

PERSPECTIVES

Pharyngitis Management: Defining the Controversy

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Despite numerous controlled trials, clinical practice guidelines and cost-effective analyses, controversy persists regarding the appropriate management strategy for adult pharyngitis. In this perspective, we explore this controversy by comparing two competing clinical guidelines. Although the guidelines appear to make widely diverging recommendations, we show that the controversy centers on only a small proportion of patients: those presenting with severe pharyngitis. We examine recently published data to illustrate that this seemingly simple problem of strep throat remains a philosophical issue: should we give primacy to relieving acute time-limited symptoms, or should we emphasize the potential societal risk of antibiotic resistance? We accept potentially over treating a minority of adult pharyngitis patients with the most severe presentations to reduce suffering in an approximately equal number of patients who will have false negative test results if the test-and-treat strategy were used.

KEY WORDS: streptococcal pharyngitis; group C; group A; fusobacterium necrophorum; lemiere's disease; tonsils; guidelines.

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Twenty-five years ago, I (RMC) first published a clinical prediction model to derive the probability of streptococcal pharyngitis in adult sore throat patients.¹ Over the years, most authors have adopted this scoring system as the best validated method for clinically evaluating adult pharyngitis. The model was developed before the introduction of rapid antigen testing to provide practicing physicians a method for making timely clinical decisions given the delay in throat culture results. Initially, the strategy we proposed of either empiric antibiotics or testing before antibiotics administration for patients with higher probability of streptococcal pharyngitis had no major

opposition. However, over the following years, we have gained a better understanding about the epidemiology of acute adult sore throat, recognizing the importance of group C beta-hemolytic streptococcus.² In addition, the technology for rapid antigen testing advanced. Consequently, thinking about adult pharyngitis changed over the recent years, raising new controversies that we address in this perspective.

Recent articles highlight competing management strategies for adult pharyngitis patients.³⁻¹⁰ Some articles, including 2001 American College of Physicians-American Society of Internal Medicine (ACP-ASIM) "Principles of Appropriate Antibiotic Use for Acute Pharyngitis in Adults"¹¹⁻¹³ emphasize patient symptom relief while the others, including 2002 release of the Infectious Disease Society of America (IDSA) "Practice Guidelines for the Diagnosis and Management of Group A Streptococcal Pharyngitis,"¹⁴ give higher priority to preventing unnecessary antibiotic use. Table 1 outlines the similarities and differences between those two guidelines for adult pharyngitis patients. Carefully considering this seemingly simple and straightforward syndrome reveals an interesting philosophical problem: should we give primacy to relieving acute time-limited symptoms, or should we emphasize the potential societal risk of antibiotic resistance?

Bisno and colleagues conclude in a 2002 viewpoint⁴:

"... that the algorithm-based strategy proposed in the ACP-ASIM guideline would result in the administration of antimicrobial treatment to an unacceptably large number of adults with nonstreptococcal pharyngitis."

The IDSA's primary concern with the algorithm-based approach is the use of a pharyngitis prediction rule they feel is not specific enough to differentiate group A Streptococcal (GAS) from acute viral pharyngitis. They explicitly assume that only group A beta-hemolytic streptococcal pharyngitis requires antibiotic treatment. By endorsing a "test-and-treat" strategy which favors testing all patients "suspected on clinical and epidemiological grounds" and treating with antibiotics only those with a positive result for group A beta-hemolytic streptococcus, the IDSA expects to decrease "unnecessary" antibiotic use, thereby, preventing further antibiotic resistance.

Although these contrasting approaches may seem far apart, the controversy actually focuses on a fraction of adult pharyngitis patients.¹⁴⁻¹⁶ Even though the IDSA guidelines do not endorse using the clinical pharyngitis score that we developed in 1981 (Commonly known as the Centor score)¹ to distinguish streptococcal from nonstreptococcal pharyngitis in high-risk patients, they acknowledge its utility in identifying the subset of patients at low risk for GAS. To use the Centor score, the

We acknowledge that the designation severe pharyngitis is somewhat arbitrary. We have used the designation previously.¹⁵ Unpublished data support that patients with scores of 3 and 4 have more severe difficulty swallowing, which we equate with severity. Some patients with lower scores will consider their symptoms severe.

