Clinical Policy Title: Strep testing

Clinical Policy Number: CCP.1345

Effective Date: December 1, 2017
Initial Review Date: October 19, 2017
Most Recent Review Date: November 6, 2018
Next Review Date: November 2019

Related policies:

CCP.1330  Seasonal influenza testing

ABOUT THIS POLICY: Prestige Health Choice has developed clinical policies to assist with making coverage determinations. Prestige Health Choice’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 Prestige Health Choice 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. Prestige Health Choice’s 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. Prestige Health Choice’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Prestige Health Choice will update its clinical policies as necessary. Prestige Health Choice’s clinical policies are not guarantees of payment.

Coverage policy

Prestige Health Choice considers the use of Streptococcus group A rapid antigen testing and bacterial culture to be clinically proven and, therefore, medically necessary when the following criteria are met (Harris, 2016; Shulman, 2012; Pelucchi, 2012):

- Acute pharyngitis characterized by one or more of the following symptoms and signs:
  - Painful swallowing
  - Reddened, swollen tonsils with or without exudate
  - Palpable, tender lymph nodes in the neck region
  - Diffuse, erythematous rash.
- The test results will directly impact management (i.e., as a result of the test, effective treatment may be offered that will alter the course of disease or outcomes).
- The test is an analytically and clinically valid test (i.e., supported by peer-reviewed published research).
Limitations:

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website may be accessed at http://ahca.myflorida.com/Medicaid/.

Routine use of back-up throat cultures for those with a negative rapid antigen test is not medically necessary for adults in usual circumstances, because of the low incidence of *Streptococcus* group A pharyngitis in adults (Pelucchi, 2012).

Anti-streptococcal antibody titers are not medically necessary in the routine diagnosis of acute pharyngitis.

All other uses of *Streptococcus* group A testing are not medically necessary.

**Alternative covered services:**

- Routine patient evaluation and management by a network healthcare provider.
- Seasonal influenza testing as outlined in CCP.1330.

**Background**

Group A Streptococcus (group A strep) is a bacterium that can cause multiple infections. Group A strep are found in the nose and are easily transferred between humans. Infection can occur through exposure to droplets after coughing or sneezing, by breathing affected air, touching affected surfaces, or sharing affected food or liquids. The latency between exposure to and manifestation of group A strep is typically 2-5 days.

Streptococcus group A infection typically presents as acute pharyngitis characterized by painful swallowing and fever. Physical signs include reddened, swollen tonsils with or without exudate, palpable tender lymph nodes in the neck region, tiny red spots on the soft or hard palate, and swollen lymph nodes in the front of the neck. Sometimes scarlet fever, headache, stomach pain, nausea, or vomiting may be present. Cough, runny nose, hoarseness, and conjunctivitis/pink eye (https://www.cdc.gov/features/conjunctivitis/) are not symptoms of strep throat (https://www.cdc.gov/groupastrep/diseases-public/scarlet-fever.html) (Centers for Disease Control and Prevention, 2018a). Strep throat is most common in children and some adults. In developed countries, 15 percent of school-age children and 4 - 10 percent of adults will have a Streptococcus group A pharyngitis episode every year (Shulman, 2012). Group A strep accounts for 20 to 40 percent of pharyngitis cases in children, with most of the rest caused by viruses (Cohen, 2016).
Crowded conditions, including schools and day care centers, increase the risk of developing group A strep (Centers for Disease Control and Prevention, 2018a). An estimated 11,000 to 13,000 annual cases of invasive group A strep disease, like cellulitis with blood infection, pneumonia, and necrotizing fasciitis, occur in the U.S., and 1,100 to 1,600 people die due to invasive group A strep disease (Centers for Disease Control and Prevention, 2018b).

No individual or group of symptoms can accurately predict the presence or absence of Streptococcus, according to a systematic review of 43 articles. In children with sore throats, the following symptoms were moderately useful in identifying those with streptococcal pharyngitis; presence of a scarlatiniform rash, palatal petechiae, pharyngeal exudate, vomiting, and tender cervical nodes (Shaikh, 2010).

