

Untreated Gonococcal and Chlamydial Infection in a Probability Sample of Adults

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UNTREATED INFECTION WITH *Neisseria gonorrhoeae* or *Chlamydia trachomatis* can result in chronic pelvic pain, infertility, and potentially fatal ectopic pregnancies among women. In addition, these bacterial sexually transmitted diseases (STDs) serve as biological cofactors that facilitate transmission of human immunodeficiency virus (HIV). Untreated chlamydial infections, for example, are estimated to increase the likelihood of HIV transmission by a factor of 1.4 to 3.3.¹⁻³

Unfortunately, the prevalence and distribution of these STDs within the population are poorly understood. Until recently, our knowledge was limited by its exclusive dependence on 2 data sources with well-recognized inadequacies—the counting of infections reported to public health departments and studies of convenience samples of special populations, such as clinic patients. While these sources can provide useful information, they are inherently incapable of characterizing untreated STD infection in the population at large. This prob-

Context The prevalence and distribution of gonococcal and chlamydial infections in the general population are poorly understood. Development of nucleic acid amplification tests, such as the ligase chain reaction assay, provides new opportunities to estimate the prevalence of untreated infections in the population.

Objective To estimate the overall prevalence of untreated gonococcal and chlamydial infections and to describe patterns of infection within specific demographic subgroups of the young adult population in Baltimore, Md.

Design and Setting Cross-sectional behavioral survey based on a probability sample of Baltimore households with collection of urine specimens between January 1997 and September 1998.

Participants A total of 728 adults aged 18 to 35 years completed the interview portion of the study, and 579 of these respondents also provided a urine specimen adequate for testing.

Main Outcome Measure Prevalence of untreated infection, as measured by the percentage of specimens testing positive for gonococcal and chlamydial infection by ligase chain reaction, weighted to reflect variations in probabilities of sample selection from the population. Alternate estimates of the prevalence of recent treated infection were derived from clinically diagnosed cases reported to the Baltimore City Health Department and by diagnoses reported by participants in the survey.

Results An estimated 5.3% (SE, 1.4%) of the population aged 18 to 35 years has an untreated gonococcal infection, and 3.0% (SE, 0.8%) is estimated to have an untreated chlamydial infection. While 7.9% (SE, 1.6%) of the population is estimated to have either an untreated gonococcal or chlamydial infection, estimated prevalence is substantially higher among black women (15.0%; SE, 3.7%). Few participants with untreated infections reported dysuria or discharge during the 6 months preceding testing. The estimated number of untreated gonococcal infections in the population (9241; SE, 2441) substantially exceeds both the number of such infections diagnosed among Baltimore adults aged 18 to 35 years and reported to the Baltimore City Health Department during 1998 (4566), and the estimated number of diagnoses derived using participants' reports for the 12 months prior to the survey (4708 [SE, 1918] to 5231 [SE, 2092]). The estimated number of untreated chlamydial infections (5231; SE, 1395) is also greater than the number of cases reported to the health department in 1998 (3664) but is slightly less than the estimated number of diagnoses derived using participants' reports of chlamydial infections diagnosed during the 12 months prior to the survey (5580 [SE, 1918] to 6975 [SE, 2441]).

Conclusion In 1997-1998, the estimated number of undiagnosed gonococcal and chlamydial infections prevalent in the population of Baltimore adults aged 18 to 35 years approached or exceeded the number of infections that were diagnosed and treated annually.

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lem is particularly severe for infections whose symptoms are mild or nonexistent. Available evidence suggests that a substantial fraction of gonococcal and

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chlamydial infections are asymptomatic.⁴⁻⁸ The Institute of Medicine has noted,⁸ such STDs spawn “. . . hidden epidemics of tremendous health and economic consequence in the United States . . . [T]he scope, impact, and consequences of [these] STDs are underrecognized by the public and health care professionals.”

The recent development of nucleic acid amplification tests (NAATs) for the diagnosis of gonococcal and chlamydial infections using urine specimens has generated new models for research on the epidemiology of these STDs.⁹⁻¹¹ Since the urine specimens required for NAAT can be obtained in population surveys, generalizations about the prevalence and patterns of infection now can be derived from surveys of probability samples of the general population rather than samples of clinic patients or other special populations. This research model provides estimates (with known margins of sampling error) for the prevalence of untreated infections both in the population at large and in identifiable subpopulations.

