



New Zealand

# Guidelines

for

Rheumatic Fever

## 2. Group A Streptococcal Sore Throat Management

Evidence-based, best practice  
Guidelines on:

1. Diagnosis, Management and Secondary Prevention
2. Group A Streptococcal Sore Throat Management
3. Proposed Rheumatic Fever Primary Prevention Programme

**Endorsed by:**

The Cardiac Society  
of Australia  
and New Zealand



**Pacific Islands  
Heartbeat  
Programme**



Evidence-based, best practice  
New Zealand Guidelines for Rheumatic Fever

## 2. GROUP A STREPTOCOCCAL SORE THROAT MANAGEMENT

*He korokoro ora he manawa ora,  
Mo tatou katoa*

*(A healthy throat, a healthy heart for us all)*

**May 2008**

## Table of Contents

1.	<b>Foreword</b>	5
2.	<b>Scope and Purpose of Guideline</b>	6
	Gaps between current practice and evidence	6
3.	<b>About the Guideline</b>	6
	Disclaimer	7
	Outline of grading methodology used	7
	Guideline development process	8
	Endorsing organisations	9
	Organisations consulted	9
	New Zealand guidelines: writing group	9
	Peer reviewers and contributors	10
	Acknowledgements	12
	Declarations	12
4.	<b>Executive Summary &amp; Recommendations</b>	13
	Key messages	13
	Algorithm	14
5.	<b>Introduction</b>	18
6.	<b>Clinical Questions</b>	20
Q1.	Which clinical signs and symptoms best correlates with group A streptococcal (GAS) pharyngitis infection in adults and children?	20
Q2.	Should patients of different ages and ethnicities have their sore throats managed differently?	21
Q3.	Which test should be done to diagnose GAS pharyngitis?	23
Q4.	Are two throat swabs more accurate than one?	24
Q5.	Which antibiotic should be used for treating GAS pharyngitis and for how long?	24
Q6.	Should GAS culture-positive pharyngitis patients be isolated?	26
Q7.	How should treatment failure and/or the recurrence of GAS pharyngitis be managed?	27
Q8.	How should asymptomatic pharyngeal carriers of GAS be managed?	28
Q9.	In patients with or without GAS pharyngitis, do antibiotics shorten symptoms of sore throat on day 3 and at one week (days six to eight)?	28
Q10.	Does treating pharyngitis with antibiotics reduce the suppurative complications of GAS pharyngitis (acute otitis media and quinsy)?	30
Q11.	Do antibiotics reduce the incidence of non-suppurative complications of GAS pharyngitis (acute post streptococcal glomerulonephritis (APSGN) and ARF)?	30
Q12.	Which measures improve adherence to antibiotic courses (prescribed for GAS pharyngitis)?	31
Q13.	Do recurrent sore throats increase the risk of a patient progressing to ARF?	31
Q14.	Does delay in the availability of the throat culture result (up to nine days) increase the risk of the development of ARF?	32
Q15.	Is seasonal prophylaxis for recurrent streptococcal pharyngitis useful?	32
Q16.	Does having a smoker in the house make GAS throat infection more likely?	33
Q17.	Is there a vaccine available for the control of GAS disease?	33

Q18.	Should throat swabs be repeated after antibiotic course has ceased?	33
Q19.	Is there a role for tonsillectomy in recurrent pharyngitis?	34
Q20.	Which factors lead to the spread of GAS pharyngitis?	34
7.	<b>Implementation of the Guideline</b>	37
	Driving forces	37
	Restraining forces	37
	Consultation	37
	Suggested implementation strategies	37
	Measuring effectiveness/outcomes	38
	Economic analysis: to come	38
8.	<b>Appendices</b>	
	Appendix A: Microbial causes of acute pharyngitis	39
	Appendix B: Guideline development process	40
	Appendix C: Rheumatic fever incidence in New Zealand per District Health Board	42
	Appendix D: Areas of New Zealand with high incidences of rheumatic fever	43
	Appendix E: Incidence of ARF in children and adolescents in studies published since 1990	44
	Appendix F: Differential diagnosis of pharyngitis	47
	Appendix G: Throat swab technique	48
	Appendix H: Once daily amoxicillin studies	49
	Appendix I: Statistics for Clinical Questions No. 9, 10 & 11	51
	Appendix J: Studies listing sore throat episodes of rheumatic fever	53
	Appendix K: Studies involving fomites in the spread of GAS	54
9.	<b>References</b>	55
10.	<b>Key Definitions</b>	63
11.	<b>Glossary</b>	64