Even though the majority of sore throats are caused by viruses, they should be checked for presence of strep A infection. When strep throat is suspected, a positive streptococcus test is needed prior to initiation of antibiotics. If a rapid strep test (swabbing the throat and quickly obtaining test results) is negative but strep throat is still suspected, a throat culture swab to confirm a strep infection is required in children and teens, as they are at risk of developing rheumatic fever (unlike adults) if group A strep is present but not treated. Another (rare) adverse outcome of strep A infection is post-streptococcal glomerulonephritis (Centers for Disease Control and Prevention, 2018a).

The traditional throat culture test to diagnose Streptococcus group A infection takes two to three days for results to be returned from labs. The rapid antigen test, in which the throat and tonsils are swabbed to collect bacteria, can produce results in 10 to 15 minutes, improving the chances for effective antimicrobial therapy to commence.

It is possible for a person to develop strep throat multiple times more than once in a lifetime. Without a vaccine to prevent strep throat, universal precautions should be used to limit the spread of the disease.

**Searches**

Prestige Health Choice searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services.

We conducted searches on September 11, 2018. Search terms were: “rapid antigen testing,” and "Streptococcus group A.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

The Infectious Diseases Society of America has updated its guidelines on the diagnosis and treatment of *Streptococcus* group A infection (Shulman, 2012). Within the target range (5 - 15 years of age) *Streptococcus* group A infection must be differentiated from viral pharyngitis. Diagnosis should be confirmed using a rapid antigen test or swab throat culture. A positive result on rapid antigen detection testing is diagnostic for group A streptococcal pharyngitis.

Harris (2016) writing for the American College of Physicians and the Centers for Disease Control and Prevention advised that clinicians should test patients with symptoms suggestive of group A streptococcal pharyngitis (i.e., persistent fevers, anterior cervical adenitis, and tonsillopharyngeal exudates or other appropriate combination of symptoms) by rapid antigen detection test and/or culture for *Streptococcus* group A. He also noted that antibiotics are often inappropriately prescribed for patients without chronic lung disease or immunocompromising conditions, and clinicians should treat patients with antibiotics only if they have confirmed streptococcal pharyngitis.

A meta-analysis of 29 articles revealed that 37 percent of children of all ages who present to a health professional with a sore throat, have group A strep. Those younger than five years had a lower prevalence (24 percent). Prevalence of group A strep carriage among well children with no signs or symptoms of pharyngitis was 12 percent (Shaikh, 2010).

An early systematic review/meta-analysis (24 studies) analyzed efficacy of rapid antigen tests for group A strep. Overall sensitivity was 85 percent (range between 65.6 and 96.4), with overall specificity of 96 percent 68.7 to 99.3, which authors classified as a “good diagnostic performance” (Ruiz-Aragón, 2010).

A prospective trial (Cohen, 2015) identified several clinical prediction rules for diagnosing group A streptococcal infection in French children who presented with pharyngitis during a one-year period (2010-2011). Definitive diagnosis was made by using two throat swabs: one obtained for a rapid antigen detection test (StreptAtest, Dectrapharm) and one obtained for culture (reference standard). Sensitivity and specificity of rules-based selective testing strategies ranged from 66 to 94 percent and from 40 to 88 percent , respectively. Use of rapid antigen detection testing following the clinical prediction rule ranged from 24 to 86 percent. None of the rules-based selective testing strategies achieved the diagnostic accuracy target (sensitivity and specificity > 85 percent).

A Cochrane review of 98 studies (n=101,121) found the sensitivity of rapid antigen detection tests to be 85.6 percent, comparable to those of enzyme immunoassay and optical immunoassay tests (85.4 and 86.2 percent). Rapid testing results had a specificity of 95.4 percent. Thus, among 100 children with
group A strep, 86 would be properly diagnosed and treated using only the rapid antigen detection test, which authors describe as “high enough to ensure against unnecessary use of antibiotics” (Cohen, 2016).

