjects detected with this model. Because screening on the basis of race would probably be viewed as inequitable, a strategy excluding race was examined. According to this strategy,

TABLE 2. UNIVARIATE ANALYSIS OF FACTORS ASSOCIATED WITH CHLAMYDIAL INFECTION IN FEMALE ARMY RECRUITS.*

RISK FACTOR	NO. OF RECRUITS	PREVALENCE OF INFECTION		
		RISK FACTOR PRESENT	RISK FACTOR ABSENT	ODDS RATIO (95% CI)
Age ≤25 yr	11,603	10.0	3.6	3.0 (2.3–4.0)
Black race†	4,733	14.9	5.5	3.0 (2.7–3.5)
Other (nonwhite, nonblack) race‡	1,726	8.1	5.5	1.5 (1.2–1.9)
Having ever had vaginal sex	12,281	9.8	1.4	7.5 (4.4–13.1)
Having had >1 sex partner in previous 90 days‡	3,478	13.5	7.7	1.9 (1.7–2.1)
Having had a new sex partner in previous 90 days§	4,076	12.4	7.8	1.7 (1.5–1.9)
Having had a partner who did not always use condoms in previous 90 days¶	10,405	9.8	NA	1.2 (1.0–1.4)
Condom use unknown¶	418	5.0	NA	0.6 (0.4–0.9)
Data on condom use missing¶	266	1.5	NA	0.2 (0.1–0.5)
Previous diagnosis of <i>Neisseria gonorrhoeae</i>	430	12.3	9.1	1.4 (1.0–1.9)
Previous diagnosis of trichomonas	611	11.6	9.1	1.3 (1.0–1.7)
History of any sexually transmitted disease	1,828	10.5	9.0	1.2 (1.0–1.4)

*CI denotes confidence interval, and NA not available.

†The reference group consisted of the white subjects.

‡The variable is dichotomized: the reference group consisted of the subjects who did not have >1 sex partner, who answered that they did not know, or for whom data were missing.

§The variable is dichotomized: the reference group consisted of the subjects who did not have a new sex partner, who answered that they did not know, or for whom data were missing.

¶The variable is dichotomized: the reference group consisted of the subjects who had a partner who always used condoms.

TABLE 3. MULTIVARIATE ANALYSIS OF FACTORS INDEPENDENTLY ASSOCIATED WITH CHLAMYDIAL INFECTION IN FEMALE ARMY RECRUITS.

RISK FACTOR	Odds RATIO (95% CI)*
Age ≤25 yr	3.0 (2.3–4.0)
Black race†	3.4 (2.9–3.8)
Other (nonwhite, nonblack) race‡	1.7 (1.4–2.1)
Having ever had vaginal sex	5.9 (3.2–10.6)
Having had >1 sex partner in previous 90 days‡	1.4 (1.2–1.7)
Having had a new sex partner in previous 90 days§	1.3 (1.1–1.6)
Having had a partner who did not always use condoms in previous 90 days¶	1.4 (1.1–1.6)
Having ever had a sexually transmitted disease	1.2 (1.0–1.4)

*CI denotes confidence interval.

†The reference group consisted of the white subjects.

‡The reference group consisted of the subjects who did not have >1 sex partner, who answered that they did not know, or for whom data were missing.

§The reference group consisted of the subjects who did not have a new sex partner, who answered that they did not know, or for whom data were missing.

¶The reference group consisted of the subjects who had a partner who always used condoms.

recruits would be tested if they were 25 years of age or less or if they reported on a questionnaire having had more than one sex partner or a new sex partner in the previous 90 days, having had a partner who did not use condoms in the previous 90 days, or having a history of sexually transmitted disease. Screening according to these criteria would still require testing 100 percent of the population. If a questionnaire could be avoided and young age (25 years or less) alone was the screening criterion, 87.9 percent (11,603 of 13,204) of the population would need to be tested and 95.3 percent (1162 of 1219) of the positive subjects would be identified.

Geographic Variation in Prevalence

There was considerable variation in the prevalence of chlamydial infection according to the state of origin of the recruits ($F < 0.001$ by one-way analysis of variance). The prevalence was more than 15 percent for recruits from South Carolina, Georgia, Alabama, Louisiana, and Mississippi. For New Jersey, North Carolina, Kentucky, Texas, Oklahoma, and Arkansas, the prevalence was 10 to 15 percent, and for 17 other states and Puerto Rico, it was 5 to 10 percent. For five states (Washington, Oregon, Minnesota, Arizona, and Massachusetts), the prevalence was less than 5 percent. Fewer than 100 recruits were tested from each of 17 states, 3 territories, and the District of Columbia, and prevalence figures from these areas were therefore not included in the analysis. The prevalence for the five states with the highest prevalence and the five states with the lowest prevalence differed significantly, since the 95 percent confidence intervals for prevalence did not overlap.

DISCUSSION

Although the diagnosis and treatment of sexually transmitted diseases has always presented a challenge, there has been no routine screening of recruits for chlamydial infections at entry into the U.S. Army.²¹ Because most chlamydial infections are asymptomatic in women and because the sequelae of disease present a severe and costly burden, screening women at entry into the Army is an appropriate way to identify infections early and to explore opportunities for a control program.^{1,6,7,22}

Civilian chlamydia-control programs have sought to identify criteria for selective screening.^{23–27} Most of these control programs have used diagnostic assays that require pelvic examinations and cervical specimens.²⁵ However, it has recently been shown that testing urine specimens by DNA-amplification techniques is cost effective for screening large numbers of persons in different settings.^{15,28} We used this new technique to determine the prevalence of chlamydia and to identify screening criteria for a program to control chlamydia in the military.^{10,12,14} Collection of urine specimens in this study was highly acceptable and easily implemented.

