Men provide a reservoir for continued transmission of *C. trachomatis* to women, thus representing a population for potential targeted screening. There are no formal recommendations by professional organizations for screening men for chlamydia, however, guidance has been provided by the Centers for Disease Control and Prevention for clinical sites wishing to screen men, who are primarily asymptomatic. This article describes and reviews the methods for laboratory diagnosis of *Chlamydia trachomatis* in men. The current recommendations for screening heterosexual men for chlamydia is using urine and testing by nucleic acid amplification tests (NAATs).

*Chlamydia trachomatis* is the most common reportable bacterial sexually transmitted disease in the United States, with estimates being 3-4 million new cases per year. While most chlamydia-associated morbidity is in women, men provide a reservoir for continued transmission for new and recurrent infection among women, and thus represent a population for targeted screening, especially if they are asymptomatic. The Centers for Disease Control and Prevention (CDC) has not made any formal recommendations for screening males for chlamydia, but has recently offered guidance for sites currently screening or planning to institute male screening. The guidelines include jailed males over 30 years of age, males attending STD clinics, men attending Job Corps training, males in the military, and males in HIV clinics, as well as males entering juvenile facilities with >2% prevalence and males in emergency departments, high schools, and adolescent clinics with high chlamydia prevalences in the community.

Clinicians have traditionally collected urethral swabs as the diagnostic specimen for detection of chlamydia and these may have posed a barrier for screening men. Now that urine-based nucleic acid amplification tests (NAATs) are available, these have been shown to perform better than urethral culture, enzyme immunoassay (EIA), direct fluorescent assay (DFA) or nucleic acid probe for detection of chlamydia. The availability of non-invasive chlamydia testing should potentially lead to more widespread screening of asymptomatic males in the community.

For men who have sex with men (MSM), rectal samples (and/or pharyngeal specimens for gonorrhea) may be the specimen of choice, as urethral swabs or urine samples may miss many infections; however these samples are not yet FDA cleared for NAAT assays, although some laboratories have performed verification studies and are using them. Pharyngeal swabs are not recommended for screening for chlamydia in men (or MSM) because of very low prevalences, but because many pharyngeal samples get tested for gonorrhea, positive pharyngeal chlamydia results may be returned to the clinician. Treatment should be given for such infections until we have further research to recommend otherwise.

**NAATs**
Although older tests for the detection of chlamydia in men include culture in tissue culture cells, direct fluorescent antibody (DFA)
tests, enzyme immunoassay (EIA), nucleic acid probe hybridization, only NAAT assays are now recommended for detecting chlamydia in men. NAAT assays include several available commercial tests; polymerase chain reaction (PCR), real time PCR, strand displacement hybridization (SDA), and transcription mediated hybridization (TMA). While all of these tests can be performed with urethral swabs, they are also FDA-cleared for use with first catch urine (FCU) samples. The NAATs are considered the most sensitive tests available. Urine is the specimen of choice when using NAAT assays because the sensitivity and specificity are not usually significantly different between urine and urethral swabs; urines may even be higher sensitivity. Urine specimens are recommended additionally because they are non-invasive and may result in more men being screened. Rapid, antigen point-of-care (POC) tests are not yet of sufficient sensitivity for use with urine specimens. Thus, the recommendation for screening symptomatic and especially asymptomatic men is to use a NAAT assay on a “first void” part (15-20 ml) of a urine (FVU) sample.

Medico-legal Issues
The moderate to poor sensitivity of C. trachomatis culture limits its diagnostic utility and the need to obtain a urethral swab followed by extensive laboratory processing restricts it from use in screening. In contrast, C. trachomatis culture is recommended for medico-legal cases for detection of chlamydia in cases of investigations of sexual abuse due to its near perfect specificity. The use of NAATs for medico-legal investigations has received some attention and the demonstrated accuracy may allow acceptance of these tests in the future by the legal system.

Patient symptom status
When men are symptomatic and are attending a clinic, they should receive a complete urogenital examination, with either urethral or urine samples obtained for diagnostic testing using the most sensitive and specific test available, i.e. a NAAT test, which has been recommended by the CDC as the test of choice. When populations of asymptomatic men, who are non-health-care-seeking, are being screened, the use of non-invasive samples, such as urine, is recommended. Such samples eliminate the requirement for a clinician for sample collection and their use can be cost-effective, especially when surveying large numbers of persons. When these non-invasive samples are used to screen asymptomatic persons for chlamydia, only a NAAT test can be used as none of the other older tests have high enough sensitivity.

