

# Recommendations For the Diagnosis of *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, Including Extra-Genital Sites

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**CHLAMYDIA TRACHOMATIS (CT) AND *Neisseria gonorrhoeae* (NG)** are the two most common reportable sexually transmitted infections (STIs) in the United States.<sup>1</sup> Adolescent girls (15 to 19 years of age) and young women (20 to 24 years of age) are at highest risk for these infections.<sup>2</sup> This likely reflects a combination of factors, including biological differences that place females at greater risk for STIs than males, as well as higher screening rates among young women. Similarly, **men who have sex with men (MSM)** are at increased risk for STIs including chlamydia and gonorrhea due to higher rates of unsafe sexual behaviors. Clinicians should be aware of current screening recommendations and diagnostic methods for detection of gonorrhea and chlamydia in genital as well as extra-genital sites to address this prevailing epidemic, particularly among younger women and MSM.

## EPIDEMIOLOGY IN RHODE ISLAND

The surveillance data on chlamydia and gonorrhea in Rhode Island are available through 2010.<sup>3</sup> Chlamydia is by far the most commonly reported STI in Rhode Island with a total of 3,480 cases (336 per 100,000 people; 2,478 females and 1,002 males) reported in 2010; this number is unchanged over the last five years. In contrast, reported cases of gonorrhea have decreased from 508 cases in 2006 (rate of 48.0 cases per 100,000) to 291 cases in 2010 (rate of 28.1 cases per 100,000), with rates unchanged since 2008. Females comprise 42% (121/291) of gonorrhea cases, compared to 71% of chlamydia cases (2,478/3,480). However, for both infections, rates are highest in 15 to 24 year olds among both males and females. By race and ethnicity, African-Americans are most disproportionately affected followed by Hispanics and non-Hispanic whites in Rhode Island.

## CLINICAL PRESENTATION

Over 50% of women with chlamydia infection are asymptomatic. The most common site of infection is the urogenital tract and, when symptomatic, usually manifests as cervicitis with mucoid vaginal discharge, bleeding, and dyspareunia. Ascending infection can present with right upper quadrant pain and/or pleuritic pain consistent with perihepatitis (Fitz-Hugh Curtis syndrome). Upper genital tract infection, otherwise known as **pelvic inflammatory disease (PID)**, can present with vaginal discharge, dysuria, lower abdominal pain, and systemic symptoms such as fever. Chlamydia-induced PID carries a higher rate of infertility for women of child bearing age than gonorrhea. In pregnant women, undiagnosed infection can cause life threatening ectopic pregnancy, premature rupture of membranes, as well as neonatal conjunctivitis and/or pneumonia.

## Pregnant women should be screened for all STIs.

As with their female counterparts, asymptomatic chlamydial infection is common among males, causing health care providers to frequently rely on screening tests in order to detect infection. Urogenital infection in men affecting the lower genital tract can present as a non-gonococcal urethritis or epididymitis. Symptoms include dysuria and urethral mucopurulent discharge. Identification of infection in men is of importance as they can serve as a reservoir for infection in women.

Gonorrhea infections in females most commonly involve the cervix. Females are asymptomatic approximately half of the time. Typical symptoms include a mucopurulent discharge, and the exam

may demonstrate friable cervical mucosa. Other symptoms may include abdominal pain, dyspareunia, dysuria, pruritus, PID, or perihepatitis. The main impetus for the early diagnosis and treatment of gonorrhea is to prevent the development of PID. Among women, gonococcal infections might not produce recognizable symptoms until complications such as PID have occurred. PID occurs in up to 40% of women with cervical infection, and can result in tubal scarring that can lead to ectopic pregnancy or infertility.

In men, gonorrhea is asymptomatic only 10% of the time.<sup>4</sup> The majority of urethral infections caused by *N. gonorrhoeae* among men produce symptoms that cause them to seek curative treatment soon enough to prevent serious sequelae, but treatment might not be soon enough to prevent transmission to others.<sup>1</sup> Gonorrhea usually causes urethritis including dysuria and a purulent penile discharge. Furthermore, gonorrhea usually does not cause other invasive disease in men, although it may progress to cause local abscesses, prostatitis, or epididymitis.