To provide a more accurate understanding of the hidden epidemics of untreated infection with *N gonorrhoeae* and *C trachomatis*, using probability sampling methods, we recruited a population sample of young adults aged 18 to 45 years to participate in a survey of sexual and other sensitive behaviors and STD history. We then used NAATs of urine specimens obtained from survey respondents aged 18 to 35 years to detect the presence of untreated gonococcal and chlamydial infections. The resultant data allowed us to estimate the prevalence and patterns of untreated infection in our target population, adults aged 18 to 35 years in Baltimore, Md.

METHODS

Sample Design

The sample for the Baltimore STD and Behavior Survey was drawn from households residing within the municipal boundaries of the city of Baltimore (1998 population: 645 664).¹² Households were selected using a stratified probability sam-

pling design that selected residences from the Baltimore Real Estate Property Registry. This registry includes all properties—both taxable and tax-exempt—within the city of Baltimore. Two sample strata were disproportionately sampled to ensure adequate representation of (1) young black men and (2) young adults living in predominantly white US Census tracts with elevated levels of STDs (based on Baltimore City Health Department [BCHD] STD surveillance statistics). Operationally, these 2 strata comprised (1) households with an age-eligible man drawn from census tracts with 95% to 100% black residents according to the 1990 US Census; and (2) adults aged 18 to 35 years residing in 13 census tracts that had the highest rates of reported gonococcal infection among tracts with 0% to 9% black residents. A third crosscutting sample stratum was created to accommodate the refueling of a 50% random subsample of cases for which our quality control procedures could not verify the integrity of the interview data (see below).

This sample design oversampled segments of the population that are known to have higher rates of STDs (ie, young black men and whites living in US Census tracts with high rates of reported STDs). Oversampling is routinely used in household surveys to ensure adequate sample sizes for difficult-to-survey or numerically rare segments of the population. Probability sampling requires that every member of the population have a nonzero probability of selection. Complex probability samples use stratification and sampling at different rates in the design stage and sample weighting (by the inverse of the sampling probabilities) at the analysis stage to yield samples representative of the targeted population. Our prevalence estimation uses sampling weights to adjust for the unequal probabilities of selection across sample strata.

Informed Consent

A 2-stage procedure was used to obtain informed consent. Informed consent (both oral and written) was first obtained from all survey participants

(aged 18-45 years) prior to the survey interview. A separate consent (both oral and written) was obtained from respondents (aged 18-35 years) participating in the urine testing. The informed consent process made explicit that the urine would not be used for drug testing and that, in compliance with state laws, specimens found positive for gonococcal and/or chlamydial infection would be reported to the BCHD. The protocol for this study was approved by institutional review boards at the Research Triangle Institute and Johns Hopkins Medical Institutions.

Interview

Respondents completed a detailed survey on sexual behavior, prior STD history, STD symptoms, drug and alcohol use, social attitudes and behaviors, and individual background characteristics. Interview data were collected by 36 trained interviewers in the respondent's home. Interviewers were instructed to conduct the interviews in a private place in the home or at an alternate location where privacy could be ensured. They were specifically instructed that they could not conduct an interview if another person was listening. To satisfy another objective of the research program, respondents were randomly assigned to complete the survey questionnaire using either traditional survey procedures (ie, computer-assisted personal interview with some paper-and-pencil self-administered questionnaires) or an audio computer-assisted self-interviewing technology.¹³⁻¹⁵ (Random assignment of respondents to interview modes ensures that there will be no systematic association between interview mode and the variable of central interest to us—NAAT-diagnosed gonococcal or chlamydial infection.) Data from these 2 interview modes are aggregated in this article. The survey took an average of 26 minutes to complete. Respondents received \$10 to \$20 at the conclusion of the interview.

Collection and Processing of Urine Specimen

At the conclusion of the interview, participants aged 18 to 35 years were asked

to provide a urine specimen for testing. Respondents who agreed to provide a urine sample for screening received an additional \$10 to \$20.

