Gonorrhea screening

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Policy contains: Gonorrhea; Neisseria gonorrhea; pelvic inflammatory disease; sexually transmitted disease.

This policy is a Sandhills Center Clinical Coverage Policy adopted from AmeriHealth Caritas of North Carolina. These clinical policies are used to assist with making coverage determinations. Sandhills Center's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Sandhills Center when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Sandhills Center clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Sandhills Center's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Sandhills Center will update its clinical policies as necessary. Sandhills Center clinical policies are not guarantees of payment.

Coverage policy

Screening for *Neisseria gonorrhoeae* (*N. gonorrhoeae*) of asymptomatic members is clinically proven and, therefore, medically necessary when any of the following criteria are met (Lefevre, 2014; U.S. Centers for Disease Control and Prevention, 2015; U.S. Preventive Services Task Force, 2014, 2016):

1. Women under age 25 who are sexually active.
    a. Retest three months after treatment.
2. Women over age 25 who are at increased risk (i.e. they have a new partner, or their sexual partner has multiple partners, or they have multiple partners).
    a. Retest three months after treatment.
3. Pregnant women, during first prenatal visit and in the third trimester.
    a. Retest three months after treatment.
4. All women who are diagnosed with gonococcal Pelvic Inflammatory Disease:
    a. Retest three months after completing treatment.
5. Sexually active men having sex with men, with no other risk factors (at least annually), at sites of contact (urethra, rectum, pharynx), regardless of condom use.
    a. Men in this category should be tested every three to six months if they are at increased risk (i.e. they or their sexual partners have multiple partners).
6. Human immunodeficiency virus-positive and sexually active members at first human immunodeficiency virus assessment, and at least annually thereafter.

a. Depending on individual risk behaviors and the local epidemic, it may be necessary to screen more frequently.

7. For the above categories 1 through 6, screening of extra-genital sites should be based on self-reported risk.

The following tests are clinically proven and, therefore, medically necessary for detection of *N. gonorrhoeae* in asymptomatic members (U.S. Centers for Disease Control and Prevention, 2014):

- Nucleic acid amplification testing when performed using a test cleared by the U.S. Food and Drug Administration for use on urogenital sites, including male and female urine; clinician-collected endocervical, vaginal, and male urethral specimens; and self-collected vaginal specimens in clinical settings. See list of approved or cleared tests for *N. gonorrhoeae* detection: https://www.fda.gov/medical-devices/vitro-diagnostics/nucleic-acid-based-tests.
- Culture for *N. gonorrhoeae*:
    - In cases of sexual assault in boys and extragenital site exposure in girls.
    - Specimens from rectal, oropharyngeal, or conjunctival sites.

Limitations

All other screening tests for *N. gonorrhoeae* are considered investigational/not clinically proven, and, therefore, not medically necessary, including, but not limited to (U.S. Centers for Disease Control and Prevention, 2014):

- Nucleic acid amplification testing to assess the efficacy of antibiotic therapy or monitor for antimicrobial resistance.
- Routine repeat testing of nucleic acid amplification test-positive genital tract specimens, because the practice does not improve the positive predictive value of the test.
    - Repeat testing may be indicated when there is a clinical or laboratory reason to question an initial test result.
- Gram stain for ruling out infection in asymptomatic men.
- Gram stains of endocervical specimens, pharyngeal, or rectal specimens in women.
- Enzyme immunoassays.
- Nucleic acid probe tests.
- Nucleic acid transformation tests.
- Serologic tests that detect a systemic immune response to infection because of the lack of precision for the detection of an active infection.
- Home-based self-specimen collection (Rönn, 2019).

Alternative covered services

No alternative covered services were identified during the writing of this policy.

Background

Gonorrhea is a sexually transmitted disease caused by infection with the *N. gonorrhoeae* bacterium (U.S. Centers for Disease Control and Prevention, 2018). It infects the mucous membranes of the reproductive tract and can also infect the mucous membranes of the mouth, throat, eyes, and rectum. Gonorrhea can also be spread perinatally from mother to baby during childbirth.

Any sexually active person can be infected with gonorrhea (U.S. Centers for Disease Control and Prevention, 2018). In 2018, there were 583,405 cases of gonorrhea, making it the second most common notifiable condition in the United States. Rates of reported gonorrhea have increased 82.6% since the historic low in 2009. The highest reported rates of infection are among sexually active teenagers, young adults, and African Americans.

Many men and most women with gonorrhea are asymptomatic (U.S. Centers for Disease Control and Prevention, 2019). Left untreated, gonorrhea can spread and cause serious and permanent health problems in both women and men, women and their newborns. Untreated gonorrhea can increase a person's risk of acquiring or transmitting human immunodeficiency virus and, if spread to the blood, can cause disseminated gonococcal infection, which can be life threatening. In newborns, vertical transmission of gonorrhea can lead to gonococcal ophthalmia neonatorum (U.S. Preventive Services Task Force, 2019).

