Evaluation and Treatment of Pharyngitis in Primary Care Practice

The Difference Between Guidelines Is Largely Academic

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Background: The guidelines from the American College of Physicians and the Infectious Diseases Society of America differ with respect to the use of clinical criteria and microbiologic testing to identify adults with pharyngitis who are likely to have group A β-hemolytic streptococci.

Methods: To measure the rate of adherence to 3 strategies, we performed a retrospective analysis of visits to Boston, Mass, area primary care clinics by adults with a diagnosis of pharyngitis (n=2097).

Results: The 4-point Centor criteria recommended by the American College of Physicians and Infectious Diseases Society of America were not predictive of streptococcal testing (results for 0, 1, 2, 3, and 4 criteria were 79%, 81%, 79%, 80%, and 74%, respectively; \( P=.63 \)) but were predictive of a positive streptococcal test (8%, 13%, 22%, 31%, and 30%, respectively; \( P<.001 \)) and of antibiotic prescribing (25%, 34%, 63%, 80%, and 89%, respectively; \( P<.001 \)). Clinicians were adherent to the American College of Physicians’ empirical strategy in 12% of visits, the American College of Physicians’ test strategy in 30% of visits, the Infectious Diseases Society of America’s strategy in 30% of visits, and adherent to none of these strategies in 66% of visits. The most common reason for nonadherence to any strategy was testing or antibiotic prescribing to patients at low risk of streptococcal pharyngitis (1076 visits; 78% of the visits in which physicians were nonadherent to any strategy), patients for whom the guidelines agree.

Conclusions: The major problem in the testing and treatment of adults with pharyngitis is not which guideline to follow, but that clinicians usually fail to follow any guideline. Interventions should focus on an area where the guidelines agree: avoiding testing and antibiotic prescribing to patients at low risk for streptococcal pharyngitis.

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Every year, patients in the United States make about 11 million visits to ambulatory practices and emergency departments that result in a diagnosis of pharyngitis. Approximately 10% of adults with pharyngitis will have group A β-hemolytic streptococci (streptococcal pharyngitis), the only common cause of pharyngitis that warrants antibiotic treatment. However, about 70% of adults with pharyngitis are treated with antibiotics in the United States. There is agreement that the antibiotic prescribing rate for adults with pharyngitis is too high, but there is open disagreement as to the optimal way to evaluate and treat adults with pharyngitis.

The American College of Physicians (ACP), the American Academy of Family Practice, and the Centers for Disease Control and Prevention recommend 2 potential strategies: (1) empirical treatment of patients who meet 3 or 4 Centor criteria (ACP empirical strategy) or (2) testing patients with 2 or 3 criteria using a rapid antigen detection test (RADT) and prescribing antibiotics to patients with a positive test or with 4 criteria (ACP test strategy).

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The Infectious Diseases Society of America (IDSA) guideline agrees with the ACP guideline that adults with 0 or 1 Centor criteria, who are at low risk for streptococcal pharyngitis, should neither be tested nor treated with antibiotics. In contrast to the ACP strategies, the IDSA recommends microbiologic confirmation for all adults with pharyngitis prior to antibiotic prescribing. The authors of the IDSA...
guideline have been openly critical of the ACP guideline owing to concern that the use of clinical criteria results in the overprescribing of antibiotics to patients who are unlikely to have streptococcal pharyngitis.7,8

To determine if clinicians in actual practice use clinical criteria or microbiologic testing, or both, in the evaluation of adults with pharyngitis, we performed a retrospective review of visits by patients with pharyngitis to clinics in the Brigham and Women’s Primary Care (BWPC) Practice-Based Research Network (PBRN) in the greater Boston, Mass, area. We measured adherence to the ACP and IDSA guidelines and calculated hypothetical streptococcal testing rates and antibiotic treatment rates, assuming perfect adherence to each strategy.

