Reconsidering sore throats

Part 1: Problems with current clinical practice

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ABSTRACT

OBJECTIVE To provide evidence-based answers to clinical questions posed by family physicians about Group A streptococcus pharyngitis and to further understanding of why management is controversial.

QUALITY OF EVIDENCE Evidence from randomized trials was not found for most questions. The most critical information came from high-quality community prevalence studies and criterion standard studies of physician clinical judgment.

MAIN FINDINGS Expert recommendations for physician management are not likely to help prevent rheumatic fever, as most people with sore throats do not seek medical care. Current clinical practices result in overuse of antibiotics because accuracy of clinical judgment is limited.

CONCLUSIONS Costs associated with visits for upper respiratory infections as well as increasing antibiotic resistance necessitate reconsidering the current clinical approach. An alternative management strategy is presented in part 2.

RÉSUMÉ

OBJECTIF À partir de données probantes, répondre aux questions cliniques des médecins de famille concernant la pharyngite à streptocoques du groupe A et améliorer notre compréhension de la controverse qui persiste quant à son traitement.

QUALITÉ DES PREUVES Les essais randomisés ne fournissent pas de preuves permettant de répondre à la plupart des questions. Le plus haut degré d'information critique nous est fourni par des études de grande qualité touchant la prévalence communautaire et par des études sur le jugement clinique du médecin à partir de critères standards.

PRINCIPAUX RÉSULTATS En termes de traitement médical, les recommandations des experts ont peu de chance de prévenir le rhumatisme articulaire aigu puisque la plupart des personnes qui présentent un mal de gorge ne consultent pas les médecins. Les pratiques cliniques actuelles entraînent un recours abusif aux antibiotiques parce que la précision du jugement clinique est limitée.

CONCLUSIONS Les coûts générés par les consultations pour infections des voies respiratoires supérieures et l'antibiorésistance accrue nous forcent à remettre en question notre approche clinique actuelle. La deuxième partie de cet article offrira une stratégie thérapeutique de rechange.

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Family physicians frequently encounter children and adults who have sore throats either as an isolated symptom or in association with an upper respiratory tract infection. Upper respiratory tract infections account for about 12% of visits to family physicians at an estimated annual cost of $200 million in Ontario alone.[1,2]

Decisions about management often relate to whether or not there is a possibility of Group A streptococcus (GAS). Should a throat culture be taken? Should an antibiotic be prescribed at the initial office visit, or should this decision be delayed until the result of the throat culture becomes available? An optimal approach continues to be debated.[3,4]

This article is the first of two examining management of people presenting with sore throats. In this part, evidence-based answers to clinical questions posed by practising family physicians are presented, and problems with both expert recommendations and current clinical practices are discussed. In part 2, an alternative approach is proposed, and a tool for implementing the strategy is presented.

Background

In 1994, physicians from the Department of Family Medicine at the Stratford General Hospital in Ontario joined researchers at the Institute for Clinical Evaluative Sciences in Ontario to review sore throat management. The goal was to determine whether existing scientific literature supported any particular management approach and, if so, to find a way of applying the approach in community practice.

The community physicians produced a series of questions they considered clinically relevant. The research partners completed a broad MEDLINE search using the key words "pharyngitis," "controlled trials," and "rheumatic fever." This search was supplemented by a manual search of bibliographies of retrieved articles. Information was then summarized and presented to physicians at an intensive half-day workshop, during which they could examine the evidence for themselves. Each question was reviewed, and an alternative management approach was presented. Feedback and suggestions for revisions were obtained, and the final review was sent to three content experts for critical comment.

