

American College of Preventive Medicine

Practice Policy Statement

Screening for *Chlamydia trachomatis*

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Overview

On the basis of a review of the current literature and recommendations, the American College of Preventive Medicine presents a practice policy statement on screening for *Chlamydia trachomatis*.

Burden of Suffering

Chlamydia trachomatis infection is the most common bacterial sexually transmitted disease in the United States,¹ affecting >4 million people yearly at a cost exceeding \$2.7 billion.^{2,3} Because up to 70% of infected women^{4,5} and 75% of infected men⁵⁻⁷ are asymptomatic, systematic screening of large populations is necessary to accurately assess the true burden of disease. In systematic clinic-based and population-based screening studies, chlamydial prevalence ranges from 1% to 24%, depending on the population studied.^{1,8-18} The median rate of chlamydia positivity among 15- to 24-year-old women tested in all states during visits to selected family planning clinics was 5.2%.¹⁹ Prevalence in men is 25% to 50% lower than in women, but data are limited.^{14,20,21} Age <25 years is the strongest risk factor for infection, with women between 15 and 24 years accounting for more than 70% of all reported cases.^{15,19,22} African-American and Native-American women have twice the risk of white women, with Hispanic and Asian women at an intermediate risk. Other risk factors include multiple sexual partners, a new partner, inconsistent use of barrier contraceptives, history of an STD, low socioeconomic status, and frequent use of marijuana.^{1,7,16,18,23,24}

Cervicitis is the most commonly reported manifestation of chlamydial infection in women. Pelvic inflammatory disease (PID) occurs in up to 30% of untreated women and causes most of the associated morbidity. Asymptomatic PID is present in a large number of women²⁵; in one study, 40% of women had no symp-

toms at the time of referral.²⁶ Up to 50% of the 1 million annual U.S. cases of PID and 17% of tubal infertility may be due to chlamydia.^{4,10,27} Other serious sequelae include chronic pelvic pain and ectopic pregnancy.^{4,28,29} Chlamydial infection also increases the likelihood of both transmitting and acquiring HIV infection.^{30,31}

The prevalence of chlamydial infection in pregnant women is at least as great as in nonpregnant women, ranging from 4% to 35%.³²⁻³⁶ Infection during pregnancy is associated with preterm contractions, premature rupture of membranes, low birth weight, and increased fetal and infant mortality.^{32,37,38} Perinatal transmission during passage through the birth canal causes conjunctivitis, chlamydial pneumonia, and rectal and vaginal infections.^{33,35,39}

Chlamydial infection in men causes urethritis, epididymitis,⁴⁰ and prostatitis,^{2,27} and may be associated with infertility.⁴¹ However, complications of infection in men are rare.⁴²

Description of Preventive Measures

There are three classes of specific screening tests: (1) cell culture; (2) "direct" antigen or nucleic acid detection assays; and (3) DNA/RNA amplification. Nonspecific tests of inflammation, such as leukocyte esterase dipstick, may also be used to screen for infection. Tests vary in the type of specimens on which they may be used, the level of skill required to collect and transport specimens, the level of skill required by the testing laboratory, and the accuracy and rapidity of results (Table 1).⁴³⁻⁵⁸ In women, specimens may be obtained from (1) the endocervix, using a swab; (2) urethra and vagina using a swab; and (3) first-catch urine. In men, specimens can be obtained by swabbing the anterior urethra as well as through first-catch urine.³³

Chlamydial culture from endocervical or urethral swabs was long the "gold standard," but it has been largely supplanted as a screening test because it requires invasive and time-consuming specimen collection, cold transportation of specimens, and a high level of laboratory technical expertise. It is also slow (3 to 7 days) and insensitive relative to newer tests.³³

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Table 1. Summary of chlamydia testing methods