## List of Tables

1.	Levels of evidence for clinical interventions and grades of recommendation	7
2.	Infectious Diseases Society of America (IDSA) – United States Public Health Service grading system for rating recommendations in clinical guidelines	8
3.	Routine antibiotics	16
		26
4.	Recurrent antibiotics	16
		27
5.	Modified Centor criteria for the management of pharyngitis in adults and children	20
6.	Scoring system for modified Centor criteria	20
7.	Notified rheumatic fever cases in New Zealand 2003 (initial cases & recurrences)	22
8.	Group A Streptococcus sensitivities 2004	24
9.	Recommendations for standard antibiotic regimes for GAS pharyngitis	24
10.	Studies on seasonal prophylaxis for pharyngitis	32
11.	Microbial causes of acute pharyngitis	39
12.	Quality of the three guidelines used as a basis for the sore throat guideline	41
13.	Areas of New Zealand with high incidences of rheumatic fever	43
14.	Incidence of ARF in children and adolescents in studies published since 1990	44
15.	Differential diagnosis of pharyngitis	47
16.	Once daily amoxicillin studies	49
17.	Statistics for clinical questions (No. 9,10 & 11) treatment and symptoms of pharyngitis, treatment and suppurative and non-suppurative sequelae	51
18.	Studies listing sore throat episodes and rheumatic fever	53
19.	Studies involving fomites in the spread of GAS	54

## [1. Foreword]

*Kia ora koutou katoa  
Kei raro te aroha o to tatou atua  
Rau rangatira ma nga mihi rangatira ki a koutou katoa  
Tena koutou*

These guidelines are an important step in controlling rheumatic fever. This disease among Māori is important for two reasons: Firstly, currently 0-20 year olds are the largest age-group for Māori and by 2021 will make up 28% of this national age group population. Secondly our tamariki (*children*)/rangatahi (*teens*) are critical in the resurgence of our culture, our reo (*language*), our tikanga (*customs*) and ultimately what we are all striving for, our hauora (*health and wellbeing*). It is unacceptable that our tamariki mokopuna living in New Zealand should suffer rates of rheumatic fever comparable to third world countries. These guidelines will give clinicians a standardised approach to managing the triggering illness for rheumatic fever and provide a tool for educating communities, and preventing and treating rheumatic heart disease, therefore going some way towards addressing the burden our children shoulder. (See <http://www.heartfoundation.org.nz> for guidelines).

It is my pleasure to be a part of the writing group to offer a tangata whenua perspective.

In addition I was asked to consider a whakatauki-*proverb* to be used with the guidelines.

***He korokoro ora he manawa ora  
Mo tatou katoa***

This translates to:  
***A healthy throat, a healthy heart for us all***

This whakatauki highlights the importance for our whānau of treating sore throats seriously as there is a link between a sore throat and heart disease. It also highlights the importance to our whānau of the contagious nature of the disease and the impact that rheumatic heart disease has, not only on the patient, but on all those close to them. This is evident in the “a healthy heart for us all” (similar to the *one heart many lives*-theme).

This whakatauki was chosen because it is succinct and clearly establishes the link between prevention and disease.

**Dr Lance O’Sullivan  
Chairman  
Te Hotu Manawa Māori  
Member of Rheumatic Fever Guidelines Writing Group**

## [2. Scope and Purpose of Guideline]

The purpose of this document is to introduce evidence-based guidelines for the diagnosis and management of group A streptococcal (GAS) sore throats (pharyngitis) in three to 45 year old New Zealanders. This guideline has been developed to clarify best practice for the management of sore throats. In particular it is to guide:

- When to perform a throat swab
- When to prescribe an antibiotic
- Which antibiotic to prescribe and the length of treatment.

Sore throats are a common medical condition which are usually viral and benign. In the New Zealand population, where, as in other industrialised countries, diphtheria has virtually disappeared,<sup>1</sup> GAS sore throats are considered to be the only clinically significant bacterial throat infection, because of the morbidity and mortality associated with the sequelae. There are other less common pharyngeal pathogens which may require treatment. This guideline has been produced specifically to address the incidence of rheumatic fever in the New Zealand community.<sup>2</sup> The underlying premise is that treating streptococcal pharyngitis will reduce the incidence of rheumatic fever.<sup>3</sup> Within the New Zealand population, not all groups are at equal risk of developing acute rheumatic fever (ARF) as a consequence of streptococcal throat infection. The aim of this guideline is to maximise diagnosis and management of sore throat in those who are at greatest risk of developing rheumatic fever, while minimising investigations and antibiotic use in those who are at the lowest risk. The clinical end point is rheumatic fever prevention, not eradication of GAS in the throat.

Target groups who may benefit from this guideline are general practitioners, doctors in emergency departments, nurses and other community health workers and paediatricians. This guideline includes clinical questions and treatment algorithms to assist in the diagnosis and management of GAS pharyngitis.

