BRIEF REPORT: The Role of Point of Care Testing for Patients with Acute Pharyngitis

Steven J. Atlas, MD, MPH, Steven M. McDermott, RN, Carol Mannone, RN,
Michael J. Barry, MD

From the General Medicine Division, Medical Services, Massachusetts General Hospital, Harvard Medical School, Boston, Mass 02114, USA.

BACKGROUND: There is no consensus favoring a particular strategy for evaluating patients with pharyngitis.

OBJECTIVE: To compare a clinical decision aid and a rapid office-based point of care (POC) test with routine culture for group A β -hemolytic streptococcus (GAS).

DESIGN: Prospective observational study.

PARTICIPANTS: Among 179 patients enrolled, 150 were eligible and 148 had POC testing and cultures initially performed.

MEASUREMENTS: An encounter form included eligibility criteria, clinical information based upon the Centor rule, and treatment provided. Sensitivity and specificity of POC test compared to routine culture for GAS.

RESULTS: Thirty-eight patients (25.7%) had a positive GAS culture. The POC test was 92.1% sensitive (95% confidence interval [CI] 80% to 98%) and 100% specific (95% CI 97% to 100%). Although the Centor rule did not adequately discriminate among symptomatic patients with or without GAS (receiver operating curve area 0.63), the 3 patients with a false-negative POC test had a Centor score of less than 2. Among patients with a negative POC test, 26% initially received antibiotics.

CONCLUSIONS: For patients with a Centor score of ≥ 2 , a POC test was highly sensitive for GAS. Future studies should confirm these results and assess whether implementation of POC testing as part of a local practice guideline can decrease variability in testing and treatment.

KEY WORDS: pharyngitis; point of care testing; diagnostic accuracy; guideline.

DOI: 10.1111/j.1525-1497.2005.0143.x

J GEN INTERN MED 2005; 20:759-761.

Acute pharyngitis is a frequent complaint for primary care providers.^{1,2} Although most commonly viral in etiology, group A β -hemolytic streptococcus (GAS) is identified in 5% to 10% of symptomatic adults.² Treatment for other less common bacterial etiologies is not routinely recommended.^{2,3} Antibiotics for GAS decrease symptom duration 1 to 2 days on average.^{4,5} Since most patients improve whether antibiotics are prescribed or not, earlier treatment may provide greater symptomatic benefit. Other antibiotic benefits, such as preventing suppurative complications or rare post streptococcal glomerulonephritis, are unproven.^{3,4,6,7} Although GAS causes acute rheumatic fever, risk is minimal in adults.^{7,8} Finally, treating infected individuals can reduce household transmission.⁹

Dr. Atlas has performed consulting for Aventis-Sanofi Pharmaceuticals for unrelated work.

This work was presented in part at a New England Regional meeting of the Society of General Internal Medicine, Boston, Mass, on March 5, 2004.

Address correspondence and reprint requests to Dr. Atlas: General Medicine Division, Massachusetts General Hospital, 50 Staniford Street, Boston, MA 02114 (e-mail: satlas@partners.org).

Etiology is traditionally identified using routine cultures, but delayed results require postponing treatment or basing it on clinical characteristics. Clinical decision rules can identify patients at increased GAS risk,^{5,10} but they increase antibiotic use compared with waiting for culture results.^{11,12} Rapid office-based point-of-care (POC) tests can identify patients with GAS during a visit, but initial tests suffered from low sensitivity.¹³ Current tests report high sensitivity and specificity,^{6,7} but sensitivity continues to vary across clinical studies.¹² Guidelines recommend that POC tests at least 80% sensitive can be used to base treatment without needing a confirmatory culture.³

Various testing strategies are available, but none is currently preferred.^{3,6,14} While developing a local practice guideline, retrospective assessment of acute pharyngitis encounters demonstrated wide variability in testing rates across 8 primary care practices. In 2002, 68% of 4033 encounters had a routine culture (practice range 40% to 80%), with few practices using POC tests. There was no relationship between testing intensity and positive culture rates (mean 12.6% positive, practice range 5.6% to 19%). To address these findings, a prospective study was designed to assess POC test sensitivity for GAS when used with the simple and well-studied Centor clinical decision rule.¹⁵ We hypothesized that diagnostic POC testing combined with clinical data could identify patients most likely to benefit from early treatment of GAS while decreasing inappropriate antibiotic use.

METHODS

A prospective study was implemented in 2 primary care settings at Massachusetts General Hospital between July 1, 2002 and June 30, 2003—a primary care practice implementing a new POC test for GAS, and a medical walk-in center where POC testing was already used. All patients were routinely managed by her/his provider. During the study, hospital policy required obtaining a confirmatory culture when POC testing for GAS was performed. The same POC test (Acceava, Thermo Electron Corporation, Waltham, Mass) and procedure guideline (POC test rapid Strep A procedure manual) was used in both practices by trained providers. Partners Healthcare Institutional Review Board approved the study with an informed consent waiver.