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Modern management practices in context

At the turn of the century, rheumatic fever cases were numerous, mortality following scarlet fever was 5%, and deaths from rheumatic heart disease were common.[5] From 1940 to 1950, death rates from chronic rheumatic heart disease in Canada were 10 to 12/100 000 persons, compared with a rate of 2 to 3/100 000 in 1985.[6] One clinician could "recall most vividly that acute rheumatic fever was one of the greatest plagues of the first half of this century."[7]

It was in this societal context that penicillin was demonstrated to prevent rheumatic fever in people with streptococcal pharyngitis.[8] In 1950, 798 military persons with "exudate on their tonsils or pharyngeal wall" received two intramuscular doses of penicillin G, while 804 did not. Rheumatic fever developed in two persons who had received penicillin and in 17 who had not. Its use was quickly adopted by physicians and accepted by the public as an effective way to prevent rheumatic fever, although some argued that sore throats not associated with epidemics conferred a low risk of rheumatic fever.[9]

Evidence-based answers to clinical questions

How often does rheumatic fever or glomerulonephritis occur and has the incidence of rheumatic fever declined because of the use of antibiotics? A study in Ontario of hospital separations from 1980 to 1986 reported 151 cases of acute rheumatic fever in people younger than 19 years.[10] The estimated incidence was 0.96/100 000 population, with no significant year-to-year variation. A Toronto Hospital for Sick Children study from 1972 to 1988 found 83 cases using strict criteria for diagnosing rheumatic fever. Incidence in this study was estimated to decline in children younger than 18 from 2.2/100 000 in 1972 to 0.5/100 000 in 1988.[11]

A worldwide decrease in rheumatic fever has been observed in many industrialized countries[5,12,13] but not in all developing countries[14] or aboriginal populations.[15,16] Although some outbreaks occurred in the United States in the mid-1980s,[17,18] death rates from rheumatic fever remain at an all-time low.[19] However,

the decline in rheumatic fever began some time before the introduction of penicillin.[20] Currently favoured theories to explain this are a combination of improved social conditions, antibiotic availability, and changes in the prevalence of virulent strains of streptococcus.[14,19,20]

What is the risk? A patient with GAS pharyngitis who does not receive antibiotic treatment risks developing rheumatic fever, glomerulonephritis, or a local complication (such as peritonsillar abscess). Experts believe that glomerulonephritis cannot be prevented by treating pharyngitis.[21] The risk of developing rheumatic fever during an epidemic is 3% or 30/1000 persons with GAS pharyngitis who do not receive antibiotics.[22] **Table 1**[23-25] shows studies of adults and children in communities with usual, or endemic, levels of GAS pharyngitis.

These studies suggest that, if 1000 persons with GAS pharyngitis are left untreated, three or four

Table 1. Occurrence of rheumatic fever after untreated streptococcal pharyngitis in the community (excluding epidemics)

STUDY	SETTING	SAMPLE	GROUP A STREPTOCOCCUS (%)	NOT TREATED	CASES OF RHEUMATIC FEVER	RISK OF RHEUMATIC FEVER
Siegel et al[23] (1961)	Pediatric practice, Chicago	2545	41	519	2	4/1000
Goslings et al[24] (1963)	Netherlands	233	60	115	0	4/1000*
Valkenburg[25] (1971)	Netherlands	1517	56	345	1	3/1000

**Estimated from four cases of rheumatic fever, which occurred in the community but were not seen in the study.*

Table 2. Effect of penicillin on symptoms

STUDY	SAMPLE N (AGE RANGE)	WAS ASSESSMENT BLINDED?	24-HOUR IMPROVEMENT		48-HOUR IMPROVEMENT	
			CONTROL	PENICILLIN	CONTROL	PENICILLIN
RELIEF OF SORE THROAT						
Merenstein and Rogers[28] (1974)	62 (any age)	No	31%	78%	—	—
Randolph et al[29] (1985)	194 (2-20 y)	No	25%	95%	—	—
Middleton et al[30] (1988)	57 (4-29 y)	Yes	61%	74%	78%	94%
Pichichero et al[31] (1987)	114 (4-18 y)	Yes	2.2*	1.8*	1.6*	1.3*
El-Daher et al[32] (1991)	229 (4-14 y)	Yes	—	—	-82%	98%
RELIEF OF FEVER						
Merenstein and Rogers[28] (1974)	62	No	46%	77%†	—	—
Krober et al[33‡] (1985)	26	Yes	38.1°C	37.1°C†	38.0°C	36.8°C†
Randolph et al[29] (1985)	194	No	95%	95%	—	—
Pichichero et al[31‡] (1987)	114	Yes	37.4°C	37.0°C†	37.1°C	36.9°C
Middleton et al[30] (1988)	57	Yes	87%	79%	100%	97%
El-Daher et al[32‡] (1991)	229	Yes	—	—	38.0°C	37.2°C†