Test class	Test method	Specimen	Sensitivity	Specificity	Advantages	Disadvantages	References
Culture	Culture	Endocervix, male urethra	30.1%–88.0%	100%	No false positives; preserves organism for later testing	Invasive sampling; labor intensive; cold transport; lab variability; slow; not sensitive	Thejls et al. ⁴³ Schachter et al. ⁴⁴ Pasternack et al. ⁴⁵ Andrews et al. ⁴⁶
Immunoassay	EIA with positive confirmation	Endocervix, male urethra, urine	64.7%–94.0%	100%	Simple automatic reading; objective results; reduced requirements for specimen transport and storage conditions; standardized technology	Lower sensitivity than amplification tests; positive results need to be confirmed	Thejls et al. ⁴³ Dean et al. ⁴⁷
	Rapid office-based EIA	Endocervix	66%–85%	98.5%–99.8%	Does not require sophisticated equipment; rapid results; qualitative results	Low sensitivity	Pate et al. ⁴⁸ Ferris et al. ⁴⁹
	DFA	Endocervix	77.8%	99.5%	Rapid test; no refrigeration of specimens during transport; simple processing of specimens	Dependent on observer's experience; used primarily as a second-stage confirmatory test	Thejls et al. ⁴³
Hybridization probe	DNA probe	Urine, endocervix, male urethra	77.2%–95.2%	98.2%–99.9%	Reduced requirements for specimen transport and storage; standardization of technology; simultaneously detects <i>N. gonorrhoeae</i> ; rapid processing	Lower sensitivity than amplification tests; positive results need to be confirmed	Kluytmans et al. ⁵⁰ Lauderdale et al. ⁵¹
DNA amplification	PCR	Urine, endocervix, male urethra	94.8%–100%	97.7%–99.9%	Sensitive; noninvasive; simple to collect (urine)	Must be first-catch urine; requires refrigeration; expensive	Gaydos et al. ⁵² Morre et al. ⁵³
	LCR	Urine, endocervix, male urethra	76.9%–96.6%	98.9%–100%	Noninvasive; simple to collect (urine)	Must be first-catch urine; requires refrigeration; expensive	Gaydos et al. ⁵² Morre et al. ⁵³ Buimer et al. ⁵⁴
	Amplified DNA probe (strand displacement amplification)	Urine, endocervix, male urethra	100%	100%	Sensitive; noninvasive; simple to collect (urine); less prone to contamination than PCR or LCR; potentially less expensive	Little clinical experience to date	Little et al. ⁵⁵
RNA amplification	TMA	Urine, male urethra, endocervix, vulva	76.0%–100%	98.7%–100%	Noninvasive; simple to collect (urine); vulvar specimens allow self-collection	Must be first-catch urine; requires refrigeration; expensive	Crotchfelt et al. ⁵⁶ Sary et al. ⁵⁷
Dipstick	LE with “trace” cut-off	Male urine	77.8%	80.9%	Noninvasive; low cost	Low specificity	Bowden ⁵⁸

DFA, direct immunofluorescent antibody; EIA, enzyme immunoassay; LCR, ligase chain reaction; LE, leukocyte esterase; PCR, polymerase chain reaction; TMA, transcription-mediated amplification.

Nonculture assays include enzyme immunoassay (EIA) (e.g., Chlamydiazyme); DNA hybridization probe (e.g., PACE 2); and direct immunofluorescent antibody (DFA). EIA and DNA probe are indicated for use on endocervical and male urethral specimens. EIA assays detect chlamydial lipopolysaccharide (LPS) antigen with an antibody that has been labeled with a color-inducing enzyme. Because antibodies to LPS may cross-react with LPS from other gram-negative bacteria, a confirmatory test is used to verify positive results. DNA probes detect chlamydia by hybridization of a luminescent DNA sequence to chlamydial ribosomal RNA. DFA assays detect either LPS or major outer membrane protein (MOMP) by staining with fluorescein-labeled specific antibody. These assays require a high degree of laboratory expertise and are therefore principally used for second-stage "confirmation" of positive results of other nonculture assays.