N gonorrhoeae and *C trachomatis* were detected in urine specimens using a ligase chain reaction (LCR) assay (Abbott Laboratories, North Chicago, Ill). The LCR assay was performed according to the manufacturer's instructions. Positive test results were reconfirmed by a repeat analysis using this same procedure. If this second analysis was negative, the case was coded as negative. (Repeat analyses were not available for 3 cases that tested positive on initial testing. These cases were coded positive based on their initial testing.)

Notification of Results

All respondents were given a telephone number they could call to learn of their test results, and study staff used a succession of methods to attempt to contact participants who tested positive (telephone, registered letter, and, if refused or undelivered, regular mail). Free, expedited treatment at one of the BCHD clinics was offered to all contacted subjects who tested positive.

Quality Control

During the course of the study, a subset of interviewers' work was subject to independent verification to confirm that the interview had been completed and that a urine specimen had been requested if the respondent was 35 years or younger. A verification interviewer (not part of the regular survey staff) contacted the household to confirm the respondent's name, participation in the survey, demographic information, date of interview, whether a urine specimen had been collected, and whether the respondent had been paid the monetary incentive. This procedure identified 7 interviewers who appeared to have fabricated some of their interviews or to have collected interview data and urine specimens from households other than those selected into the sample. All of the interviews submitted by these interviewers were subject to verification, and data were retained only if the verification result was

positive. (A full account of these procedures has been presented elsewhere.¹⁶)

Over the course of the study, 56% of all completed survey interviews included in the final database were subject to independent verification.

Statistical Analyses

Prevalence estimates were derived using case weights that are inversely proportional to the probabilities of case selection and that incorporate a poststratification weighting to ensure that the sample distribution matched the 1997 US Census tabulation of the Baltimore population by race, sex, and age. Statistical algorithms that take account of the impact of complex sample designs on variance estimates, as implemented in the survey data component of Stata 6.0,^{17,18} were used in all analyses and calculation of variance estimates. We tabulated frequencies of demographic characteristics to obtain a descriptive profile of the sample. Logistic regression and χ^2 tests were used to assess the association between estimates of infection status and other subject characteristics. Tests of the equivalence of prevalence estimates for gonococcal vs chlamydial infections take account of the covariance that arises when estimates are derived using measurements made on the same subjects.

Impact of Assay Performance on Estimated Prevalence

To assess the potential impact of assay performance on prevalence estimates, sensitivity analyses were conducted using a plausible range of estimates for the specificity (0.990-0.999) and sensitivity (0.90-0.94) of the LCR assays used in this research. Past research indicates that NAAT assays have high sensitivity (>0.90) and specificity (>0.99) for the detection of chlamydial and gonococcal infections because genetic material from the target organisms is detected.¹⁹⁻²⁴ In the present study, specificity was optimized by retesting almost all positive specimens and considering a specimen positive only if both initial and repeat test results were positive. Sensitivity analyses were performed using

spreadsheets constructed in Excel 2000 (Microsoft, Redmond, Wash).

Impact of Missing Data on Estimated Prevalence

To assess the impact of respondents' refusal or inability to provide urine specimens on our prevalence estimates, we used logistic regression to model the likelihood that respondents would test positive for either gonococcal or chlamydial infection based on a range of sociodemographic and behavioral variables collected in the survey interview. This model was estimated using data from those respondents who provided urine samples adequate for testing. The parameter estimates derived for this model were then used to impute the probability that individual nonrespondents in the urine collection would have tested positive for either pathogen had they been tested. These imputed probability values for respondents who did not provide a urine specimen were combined with the actual gonococcal and chlamydial infection test results for respondents who did provide specimens. The synthetic estimate derived by this imputation process (8.1% for infection with *C trachomatis* and/or *N gonorrhoeae*) was quite similar to the unadjusted estimate derived from tested specimens alone (7.9%). Since imputation for nonresponse did not have a substantial effect on the overall prevalence estimate, we used unadjusted estimates based on complete data in our analyses.