**Score where 1 = mild sore throat, 2 = moderately severe, and 3 = severe.*
†$P \leq 0.01$.
‡Average temperature.

Table 3. Ontario Medical Association Adverse Drug Reaction Reporting Program: *Serious reactions and fatalities for selected drug classes, 1984[45] and 1992[44]*

	TOTAL REPORTS		SERIOUS REACTIONS		FATALITIES	
DRUG CLASS	1984	1992	1984	1992	1984	1992
Antimicrobials	138	193	41	44	3	3
Nonsteroidal anti-inflammatory drugs	46	34	28	15	12	2
Vaccines	21	18	15	5	0	0

cases of rheumatic fever occur. This is a 10-fold decrease in risk compared with an epidemic and supports the view the attack rate in endemic setting is lower.[22] An overview of randomized treatment trials estimated that penicillin would reduce this risk by 75%.[26] Although most rheumatic fever occurs in children, a 1987 outbreak involved 10 male naval recruits ranging in age from 19 to 31.[17]

Does penicillin work better than placebo? A study of tonsillitis in 17 countries found the mean duration of fever was 2 to 3 days even among those not treated with antibiotics.[27] **Table 2**[28-33] shows other studies of the effects of penicillin on symptoms adapted and updated from an overview by Del Mar.[26]

It is important to rely on randomized, double-blind trials where patients and investigators do not know who has placebo and who has antibiotics when assessing a subjective symptom like sore throat (**Table 2**[28-33]). Studies with inadequate blinding[28,29] showed a larger benefit for penicillin than studies where a placebo indistinguishable from penicillin was used.[30-32]

Table 4. Prevalence of throat findings in people with and without Group A streptococcus

STUDY	GAS (%)	NON-GAS (%)
RED THROAT		
Siegel et al[23]	88	84
Stillerman and Bernstein[47]	78	43
Walsh et al[48]	98	84
EXUDATE		
Siegel et al[23]	40	21
Stillerman and Bernstein[47]	26	12
Walsh et al[48]	47	21

Even with adequate blinding, it is difficult to interpret the clinical importance of observed sore throat relief. For instance, one study asked people to score their sore throat as 1 if mild, 2 if moderate, or 3 if severe.[31] There was a statistical difference in the scores obtained, but the clinical relevance of a score of 2.2 (just above moderately severe sore throat) compared with a score of 1.8 (just below moderately severe) is questionable. However, in a group of children with more severe symptoms and an average temperature of 38.8°C, the proportion with a severe sore throat in those not receiving penicillin until culture results were known increased from 34% to 52% at 48 hours.[32] In children given antibiotics immediately, severe sore throat declined from 41% to 1%. Symptoms of irritability, abdominal pain, and headache were all similarly improved with early penicillin treatment.

In most studies, the temperature difference between treated and untreated groups was about 1°C in favour of penicillin (**Table 2**[28-33]). Only one study reported on return to work or school and found no difference in the first 24 hours, but it is doubtful that the study had enough participants to detect a significant difference if it existed.[30]

While these studies suggest quicker relief of sore throat with penicillin therapy, at least in children with severe symptoms, symptoms resolve even without antibiotic treatment. It is unclear whether symptoms in milder presentations are relieved just as effectively with antipyretics while awaiting culture results. There is little information about adults. Also, in relation to concerns about delaying antibiotics, expert opinion is that penicillin prevents rheumatic fever even when administered several days after symptom onset.[22]

What are the risks of treating pharyngitis with antibiotics? An important concern about widespread antibiotic use is the promotion of antibiotic resistance.[34,35] A recent Canadian survey found 40% of