### Gaps between current practice and evidence

There are limited New Zealand publications on current sore throat management practice. Between 2001 and 2002, Kljakovic and Crampton analysed 335 General Practitioner visits for sore throat and found that a diagnosis was recorded in 59% of the patient's notes. Despite this uncertainty, 6.6% of patients received a throat swab and overall 60.7% received antibiotics. The explicit diagnosis of likely viral sore throat was documented in 14.8% of visits.<sup>4</sup>

## [3. About the Guideline]

Sore throats are a frequent cause of presentation to healthcare professionals that require accurate diagnosis and management to minimise the unnecessary use of antibiotics in the current era of rising health costs and increasing antibiotic resistance.<sup>4</sup>

Although ARF is now rare in industrialised countries and in New Zealanders of European descent/Pakeha, it remains a significant disease among Māori and Pacific children in New Zealand. Currently Māori and Pacific rheumatic fever rates are similar to those of European New Zealanders in the 1920's.<sup>5</sup> ARF rates in southern New Zealand are similar to those in western industrialised countries, while rates in the North Island remain high.<sup>6</sup> The persistence of ARF in New Zealand is likely to be due to a combination of factors including; crowded living conditions, difficulties accessing health care and poor health knowledge.

ARF may result in damage to cardiac valves and consequently rheumatic heart disease (RHD). Recurrences are likely in the absence of preventative measures and may cause further valve damage. Consequently, the prevalence of RHD is high among these populations,<sup>7</sup> with significant rates of hospitalisations, procedures and death among young and middle-aged adults.<sup>7</sup>

Appropriate treatment of sore throats in high-risk populations will eradicate GAS in most cases,<sup>8,9</sup> prevent individual cases of ARF<sup>3</sup> and subsequent chronic heart disease. The profile of ARF needs to be raised, with better awareness in high-risk communities that this is a preventable disease. Part of the solution may

be to establish a school-based pharyngitis clinic programme in high-ARF risk areas (see New Zealand Guidelines for Rheumatic Fever 3. Proposed Rheumatic Fever Primary Prevention Programme, available at: <http://www.heartfoundation.org.nz>).

## Disclaimer

The production of this document has been supported by The National Heart Foundation of New Zealand and the Cardiac Society of Australia and New Zealand for the guidance of health professionals. The statements and recommendations it contains are, unless labelled as “expert opinion”, based on independent review of the available evidence. Interpretation of this document by those without appropriate health training is not recommended, other than at the request of, or in consultation with, a relevant health professional.

In addition, the recommendations in this guideline are not intended to replace clinical judgement. Treatment of individuals should take into account co-morbidities, drug tolerance, lifestyle, living circumstances, cultural sensibilities and wishes. When prescribing medication, clinicians should observe usual contra-indications, be mindful of potential adverse drug interactions and allergies, monitor responses and ensure regular review. This guideline focuses on group A streptococcal pharyngitis and does not attempt to address other causes of sore throat including rarer bacterial pathogens which may need clinical treatment (see [Appendix A](#)).

## Outline of grading methodology used

The review includes levels of evidence and accompanying grades of recommendation ([Table 1](#) and [2](#)). There are two similar, but different, evidence ratings used. [Table 1](#) has been customised for use in these guidelines, and is used where the writing group has assessed the evidence.

**Table 1. Levels of Evidence for Clinical Interventions and Grades of Recommendation**

LEVEL OF EVIDENCE	STUDY DESIGN	GRADE OF RECOMMENDATION
I	Evidence obtained from a systematic review of all relevant randomised controlled trials (RCT)	A Rich body of high-quality randomised controlled trial (RCT) data
II	Evidence obtained from at least one properly designed randomised controlled trial	B Limited body of RCT data or high-quality non-RCT data
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method)	C Limited evidence
III-2	Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group	D No evidence available – panel consensus judgment
III-3	Evidence obtained from comparative studies with historical control, 2 or more single-arm studies, or interrupted time series with a parallel control group	
IV	Evidence obtained from case series, either post-test or pre-test and post-test	

**Source:** The levels of evidence and grades of recommendations are adapted from the National Health and Medical Research Council levels of evidence for clinical interventions and the US National Institute of Health clinical guidelines. Details can be found at [www.nhlbi.nih.gov/guidelines/index.htm](http://www.nhlbi.nih.gov/guidelines/index.htm).

Table 2 has been used in this guideline, where recommendations have been taken directly from the Infectious Diseases Society of North America's (IDSA) review of relevant studies.<sup>10</sup> It was decided not to give a new rating to the IDSA studies, due to resource and time constraints.

**Table 2. Infectious Diseases Society of America (IDSA). United States Public Health Service Grading System for Rating Recommendations in Clinical Guidelines<sup>10</sup>**

CATEGORY, GRADE	DEFINITION
<b>Strength of recommendation</b>	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use
<b>Quality of evidence</b>	
I	Evidence from ≥1 properly randomized, controlled trial
II	Evidence from ≥1 well-designed clinical trial, without randomization, from cohort or case-controlled analytic studies (preferably from >1 centre), from multiple time-series, or from dramatic results of uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

**Source:** Bisno et al. Clinical Infectious Diseases. 2002; 35: 113-125, University of Chicago. Copyright © 2002 by the Infectious Diseases Society of America. All rights reserved.