Eligibility criteria included age 18 years or older and symptoms of acute pharyngitis. Patients were excluded for symptoms >7 days, antibiotics within 24 hours, immunocompromised state, or diagnosis of acute pulmonary disease flare. Providers completed a standard encounter form including demographics, clinical symptoms (Centor score criteria), POC test and routine culture results, treatment, and follow-up.

Clinical characteristics using the Centor score, results from POC tests, and routine cultures were compared. Positive

Received for publication March 29, 2004

and in revised form January 26, 2005

Accepted for publication March 2, 2005

Table 1. Patient Clinical Features at Baseline Evaluation

Variable	N=150	%
Practice site, walk-in center	76	50.7
Age, mean (SD)	150	35.6 (10.9)
Gender, female	110	73.3
Ethnicity		
Non-Hispanic white	133	90
Hispanic	7	5
Asian	4	3
African American	3	2
Clinical data used in Centor score		
History of fever*	61	40.6
Tonsillar exudates on exam	55	36.7
Swollen anterior cervical lymph nodes	70	46.7
Absence of cough (patient report)	114	76
Centor score [†]		
0–1	56	37.3
2	45	30.0
3	31	20.7
4	18	12.0

*Patient report or measured temperature > 100.4°F.

[†]A positive response to each of the 4 clinical variables is associated with 1 point. A negative response is given 0 points. The sum of the responses to each variable provides the total score that ranges from 0 to 4 points. Higher scores are more likely to indicate pharyngitis due to GAS. GAS, group A β -hemolytic streptococcus.

cultures for GAS were the gold standard. POC test sensitivity and specificity for GAS was calculated with 95% confidence intervals (CI) and stratified by the Centor score. Positive and negative likelihood ratios were calculated using lower 95% CI limits for test specificity (no false-positive results), and sensitivity. Antibiotic prescriptions at the clinical encounter were compared among patients with a positive or negative POC test. Analyses were performed using SAS (SAS Institute, Cary, NC).

RESULTS

Among 179 patients with completed data forms, 29 were excluded (symptoms > 7 days (16), prior antibiotics (4), immunocompromised (3), acute pulmonary disease (6)). The clinical features of 150 eligible patients are presented in Table 1. Initial POC tests and routine cultures were obtained for 148 patients. Two patients only had a POC test available (1 positive). Forty patients (27%) had a positive culture for any bacterial organism. Two patients (1.4%) had non-GAS (1 group C and 1 group G streptococcus), with negative POC tests and Centor scores of 2 and 4, respectively.

Thirty-eight patients (25.7%) had positive GAS cultures (Table 2). Positive cultures were more frequent in patients with Centor scores of 2 or higher, but the percentage of GAS did not differ among Centor scores of 2 to 4. Among specific Centor score items, presence of tonsillar exudates correlated best with GAS (odds ratio [OR] 2.4, 95% CI 1.1 to 5.0) followed by a history of fever (OR 1.9, 95% CI 0.9 to 4.1), cervical adenopathy (OR 1.5, 95% CI 0.7 to 3.1), and absence of cough (OR 0.9, 95% CI 0.4 to 2.1). In multivariate models, only tonsillar exudate independently predicted GAS. Overall, the sum of the Centor score was a modest predictor of risk (OR 1.5, 95% CI 1.1 to 2.0, receiver-operating characteristic $r=0.633$, $P=.02$).

POC tests were positive for GAS in 35 of 38 patients with positive cultures (92.1% sensitivity, 95% CI 80% to 98%) (Table 2). Among 3 false-negative POC tests, two patients had Centor scores of 0 or 1 (67% POC test sensitivity for these Centor scores, 95% CI 22% to 96%). A third patient had a Centor score of 2. For patients with a Centor score of 2 or more, POC test sensitivity was 98% (95% CI 88% to 100%). No patient had a positive POC test and a negative culture (100% specificity, 95% CI 97% to 100%). Positive and negative likelihood ratios calculated using lower 95% CIs were good to excellent for the POC test in patients with a Centor score of 2 or more.

All patients with positive POC tests for GAS as well as 30 of 114 (26%) patients with negative POC tests received antibiotic prescriptions (Table 3). Patients with positive POC tests were more likely to be prescribed penicillin or erythromycin than patients with negative POC tests (75% vs 50%, respectively, $P=.03$).