Haemophilus influenzae were resistant to amoxicillin, while penicillin-resistant pneumococcus had increased from 1.5% in 1988 to 9% in 1994.[36,37] Group A streptococci remain sensitive to penicillin,[34,38,39] but resistance to erythromycin has been reported.[40,41] Although prescribing habits are not the sole cause, penicillin-resistant pneumococcus declined in Hungary when prescribing decreased.[42]

Antibiotics are also the most commonly prescribed drugs[43]; while death is uncommon, these drugs account for the greatest proportion of adverse drug events (**Table 3**[44,45]). In a large US health maintenance organization, 12 cases of serum sickness occurred in 3487 children prescribed antibiotics for either otitis media or pharyngitis.[46] Early antibiotic treatment might also have other effects. Two randomized trials reported 29% to 37% of children treated immediately suffered recurrences of GAS pharyngitis in the next 4 months, compared with 8% to 16% of those who were not treated until culture results were available 48 hours later.[31,32]

How accurate is clinical diagnosis? **Table 4**[23,47,48] shows the proportion of people with throats positive for GAS who have a red throat or exudate, compared with those with negative cultures. Throat findings are similar among those with and without GAS. Reliance on red throat alone would cause up to 80% of those with a negative throat culture to be incorrectly diagnosed as having GAS pharyngitis. Pharyngeal or tonsillar exudate has a higher specificity but will miss 50% to 75% of GAS cases.

Table 5[23,49-54] shows studies comparing physician clinical judgment with throat culture results. The sensitivity of clinical diagnoses ranged from 45% to 93%, although the New Zealand study used antibiotic treatment as a proxy for diagnosis. This study could be less relevant, as 74% of those with a negative throat culture also received antibiotics.[51] Similarly, the Japanese study could also be less generalizable, as only three physicians with a special interest in GAS were involved.[54]

In the remainder, sensitivity of clinical judgment was 45% to 72%. The implication is that clinical diagnosis as

Table 5. Physicians' accuracy at diagnosing Group A streptococcus pharyngitis on clinical grounds

STUDY	SETTING	SAMPLE	GROUP A STREPTOCOCCUS PREVALENCE (%)	SENSITIVITY (%)	SPECIFICITY (%)
Hart[49] (1976)	General practice in Winnipeg	540	10	56	57
Shank and Powell[50] (1984)	General practice in United States	3982	16	45	80
Kljakovic[51] (1993)	General practice in New Zealand	329	12	93	26
Centor et al[52] (1981)	Emergency department in United States	286	17	72	76
Siegel et al[23] (1961)	Pediatric hospital in United States	2545	48	55	73
Cebul and Poses[53] (1986)	Student service in United States	310	5	53	67
Fujikawa and Ito[54] (1985)	Pediatric hospital in Japan	271	40	90	71

Table 6. Physicians' stated practices for managing patients presenting with pharyngitis