DATA EXTRACTION

We used the Research Patient Data Repository to identify patients with potential diagnoses of pharyngitis who visited the BWPC-PBRN Clinics. We found encounters by patients 18 years or older with an ICD-9-CM diagnosis code of streptococcal sore throat and scarlet fever (ICD-9-CM code 034) and acute pharyngitis (ICD-9-CM code 462) who were seen from October 1, 2003, to May 31, 2005. From the visit note, we extracted the diagnoses assigned by the treating physician. We excluded encounters that had no associated visit note; duplicate notes; a nonpharyngitis acute respiratory infection diagnosis; a nonacute respiratory infection diagnosis; a concomitant, nonpharyngitis, antibiotic-appropriate diagnosis; or visits by patients with symptoms for more than 30 days.

If the treating physician diagnosed the patient as having pharyngitis (including streptococcal pharyngitis, nonstreptococcal pharyngitis, or nonspecific pharyngitis), we collected information about symptoms, vital signs, physical examination findings, testing performed, and medications prescribed. We abstracted information about whether an RADT or throat culture, or both, was performed. Most data in the Longitudinal Medical Record are captured as free text. Clinicians are not prompted to enter the Centor criteria.

We abstracted information on up to 4 medications, giving preference to antibiotics if more than 4 were mentioned (which occurred in <1% of visits). For the purposes of this analysis, we included only oral, antibacterial agents as antibiotics (ophthalmic and otic antibiotics were classified as “other medications”; there were no uses of intramuscular antibiotics). We further subdivided antibiotics into 12 classes: penicillin, amoxicillin, amoxicillin/clavulanate, cephalosporins, fluoroquinolones, erythromycin, extended spectrum macrolides (including azithromycin and clarithromycin), sulfaba-based antibiotics, tetracyclines, metronidazole, clindamycin, and other antibiotics.

To assess data quality, we randomly selected 100 visits for repeated medical chart abstraction by the first author (J.A.L.) for the diagnosis and other variables. For determining whether the clinician had diagnosed the patient as having pharyngitis, interobserver agreement was 94%. For included visits, antibiotic prescribing had an interobserver agreement of 99%. For all variables combined—including diagnosis, symptoms, physical examination findings, testing, and medications—interobserver agreement was 94%.

DATA ANALYSIS

Using collected signs and symptoms, we considered the 4 Centor criteria: (1) subjective complaint of fever or measured temperature of 100.3°F or higher, (2) documented absence of cough, (3) tender anterior cervical lymphadenopathy, and (4) tonsilar exudate. To evaluate the use of streptococcal testing, we combined the use of RADTs, throat cultures, or both, into a single variable of streptococcal testing. We collapsed the antibiotic categories into recommended antibiotics, including penicillin and erythromycin, and nonrecommended antibiotics, including all other antibiotics.9,12

For all 3 strategies, we considered physicians as being in adherence depending on the number of Centor criteria that were applied.5,10,12

1. For the ACP empirical strategy, we considered physicians in adherence for visits with 0, 1, or 2 Centor criteria if no streptococcal test was performed and no antibiotic was prescribed. We considered physicians in adherence for visits with 3 or 4 Centor criteria if no streptococcal test was performed and an antibiotic was prescribed.

2. For the ACP test strategy, we considered physicians in adherence for visits with 0 or 1 Centor criterion if no streptococcal test was performed and no antibiotic was prescribed. We considered physicians in adherence for visits with 2 or 3 Centor criteria if a test was performed and a positive test was associated with an antibiotic prescription or a negative test was not associated with an antibiotic prescription. We considered physicians in adherence for visits with 4 Centor criteria if no streptococcal test was performed and an antibiotic was prescribed.

3. For the IDSA Strategy, we considered physicians in adherence for visits with 0 or 1 Centor criteria if no test was performed and no antibiotic was prescribed. We considered physicians in adherence for visits with 2, 3, or 4 Centor criteria if a streptococcal test was performed and a positive test was associated with an antibiotic prescription and a negative test was not associated with an antibiotic prescription.