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Table 1. Comparison of adult pharyngitis guideline recommendations for diagnostic testing and antibiotic treatment stratified by centor score

Centor Score		IDSA	ACP-ASIM
0	Test	No	No
	Treat	No	No
1	Test	No	No
	Treat	No	No
2	Test	Rapid antigen test*	Rapid antigen test
	Treat	PCN-V if rapid antigen test is positive	PCN-V if rapid antigen test is positive
3	Test	Rapid antigen test	No test or Rapid antigen test
	Treat	PCN-V if rapid antigen test is positive	Empiric PCN-V or PCN-V if rapid antigen test is positive
4	Test	Rapid antigen test	No Test
	Treat	PCN-V if rapid antigen test is positive	Empiric PCN-V

*While the original IDSA (Infectious Disease Society of America) guidelines recommended throat cultures for negative rapid antigen tests, the current revision no longer endorses routine throat cultures for adult patients with a negative rapid antigen test. The ACP-ASIM guidelines also do not recommend backup throat cultures for negative rapid antigen tests.

examining clinician assigns 1 point each for: tonsillar exudates, swollen tender anterior cervical nodes, fever history, and lack of a cough, resulting in a score with a possible range of 0 to 4. The ACP-ASIM and IDSA agree that patients with scores of 0 or 1 (mild pharyngitis) should be treated symptomatically with no testing and no antibiotics because these patients have a very low probability of streptococcal pharyngitis. Both agree that patients having a score of 2 should undergo further testing. The controversy, therefore, centers only on those patients with scores of 3 or 4, herein referred to as severe pharyngitis. Figure 1 shows the approximate severity distribution of adult patients presenting with sore throat, only 30% of whom have severe symptoms.¹

As noted by Bisno and reported by Linder, 73% of adult pharyngitis patients currently receive antibiotics.^{4,17} In our 1981 pharyngitis study, almost half of the patients had mild pharyngitis. If generalists simply followed the ACP-ASIM guidelines and neither tested nor provided antibiotics to these patients, we would immediately decrease antibiotic use by approximately one-third. Both guidelines agree with testing the 25% of patients with scores of 2. As less than 20% of patients with scores of 2 will test streptococcal positive, this strategy would further decrease antibiotic use. By following the ACP-ASIM guidelines as written (even with empiric antibiotics for all severe pharyngitis), antibiotic usage would decrease from 73% to 35%. Thus, the “unacceptably large number of adults” receiving unnecessary antibiotics represent, at most, a small proportion of the 30% of adult patients with severe pharyngitis.

The four commonly cited reasons for treating group A beta-hemolytic streptococcal pharyngitis are prevention of non-suppurative complications, prevention of suppurative complications, symptom resolution, and decreased transmission to contacts. Below, we contrast the rationale for treating all patients with severe pharyngitis with antibiotics with the two main reasons proposed for the “test-and-treat” strategy: antibiotic anaphylaxis and generation of antibiotic resistance.