Rapid "point-of-care" tests are self-contained EIA kits that can be completed in 30 minutes in the clinician's office.^{48,51,59} These tests are designed to require very little expertise, but in practice they have significantly lower sensitivity than laboratory-based EIA testing.

The newest generation of chlamydia-detection tests utilizes nucleic acid amplification methods. These methods, which are indicated for use on all types of specimens, use oligonucleotide primers to replicate and detect minute quantities of chlamydial DNA or RNA. DNA-based amplification methods include polymerase chain reaction (PCR), ligase chain reaction (LCR), and DNA probe based on simultaneous strand displacement amplification. Transcription-mediated amplification (TMA) is an RNA amplification method. These methods are increasingly used in public health laboratories in the United States because they are highly sensitive and specific, and use noninvasive sampling techniques. Although presently their cost is higher than that of other nonculture tests, increased competition and new amplification tests being developed will likely lower future costs. Additionally, in low-prevalence populations, cost saving can be accomplished through pooling urine specimens for testing.^{60,61}

Numerous observational studies have examined the sensitivity and specificity of existing screening methods; these are summarized in Table 1. The broad ranges in sensitivity for a given method are a function of both technique and the definition of what constitutes a "true positive" infection. All screening tests currently in use are highly specific. The nucleic-acid amplification tests have higher sensitivity than either culture or antigen-based tests. When evaluating screening effectiveness, attention must be paid to the test type and methodology in order to avoid comparisons based on diagnostic misclassification.⁶²

Evidence of Effectiveness

Clinic-based screening programs for *Chlamydia trachomatis* have been associated with declining prevalence in selected populations.^{14,17,63,64} Test positivity has declined as much as 59% among women participating in the U.S. Department of Health and Human Services' Region X family planning screening programs.¹⁹ Only one randomized controlled trial on the effect of screening and treatment of women at risk has been reported. The setting was a health maintenance organization. Women randomized to screening had a 56% reduction in PID compared to controls who received usual care.⁶⁵ Moreover, in two large studies,^{32,37} screening and treatment for chlamydia in pregnancy was associated with a reduction in premature rupture of membranes and small-for-gestational-age infants. *Chlamydia trachomatis* infections in nonpregnant patients can be effectively treated with azithromycin, doxycycline, or erythromycin base.⁶⁶ Pregnant women can be treated with erythromycin base, amoxicillin, or azithromycin.^{34,66,67}

Potential disadvantages of screening include patient anxiety, embarrassment, and the risk of unnecessary treatment of patients with false-positive results, including potential side effects of drugs.⁶⁸ However, because a single oral dose of azithromycin is highly effective, simple to administer and well tolerated, there are few disadvantages to treatment.^{34,69}

Public Policy Considerations

The cost-effectiveness of screening for *Chlamydia trachomatis* depends on its prevalence in the population being screened. Moreover, it is affected by the cost and accuracy (sensitivity and specificity) of the screening test. Although optimal screening strategies vary in different populations, the economic benefit to society of screening compared to no screening has been demonstrated in several cost-effectiveness analyses. One study compared culture, nonculture nonamplification, and amplification methods in a large population of women aged <30 years. Screening with any method was cost saving compared with a no-screening strategy. A screening strategy combining the use of DNA amplification on cervical specimens in women receiving pelvic examinations and DNA amplification of urine in other women prevented the most cases of PID and provided the most savings.² Another study compared three screening strategies—screening according to Centers for Disease Control and Prevention (CDC) criteria (testing all women with mucopurulent cervicitis, all women <20 years of age, as well as testing all women ≥20 years who have not consistently used barrier contraception or have had a new sex partner or >1 sex partner during the past 90 days); screening all women <30 years of age; and universal screening of women. The results suggested that age-based screening pro-

vided the greatest cost savings.⁶⁸ Similarly, a recent study compared targeted screening of women aged ≤ 25 years with universal screening and universal empiric antibiotic treatment in female military recruits. Targeted screening by age provided the greatest cost savings.⁶⁹ Another recent study compared screening women aged 15 to 19 years using the EIA method or DNA hybridization probe with a no-screening strategy. The prevalence of infection in this population was 12.6%, and DNA-probe screening proved to be most cost-effective.³⁶