## Guideline development process

This guideline has been developed by a writing group comprised of experts in primary care, paediatric infectious diseases, public health and rheumatic fever. Selected individuals with experience in sore throat and ARF management and relevant stakeholders were also involved. These included a range of general and specialist clinicians, nurses, Māori and Pacific professionals and lay representative groups.

Three sore throat guidelines and one major article on the diagnosis of GAS pharyngitis have been used as a framework. The guidelines used are from:

- The Infectious Disease Society of America<sup>10</sup>
  - The American Academy of Family Physicians and The American College of Physicians<sup>11</sup>
  - The 2006 Report of the Committee on Infectious Diseases by the American Academy of Pediatrics.<sup>12</sup>
- The article used in this framework is Mclsaac's revised Centor criteria for diagnosing GAS pharyngitis.<sup>13,14</sup>

This guideline has been produced for New Zealand and is endorsed by New Zealand organisations. It has been piloted among target users.

The development process is described in more detail in [Appendix B](#) and a full description of the guideline development process is available to download from <http://www.heartfoundation.org.nz>

There are no current plans to update the guideline.

## Endorsing organisations

- The Cardiac Society of Australia and New Zealand
- The National Heart Foundation of New Zealand
- Te Ohu Rata o Aotearoa/Te Ora Māori Medical Practitioners Association
- New Zealand Nurses Organisation
- Paediatric Society of New Zealand
- The Rheumatic Fever Trust
- Te Hotu Manawa Māori
- Pacific Islands Heartbeat
- Australasian Society for Infectious Diseases.

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## **Declaration**

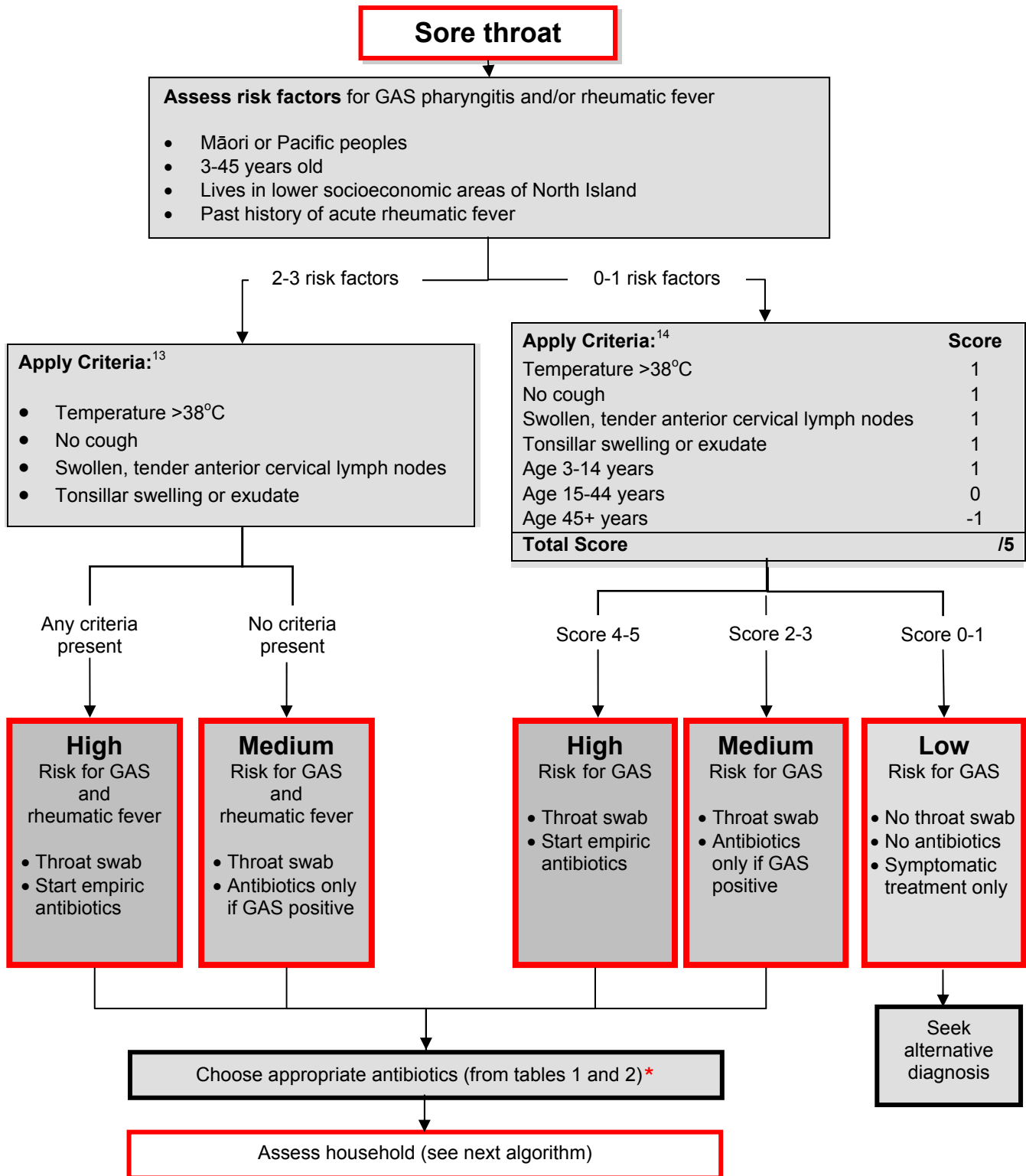
No conflicts of interest were apparent in the development of this guideline. Dr Melissa Kerdemelidis who co-ordinated the writing of this guideline was funded by The Rheumatic Fever Trust and The National Heart Foundation of New Zealand. Office space was funded by the New Zealand Guidelines Group.