Other Data Sources

In addition to prevalence estimates derived from LCR testing of urine specimens, we derived alternate prevalence estimates from physician- and laboratory-diagnosed cases of gonococcal and chlamydial infection reported to the BCHD in 1998 (G. Olthoff, MHA, written communication, November 2, 2001). Health Department estimates are derived from the Baltimore STD reporting system and eliminate instances (as duplicate reports) in which infection with the same pathogen is reported in the same individual 2 (or more) times

within a 30-day period (W. Braithwaite, BA, written communication, December 5, 2001). Reports of infection of the same individual outside of this 30-day period are included in the case counts.

Alternate prevalence estimates were also derived from survey respondents' answers to questions asking whether they had ever heard of gonorrhea and chlamydia and, if so, had they been diagnosed as having these infections in the 12 months prior to the survey. Respondents' answers provide 2 estimates of the prevalence of diagnosed infection. The first and lower estimate assumes that respondents who had not heard of a disease (gonorrhea or chlamydia) had not been diagnosed as having the disease in the previous 12 months. A second and higher estimate assumes that persons who had never heard of the infection were just as likely to have been diagnosed as having this infection in the past 12 months as respondents who had heard of the infection.

For both diagnoses reported to the BCHD and those reported by survey respondents, we assume that diagnosis is accompanied by treatment, although in a small but unknown number of cases this may not be true.

RESULTS

Survey Execution

Of the 3182 households selected for interview, 2727 (85.7%) were successfully screened. Screening identified a total of 1224 English-speaking adults who were between the ages of 18 and 45 years and eligible for interview. Survey interviews were completed with 1014 respondents (82.8%) between January 1997 and September 1998.

The protocol specified that only respondents between the ages of 18 and 35 years were eligible to provide urine for gonorrhea and chlamydia testing. Of the 1014 respondents between the ages of 18 and 45 years who completed the interview, 728 respondents aged 18 to 35 years were asked to provide urine for testing. Of the 728 age-eligible respondents, 579 (79.5%) provided a urine

specimen adequate for testing, 119 (16.3%) refused to provide a urine specimen, and 30 (4.1%) were not tested because of inadequate urine volume, interviewer error, or other logistical problems. TABLE 1 presents the unweighted numbers of adults providing urine samples and weighted percentage distributions for selected sociodemographic groups.

Estimated Prevalence of Untreated Infections

Among Baltimore adults aged 18 to 35 years, we estimate the prevalence of untreated chlamydial infection is 3.0% (SE, 0.8%) and the prevalence of untreated gonococcal infection is 5.3% (SE, 1.4%) (TABLE 2). Overall, 0.4% (SE, 0.3%) of adults are estimated to have both infections (data not shown), and 7.9% (SE, 1.6%) of Baltimore adults aged 18 to 35 years are estimated to have either gonococcal or chlamydial infection (or both). The difference be-

tween the estimated prevalence of these 2 infections is not statistically significant ($P = .16$). All respondents who reported a diagnosis of gonococcal (unweighted sample of 9) or chlamydial (unweighted sample of 13) infection in the past 12 months tested negative by LCR for the diagnosed (and presumably treated) pathogen.

Table 2 includes both weighted population prevalence estimates and unweighted counts of the numbers of infections detected and subjects tested. The unweighted sample counts represent the results of our NAAT analysis; they do not provide valid estimates of the prevalence of infection in the population as a whole or in any subpopulation. Since we used a complex sample design that purposely oversampled certain segments of the population (see above), only the weighted estimates can be used to make inferences about the prevalence of NAAT-detectable infections in the population.

Table 1. Demographic and Social Characteristics of Respondents: 1997-1998 Baltimore STD and Behavior Survey (n = 579)*

Characteristic	Unweighted Sample Size†	Weighted Percentage
Race		
White	221	28.7
Black	319	65.7
Other	39	5.6
Sex		
Women	335	52.0
Men	244	48.0
Age, y		
18-20	76	16.8
21-25	138	23.9
26-30	158	26.2
31-35	207	33.2
Marital status		
Never married	305	53.6
Married	123	21.1
Cohabiting‡	80	15.6
Widowed, divorced, or separated	71	9.6
Education		
≤Eighth grade	40	6.1
Some high school§	106	16.0
High school graduate	183	36.6
Trade or business school	36	7.6
Some college	122	20.2
≥College graduate	90	13.5

*STD indicates sexually transmitted disease.
 †Sample sizes may not sum to 579 due to respondents refusing to answer all questions, responding that they did not know, or similar survey problems.
 ‡Based on response of "not married, living with a partner."
 §Includes 16 persons who were aged 18 years at time of interview. Some respondents may still have been in school.