A meta-analysis (Lean, 2014) of 48 studies compared sensitivity and specificity of diagnosing *Streptococcus* group A pharyngitis using either optical immunoassay (19 studies) or molecular (six studies) techniques. Molecular techniques were found to be superior to optical immunoassay in sensitivity (0.92 versus 0.86) and specificity (0.99 versus 0.94). In addition, findings from studies of the molecular technique varied less than did findings from the optical immunoassay studies.

The European Society for Clinical Microbiology and Infectious Diseases (Pelucchi, 2012) established the Sore Throat Guideline Group to write an updated guideline to diagnose and treat patients with acute sore throat. A symptom score was used to screen for individuals likely to test positive on rapid antigen test. The authors concluded that throat culture is not necessary after a negative rapid antigen test for the diagnosis of group A streptococci. Furthermore, antibiotics should not be used in patients with less severe presentation of sore throat in deference to the possibility of side effects, the effect of antibiotics on microbiota, increased antibacterial resistance, medicalization and costs. If antibiotics are indicated, penicillin V, twice or three times daily for 10 days is recommended. At the present, there is not enough evidence that indicates shorter treatment length is appropriate.

A meta-analysis of 285 studies of Group A streptococcus pharyngitis observed a prevalence of 24.1 percent in clinical settings using passive recruitment methods, and 10.0 percent in sore throat management programs using active recruitment, The condition was more prevalent in high-income countries than in low/middle income countries (24.3 versus 17.6 percent). In clinical settings, 10 percent of children with a sore throat who were swabbed have serologically-confirmed group A strep pharyngitis, rising to 50-60 percent when the child is culture-positive (Oliver, 2018).

A systematic review/meta-analysis of 59 studies (n=55,766) compared the ability of various rapid antigen strep A tests to diagnosis pharyngitis. For children and adults, sensitivity was 88 percent (n=10,325) and 91 percent (n=1216) for higher-quality immunochromatographic tests, and specificity was 86 and 93 percent. Authors conclude that the data show immunochromatographic methods appear to be effective in diagnosing group A strep pharyngitis in adults but not children (Stewart, 2014).

The Centor score (cough absent, exudate, notes, temperature (fever), young or old modifier is a set of criteria governing the probability that pharyngitis is streptococcal. Scores are from 1 to 5, with high higher scores representing higher probability and greater need for rapid testing. A systematic review of 21 studies (n=4,839) showed that individual signs and symptoms generate only small shifts in post-test probability. The Centor score has reasonable (82 percent) specificity, and thus can enhance appropriate antibiotic prescribing, but should be used cautiously in low prevalence settings (Aalbers, 2011).

Rojas-Ramírez (2017) concluded that a shortened antibiotic regimen is probably similar, or with minimal differences, to a longer course, and might not make any difference regarding complications related to *Streptococcus* group A infection.
**Policy updates:**

A total of two guidelines/other and seven peer-reviewed references were added to this policy in September 2018.