A physician potentially could be adherent in an individual visit with any combination of the 3 strategies. We assessed the hypothetical effect of perfect ACP or IDSA guideline adherence on streptococcal testing and antibiotic prescribing in this cohort. We also examined a hypothetical strategy of performing a streptococcal test on all patients. For these hypothetical assessments, we assumed that the Centor criteria were distributed as in the actual cohort. We also assumed that the rate of positive streptococcal tests among patients who had streptococcal tests was the same in each stratum of Centor criteria as in the actual cohort.
STATISTICAL ANALYSIS

We used standard descriptive statistics. We used the χ²-test to compare categorical variables and the t-test to compare continuous variables. Adjustment for clustering by clinician or clinic did not change the results appreciably. All statistical analyses were performed using SAS statistical software (version 9.1; SAS Institute, Cary, NC). We considered P values smaller than .05 to be significant. The institutional review board of Brigham and Women's Hospital approved the study protocol, including a waiver of informed consent for the study subjects.

SAMPLE DERIVATION AND CHARACTERISTICS

There were 4599 encounters with a primary claim diagnosis of streptococcal pharyngitis or acute pharyngitis and 2097 visits in the cohort that met the inclusion criteria (Figure). The cohort had a mean (SD) age of 37 (12) years; 81% were women, and 50% were white (Table 1). The most common chief complaints were sore throat (83%); “strep throat” or pharyngitis (8%); cold, flu, or upper respiratory tract symptoms (3%); fever (2%); cough (1%); and other chief complaints (3%). Visits were made to all 9 clinics, ranging from 13 to 532 visits per clinic. Visits were made to 190 different clinicians, including attending physicians, residents, and nurse practitioners.

STREPTOCOCCAL TESTING

Clinicians performed a streptococcal test in 1671 visits (80%), which included RADTs in 520 visits (25%), a throat culture in 815 visits (39%), and both an RADT and a throat culture specimen in 336 visits (16%). One or both tests were positive in 357 visits (21%) in which testing was done. Among visits when only an RADT was performed, 173 (33%) of 520 had positive results.
The 9 clinics (antibiotic prescribing rate differed significantly among tetracycline (3), metronidazole (2), and sulfa-based antibiotics (1), miscellaneous antibiotics (8), clindamycin (6), fluoroquinolones (5), recommended antibiotic and a nonrecommended antibiotic prescription. To a subclass, but for a single visit to be counted, we considered clinicians to have prescribed a recommended antibiotic if they prescribed both a recommended antibiotic and a nonrecommended antibiotic prescription.

Streptococcal testing was more common among women than men and more common among patients who were white or of other race and ethnicity than among black and Latino patients (Table 1). Streptococcal testing was less common among patients with tonsillar exudates and marginally less common among patients with tender anterior cervical lymphadenopathy. There were large differences among the 9 clinics in the rates of streptococcal testing (P < .001), ranging from 31% testing at the clinic with the fewest number of visits to 100% testing at a clinic with 208 visits. The clinic with 100% testing had a policy that all patients with a sore throat received a streptococcal test before seeing the physician.

**ANTIBIOTIC PRESCRIBING**

Clinicians prescribed antibiotics in 988 visits (47%) overall. Patients who were prescribed antibiotics were younger, had symptoms for a shorter duration, and had a higher mean temperature (Table 1). Antibiotic prescribing was more common for Latinos and blacks than for whites and patients of other race and ethnicity. Antibiotic prescribing was less common for patients with cough and pharyngeal vesicles and more common in patients with fever, tender anterior cervical lymphadenopathy, tonsillar exudates, and tonsillar swelling. Clinicians prescribed recommended antibiotics in 588 visits (28%) and nonrecommended antibiotics in 400 visits (19%; Table 2). The antibiotic prescribing rate differed significantly among the 9 clinics (P < .001), ranging from 24% at the clinic with the 100% testing rate to 77% at the clinic with the fewest visits and the lowest testing rate. Clinicians prescribed antibiotics to 45% of patients who had a streptococcal test and to 57% of patients who did not have a streptococcal test (P < .001, Table 3).