Impact of Assay Performance on Estimated Prevalence

Assuming the sensitivity of the LCR assay was 0.90 to 0.94 and specificity was 0.990 to 0.999, sensitivity analysis indicates that the “true” underlying prevalence of chlamydial infection would be 2.2% to 3.2%, given our population prevalence estimate of 3.0%. For gonorrhea, the “true” underlying prevalence would be 4.6% to 5.8%, given our population prevalence estimate of 5.3%. This sensitivity analysis suggests that our prevalence estimates are not substantially affected by the imperfection of the LCR assay.

Untreated Infections by Sex, Race, and Age

The prevalence of gonococcal and chlamydial infections varies substantially across subpopulations (Table 2). We estimate that 15.0% (SE, 3.7%) of black women have gonococcal and/or chlamydial infections while the estimated infection rates are significantly lower for black men (6.4% [SE, 2.1%]; $P=.02$) and nonblack women (1.3% [SE, 0.5%]; $P<.001$). Estimated prevalence was lower among nonblack men (2.8% [SE, 1.3%]) than among black men, although the difference was not significant. For both blacks and for women, gonococcal infec-

tion appears to be more prevalent than chlamydial infection, but this difference is also not statistically significant.

TABLE 3 shows a significant decline with age in the estimated prevalence of NAAT-detectable chlamydial infections ($P=.006$ for trend) and subjects' reports of diagnoses of gonococcal infections during the past 12 months ($P=.02$ for trend). A parallel, although less uniform and nonsignificant, trend occurs for chlamydial infections diagnosed in the past year.

Current untreated gonococcal infections show a different pattern. The highest prevalence of detectable gonococcal

Table 2. Estimated Prevalence of Untreated Gonococcal and Chlamydial Infections by Race and Sex: 1997-1998 Baltimore STD and Behavior Survey*

	Black		Other Race		Total
	Women	Men	Women	Men	
Unweighted sample size	193	126	142	118	579
<i>Neisseria gonorrhoeae</i> and/or <i>Chlamydia trachomatis</i>					
No. of cases (unweighted)†	21	14	8	6	49‡
Prevalence (weighted), % (SE)§	15.0 (3.7)	6.4 (2.1)	1.3 (0.5)	2.8 (1.3)	7.9 (1.6)
<i>N gonorrhoeae</i>					
No. of cases (unweighted)†	12	10	8	3	33
Prevalence (weighted), % (SE)§	9.3 (3.3)	5.3 (2.0)	1.3 (0.5)	1.3 (0.9)	5.3 (1.4)
<i>C trachomatis</i>					
No. of cases (unweighted)†	10	4	0	4	18
Prevalence (weighted), % (SE)§	6.4 (2.2)	1.1 (0.7)	0	2.4 (1.3)	3.0 (0.8)

*STD indicates sexually transmitted disease. Estimates are based on age-eligible respondents who provided urine specimens for *N gonorrhoeae* and *C trachomatis* testing (ligase chain reaction assay). The estimates are weighted to account for differing probabilities of selection and poststratification adjustments to match US Census marginals. The estimates presented differ slightly from preliminary estimates for sexually experienced subjects presented at the International Society for Sexually Transmitted Diseases Research meetings.²⁵ In addition to the difference in population definition (all subjects vs subjects with sexual experience), subsequent comparison of laboratory records and the preliminary analysis file revealed 1 instance in which a subject who tested positive for gonococcal infection was mistakenly coded as positive for both pathogens in the preliminary analysis file.

†Unweighted case counts are not appropriate for making inferences about the prevalence of infection in populations since they do not take account of the differing probabilities of selection of households and individuals.

‡Includes 2 cases that were positive for both infections.

§SEs were calculated from weighted data using statistical algorithms that take account of impact of complex sample design on variance estimates.