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oliver (2018)</td>
<td></td>
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<tr>
<td>Preventing unnecessary</td>
<td>Key points:</td>
</tr>
<tr>
<td>antibiotic use in group A</td>
<td>• A meta-analysis of 285 studies</td>
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<tr>
<td>streptococcus carriers</td>
<td>of Group A streptococcus pharyngitis.</td>
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<tr>
<td>with acute viral infections</td>
<td>• The prevalence of group A strep was 24.1 percent (%) (95% Confidence Interval (CI) 22.6 to 25.6%) in clinical settings using passive recruitment methods, and 10.0% (CI 8.1 – 12.4%) in sore throat management programs using active recruitment.</td>
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<td></td>
<td>• Prevalence of group A strep was greater in high-income countries than in low/middle income countries (24.3% (CI 22.6 – 26.1%) versus 17.6% (CI 14.9 – 20.7%).)</td>
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<td>• In clinical settings, 10% of children swabbed with a sore throat have serologically-confirmed group A strep pharyngitis; which rises to 50-60% when the child is culture-positive.</td>
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<td></td>
<td>• The prevalence of serologically-confirmed group A strep pharyngitis was 10.3% (CI 6.6-15.7%) in children from high-income countries and their asymptomatic GAS carriage prevalence was 10.5% (CI 8.4-12.9%). A lower carriage prevalence of 5.9% was detected in children from low/middle income countries (CI 4.3-8.1%).</td>
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<tr>
<td>Cohen (2016)</td>
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<tr>
<td>Determining the accuracy</td>
<td>Key points:</td>
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<tr>
<td>of various rapid antigen</td>
<td>• A Cochrane review of 98 studies (n=101,121).</td>
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<tr>
<td>detection tests</td>
<td>• Over half (n=58,244) of subjects underwent both rapid antigen detection tests and throat culture; median prevalence of participants with group A strep was 29.5%.</td>
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<td>• Rapid antigen detection tested subjects had a sensitivity of 85.6%, similar to those of enzyme immunooassay and optical immunoassay tests (85.4 % and 86.2%).</td>
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<tr>
<td>Harris (2016)</td>
<td></td>
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<tr>
<td>Appropriate antibiotic use</td>
<td>Key points:</td>
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<tr>
<td>for acute respiratory tract</td>
<td>• Advocated that clinicians test patients with symptoms suggestive of group A streptococcal pharyngitis by rapid antigen detection test and/or culture for Streptococcus group A.</td>
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<tr>
<td>infection in adults</td>
<td>• Also noted that antibiotics are often inappropriately prescribed for patients without chronic lung disease or immunocompromising conditions</td>
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<td></td>
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<tr>
<td>Cohen (2015)</td>
<td><strong>Key points:</strong></td>
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</table>
| Selective testing strategies for diagnosing group A streptococcal infection in children with pharyngitis | - A prospective trial identified several clinical prediction rules for diagnosing group A streptococcal infection in French children who presented with pharyngitis during a one-year period (2010-2011).  
- Definitive diagnosis was made by using two throat swabs: one obtained for a rapid antigen detection test (StreptAtest, Dectrapharm) and one obtained for culture (reference standard).  
- Sensitivity and specificity of rules-based selective testing strategies ranged from 66 percent (%) (95% confidence interval [CI] 61–72) to 94% (95% CI 92–97) and from 40% (95% CI 35–45) to 88% (95% CI 85–91), respectively.  
- Use of rapid antigen detection testing following the clinical prediction rule ranged from 24% (95% CI 21–27) to 86% (95% CI 84–89).  
- None of the rules-based selective testing strategies achieved the diagnostic accuracy target (sensitivity and specificity > 85 percent). |
| Lean (2014)       | **Key points:**                                                                                                                                                                                                                   |
| Rapid diagnostic tests for group A streptococcal pharyngitis: a meta-analysis | - Meta-analysis compared sensitivity and specificity of optical immunoassay (19 studies) versus molecular (six studies) techniques.  
- Molecular techniques were found to be superior to optical immunoassay in sensitivity (0.92 versus 0.86) and specificity (0.99 versus 0.94).  
- Findings from studies of the molecular technique varied less than did findings from the optical immunoassay studies. |

**References**

**Professional society guidelines/other:**


U.S. Centers for Disease Control and Prevention.  Diseases Caused by Group A Strep.  Atlanta GA: National Center for Immunization and Respiratory Diseases, Division of Bacterial Diseases, last updated


Peer-reviewed references:


**Centers for Medicare & Medicaid National Coverage Determinations:**

No National Coverage Determinations identified as of the writing of this policy.

**Local Coverage Determinations:**

No Local Coverage Determinations identified as of the writing of this policy.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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<thead>
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<th>CPT Code</th>
<th>Description</th>
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<tr>
<td>87651</td>
<td>Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, amplified probe technique</td>
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<tr>
<td>87880</td>
<td>Infectious agent antigen detection by immunoassay with direct optical observation; Streptococcus, group A</td>
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<tr>
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<tr>
<td>R59.0</td>
<td>Localized enlarged lymph nodes</td>
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<thead>
<tr>
<th>HCPCS Level II Code</th>
<th>Description</th>
<th>Comments</th>
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<tbody>
<tr>
<td>N/A</td>
<td>Not Applicable</td>
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