The Clinical Diagnosis of Streptococcal Pharyngitis

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SYSTEMATIC REVIEW SOURCE

This is a rational clinical examination abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine series. Each features an abstract of a Rational Clinical Examination review from the *Journal of the American Medical Association* and a commentary by an emergency physician knowledgeable in the subject area.

The source for this rational clinical examination review abstract is: Ebell MH et al. The rational clinical examination: does this patient have strep throat? *JAMA*. 2000; 284:2912-2918.

The *Annals'* Evidence-Based Emergency Medicine editors assisted in the preparation of the abstract of this rational clinical examination review, as well as selection of the Evidence-Based Medicine Teaching Points.

OBJECTIVE

The purpose of this abstract is to review the accuracy and value of the physical examination in diagnosing group A [β]-hemolytic streptococcal pharyngitis.

DATA SOURCES

The authors conducted a MEDLINE search from 1966 to 2000 using the MeSH headings ''sensitivity and specificity,'' ''predictive value of tests,'' ''medical history taking,'' ''physical examination,'' and ''pharyngitis.'' The authors identified 917 articles using this search.

STUDY SELECTION

Studies were included that described the precision and accuracy of clinical examination in diagnosing group A [β]-hemolytic streptococcal pharyngitis in patients complaining of sore throat. The author's inclusion criteria required individual studies to have at least 300 patients, have all data collected prospectively, and use a throat culture as the reference standard for diagnosis. In addition, study investigators must not have been aware of any of the rapid streptococcal or throat culture results before the history and physical examination was performed. Of the initial 917 articles identified by the author's MEDLINE search, 9 studies met all inclusion criteria (17 studies met all criteria except a sample size ≥300 subjects), representing 5,453 total patients.

DATA EXTRACTION AND ANALYSIS

The methods of data extraction are not discussed. Pooled sensitivity, specificity, and positive and negative likelihood ratios were calculated using a random-effects model when possible; otherwise, a range for each variable was reported. The area under the receiving operator characteristic curve for disease signs and symptoms was also reported if more than 3 studies reported the variable's sensitivity and specificity.

MAIN RESULTS

The variables with the greatest area under the receiving operator characteristic curve, and therefore representing the most valuable medical history and physical features for distinguishing individuals with and without strep throat, were the presence of pharyngeal or tonsillar exudates, fever by history, tonsillar enlargement, tenderness or enlargement of the anterior cervical lymph nodes, and the absence of cough. Individual clinical factors with the highest positive and lowest negative likelihood ratios are shown in Table 1.

Because individual clinical findings in isolation are not sufficient to accurately diagnose streptococcal pharyngitis, clinical prediction rules have been developed that use a combination of history and physical variables to estimate disease probability. The Centor's score represents the single most well-validated clinical prediction rule for the prediction of streptococcal pharyngitis[1] and has been recently modified and validated to include a pediatric population (Tables 2 and 3).[2] The prediction rule demonstrates an area under the receiving operator characteristic curve of 0.79 in clinical trials.

CONCLUSIONS

No single element of the medical history or physical examination is sufficient to accurately diagnose streptococcal pharyngitis in isolation. However, a combination of findings, including tonsillar exudates, tender or enlarged anterior cervical lymph nodes, the absence of cough and a history of fever, is helpful in predicting an increased probability of the disease. These findings should be coupled with additional clinical factors such as the patient's age, the results of rapid antigen testing or culture, and clinician judgment.

Table 1. Accuracy for selected elements in determining bacterial throat infection.*

Symptoms or Signs	LR+ (95% CI)	LR− (95% CI)
Any exudates	1.5–2.6	0.66–0.94
Reported fever	0.97–2.6	0.32–1.0
Measured temperature >37.8°C (100.0°F)	1.1–3.0	0.27–0.94
Swollen cervical nodes	0.47–2.9	0.58–0.92
Pharyngeal exudates	2.1 (1.4–3.1)	0.90 (0.75–1.1)
Tonsillar swelling/ enlargement	1.4–3.1	0.63 (0.56–0.72)
Tonsillar/pharyngeal exudates	1.8 (1.5–2.3)	0.74 (0.66–0.82)
Anterior cervical nodes tender	1.2–1.9	0.60 (0.49–0.71)
Tonsillar exudates	3.4 (1.8–6.0)	0.72 (0.60–0.88)
No cough	1.1–1.7	0.53–0.89
Headache	0.81–2.6	0.55–1.1
Pharynx injected	0.66–1.63	0.18–6.42
Male sex	0.87 (0.72–1.05)	1.1 (0.93–1.2)
Palatine petechiae	1.4 (0.48–3.1)	0.98 (0.92–1.1)
Strep exposure previous 2 wk	1.9 (1.3–2.8)	0.92 (0.86–0.99)
Rash	0.06–35	0.90–1.1