Using the ligase chain reaction with urine samples, we found a high prevalence of *C. trachomatis* infection (9.2 percent). This prevalence was higher than that observed in family-planning clinics²⁸ but not as high as that reported in some adolescent health clinics.^{29,30} Our data agree with those from previous studies of chlamydial infections in Army women, in which prevalence rates ranged from 8.2 percent to 9.8 percent.^{17,18} In one large, community-based screening study, the overall prevalence of chlamydia in young women was 8.6 percent, as detected by the urine ligase chain reaction, a prevalence similar to that found in our study.³¹ Because our population was not clinic-based and was not made up of women seeking health care, the finding of such a high prevalence in these women warrants the institution of a control program for the routine identification and treatment of chlamydial infections in order to prevent sequelae and transmission to sex partners.⁸

The study population consisted of a young, sexually active group of female recruits with sexual risk factors known to be associated with chlamydial infection.²⁵ Although 9.1 percent of the subjects reported having had chlamydial infection in the past, this factor was not associated with the risk of current infection. The highest prevalence was observed among 17-year-olds. This prevalence is similar to comparable age-specific rates in other studies, confirming that young age is associated with chlamydial infection.^{28,31} In our study, young age was associated with being chlamydia-positive in both univariate and multivariate analyses (odds ratio, 3.0). In order to include more positive subjects, we used an age cutoff of 25 years, which allowed the detection of 95.3 per-

cent of the chlamydial infections. Other studies have supported age-based screening for chlamydia.^{27,31,32}

Thus, for this group of female recruits coming from a civilian background, who were tested within three days of starting basic training, young age alone can be recommended as a single indicator of who should be tested for chlamydial infection. Other models considered in this study offered high sensitivity, but the models were more complex and required valid sexual-risk histories. We documented 13 chlamydial infections (prevalence, 1.4 percent) among 914 recruits who denied being sexually active, as well as chlamydial infections in 8.4 percent of those who reported that their partners consistently used condoms. These figures indicate that self-reported sexual-risk histories are not always valid.³³ The lower prevalence of chlamydial infection among recruits for whom the data on condom use were missing, or who indicated on their questionnaires that they did not know whether their partners always used condoms, may be due to lack of sexual activity, because 58.6 percent of the 684 recruits in these categories reported that they had never had vaginal sex. There is a fixed laboratory budget available for population screening in the Army. Young age is the simplest, least expensive, and most easily documented risk factor on which to base a recommendation for a screening program, as well as being highly sensitive. Alternatively, since the use of age as a selective screening criterion would have missed 4.7 percent of the infections, universal screening might be more cost effective from a societal perspective, and future studies of cost effectiveness are warranted.²⁸

This was one of the largest programs for screening young, sexually active subjects that was not clinic-based and whose results were derived from urine DNA-amplification assays. The geographic variation in prevalence was striking. From more than 15 percent in the five states with the highest prevalence to less than 5 percent in the five states with the lowest, these differences may reflect the levels of disease burden in certain states. These regional variations also appear to reflect regional differences in chlamydial disease, as reported by the Centers for Disease Control and Prevention.^{34,35} For example, the prevalence in North Carolina reportedly varied from 10 percent to 17 percent.³⁵ The prevalence is lower in regions such as Wisconsin and Washington State, where clinic-based chlamydia-control programs are in place and where declining rates of prevalence of chlamydia have been reported.^{26,27,32,36} In our study, the prevalence was 11.3 percent for North Carolina and 3.8 percent for Washington State. Our data imply that chlamydial infection remains common in young women across the United States. With a volunteer rate of 80 percent among women who were approached and representation from 50 states and 4 territories, our study had a wide geographic sampling.

One limitation of our study is that it is not known whether the prevalence of risk factors for chlamydial infection differs between young women who decide to join the military and those who do not. However, the demographic and sexual risk-factor characteristics of our subjects appear to be similar to those of other regional and clinic-based populations,²⁵ as well as those from a large, community-based study.³¹ An additional limitation is that the nonvolunteers in our study differed from the volunteers with regard to sexual risk factors for chlamydia. However, the nonvolunteers represented a group who were mostly sexually active, who had had new sex partners in the previous 90 days, and whose partners did not use condoms. Thus, their risk of chlamydial infection may have been as high as that of the subjects in our study.

Although amplified-DNA tests are more expensive than traditional nonculture tests, the savings associated with not having to have a clinician collect specimens from a pelvic examination and the advantages of being able to use urine as a diagnostic specimen may outweigh the extra cost of the test.¹⁵ In addition, it has been demonstrated that amplified-DNA testing of urine specimens is cost effective, and treating chlamydial infections prevents serious complications such as pelvic inflammatory disease, ectopic pregnancy, and infertility.^{15,28,37}

In conclusion, our study indicates that with the limited funding available at present, young age (25 years or less) would be the best criterion on which to base a screening program using amplified-DNA testing of urine for female Army recruits and perhaps for other young women. Institution of such a control program has the potential to reduce drastically the burden of chlamydial disease in the U.S. Army and to prevent morbidity due to these infections.³⁷

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