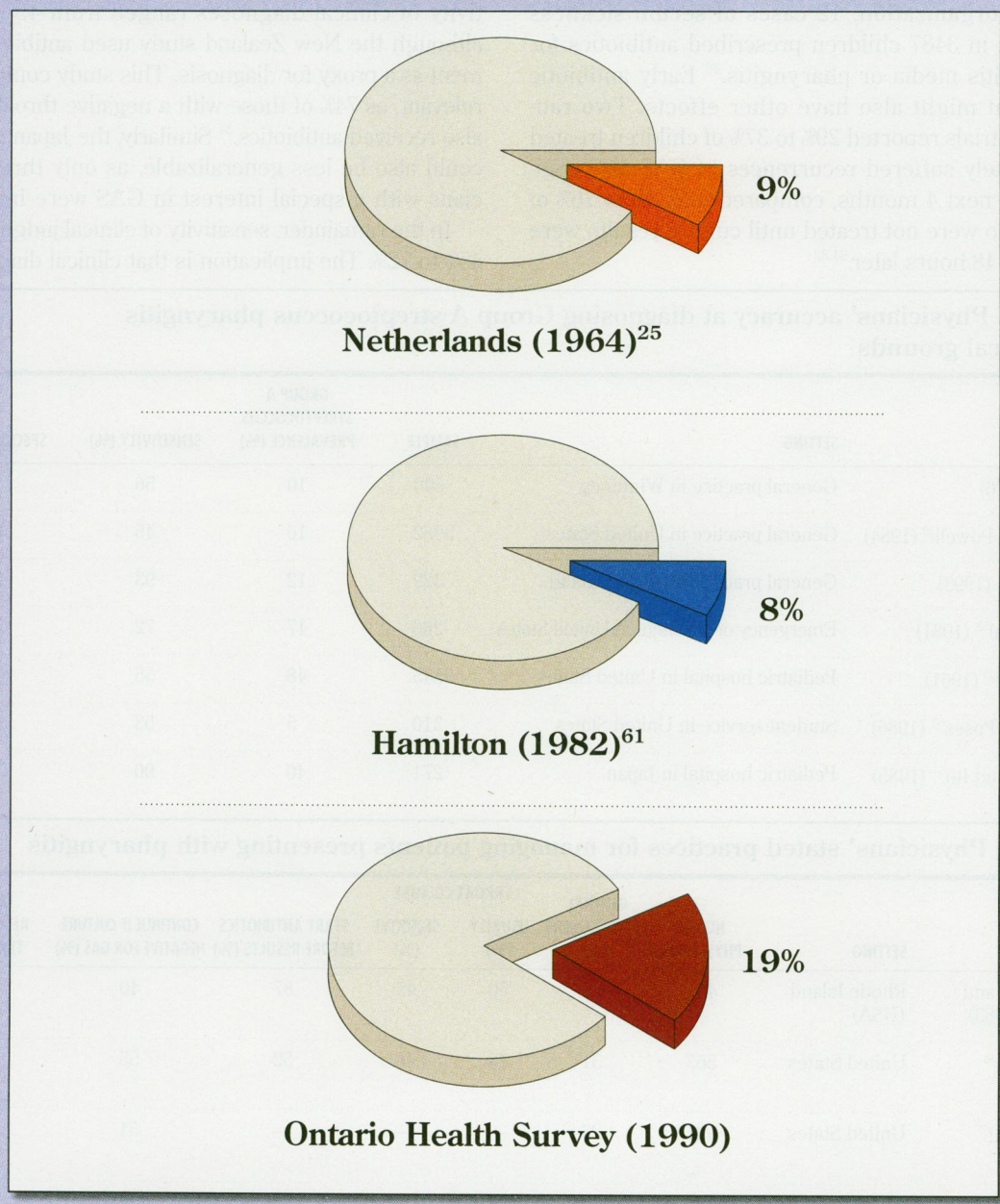
STUDY	SETTING	NO. OF PHYSICIANS	GENERAL PRACTITIONERS (%)	THROAT CULTURE		START ANTIBIOTICS BEFORE RESULTS (%)	CONTINUE IF CULTURE NEGATIVE FOR GAS (%)	CULTURE RESULTS NOT TIMELY (%)
				USUALLY (%)	SELECTIVE (%)			
Holmberg and Faich[55] (1983)	Rhode Island (USA)	491	29	50	45	87	40	44
Cochi et al[56] (1984)	United States	567	31	18	46	52	55	54
Arthur et al[57] (1984)	United States	921	23	—	—	—	51	—
Berger et al[58] (1989)	Alberta (Canada)	85	100	53	—	78	12	56

it is usually practised misses from one quarter to half of GAS pharyngitis cases. The 57% to 80% range for specificity suggests that clinical diagnosis labels 20% to 40% of those with negative throat cultures as having GAS. Given the prevalence of GAS of 10% to 20%, 80% to 90% of sore throats typically seen by family physicians will likely have throat cultures negative for GAS. Reliance on clinical diagnosis as a basis for prescribing decisions will result in overuse of antibiotics.