Males often experience urethritis and painful urination within a few days after exposure, generally prompting them to seek medical treatment, but often not in time to prevent transmission to their sexual partners (U.S. Centers for Disease Control and Prevention, 2019). Cervical, oral, and rectal infections tend to be asymptomatic or to result in mild symptoms, making identification and treatment more challenging. It is unknown whether untreated reservoirs of infection in these tissues are contributing to the current increase in multi-drug resistant gonorrhea.

Adolescent or adult ocular infection is likely to have a unilateral presentation and patients may initially be treated for presumptive bacterial conjunctivitis before receipt of laboratory results (Sadowska-Przytocka, 2016). Infants are prophylactically treated at birth to prevent ocular infection, in case gonorrhea bacteria are present in the vagina (U.S. Preventive Services Task Force, 2019).

Drug resistance presents a major and ongoing threat to treatment effectiveness. The genetic material of gonorrhea bacteria has an ability both to mutate and to acquire resistant material from other bacteria (Wetzler, 2016). As a result, antimicrobial resistance patterns are shifting recommendations based on gonococcal susceptibility. Dual treatment with ceftriaxone and azithromycin is the recommended treatment for gonorrhea (U.S. Centers for Disease Control and Prevention, 2019).

Reinfection after treatment is common, and inoculation and treatment do not confer immunity (U.S. Centers for Disease Control and Prevention, 2019). Efforts to prevent reinfection and limit further transmission include refraining from sexual contact during treatment and treating sexual partners from the past 60 days. Sexual partners may be referred for free treatment to local public health authorities.

Many laboratory test options can be used to detect gonorrhea, although some might not be recommended for routine use based on inferior performance. Direct detection options of *N. gonorrhoeae* include nucleic acid amplification testing or gonorrheal culture, depending on the specimen type (U.S. Centers for Disease Control and Prevention, 2019).

Nucleic acid amplification tests are designed to amplify and detect nucleic acid sequences that are specific for the organism being detected. These tests do not require viable organisms and can detect a positive signal from as little as a single copy of the target deoxyribonucleic acid or ribonucleic acid, yielding high sensitivity. This high sensitivity has allowed the use of less invasively collected specimens such as first catch urines and vaginal swabs and facilitates screening. Several nucleic acid amplification tests have been approved for detection of *N. gonorrhoeae* (U.S. Food and Drug Administration, 2020).

Findings

Testing for gonorrhea is recommended for patients presenting with genital symptoms of gonorrhea, and screening is indicated for asymptomatic individuals at risk for infection. Early detection of *N. gonorrhoeae* infection through screening results in a moderate magnitude of benefit based on the large proportion of cases that are asymptomatic, the high morbidity associated with untreated infections, and the effectiveness of antibiotic treatment to reduce infections (Lefevre, 2014).

The U.S. Preventive Services Task Force (Lefevre, 2014) recommend gonorrhea screening in sexually active females aged 24 years or younger and in older women who are at increased risk for infection, including pregnant

women. Screening of non-urogenital sites should be risk-based and based on patient self-reported behavior. There are currently no recommendations for screening women at extragenital sites. A two-year prospective study in two Baltimore public sexually transmitted disease clinics found an extragenital gonococcal prevalence of 2.4% among women who reported extragenital exposure (Trebach, 2015). Gonorrhea and chlamydia have the same risk factors and similar symptoms, but require different treatment. Therefore, patients are usually tested for both.

Neither organization recommends routine gonorrhea screening in men at low risk of infection due to insufficient evidence examining the balance of benefits and harms in this population. However, because extragenital infections are common in men who have sex with men and most of those infections are asymptomatic, both organizations recommend routine (annual) laboratory screening of genital and extragenital sites for all sexually active men who have sex with men at risk for infection.

The Centers for Disease Control and Prevention (2021) recommends nucleic acid amplification tests that are cleared by the Food and Drug Administration for detection of genital tract infections caused by *N. gonorrhoeae* infections in men and women with and without symptoms. The optimal specimen types are vaginal swabs from women and first catch urine from men. Older nonculture tests and non-nucleic acid amplification tests have inferior sensitivity and specificity characteristics and no longer are recommended. *N. gonorrhoeae* culture capacity is still needed for evaluating suspected cases of treatment failure and monitoring antimicrobial susceptibility, and may be needed in instances of child sexual assault in boys and extragenital infections in girls.

Although nucleic acid amplification tests have not been cleared by the U.S. Food and Drug Administration for the detection of rectal and oropharyngeal infections caused by *N. gonorrhoeae,* the Centers for Disease Control and Prevention (2021) recommends these tests for extragenital infections based on increased sensitivity and ease of specimen transport and processing. Laboratories must establish performance specifications when using these specimens to meet regulatory requirements, as applicable, prior to reporting results for patient management.