**Table 2. Recommended and Nonrecommended Antibiotic Prescribing to Adults With Pharyngitis**

<table>
<thead>
<tr>
<th>Type of Antibiotic</th>
<th>Visits, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommended antibiotics</td>
<td>588 (28)</td>
</tr>
<tr>
<td>Penicillin</td>
<td>536 (26)</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>52 (2)</td>
</tr>
<tr>
<td>Nonrecommended antibiotics</td>
<td>400 (19)</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>195 (9)</td>
</tr>
<tr>
<td>Extended-spectrum macrolides</td>
<td>149 (7)</td>
</tr>
<tr>
<td>Other antibiotics†</td>
<td>60 (3)</td>
</tr>
<tr>
<td>Any antibiotic</td>
<td>988 (47)</td>
</tr>
<tr>
<td>Total visits</td>
<td>2097 (100)</td>
</tr>
</tbody>
</table>

*Numbers may not sum to total because at 5 visits multiple antibiotics were prescribed. Each antibiotic mention was counted in its respective subclass, but for a single visit to be counted, we considered clinicians to have prescribed a recommended antibiotic if they prescribed both a recommended antibiotic and a nonrecommended antibiotic prescription.
†Other antibiotics were amoxicillin-clavulanate (19), cephalosporins (17), miscellaneous antibiotics (8), clindamycin (6), fluoroquinolones (5), tetracycline (3), metronidazole (2), and sulfa-based antibiotics (1).

visits when only a throat culture was performed, 124 (15%) were positive. Among visits when an RADT and a throat culture were performed, 41 RADTs (12%) and 50 cultures (15%) were positive.

Streptococcal testing was more common among women than men and more common among patients who were white or of other race and ethnicity than among black and Latino patients (Table 1). Streptococcal testing was less common among patients with tonsillar exudates and marginally less common among patients with tender anterior cervical lymphadenopathy. There were large differences among the 9 clinics in the rates of streptococcal testing (P < .001), ranging from 31% testing at the clinic with the fewest number of visits to 100% testing at a clinic with 208 visits. The clinic with 100% testing had a policy that all patients with a sore throat received a streptococcal test before seeing the physician.

**Table 3. Recommended and Nonrecommended Antibiotic Prescribing to Adults With Pharyngitis**

<table>
<thead>
<tr>
<th>Test</th>
<th>Antibiotics</th>
<th>No Antibiotics</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any test</td>
<td>747 (45)</td>
<td>924 (55)</td>
<td>1671 (80)</td>
</tr>
<tr>
<td>No test</td>
<td>241 (57)</td>
<td>185 (43)</td>
<td>426 (20)</td>
</tr>
<tr>
<td>Positive test</td>
<td>350 (98)</td>
<td>7 (2)</td>
<td>357 (17)</td>
</tr>
<tr>
<td>No positive test</td>
<td>638 (37)</td>
<td>1102 (63)</td>
<td>1740 (83)</td>
</tr>
<tr>
<td>Totals</td>
<td>988 (47)</td>
<td>1109 (53)</td>
<td>2097 (100)</td>
</tr>
</tbody>
</table>

*Clinicians prescribed antibiotics to 397 (30%) of the 1314 patients who had a negative streptococcal test result. P < .001 for the association between streptococcal testing and antibiotic prescribing. P < .01 for the association between a positive test result and antibiotic prescribing.