Table 3. Estimated Prevalence of Untreated Gonococcal and Chlamydial Infection and Self-reports of Diagnosed Infections by Age: 1997-1998 Baltimore STD and Behavior Survey*

	Age Group, y				Total
	18-20	21-25	26-30	31-35	
Unweighted sample size†	68-76	122-138	133-158	145-207	468-579
<i>Chlamydia trachomatis</i>					
Untreated infections‡	8.0 (3.9)	3.5 (1.4)	2.6 (1.3)	0.5 (0.5)	3.0 (0.8)
Diagnosed in past year§	8.2-9.2 (4.9-5.4)	2.6-2.9 (1.3-1.5)	0.8-1.0 (0.8-1.0)	2.9-4.4 (1.6-2.4)	3.2-4.0 (1.1-1.4)
<i>Neisseria gonorrhoeae</i>					
Untreated infections‡	4.5 (2.4)	3.5 (1.9)	1.4 (0.8)	10.2 (3.3)	5.3 (1.4)
Diagnosed in past year§	7.4-7.9 (5.0-5.4)	4.6-5.3 (2.2-2.5)	0	0.9-1.0 (0.6-0.7)	2.7-3.0 (1.1-1.2)

*STD indicates sexually transmitted disease. Estimated prevalence is reported as percentage (SE).

†Values reflect 2 alternate measurements. See section symbol footnote.

‡Diagnosed by ligase chain reaction assays.

§Range of estimates reflects alternative treatment of cases in which respondents reported they had never heard of the disease (gonorrhea or chlamydia). The lower estimate assumes that such respondents had not been diagnosed with the disease in the previous 12 months. The higher estimate assumes that persons who had never heard of the infection were just as likely to have been diagnosed with the infection in the past 12 months as respondents who had heard of the infection.

infection (10.2% [SE, 3.3%]) occurs among persons aged 31 to 35 years. While the number of infections detected is small (unweighted counts: 33/579 [aged 18-35 years] and 17/207 [aged 31-35 years]), the unexpectedly high prevalence estimated for gonococcal infection among older respondents is unlikely to be due to the small sample sizes. (The null hypothesis that the population prevalence of gonococcal infections is equivalent among adults aged 31 to 35 years and those aged 18 to 30 years is rejected with $P < .001$.) High estimated prevalences of untreated gonococcal infections are observed among both men (7.8%) and women (12.2%) in the group aged 31 to 35 years (data not shown).

Symptoms and Antibiotic Use

The high prevalence of untreated infections estimated for the Baltimore population raises questions about the reasons why medical diagnosis and treatment were not obtained. Interview data indicate that symptoms were rarely reported among persons with untreated gonococcal or chlamydial infections. Excluding persons receiving treat-

ment for a gonococcal or chlamydial infection in the previous 6 months, only 2.0% of currently infected respondents reported dysuria (burning on urination) and 4.7% reported discharge within the past 6 months. Untreated infections were found less frequently among persons reporting dysuria during the preceding 6 months than among those who did not report this symptom (prevalence: 2.0% vs 8.8% [odds ratio {OR}, 0.21]; $P = .08$). Similarly, infections were less likely to be reported among persons who report dripping or discharge in the past 6 months than among those who did not, but this difference did not approach statistical significance (4.7% vs 8.4% [OR, 0.54]; $P = .43$).

Persons who reported antibiotic use in the 6 months prior to testing were less likely to test positive for gonococcal and/or chlamydial infection than those who reported no antibiotic use in this period (4.4% vs 10.5% [OR, 0.40]; $P = .04$). In theory, variation in the use of antibiotics could produce a negative association between symptom reporting and current infection status if antibiotics were administered presumptively on the reporting of dysuria or dis-

charge. To control for this possibility, we examined the relationship of symptoms and current infection status in persons reporting no antibiotic use and no diagnosed gonococcal or chlamydial infections in the 6 months prior to testing. A trend toward asymptomatic infection remains (OR, 0.24 for dysuria; and OR, 0.32 for discharge), however, with the diminished sample sizes, these results are not statistically significant ($P = .19$ and $P = .30$, respectively).