PREVENTING NON-SUPPURATIVE COMPLICATIONS

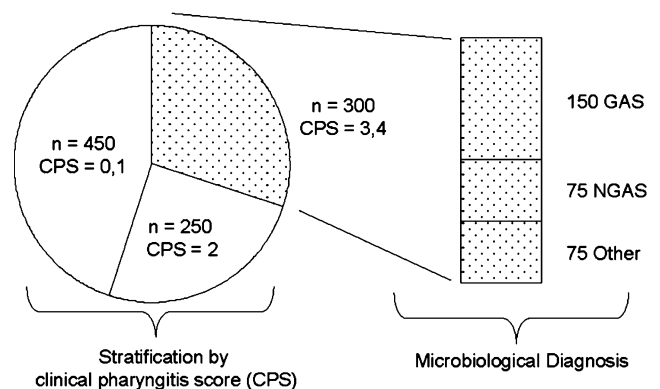
All strategies (immediate antibiotics, culture, or rapid testing) will prevent most non-suppurative complications (acute rheumatic fever). Given the imperfect sensitivity of both culture and rapid testing, these strategies may fail to prevent a low percentage of acute rheumatic fever cases, but given the low rate of this complication in the United States, acute rheumatic fever risk should not influence our decision making. We have no evidence that treatment prevents other non-suppurative complications. We know of no evidence that the non-group A streptococci cause non-suppurative complications.

PREVENTING SUPPURATIVE COMPLICATIONS

Preventing suppurative complications is more challenging.¹⁸ One could argue that prompt antibiotics (either with empiric therapy or rapid testing) will decrease the risk of peritonsillar abscess compared to a 2-day delay in antibiotics experienced from the culture strategy. A recent review of the microbiology of peritonsillar abscess included group A and group C streptococci and anaerobic bacteria.¹⁹ Most patients with positive cultures (aspiration of the abscess) have negative throat swabs.²⁰ Empiric antibiotics would likely prevent some suppurative complications above those prevented when treating only rapid test positive patients.

Another potential reason for antibiotic therapy for severe pharyngitis is to treat *Fusobacterium necrophorum*. Recent data suggest that these bacteria may cause endemic acute pharyngitis. *F. necrophorum* infections can cause Lemierre’s Disease, peritonsillar abscess and persistent sore throat symptoms.²¹⁻²⁴ While we do not yet know the probability of progression to these complications, certainly empiric antibiotic treatment would likely decrease their incidence. A recent pediatric paper has documented the increasing incidence of *F. necrophorum* infections (including Lemierre’s Syndrome) over a recent 6-year period. The authors speculate that

Characteristics of 1000 Hypothetical Patients with Sore Throat



Abbreviations: GAS - Group A Streptococcus; NGAS - Non Group A Streptococcus;

Figure 1 Characteristics of 1,000 hypothetical patients with sore throat.

Table 2. Treatment appropriateness for 300 hypothetical patients (from Fig. 1) with severe pharyngitis: test and treat when positive versus treat all

Patient number (%)	Pharyngitis etiology	Rapid antigen test		Appropriateness	
		Results	Classification	“Test-and-treat if positive”	“Treat all”
135 (45%)	GAS	+	True Positive	A	A
15 (5%)	GAS	-	False Negative	I	A
75 (25%)	NGAS	-	True Negative	I	A
75 (25%)	Other	-	True Negative	A	I

GAS Group A streptococcus, NGAS non-group A streptococcus, A appropriate, I inappropriate.

decreased empiric antibiotic use may be contributing to the resurgence of this infection.²⁵

SYMPTOM RELIEF

Starting antibiotics on the day of clinical presentation will decrease symptom duration. Zwart and colleagues showed that immediate penicillin V, given for 7 days, decreased group A streptococcal symptoms in 2.5 days, and non-group A streptococcal symptoms, in 1 day in adult patients.²⁶ Previous analyses suggested that antibiotics decrease symptom duration by only 1 day. Zwart’s finding of greater benefit most likely resides in the study population. His study focused on patients at the heart of the controversy: those with pharyngitis scores of 3 or 4. No previous study of symptom benefit either restricted enrollment to adults or just those patients having severe pharyngitis.

As the Centor score increases, we suspect that symptom severity also increases. Acute adult pharyngitis causes a substantial several day quality of life decrement. Because prompt antibiotics speed recovery from this discomfort, symptom relief may dominate the treatment decision for many patients with severe adult pharyngitis.