**Table 4. Centor Criteria, Streptococcal Testing, and Antibiotic Prescribing**

<table>
<thead>
<tr>
<th>Centor Criteria</th>
<th>Sample, No. (%)</th>
<th>Streptococcal Test†</th>
<th>Positive Test†</th>
<th>Antibiotic Prescribing†</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>502 (24)</td>
<td>396 (79)</td>
<td>40 (8)</td>
<td>123 (25)</td>
</tr>
<tr>
<td>1</td>
<td>726 (35)</td>
<td>589 (81)</td>
<td>95 (13)</td>
<td>248 (34)</td>
</tr>
<tr>
<td>2</td>
<td>499 (24)</td>
<td>394 (79)</td>
<td>108 (22)</td>
<td>314 (63)</td>
</tr>
<tr>
<td>3</td>
<td>300 (14)</td>
<td>240 (80)</td>
<td>93 (31)</td>
<td>241 (80)</td>
</tr>
<tr>
<td>4</td>
<td>70 (3)</td>
<td>52 (74)</td>
<td>21 (30)</td>
<td>62 (89)</td>
</tr>
<tr>
<td>Total</td>
<td>2097 (100)</td>
<td>1671 (80)</td>
<td>357 (17)</td>
<td>988 (47)</td>
</tr>
</tbody>
</table>

*The Centor criteria are (1) subjective complaint of fever or measured temperature of 100.5°F or higher, (2) absence of cough, (3) tender anterior cervical lymphadenopathy, and (4) tonsillar exudate. P < .63 for association between Centor criteria and streptococcal testing. P < .001 for the association between the number of Centor criteria and a positive streptococcal test. P < .001 for the association between the number of Centor criteria and antibiotic prescribing.
†Data are given as number (percentage of stratum).

Clinicians prescribed antibiotics to 52% of patients who had an RADT, 46% of patients who had a throat culture, and 30% of patients who had an RADT as well as a culture (P < .001). Patients who had an RADT, a throat culture, both, or no test accounted for 27%, 38%, 10%, and 24% of antibiotic prescribing, respectively.

Among patients who had a positive streptococcal test, 350 (98%) of 357 received antibiotics (Table 3). Among the 1314 patients who had a negative test, 397 (30%) received antibiotics. Patients who had a positive test, negative test, or no test accounted for 35%, 40%, and 24% of antibiotic prescribing, respectively.

**CENTOR CRITERIA AND ADHERENCE TO GUIDELINES**

Clinicians explicitly documented the use of any clinical prediction rule in only 23 visits (1%). The Centor criteria were not associated with streptococcal testing (P = .63) but were associated with both a positive streptococcal test result (P < .001) and antibiotic prescribing (P < .001; Table 4).

Clinicians were adherent to the ACP empirical strategy in 12% of visits, the ACP test strategy in 30% of visits, and no strategy in
66% of visits. The most common reason for nonadherence to any strategy was streptococcal testing or antibiotic prescribing to patients at low risk for streptococcal pharyngitis with 0 or 1 Centor criteria (1076 visits, 78% of visits in which the clinician was nonadherent to any guideline). Of these 1076 visits, clinicians performed a streptococcal test in 985 visits (92%) and prescribed antibiotics in 371 visits (34%).

We examined the effect that perfect adherence to each management strategy would have on the testing and antibiotic treatment rates assuming the same distribution of Centor criteria and the same rate of positive test results in each stratum of the Centor criteria as in the actual cohort (Table 5). Perfect adherence to the Test All strategy would result in the lowest antibiotic prescribing rate. Perfect adherence to the IDSA strategy would result in the lowest rate of antibiotic prescribing.

We found that physicians prescribed antibiotics to 47% of adults diagnosed with pharyngitis in our practice-based research network. Although this rate is lower than national rates of antibiotic prescribing to adults with pharyngitis, it still greatly exceeds the expected prevalence of group A β-hemolytic streptococci. The antibiotic prescribing rate of 47% is particularly striking given the performance of streptococcal testing in 80% of visits and a positive test result in only 17% of visits.