LR+, Positive likelihood ratios; *LR−*, negative likelihood ratios.
*Ranges reported when pooled results not available.
Reprinted from: Ebell MH, Smith MA, Barry HC, et al. The rational clinical examination: does this patient have strep throat? *JAMA*. 2000;284:2912-2918.

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COMMENTARY: CLINICAL IMPLICATION

Sore throat is a common medical complaint, representing 2.1% of total US ambulatory visits and second only to complaints of cough.[3] Group A [β]-hemolytic streptococci remains the most common bacterial cause, with an incidence of 15% to 36% in children and 5% to 17% in adults with a sore throat. Despite low bacterial prevalence, of the 6.7 million annual visits in the United States by adults for sore throats between 1989 and 1999, it is estimated 73% were likely to have been treated with antibiotics.[4,5] Although the value of antibiotics has been debated in this generally self-remitting disease, antibiotics are still frequently recommended for patients with a high likelihood of, or else culture-confirmed, streptococcal throat infection. A uniform standard diagnostic testing guideline has not been established and remains controversial because each recommended approach carries strengths and weaknesses.[6] Most guidelines propose a strategy based on the score derived from a clinical prediction rule that indicates to omit treatment, further test using a rapid antigen strep test (with or without confirmatory culture), or empirically treat with antibiotics. The sensitivity of the rapid antigen strep test has recently been shown to vary with the spectrum of disease (spectrum bias). As the Centor's score increases (0 or 1, 2, 3, or 4), there is an associated increase in the sensitivity of the rapid antigen strep test (61%, 76%, 90%, and 97%).[5]

Table 2. McIsaac modification of the Centor Strep Score: add up points for patient symptoms or signs.[2,12]*

Symptom or Sign	Points
History of fever or measured temperature >38°C (100.3°F)	1
Absence of cough	1
Tender anterior cervical lymph nodes	1
Tonsillar swelling or exudates	1
Age <5 y	1
Age >45 y	−1

*Reprinted from: Ebell MH, Smith MA, Barry HC, et al. The rational clinical examination: does this patient have strep throat? *JAMA*. 2000;284:2912-2918. Centor RM, Witherspoon JM, Dalton HP, et al. The diagnosis of strep throat in adults in the emergency room. *Med Decis Making*. 1981;1:239-246.

Table 3. McIsaac modification of the Centor Strep Score: risk of streptococcal infection.[2,12]*

Points	Likelihood Ratio	Percentage With Strep (Patients With Strep/Total)
−1 or 0	0.05	1 (2/179)
1	0.52	10 (13/134)
2	0.95	17 (18/109)
3	2.5	35 (28/81)
4 or 5	4.9	51 (39/77)

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This rational clinical examination installment explores the usefulness of factors in the medical history and physical examination for diagnosing strep throat. Although few studies are perfect or universally applicable, the studies chosen for this review (and their summary) appear to be of relatively high quality, power, and applicability to the emergency department setting, making this a subject with an uncommonly rich evidentiary foundation and therefore uncommonly valid results. The authors note that no single element in the medical history or physical examination is sufficient to confirm or exclude streptococcal pharyngitis and recommend using the combination of clinical prediction rules, rapid antigen testing or throat culture, and clinician judgment. Although features of the clinical examination are not helpful in isolation, clinical prediction rules do appear to be effective in stratifying which patients are less and more likely to have bacterial infection. Clinical prediction rules have been noted to have an overall sensitivity of 64% to 83% and a specificity of 67% to 91% for predicting positive throat culture results in academic and community practices.[7] Under most diagnostic and treatment strategies, antibiotic use for viral pharyngitis, an extremely common occurrence according to current observational data, would be significantly reduced by using such rules, with little or no reduction in antibiotic coverage for bacterial disease.[6]