## DIAGNOSTIC CONSIDERATIONS

The current standard laboratory test for detection of urogenital chlamydia and gonorrhea is a **nucleic acid amplification test (NAAT)**.<sup>5</sup> These tests are extremely sensitive and specific for detection of both organisms (>90%) using a noninvasive urine sample, thus reducing the need for pelvic examination or urethral sampling. These tests are FDA-cleared for the diagnosis of gonorrhea and chlamydia urogenital infections. Current guidelines<sup>1,6</sup> recommend screening all women age 25 years or younger for chlamydia and gonorrhea, as well as women older than 25 who have a history of STIs, new or multiple sex partners, or exchange sex for drugs or money. Pregnant women should be screened for all STIs. Men with risk factors for infection should be screened

**Table 1: Anatomic site specific *Chlamydia trachomatis* and *Neisseria gonorrhoea* infections as determined by nucleic acid amplification testing (NAAT).\***

Specimen Site	Total tested CT	Number positive	% positive of total	Total tested GC	Number positive	% positive of total
Urine	19449	1111	5.7	31201	159	0.9
Pharyngeal	291	5	1.7	320	11	3.4
Rectal	178	21	11.8	188	10	5.3
<b>Total tested</b>	<b>32589</b>			<b>31201</b>		

\*Diagnostic testing was with the Gen-Probe APTIMA Combo 2 assay over a time period of 17 months during 2011-2012. Validation of pharyngeal and rectal sites was performed by the Microbiology laboratory at Lifespan Laboratories.

CT=Chlamydia; GC=Gonorrhoea.

including gay, bisexual, transgender, or other MSM. Screening for STIs including gonorrhoea and chlamydia should occur for MSM on an annual basis, and more frequently if multiple or anonymous partners or intravenous drug use is involved (as often as three to six months).

Clinicians should be aware of extra-genital mucosal sites of infection for both gonorrhoea and chlamydia, specifically the oropharynx and rectum.<sup>7</sup> Anorectal gonorrhoea infection in women is usually asymptomatic. Symptoms of proctitis such as anal pruritus, discharge, and pain on defecation are seen in a minority of patients (3%).<sup>8</sup> For women, many infections occur in the setting of urethral, vaginal, or cervical infection (46%). However, anorectal infection may be found solely in the rectum (4-6%).<sup>8,9</sup> It is unclear whether anal infection is due to anal intercourse or due to autoinfection from a urogenital source. Gonorrhoeal infection of the oropharynx is also common in women, occurring in 2-6% of individuals.<sup>10,11</sup>

Among men and especially MSM, extra-genital sites of infection are common, and MSM are a high-risk group in which rates of STIs are increasing.<sup>12,13</sup> Anorectal gonorrhoea in men, compared to women, may be the only site of infection in up to 40%. Symptoms may include a purulent discharge, tenesmus, pain, and/or constipation. Infection may be due to gonorrhoea alone, or may be in conjunction with other STIs including herpes simplex, chlamydia, and/or syphilis. Oropharyngeal infections are

usually asymptomatic but can present with pharyngitis. Surveillance studies have suggested that the pharynx is the most common site of gonorrhoea infection among MSM ranging from 3 to 15%.<sup>14,15</sup> Interestingly, oropharyngeal gonorrhoea is self-limiting with resolution of infection in the majority of cases. This may suggest that oropharyngeal treatment is unnecessary; however, the infection may be passed to the genital tract causing more invasive or disseminated disease.

Although no NAAT tests are FDA-cleared for use with rectal or oropharyngeal specimens for the diagnosis of gonorrhoea and chlamydia, some laboratories have validated these specimen sites for clinical use.<sup>13</sup> Cultures from these sites yield poor sensitivity at less than 50%. Over a 17 month period during 2011-2012, Lifespan laboratories tested a total of 32,589 and 31,201 samples for chlamydia and gonorrhoea, respectively. (Table 1) Chlamydia was positive in 5.7% (111/19449) of urine specimens, (the most common specimen received for testing of CT and GC), 1.7% (5/291) of pharyngeal, and 11.8% (21/178) of rectal specimens. Gonorrhoea was positive in 0.9% (159/31,201) of urine, 3.4% (11/320) of pharyngeal, and 5.3% (10/188) of rectal specimens. The high rates of oropharyngeal and rectal infections with both chlamydia and gonorrhoea are consistent with previous studies demonstrating significant infection in patients selected for screening at these anatomic sites secondary to identification of risk factors.

## CONCLUSION

Aggressive STI screening of the oropharynx, rectum, and urethra should be performed in individuals who perform sexual practices involving these sites, especially in MSM. Comprehensive STI screening for chlamydia and gonorrhoea should include a NAAT of the urine, rectum (for men and women who have receptive anal intercourse), and the pharynx (for men with gonorrhoea and women who have receptive oral intercourse). Recognition and diagnosis of chlamydia and gonorrhoea is essential to decrease the morbidity associated with these diseases, as well as prevent the transmission of other STIs including HIV.<sup>16,17</sup>

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