Number of Treated vs Untreated Infections

Overall, 4566 gonococcal infections were diagnosed in persons aged 18 to 35 years and reported to the BCHD in 1998 (TABLE 4). This would represent a maximum population prevalence of 2.6% (under the assumption that no person had ≥ 2 infections recorded during the year). Interview data provided by our survey respondents suggest that between 4708 (2.7%) and 5231 (3.0%) individuals in this age group were diagnosed as having (and presumably received treatment for) gonococcal infections in the 12 months prior to our survey. Based on NAAT assays of urine

Table 4. Estimates of Baltimore Population With Treated and Untreated Gonococcal and Chlamydial Infections

	Men		Women		Total	
	No. (SE)	Population, %	No. (SE)	Population, %	No. (SE)	Population, %
<i>Neisseria gonorrhoeae</i>						
Health department STD reports (patients diagnosed in 1998)*	2502	3.0	2051	2.3	4566	2.6
Survey estimate of population diagnosed in past 12 months†						
Lower bound	3340 (1670)	4.0	1272 (727)	1.4	4708 (1918)	2.7
Upper bound	3674 (1837)	4.4	1454 (818)	1.6	5231 (2092)	3.0
Population with untreated infection‡	3173 (1086)	3.8	6087 (2090)	6.7	9241 (2441)	5.3
<i>Chlamydia trachomatis</i>						
Health department STD reports (patients diagnosed in 1998)*	391	0.5	3255	3.6	3664	2.1
Survey estimate of population diagnosed in past 12 months†						
Lower bound	1587 (1253)	1.9	3998 (1363)	4.4	5580 (1918)	3.2
Upper bound	2088 (1754)	2.5	4634 (1635)	5.1	6975 (2441)	4.0
Population with untreated infection‡	1336 (501)	1.6	3907 (1363)	4.3	5231 (1395)	3.0

*Baltimore City Health Department (BCHD) estimates are counts of number of cases reported to the health department by clinicians and laboratories. Duplicate reports for the same person within 30 days were eliminated by the BCHD, although some duplicate counting may occur due to clerical error. Percentages for population prevalence were calculated using 1998 US Census estimates of population size as the denominator. The BCHD records do not indicate the sex of 18 persons diagnosed as having chlamydia and 13 persons diagnosed as having gonorrhea in 1998. These cases are included in the totals but not in the breakdowns by sex. The BCHD tabulations exclude 42 cases of chlamydial infection and 24 cases of gonococcal infection for which patient's age was unknown. STD indicates sexually transmitted disease.

†Lower bound estimate assumes that respondents who had not heard of a disease (gonorrhea or chlamydia) had not been diagnosed as having the disease and the higher bound estimate assumes that persons who had never heard of the disease were just as likely to have been diagnosed as those who had heard of the infection.

‡Urine specimens tested by ligase chain reaction assay. The estimated number of persons with untreated infections calculated as a product of the Baltimore STD and Behavior Survey estimated prevalence rates for *N gonorrhoeae* and *C trachomatis* and US Census estimates of the number of Baltimore residents aged 18 to 35 years in 1998.

specimens, we estimate that 9241 (5.3%) of this age group had a current and untreated gonococcal infection at the time of our survey. The divergence in estimates of diagnosed and undiagnosed gonococcal infections is most striking for women. Three estimates of the number of women (aged 18-35 years) diagnosed as having gonococcal infection annually in Baltimore lie in the range of 1272 (1.4%) to 2051 (2.3%). NAAT analysis of urine specimens from our probability sample of this population leads us to estimate that 6087 women (6.7%) were carrying an undiagnosed gonococcal infection at the time of the survey.

For chlamydial infection, BCHD records indicate that 3664 infections were diagnosed in this age group in 1998. This represents a maximum prevalence of 2.1%. Responses during the survey interview suggest that 5580 (3.2%) to 6975 (4.0%) of the population were diagnosed as having and presumably treated for chlamydial infections in the 12 months prior to our survey. Testing of urine specimens yields an estimate that 5231 (3.0%) of this age group had a current and untreated chlamydial infection. Examination of the results by sex indicates that only 391 men (0.5%) were diagnosed as having chlamydial infections and reported to the BCHD in 1998 while our testing of urine specimens yields an estimate that 1336 men in this age group (1.6%) had a current untreated chlamydial infection. Male respondents reported diagnoses of chlamydial infection by their health care providers at rates that are considerably higher than recorded in BCHD statistics (1.9%-2.5% vs 0.5%). This may reflect presumptive treatment (eg, for nongonococcal urethritis) without diagnostic testing.