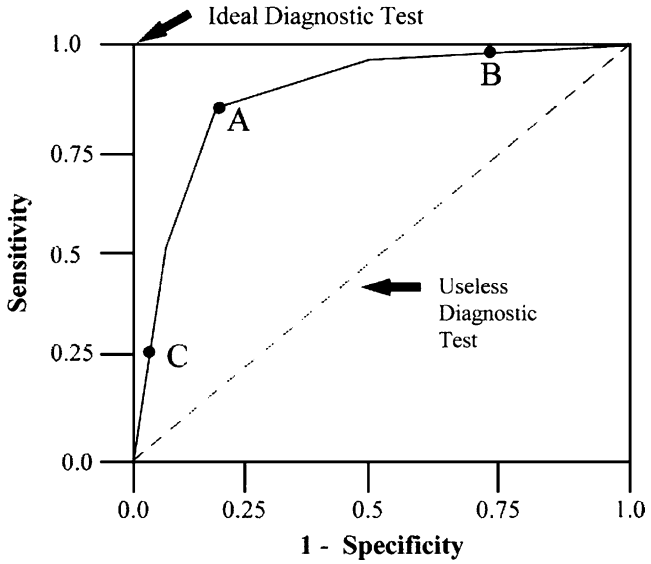

Figure. Receiver operating characteristic curve demonstrating various cutoff points and their impact on sensitivity and specificity. Note: *x*-axis is 1, specificity. Cutoff point A has equal false positives and false negatives, with sensitivity and specificity of approximately 80%. Point C represents a cutoff point with low sensitivity and high specificity, whereas point B has a high sensitivity and low specificity.
Reprinted from: Boardman LA, Peipert JF. Screening and Diagnostic Testing. *Clin Obstet Gynecol*. 1998;41:267-274.

TAKE HOME MESSAGE

Streptococcal pharyngitis is a common disease that cannot be identified by individual factors in the clinical examination. However, the clinical examination may be very helpful when combined with a clinical prediction rule, such as the Centor's criteria, to stratify the pretest probability of strep throat. Centor's scores of 0 or less and 4 or greater appear to be associated with quite useful likelihood ratios of 0.05 and 4.9, respectively. The likelihood of bacterial disease in those with scores from 1 through 3 appears to be only slightly modified by these findings. Results of this stratification can then inform the need for rapid antigen testing or throat culture to confirm disease, thereby limiting unnecessary antibiotic therapy.

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EBEM TEACHING POINT

Receiver operating curve. Receiver operating characteristic curve analysis was originally developed in the 1950s for use with radar technology in distinguishing inherent signal noise from true observations.[8] It has gained popularity in medicine for evaluating diagnostic test performance. Diagnostic tests are frequently defined in terms of "positive" or "negative" using a predefined threshold point to establish the classification. The cutoff point for a positive test will then subsequently determine the number of true positives, false positives, true negatives, and false negatives for the diagnostic test. Changes in a test's positive threshold level will affect these values, as well as the derived sensitivity and specificity. A lower positive test threshold level results in a higher sensitivity and a corresponding lower specificity. Inversely, a higher positive test threshold level will result in a lower sensitivity and a higher specificity. Receiving operator characteristic curves are a graphic plot of the number of true positives versus the number of false positives and represent the test's complete sensitivity and specificity range (Figure).[9] The receiving operator characteristic curve displays sensitivity (the true positive rate) on the vertical axis against the complement of specificity (1, specificity or the false positive rate) on the horizontal axis.[10] The area under the receiving operator characteristic curve describes the test's accuracy, with an area of 1.0 reflecting a perfect test, an area of 0.7 representing moderate-accuracy test, and an area 0.5 representing a test no better than chance (represented as a diagonal line in the Figure).[11] The receiving operator characteristic curve also graphically displays all of the possible threshold values, as well as the resulting sensitivity and specificity, for a diagnostic test. The point closest to the upper left corner on a receiving operator characteristic curve represents the test's optimal threshold level, diagnosing the most true positives with the least false-positive results.[9]

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