## [4. Executive Summary and Recommendations]

### Key Messages

- In the New Zealand setting, Māori and Pacific three to 45 year olds from lower socioeconomic areas have the highest rate of acute rheumatic fever (ARF). A targeted approach to sore throat management is required to reflect this difference in risk (see sore throat management algorithm, [page 14](#))
- Treatment of group A streptococcal (GAS) pharyngitis infection with the appropriate antibiotics reduces the risk of ARF
- In New Zealand, culture of throat swabs is recommended to confirm diagnosis of GAS pharyngitis
- If there are three or more episodes of GAS pharyngitis within a household, within a three month period, diagnosed using throat swabs, management of the household is required (see household sore throat management algorithm, [page 15](#)). The entire household should have throat swabs and be treated with antibiotics if GAS positive, whether they have a sore throat or not
- To facilitate the tracking of GAS pharyngitis, it should become a notifiable disease to the Ministry of Health once again
- Routine antibiotics are suggested if it is the patient's first or second episode of GAS pharyngitis inside a three month period (see [Table 3](#))
- Ten days of oral penicillin V should be administered for the routine treatment of GAS pharyngitis
- If the patient has had three or more episodes of pharyngitis inside a three month period, treat using recurrent antibiotics (see [Table 4](#))
- If a patient is on intramuscular benzathine penicillin prophylaxis for ARF and develops a sore throat which is GAS positive on throat swab culture, treatment depends on whether the pharyngitis has occurred in the first two weeks after the injection or in the second two weeks
- Children with GAS pharyngitis should be kept home from school or day-care for 24 hours if possible
- Treatment of GAS pharyngitis can be delayed until culture results are available for up to nine days, as rheumatic fever is unlikely to occur in this time
- No recommendations are able to be made around seasonal prophylaxis
- Rapid streptococcal tests are not funded in New Zealand and need further investigation regarding their sensitivity and specificity in this country
- No vaccine for GAS has yet been developed
- There is no agreement about the role of tonsillectomy in recurrent GAS pharyngitis.