COMMENT

The foregoing estimates indicate that nearly 1 in 12 (7.9%) Baltimore adults between the ages of 18 and 35 years has an untreated infection with either *N gonorrhoeae* or *C trachomatis*. The estimated prevalence for black women is

greater than 1 in 7 (15.0%). Two important conclusions emerge when these estimates, which represent undiagnosed infections prevalent in the population, are compared with estimates of the number of infections diagnosed annually. First, the combined number of gonococcal and chlamydial infections that persist undiagnosed and untreated in this population exceeds the number of infections that are diagnosed and treated in a given year. Second, there appears to be a large reservoir of undiagnosed gonococcal infections in Baltimore, particularly among women.

It is impossible to know the duration of the infections detected in this study. We note, however, that nearly all of the detected infections occurred among adults who reported no recent symptoms. In addition, elevated levels of gonococcal infection were detected among older adults aged 31 to 35 years. The lack of symptoms and high levels of gonococcal infection among the oldest sampled age group suggest that persistent infections may be responsible for the high prevalence of untreated asymptomatic infections detected in this study. Longstanding infections may represent low organism burden, partial immunological clearance,²⁶ or infection with organism strains that cause less symptomatic disease.²⁷ In some cases, these persistent asymptomatic infections may be associated with significant sequelae, such as infertility. In other cases, the clinical importance and transmissibility of these infections is less clear.²⁸ Although there is some uncertainty about the interpretation of NAAT-detected infections, we believe our findings have 2 important implications.

First, prompt consideration should be given to strategies for improving the diagnosis and treatment of asymptomatic infections in this population. The urine-based NAAT assays used in this research are approved by the Food and Drug Administration for diagnosis of gonococcal and chlamydial infections. As such, we believe it is prudent to plan appropriate public health actions in response to the high prevalence rates we have detected. Strategies for reducing the

prevalence of infection in this population might include screening or routine testing in health care settings for the entire population of young adults, including persons who formerly would be considered to be at low risk of infection. (Such efforts will require confronting issues that are beyond the scope of the present article, including identification of appropriate methods for delivering and financing such testing, and the role to be played by public health facilities and private health care providers.)

In support of this recommendation, we note that Mehta et al²⁹ recently reported testing 454 patients (aged 18-31 years) seeking medical care for reasons other than STD symptoms at the adult emergency department at Johns Hopkins Hospital and Health System (Baltimore, Md). Using urine-based NAAT assays, investigators found that 9.3% of these patients tested positive for chlamydial infection and 5.3% tested positive for gonococcal infection. Their sample is not directly comparable with our own since they recruited patients in a large Baltimore emergency department. However, both our estimates and those of Mehta et al are derived from screening adult populations outside of an STD care setting.

The second implication of our findings is that research is urgently needed to improve our understanding of the clinical and public health significance of NAAT-detectable infections. It is possible that NAAT assays are identifying clinically inconsequential infections because of the assays' ability to detect extremely low levels of viable organisms (ie, below the infectious inoculum) or amplifiable DNA (or RNA) from residual pathogens (ie, nonviable organisms) of past infections that are well on their way to being cleared. One potentially informative line of research may be to compare the transmissibility and clinical consequences of infections that are detectable only by NAAT assay vs those that are detectable by traditional assays.³⁰

In addition to its substantive findings, the present study provides an example of the feasibility and benefits of

combining population survey techniques and NAAT analysis of urine specimens in research on the epidemiology of STDs. Such research can complement and enrich the epidemiological insights gained from studies using case reporting systems and studies of clinical and other special populations. Most importantly, this research permits generalizations about the prevalence in the population at large—or at least in that fraction of the population who consents to being surveyed.

Interpretation of our research findings will benefit from replication. Since teenagers both contract infections from and transmit infections to the adult population, any replication should include this segment of the population. Annual or biannual monitoring of STD prevalence using population survey techniques in Baltimore and else-

where could enrich our understanding of the epidemiology of these STDs. It could also provide important guidance on the appropriate roles of population prevalence data and STD case reports in tracking trends in these STDs and identifying subpopulations that might benefit from screening or other interventions designed to inhibit the spread of these infections.

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