Use of NAAT assays has the ability to influence the epidemiology of chlamydia in male population groups
The number of infections detected by NAAT may be up to 80% higher than those found with the use of older tests. NAATs are quite accurate in screening asymptomatic men, even though the burden of bacterial load may be low. A national household survey sample demonstrated a prevalence of chlamydia infection of 2.8%. A large screening program in four cities in the U.S. demonstrated a chlamydia prevalence of 7% in mostly asymptomatic males. High prevalence (4-5%) of chlamydia infections in male military recruits has been demonstrated. Recent surveys of young adults and adolescents in the Adolescent Health Study originally enrolled in schools using NAAT technology also indicated substantial prevalence of chlamydia in men age 18-26 yr (overall, 3.67%; White men, 1.38%; Black men, 11.12%). A large city-wide school survey has indicated prevalence for males of 2.5%. Screening in nontraditional settings such as the National Job Training Program for males has indicated that the overall chlamydia prevalence was 8.2%. Detention centers, jails, urban shelters, community cohorts of injection drug users, and emergency departments have also been screened for chlamydia in men with prevalences as high as 14.3%-15% and encouraging results for a high proportion of infected men receiving treatment.
Urine-based screening for chlamydia is also acceptable to males in screening settings. Without NAAT testing of urine from males these studies would not have been performed. Increasing public health interest in screening males is an important prevention message to reduce reservoirs of infection available for transmission to females.

**Other Laboratory Considerations**

NAATS measure DNA or RNA rather than live organisms; therefore, care should be used in using amplification tests for test-of-cure assays. Residual nucleic acid from cells rendered non-infectious by antibiotic therapy may give a “positive” amplified test for up to 3 weeks after therapy, when the patient is actually cured of viable organisms. Ordinarily, the CDC does not recommend a test-of-cure test for either men or women. Additionally it is not necessary to confirm positive NAATs in screening populations of low prevalence.  

**Cost Issues**

NAATs assays are more expensive than older non-culture, non-amplified tests and are often too expensive for many public health programs. Studies in males have indicated they are cost-effective for preventing sequelae in women. The high cost of NAATs relative to other FDA cleared technologies and competing responsibilities created difficulty the public health sector in implementing NAAT screening.

**Summary**

NAAT assays are the test of choice for testing males for chlamydia and urine is the specimen of choice. For those programs interested in testing males in various high-prevalence venues, guidance is available from the CDC. Future research is needed to definitively make official recommendations for screening males.

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Table 1. Diagnostic Tests for the Detection of Chlamydia trachomatis in Males.

<table>
<thead>
<tr>
<th>Diagnostic Method</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue Culture</td>
<td>70-85%</td>
<td>100%</td>
</tr>
<tr>
<td>Direct Fluorescent Antibody</td>
<td>80-85%</td>
<td>99%</td>
</tr>
<tr>
<td>Enzyme Immunoassay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Urine</td>
<td>53%</td>
<td>99-100%</td>
</tr>
<tr>
<td>Male Urethra</td>
<td>53-76%</td>
<td>95%</td>
</tr>
<tr>
<td>Hybridization (Pace2) (urethral swab)</td>
<td>65-83%</td>
<td>99%</td>
</tr>
<tr>
<td>Polymerase Chain Reaction (AMPLICOR/COBAS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Urine</td>
<td>86.5-92.0%</td>
<td>91.9-95.7%</td>
</tr>
<tr>
<td>Male Urethral Swab</td>
<td>95.7-98.7%</td>
<td>95.2-97.7%</td>
</tr>
<tr>
<td>Strand Displacement Amplification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Urine</td>
<td>94.5%</td>
<td>91.4%</td>
</tr>
<tr>
<td>Male Urethral Swab</td>
<td>94.6%</td>
<td>94.2%</td>
</tr>
<tr>
<td>Transcriptional Mediated Amplification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combo 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Urine</td>
<td>97.0%</td>
<td>99.1%</td>
</tr>
<tr>
<td>Male Urethral Swab</td>
<td>95.2%</td>
<td>98.2%</td>
</tr>
<tr>
<td>APTIMA CT</td>
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<td></td>
</tr>
<tr>
<td>Male Urine</td>
<td>96.2%</td>
<td>98.1%</td>
</tr>
<tr>
<td>Male Urethral Swab</td>
<td>97.5%</td>
<td>96.1%</td>
</tr>
</tbody>
</table>

*Synopsis compared to infected patient status; package inserts, clinical trials, published papers.

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Special thanks to Charlotte Gaydos, DrPh, International Union against Sexually Transmitted Infections (IUSTI), and The Johns Hopkins University for writing this brief. Information presented is adapted from the article “Laboratory Aspects of Screening Men for Chlamydia trachomatis in the New Millennium” by Gaydos CA, Ferrero DV, Papp J., published in Sex Transm Dis 35(11 suppl): S44-50, 2008.
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