## Algorithm: Guide for sore throat management



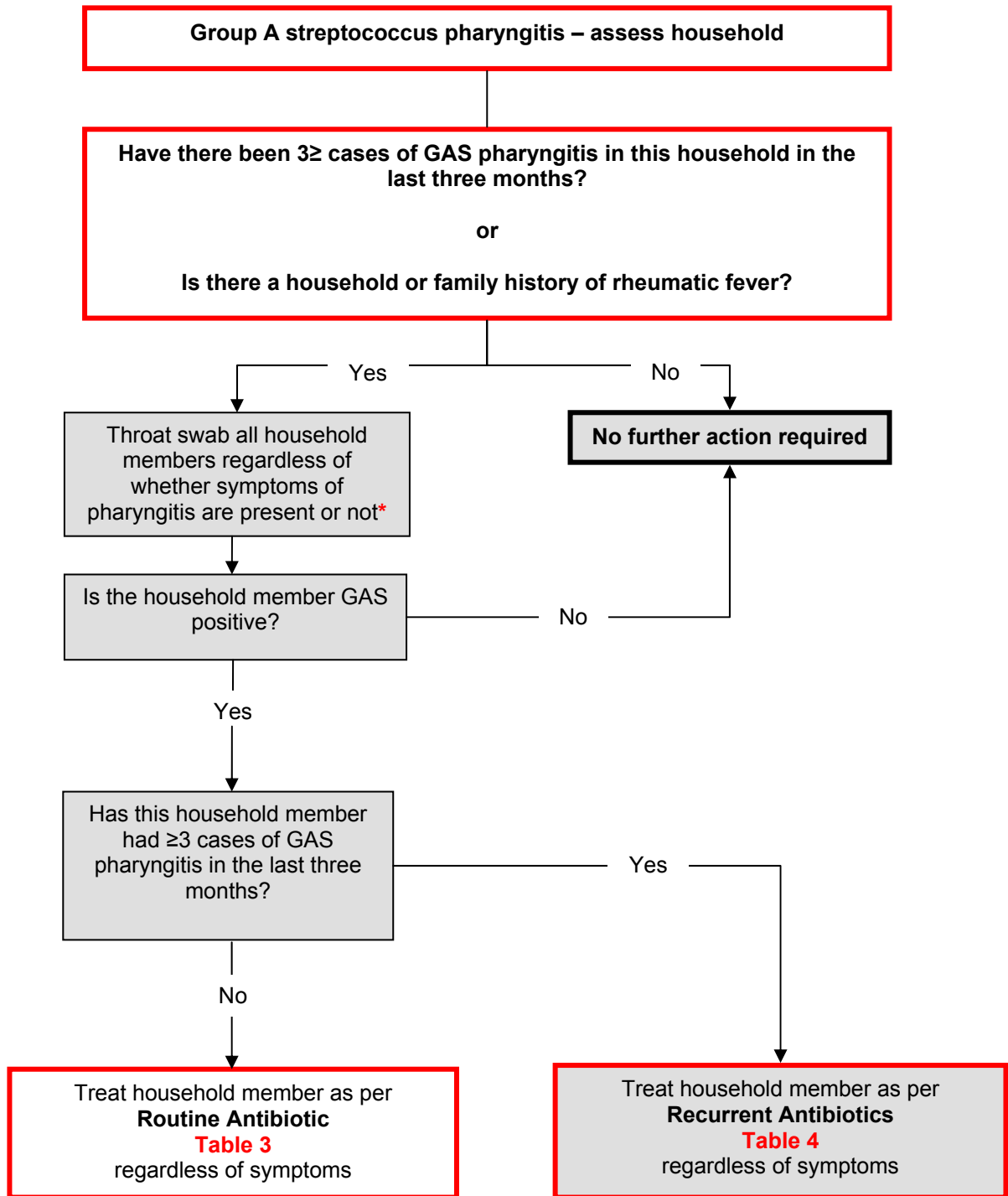
- \* If patient is on benzathine penicillin IM prophylaxis for acute rheumatic fever, and is GAS positive on throat swab, treat in the following way:
- If GAS positive in the first two weeks after IM penicillin injection has been given, treat with a 10 day course of erythromycin (see Table 3)
  - If GAS positive in the 3<sup>rd</sup> and 4<sup>th</sup> weeks after IM penicillin injection, treat with a 10 day course of oral penicillin (see Table 3).

**Sources:**

<sup>13</sup> Centor RM, Witherspoon JM, Dalton HP, Brody CE, Link K. Med Decis Making. (1:3) pp.239-246, copyright (c) 1981 by (Sage Publications Inc). Reprinted by Permission of SAGE Publications, Inc.

<sup>14</sup> Copyright © 2004, American Medical Association, All rights reserved.

## Algorithm: Guide for household sore throat management



Abbreviations:  
 GAS = group A streptococcus  
 IM = intramuscular

\* If impractical to swab, consider empiric antibiotic treatment

## Algorithm: Notes

**Table 3: Routine Antibiotics**

Standard treatment of GAS positive pharyngitis for patient's first or second case of GAS pharyngitis in a three month period.

ANTIBIOTIC	ROUTE	DOSE	DURATION
<b>Penicillin V</b> Give as first choice Give on empty stomach	PO	Children: 20mg/kg/day in 2-3 divided doses Maximum 500mg 3 times daily (250mg 3 times daily for smaller children)  Adults: 500mg twice daily	10 days
<b>Erythromycin Ethyl Succinate (EES)</b> Give if allergy to penicillin reliably documented	PO	Children: 40mg/kg/day in 2-4 divided doses Maximum 1g/day  Adults: 400mg twice daily	10 days
<b>Benzathine Penicillin G (BPG)</b> Give if compliance with 10 day regime likely to be a problem	IM	Children <20kg: 600,000 U once only  Adults and children >20kg: 1,200,000 U once only	Single dose
<b>Amoxicillin</b> Useful alternative as can be given with food, may improve compliance	PO	Weight <30kg: 750mg once daily Weight >30kg: 1500mg once daily	10 days

**Table 4. Recurrent Antibiotics**

Recommendations for treatment of symptomatic persons with multiple, recurrent, episodes of GAS pharyngitis proven by culture or rapid antigen testing.<sup>10</sup> This table should be used if this is the patient's third, or more, case of GAS pharyngitis in a three month period.

ANTIBIOTIC	REGIMEN	DURATION	RATING <sup>§</sup>
<b>Oral</b>			
<b>Clindamycin</b>	Children: 20-30mg/kg/day in 3 divided doses	10 days	B-II
	Adults: 600mg/day in 2-4 divided doses*	10 days	B-III
Amoxicillin; clavulanic acid	Children: 40mg/kg/day in 3 equally divided doses***	10 days	B-II
	Adults: 500 mg twice daily	10 days	B-III
<b>Parenteral with or without oral</b>			
Benzathine penicillin G	For IM dosages, see <a href="#">Table 3</a> or refer to IDSA guidelines <sup>#</sup>	1 dose	B-II
Benzathine penicillin G with rifampicin	For IM dosages, see <a href="#">Table 3</a> , or refer to IDSA guidelines <sup>#</sup> Rifampicin: 20mg/kg/day orally in 2 divided doses	4 days	

**Source:** Modified from Table five. Bisno et al. Clinical Infectious Diseases. 2002; 35: 113-125. University of Chicago.<sup>10</sup> ©2002 by the Infectious Diseases Society of America. All rights reserved.