Most articles assume that only group A beta-hemolytic streptococcal pharyngitis requires treatment. However, adult patients clearly develop significant pharyngitis because of non-group A beta-hemolytic streptococci, especially from groups C and G.^{2,27-29} Randomized trial data also suggest a symptomatic benefit for treating these patients.²⁶

PREVENTING TRANSMISSION

Immediate antibiotics decrease the communicability of bacterial pharyngitis. Thus, immediate antibiotics convey an advantage to household contacts (important to many patients with children). Because non-group A streptococci can cause epidemic pharyngitis,²⁷ we assume that immediate treatment will decrease communicability of those infections also.

ANTIBIOTIC ANAPHYLAXIS

Immediate treatment does give penicillin to more patients, putting a few additional patients at risk for allergic reactions.

Penicillin allergic reactions did not have a significant influence on the treatment decision when tested in previous decision and cost-effectiveness models.^{6,9}

ANTIBIOTIC RESISTANCE

We cannot quantify the contribution that oral penicillin for severe pharyngitis makes to the antibiotic resistance problem. Despite over 50 years of penicillin use, we still do not have penicillin resistant group A beta-hemolytic streptococci. Certainly, penicillin use could select out other bacteria for resistance. As most other bacteria already have penicillin resistance, we consider this risk less significant. Both guidelines argue for narrow spectrum antibiotics. Linder and colleagues have shown in two articles that the use of broad-spectrum antibiotics for pharyngitis is a major problem.^{16,17} All experts agree that we should join in correcting these inappropriate antibiotic prescriptions.

SUMMARY

Summarizing the strategy differences in Table 2, we present percentage estimates from Zwart’s prospective study of adult severe pharyngitis patients. In Zwart’s study, the prevalence of group A streptococci is 50% and non-group A strep, 25%. The “treat all severe pharyngitis patients” strategy provides antibiotic prescriptions to all adult patients having group A and non-group A streptococcal pharyngitis. This strategy would likely also prevent some cases of Lemierre’s Disease. The “test-and-treat” strategy misses 10% of group A streptococcal pharyngitis and all the non-group A pharyngitis. These cases are missed because the rapid antigen test has a sensitivity of approximately 90% for group A streptococci³⁰ and does not test for either group C or group G streptococci. We favor treating all severe pharyngitis to benefit this approximately 30% of severe pharyngitis patients that the testing strategy would omit. Our analysis is certainly sensitive to both the prevalence of group A and non-group A streptococci and the sensitivity of the rapid antigen test utilized. Although Zwart’s prevalence estimates are higher than previously reported in the literature, we use these data from the only randomized controlled trial that focused solely on patients with severe pharyngitis.

Our strategy does result in prescribing antibiotics to 25% of the severe pharyngitis patients having no streptococcal infection. However, we believe that relieving suffering remains the physician’s primary objective. Adult group A and non-group A streptococcal pharyngitis causes severe, albeit limited, symptoms, which improve more rapidly with narrow spectrum antibiotics. Using narrow spectrum antibiotics (penicillin V or erythromycin for those who are penicillin allergic) and limiting antibiotics to severe pharyngitis will minimize new antibiotic resistance while affording ill patients a faster recovery.

In summary, we believe the differences between the two guidelines result from a difference in the perceived importance of antibiotic over versus under use.¹⁰ We do not believe that the ACP-ASIM algorithm-based guideline results in an unacceptably large amount of unnecessary antibiotic use. On the contrary, we accept over treating a minority of

adult pharyngitis patients with the most severe presentations in an effort to reduce suffering in an approximate equal number of patients who will be under treated with the test and treat strategy. The problem of antibiotic overuse for sore throat is not a result of the algorithm-based approach outlined in the ACP-ASIM guideline, but instead, reflect poor adherence to the guideline as written.¹⁶ Furthermore, we believe strict adherence to the IDSA guideline will only marginally reduce antibiotic overuse, and quite possibly, increase undue suffering.

Potential Financial Conflicts of Interest: None disclosed.

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