Three additional studies suggest that to ensure cost savings of a screening program, the prevalence of chlamydial infection must be $>3\%$ to 7% .^{70–72} A fourth study, however, concluded that a universal screening program of 15- to 40-year-old asymptomatic women in the Netherlands was not cost-effective unless prevalence exceeded 41.8%.⁷³

Recommendations of Other Groups

The American Medical Association⁷⁴ and the American Academy of Pediatrics⁷⁵ recommend that all sexually active adolescents should be screened annually for chlamydia. The CDC⁷⁶ recommend screening sexually active women aged <20 years for chlamydial infection during routine annual examinations. The CDC⁷⁶ also recommend annual screening of women aged >20 who use barrier contraceptive measures inconsistently and who have new or multiple sex partners during the previous 3 months. The U.S. Preventive Services Task Force⁷⁷ recommends routine screening for all sexually active women aged ≤ 25 years, all asymptomatic pregnant women aged ≤ 25 and/or at high risk for infection, as well as other asymptomatic women at high risk for infection. High-risk characteristics include being unmarried or African American, having a prior history of STD, having new or multiple sexual partners, having cervical ectopy using barrier contraceptives inconsistently. The Canadian Task Force on the Periodic Health Examination⁷⁸ recommends screening of pregnant women during the first trimester, as well as annual screening of high-risk groups, including sexually active women aged <25 years, men and women with a new sexual partner or more than one partner in the preceding year, women who use non-barrier contraceptive methods, and symptomatic women.

Rationale Statement

Chlamydia trachomatis urogenital infections are highly prevalent among adolescents and young adults. Sequelae of undetected, untreated infections account for substantial healthcare costs. Treatment is effective, simple, and well tolerated. The majority of infected women and many men are asymptomatic; thus, screening is necessary for detection. Recently screening for *Chlamydia trachomatis* was simplified through the devel-

opment of noninvasive, highly sensitive, amplification screening tests.

Screening programs can be effective, both in lowering disease prevalence and decreasing the incidence of sequelae.^{14,17,63–65} One of the controversies regarding screening is whether to implement universal or selective screening programs. Although selective screening has been suggested as the least costly strategy,^{8,64,68} universal screening may be cost-effective in high-prevalence populations.⁷¹ Another controversy centers on whether new higher-cost amplification technologies that are more sensitive should replace lower-cost, less-sensitive methods. In addition to high sensitivities, amplification methods have specificities high enough to make their utilization feasible even in low-prevalence populations.⁷⁹ Consequently, the decision as to which screening test to utilize must be based both on the estimated prevalence in the screened population and available funding. When economically feasible, the use of amplification tests is preferable.

Data on the optimal interval for screening are not available. Several groups, however, recommend annual screening intervals.^{66,78} Re-screening at 6 to 12 months may be considered in previously infected women due to high rates of re-infection.^{12,80–82}

Recommendations of the American College of Preventive Medicine

- Assessment of risk factors for infection with *Chlamydia trachomatis* should be performed during every routine healthcare contact of sexually active women.
- Sexually active women with risk factors should be screened annually by any well-validated, laboratory-based amplification or antigen method, using cervical or urine specimens. Risk factors include age ≤ 25 years, a new male sex partner or two or more partners during the preceding year, inconsistent use of barrier contraception, history of a prior STD, African-American race, and cervical ectopy. All partners of women with positive tests should be tested for *Chlamydia trachomatis*. Women with mucopurulent discharge, suggestive of cervicitis, should be tested immediately.
- Pregnant women should be screened during their first trimester or at their first prenatal visit. Those with risk factors should be re-screened during their third trimester.
- Recommended research priorities include well-designed, randomized controlled trials studying the long-term effects of screening and treatment of various populations, prevalence studies of asymptomatic males, and cost-effectiveness studies of office-based rapid tests.

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