Macrolides (e.g. erythromycin) and cephalosporins are not included in the table, because there is insufficient data to support their efficacy in this specific circumstance.

\* Adult doses are extrapolated from data for children. Use of this drug for this indication has not been studied in adults. Further references on clindamycin available from Tanz RR et al. 1991<sup>15</sup> and Orling A et al. 1994<sup>16</sup>

\*\* Maximum dose, 750mg of amoxicillin per day

\*\*\* Refers to amoxicillin component. Note that the amount of clavulanic acid may vary between formulations. Further reference from Kaplan and Johnson 1988<sup>17</sup>

# Treatment with benzathine penicillin G is useful for patients in whom compliance with previous courses of oral antimicrobials is in question. Addition of rifampicin to benzathine penicillin G may be beneficial for eradication of streptococci from the pharynx.<sup>18</sup> It has also been reported that addition of rifampicin (20mg/kg/day, once daily) during the final four days of a ten day course of oral penicillin V may achieve high rates of eradication.<sup>19</sup> The maximum daily dose of rifampicin is 600mg; rifampicin is relatively contraindicated for pregnant women.

§ Refer to the IDSA evidence rating in [Table 2](#).

## [ 5. Introduction ]

Sore throats are a frequent cause for presentation to primary healthcare professionals. Based on their study of 10,506 visits, Kljakovic and Crampton estimated the rate was 3.6 visits per 100 to New Zealand general practitioners.<sup>4</sup> A similar consultation rate of 4.7 per 100 visits was found in the Waikato.<sup>20</sup>

Most sore throats are viral in origin. Approximately 10% of adult and 15 to 30% of paediatric sore throats presenting at doctor visits are estimated to be due to group A streptococcus (GAS).<sup>21-27</sup> Other rarer pathogens may be clinically significant (see [Appendix A](#)). An Australian family cohort study of 852 individuals found the incidence of GAS pharyngitis was 14 per 100 person-years for children.<sup>28</sup> Group A streptococci spreads in crowded situations, such as army barracks and schools,<sup>29</sup> presumably by droplet and spread from saliva or nasal secretions. Studies in the United States found the peak incidence occurs during the colder months of the year.<sup>21</sup> Evidence from other climatic conditions is sparse. In Auckland, streptococcal pharyngitis has had no clear seasonal peak over a four year period (Lennon, personal communication, 2006). Pharyngitis caused by GAS may present with fever, red tonsils, with or without exudate and tender anterior cervical lymph nodes.<sup>13</sup> Some patients, however, present with non-specific symptoms.

In a sub-group of people, GAS throat infections may lead to acute rheumatic fever (ARF) and acute post-streptococcal glomerulonephritis (APSGN), although very rarely in the same individual.<sup>30</sup> It has not been possible to predict which patients will develop post-streptococcal sequelae. GAS from other sites, in particular the skin, have not been proven to cause rheumatic fever<sup>30</sup> although skin-associated GAS have been found in the throats of patients who have developed rheumatic fever<sup>31,32</sup> and ARF is common in some populations with endemic skin disease.<sup>31,33,34</sup> The process by which GAS pharyngitis leads to rheumatic fever is poorly understood, but has been postulated to have an autoimmune basis.<sup>35</sup>

The rate of rheumatic fever in New Zealand, 3.8 per 100,000 in 2003, exceeds that in other western countries.<sup>36</sup> One hundred and forty one new cases were reported in 2003, most of which occurred in the ten to 14 year age group (n=82) and the five to nine year age group (n=27).<sup>36</sup> Seventy cases occurred in Māori and 58 among Pacific peoples.<sup>36</sup> The geographical distribution of rheumatic fever in New Zealand is complex and is summarised in the map found in [Appendix C](#). Pockets of rheumatic fever found in New Zealand are summarised in [Appendix D](#). The main areas of rheumatic fever occurrence are in lower socioeconomic areas of the North Island, in areas such as parts of Auckland, Waikato, Northland, Bay of Plenty, Rotorua, Gisborne, Hawke's Bay and Porirua.

In comparison, rheumatic fever declined sharply in Denmark from the early 1960s.<sup>37</sup> In western Scotland, between 1976 to 1979, the rate of rheumatic fever was 0.6 per 100,000 children per year.<sup>38</sup> Del Mar et al estimates that it would have taken twelve general practitioners' working lifetimes to find one new case of rheumatic fever in western Scotland in the 1980s.<sup>39</sup> Studies from the last 20 years assessing the incidence of rheumatic fever in children around the world are summarised in [Appendix E](#).