Although guidelines have been promoted as a potential tool for reducing inappropriate antibiotic prescribing for pharyngitis, there has been substantial debate as to which guideline performs best in identifying adults likely to have group A β-hemolytic streptococci. Our analysis suggests that the issue is not which guideline to follow—perfect adherence to the various strategies would result in only modest differences in the antibiotic prescribing rate—but that clinicians fail to follow any guideline. Most debate has been about whether to treat empirically at the high end of the probability range. However, the major problem in the evaluation and treatment of adults with pharyngitis in actual practice was the testing of and antibiotic drug prescribing to adults with a low probability of having streptococcal pharyngitis, a point on which the ACP and IDSA guidelines agree.

Our hypothetical results for perfect adherence were similar to the results of a study by McIsaac et al, who performed a prospective empirical validation of various strategies for the evaluation and treatment of adults with pharyngitis. The ACP empirical strategy resulted in the highest antibiotic prescribing rate, and the IDSA strategy resulted in the most testing and the lowest antibiotic prescribing rate. However, because McIsaac et al excluded patients with fewer than 2 Centor criteria, they “missed” the main problem in the treatment of adults with pharyngitis in actual practice: the testing and treatment of adults at low risk of streptococcal pharyngitis.

Several clinical factors were associated with streptococcal testing and antibiotic treatment. Most of the components of the Centor criteria were not associated with streptococcal testing but were associated with an increased antibiotic prescribing rate. This seems to be mediated not through clinician behavior but through the association of the Centor criteria with positive streptococcal tests. Similarly, pharyngeal vesicles, a sign of viral infection, were not associated with streptococcal testing but were associated with a decreased antibiotic prescribing rate. Our finding that younger age was associated with antibiotic prescribing is consistent with the higher prevalence of streptococcal pharyngitis in younger patients.

This study has several limitations. First, it is a retrospective medical chart review and thus dependent on clinicians’ documentation of their care to assess patient symptoms, physical examination findings, and treatment decisions. Our reliance on clinicians’ documentation could have caused us to underestimate number of patients with the Centor criteria. According to the documentation, only 3% of our cohort had 4 Centor criteria, whereas in previous studies 10% to 18% of patients had 4 Centor criteria. This could reflect a true difference between studies or clinicians’ lack of familiarity with or failure to recognize or document the Centor criteria. The finding that clinicians explicitly referred to a clinical decision rule in only 1% of visits supports this latter hypothesis. However, in previous studies 35% to 60% of patients had fewer than 2 criteria, so the problem of testing and antibiotic prescribing to these patients would still be present.

Second, we used claims diagnoses to identify visits. Patients with sore throat who were diagnosed as having other acute respiratory infections, such as nonspecific upper respiratory tract infection, were not included. This would skew the cohort toward having more specific findings of streptococcal pharyngitis and a higher prevalence of group A β-hemolytic streptococci (as evidenced by the fact that the 17% of the cohort had a positive streptococcal test result). Third, this was an analysis of actual practice without a gold standard test to indicate exactly which patients had streptococcal pharyngitis. Fourth, this study was performed in mainly urban, academically affiliated practice-based research network clinics, staffed primarily by internists. The results may not be generalizable to other settings or provider groups.

Antibiotic treatment of patients with streptococcal pharyngitis reduces the duration of symptoms, limits...
the spread of streptococci, and reduces suppurative complications and nonsuppurative complications. The antibiotic of choice remains penicillin, which is effective, well tolerated, and inexpensive, and to which group A β-hemolytic streptococci are universally susceptible. For the vast majority of adults with sore throat who have nonstreptococcal pharyngitis, antibiotic treatment is not associated with clinical benefit and exposes patients to the possibility of adverse drug events, increases the prevalence of antibiotic-resistant bacteria, and increases costs.

Because the major problem in actual practice in the evaluation and treatment of adults with pharyngitis is the testing of and antibiotic prescribing to adults with a low risk of having streptococcal pharyngitis, solutions should not focus on which guideline is implemented. The argument about which guideline to follow seems largely academic. Rather, the consistent application of any clinical guideline for the evaluation and treatment of adults with pharyngitis has a much greater potential to reduce inappropriate streptococcal testing and antibiotic prescribing.

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