DISCUSSION

In this study, the Centor rule did not perform as well as in prior reports, but the POC test demonstrated high sensitivity for GAS and led to appropriate treatment for those diagnosed during the visit. Practice guidelines for acute pharyngitis recommend a number of different evaluation strategies with similar effectiveness and costs rather than a single preferred approach.^{3,6,11} One guideline supports POC testing alone if it is at least 80% sensitive.³ However, a recent study examining various evaluation strategies concluded that routine cultures were an optimal strategy in adults.¹²

The current results are consistent with McIsaac et al. with regard to the limited ability of the clinical decision rule to identify individuals at high enough risk to justify empiric therapy.⁶ Using clinical decision rules alone to base treatment would

Table 2. Routine Culture and POC Testing Results by Clinical Status for Patients with Acute Pharyngitis

Centor Score*	Patients, #	Routine Cultures with GAS, # (%)	POC Tests with GAS, #	Sensitivity of POC Test (95% CI)	Specificity of POC Test (95% CI)	Likelihood Ratio [†]	
						Positive	Negative
0–1	55	6 (11)	4	67 (22 to 96)	100 (93 to 100)	3.0	0.8
2	45	16 (36)	15	94 (71 to 100)	100 (88 to 100)	5.9	0.3
3	30	10 (33)	10	100 (69 to 100)	100 (83 to 100)	4.1	0.4
4	18	6 (33)	6	100 (59 to 100)	100 (74 to 100)	2.2	0.6
3 or 4	48	16 (33)	16	100 (88 to 100)	100 (89 to 100)	8.1	0.1
2–4	93	32 (34)	31	98 (88 to 100)	100 (94 to 100)	15.7	0.1
Any	148	38 (26)	35	92 (80 to 98)	100 (97 to 100)	24.2	0.2

*Clinical status assessed using the Centor score.

[†]Calculated to assess the minimum value for likelihood ratio positive using the following calculation: likelihood ratio positive = sensitivity (lower bound of 95% CI) / (1 – specificity [lower bound of 95% CI]); likelihood ratio negative = (1 – sensitivity [lower bound of 95% CI]) / Specificity (lower bound of 95% CI). GAS, group A β -hemolytic streptococcus; POC, point of care; CI, confidence interval.

Table 3. Initial Antibiotic Prescriptions According to Results of POC Testing for GAS

Antibiotic Prescription at Initial Visit	Number with Positive POC Test (%)	
	Yes*	No
Yes	36 (100)	30 (26)
Penicillin or erythromycin	27 (75)	15 (50)
Other	9 (25)	14 (47)
Unknown	0 (0)	1 (3)
No	0 (0)	73 (64)
Unknown	0 (0)	11 (10)

*The total number of positive POC tests is 36. 1 patient had a positive POC test without a routine culture performed.

POC, point of care; GAS, group A β -hemolytic streptococcus.

increase antibiotic use in individuals without GAS. Unlike similar Centor score performance in this study and McIsaac's, POC test sensitivity was higher in this study (92.1% vs 76.7%, respectively). Differences in reported POC test sensitivity have important implications. For McIsaac, the modest ability of the modified Centor score to identify those at high risk for GAS (27.5% with score 3 and 30.8% with score 4 to 5) and lower POC test sensitivity led to recommending routine cultures alone even though this would entail withholding treatment for 24 to 48 hours until culture results were available. Although McIsaac states that "timely treatment of GAS pharyngitis was considered a secondary outcome", many patients expect timely treatment for acute symptoms.¹⁶ Despite modest sensitivity of the Centor rule, higher POC test sensitivity in the current study combined with the low risk of complications associated with missing GAS in adults makes not performing routine cultures after negative POC testing justifiable for patients with higher Centor scores.⁶

Study limitations include a relatively small patient population that generally reflected patients seen in the 2 sites. Practices considering POC testing should first define its sensitivity. The rate of GAS in this study was higher than overall practice rates of GAS. Since the study required routine and POC tests as part of usual care, patients with less severe symptoms were likely excluded to meet eligibility criteria. It is possible that by excluding less symptomatic patients, the study underestimates the Centor rule's true value. POC testing should be evaluated along with other clinical decision aids besides the Centor rule. Finally, these results are not applicable in children.¹²

Historic data from our local practices highlight wide variations in current testing. Even if the test characteristics of the POC test and clinical rule are validated in follow-up studies, their use is unlikely to lead to more appropriate testing and treatment without efforts to implement them as part of a clinical guideline with ongoing provider feedback.¹⁷ The 25% of patients with a negative POC test who initially received antibiotics highlight the challenges of meeting patient expectations without antibiotic prescriptions.¹⁸ Our local guideline recommends that POC test results in patients with a Centor score of 2 or more can be used to base treatment. If one would treat individuals with a Centor score of less than 2 (for example

to decrease household spread), a routine culture without POC testing is recommended. Future study is needed to determine whether implementing such a guideline can improve care and decrease provider variability.

The authors gratefully acknowledge the assistance of Nancy Wong, B.S. with data management and statistical analyses. We also appreciate the assistance of the medical assistants, nurses, nurse practitioners, and physicians who managed the patients identified in this study.

This work was supported by institutional funding through the Massachusetts General Hospital Primary Care Operations Improvement program.

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