Expert recommendations and physician practice patterns

Expert groups support continued reliance on throat cultures. In 1988 the American Heart Association Committee on Rheumatic Fever concluded that preventing rheumatic fever depended on "control of Group A β-hemolytic streptococcal upper respiratory tract infections."[22] Antibiotics could be safely withheld with a negative culture, and GAS was almost

Figure 1. Proportion of people with sore throats who contact a physician



always found on culture in people with active infections. Both the American Academy of Pediatrics[21] and the Canadian Paediatric Society[38] recommend throat cultures as the basis for managing children with pharyngitis.

Studies of physicians' practices in managing sore throats are few (**Table 6**[55-58]). Three surveys done in the United States included a mix of internists, pediatricians, and family physicians who provided primary care services. A Canadian study involved 85 family physicians from one region in Alberta attending a continuing medical education conference. These researchers reported that 20% to 50% of physicians said they took throat cultures "most of the time." Another 45% would take a throat culture "in selected cases" based on clinical presentation. Most physicians initiate antibiotics before receiving culture results, if they consider it warranted clinically. If no throat culture was taken, 81% of Canadian physicians rely on clinical findings to make a prescribing decision.

These surveys suggest differences between expert recommendations and actual clinical practice. At least half of physicians use cultures selectively, relying on clinical judgment instead. Experts cite difficulties in clinically differentiating viral and GAS infections.[22] Practitioners are advised to wait for culture results before instituting therapy, but most initiate antibiotics immediately based on clinical judgment. Anecdotal reports from other countries suggest similar practices.[59,60]

Which sore throats reach medical attention?

Figure 1 shows the proportion of people with sore throats or colds who seek medical attention. In 1964, 7.1% of people in two villages in the Netherlands experienced a sore throat over 2 months.[25] While this represented 800 persons, only 247 persons with pharyngitis visited physicians that year. It was estimated that 9% of streptococcal sore throats were seen by a physician.

In Ontario, 500 persons aged 21 to 60 kept a diary of symptoms and any action they took for 3 months.[61] An upper respiratory symptom was noted in 11% of diaries, while 5% recorded a sore throat on at least 1 day. Contact with a health professional was made for 16% of sore throat episodes, while 8% led to a family physician visit. The 1990 Ontario Health Survey revealed 4.5% of people experienced a cold in any 2-week period that caused them to stay in bed, see a professional, take a prescription drug, or use an over-the-counter medication (unpublished data; personal communication from Iron K). Almost 19% reported contact with a general practitioner. The higher proportion contacting medical professionals in this study could reflect the fact that minor "colds" were not counted. These studies suggest that family physicians see only a small fraction of all sore throats in a given community.

Are sore throats seen by physicians worse?

Those who rated their sore throats as either 4 or 5 on a 5-point severity scale were more likely to make medical contact in the health diary study. Still, only 50% sought medical help.[61] In 6000 episodes of respiratory illness in children from 1953 to 1967, 21% of GAS cases and an estimated 20% of cases demonstrating a two-fold rise in antistreptolysin-O titre occurred in children without sore throats.[62] Children with mild presentations (sore throat, fever lower than 38°C or runny nose; cough and fever lower than 38°C) accounted for 30% of GAS cases and 21% of significant changes in antistreptolysin-O titre.

These studies could explain in part the observation that "it is not uncommon for episodes of rheumatic fever to result from inapparent streptococcal infections for which patients do not seek medical care."[22] They suggest that the small fraction of people with sore throats visiting doctors probably does not represent all clinically important GAS disease in a community.

Conclusion

Expert recommendations encourage widespread use of throat cultures to identify GAS disease as a basis for rheumatic fever prevention. This strategy fails to recognize the passive nature of office-based prevention; only those who seek medical care are treated. This is likely only a small proportion of the population at risk and would necessitate a great increase in use of throat cultures for marginal gains in rheumatic fever prevention, given current low incidence.

Physicians have rejected these recommendations in favour of selective use of throat cultures, incorporating clinical judgment in decision making. The trade-off has been widespread use of antibiotics in self-limited respiratory illnesses. In the second article we present an alternative strategy that seeks to balance these two approaches.

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