Culture for *N. gonorrhoeae* from genital sites is inexpensive to perform and is specific and sensitive when handled properly, but it is suboptimal for routine diagnostics because of stringent collection, transport requirements, and lengthy processing time (Centers for Disease Control and Prevention, 2014). The primary advantage of *N. gonorrhoeae* culture is the ability to characterize the isolate further by antimicrobial susceptibly testing and genetic analysis if necessary.

The Centers for Disease Control and Prevention (2014) does not recommend the following tests based on inferior test performance for screening for *N. gonorrhoeae*:

- Routine repeat testing of nucleic acid amplification test-positive genital tract specimens, because the practice does not improve the positive predictive value of the test.
- Enzyme immunoassays.
- Nucleic acid probe tests.
- Nucleic acid transformation tests.
- Serologic tests that detect a systemic immune response to infection because of the lack of precision for the detection of an active infection.
- Gram stain of *N. gonorrhoeae* in urethral specimens of asymptomatic men.

A scoping systematic review (Nelson, 2014) produced for the U.S. Preventive Services Task Force concluded that various types of U.S. Food and Drug Administration-cleared nucleic acid amplification tests are highly accurate in diagnosing gonorrhea in asymptomatic persons regardless of specimen, anatomical site, or test. Their high sensitivity has surpassed that of culture as the current gold standard. Some nucleic acid amplification tests have been cleared for use on clinician- and self-collected (in clinical settings) vaginal

specimens. The authors supported additional studies using self-collected specimens at various anatomical sites to assess diagnostic performance and acceptability.

In cases of suspected or documented treatment failure, providers should perform both culture and antimicrobial susceptibility testing. With gonorrheae's strong nutritional and growth requirements, optimal recovery rates are acquired when the specimens are inoculated directly and when the growth medium is properly inoculated in an increased carbon dioxide environment. A Gram stain of urethral discharge or secretions that have polymorphonuclear leukocytes with intracellular gram-negative diplococci can be considered diagnostic for infection with N. gonorrhoeae among symptomatic men because of high sensitivity (95%) and specificity (>99%). However, because of the lower sensitivity (>95%), a negative Gram stain should not be considered sufficient for ruling out infection among asymptomatic men. In addition, gram stain of endocervical, pharyngeal, and rectal specimens are not recommended due to the same considerations (U.S. Centers for Disease control and Prevention, 2021).

In populations without the option of clinic-based testing, or who refuse a clinical exam or may not go for testing, home-based self-specimen collection for gonorrhea through use of a vaginal swab for women or a urine sample for men has the potential of reaching individuals for testing, diagnosis, and treatment of infection in urogenital tracts. While one meta-analysis found that the sensitivity and specificity of home tests were acceptable but noted that there are no guidelines for collection (Lunny, 2015), a systematic review found that high heterogeneity prohibiting pooling of the samples, and concluded that the matter needs further study (Farjardo-Bernal, 2015).

In 2018, the policy ID changed from 13.01.09 to CCP.1344. We did not identify any additional publications.

In 2019, we added one new guideline, and updated two U.S. Centers for Disease Control publications. We note that the Centers for Disease Control plan an update of the report "Antibiotic resistance threats in the United States, 2013," expected to be published in 2019.

In 2020, we added an updated American College of Obstetricians and Gynecologists' Committee Opinion (2020) on the initial reproductive health visit, which recommends annual screening for gonorrhea if the patient is sexually active. We added a systematic review (Rönn, 2019) of six studies comparing the sensitivity of nucleic acid amplification tests for detecting gonorrhea infection in vaginal specimens to that of cervical or urine specimens. Variable methodology prevented statistical pooling of summary estimates. Testing performance was similar among all three specimen types (vaginal 64% to 100%, cervical 85% to 100%, urine 67% to 94%). As vaginal samples have a higher acceptability and lower cost, the results suggest they may be suitable alternatives to traditionally used specimens, but their role in population screening requires further study. The new findings are consistent with the current policy.

In 2021, we confirmed that the current testing is still validated and added the most current U.S. Centers for Disease Control and Prevention guidelines.

The policy was reorganized to align with U.S. Centers for Disease Control and Prevention and U.S. Preventive Services Task Force recommendations for asymptomatic populations and testing. We added a list of tests considered investigational to the limitations section.

References

On September 15, 2021, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "Gonorrhea" (MeSH), "gonorrhea screening," "test," and "diagnosis." We included the best available evidence according to established evidence hierarchies

(typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

10/2017: initial review date and clinical policy effective date: 12/2017

12/2018: Policy references updated. Policy ID changed.

12/2019: Policy references updated.

12/2020: Policy references updated. Policy coverage amended.

12/2021: Policy references updated.