Treating GAS throat infections with appropriate antibiotics, aiming for eradication in most cases, reduces the likelihood of subsequent development of ARF. This has been demonstrated in a number of studies.<sup>10,14,39,40</sup> Shortly after the introduction of penicillin, epidemic rheumatic fever in the American armed forces was controlled using injectable penicillin.<sup>8</sup> A recent meta-analysis demonstrated this effect in a further nine studies, eight of which were in a military setting, that also used injectable penicillin.<sup>3</sup> Subsequently, observational studies in Baltimore,<sup>41</sup> Costa Rica<sup>42</sup> and the French Caribbean,<sup>43</sup> the latter two in low-resource environments, have shown ARF reduction.

Inner-city comprehensive primary care programmes were set up in Baltimore, USA in the 1960s. The rate of rheumatic fever decreased 60% from 1960 to 1964 through to 1968 to 1970 in the programme areas but was unchanged in the rest of the city. A ten year programme in the French Caribbean reduced the incidence of rheumatic fever by 78% in Martinique and 74% in Guadelupe. It appears the rate of rheumatic fever fell largely due to secondary prevention, although primary prevention measures also contributed. In Costa Rica, suspected GAS pharyngitis was diagnosed on clinical criteria alone i.e. no throat swabs were performed and patients were treated with intramuscular (IM) benzathine penicillin. New cases (first attacks) of rheumatic fever fell from 94 in 1970 to just four in 1991, which may or may not have been a consequence.

Since ARF can be reduced by treating GAS sore throats with antibiotics and rheumatic fever is still a problem in New Zealand, local pharyngitis protocols are required. This guideline provides details on recommended management of sore throats in the New Zealand setting. A further guideline, dealing with

rheumatic fever primary prevention and equitable access to health care for all New Zealanders, is currently under development.

## [6. Clinical Questions]

To aid clinicians, some key clinical questions around diagnosis, treatment and management of pharyngitis have been identified and answered below.

A patient's risk of rheumatic fever should be made at the start of the consultation as per the sore throat management algorithm (page 14). High risk patients are Māori or Pacific peoples, those aged three to 45 years, and those with a past history of rheumatic fever. Living in a lower socioeconomic area of the North Island is also a risk factor (see Appendix C and D). Households with more than three cases of GAS pharyngitis within a three month period should be managed as per the household sore throat management algorithm (page 15).

### **Question 1. Which clinical signs and symptoms best correlates with group A streptococcal (GAS) pharyngitis infection in adults and children?**

Evidence from key studies is available, including Mclsaac and Centor's criteria.<sup>13,14</sup> Mclsaac et al modified a scoring system for the management of pharyngitis in children and adults first developed by Centor.<sup>11</sup> The modified Centor approach is as follows:

**Table 5. Modified Centor Criteria for the Management of Pharyngitis in Adults and Children**

APPLY CRITERIA	POINTS
Temp > 38°C	1
No cough	1
Swollen, tender anterior cervical lymph nodes	1
Tonsillar swelling or exudate	1
Age 3-14 years	1
Age 15-44 years	0
Age 45+ years	-1
<b>Total Score</b>	<b>/5</b>

**Source:** Table modified by Mclsaac et al. Journal of the American Medical Association. 2004; 291: 1587-1595.<sup>14</sup> Copyright © 2004, American Medical Association. All rights reserved.

The following scoring system predicts the probability of group A streptococcal pharyngitis.

**Table 6. Scoring System for Modified Centor Criteria**

SCORE (OUT OF 5)	RISK OF STREPTOCOCCAL INFECTION <sup>44,45</sup>	SUGGESTED MANAGEMENT
=<0	1-2.5%	No further testing or antibiotics
1	5-10%	No further testing or antibiotics
2	11-17%	Culture all, antibiotics for positive culture only
3	28-35%	Culture all, antibiotics for positive culture only
>=4	51-53%	Treat empirically with antibiotics and/or culture

**Source:** Table from Mclsaac et al. Journal of the American Medical Association. 2004; 291: 1587-1595<sup>14</sup> adapted from Centor by Mclsaac. Copyright © 2004, American Medical Association, All rights reserved.

In children, the specificity of this approach is 90.3% (95% CI, 86.4-93.4%) using the modified Centor score and throat culture. For adults specificity is 43.8% (95% CI, 37.7-50.1%) for empirical treatment based on a modified Centor score of 3 or 4.<sup>14</sup> The microbial causes of acute pharyngitis and differential diagnosis of pharyngitis are shown in [Appendix A](#) and [F](#).

<b>Recommendation:</b>	The modified Centor criteria can be used to evaluate the likelihood of infection with GAS
<b>Recommendation grade:</b>	B
<b>Evidence level:</b>	II

## **Question 2. Should patients of different ages and ethnicities have their sore throats managed differently?**

In the New Zealand setting, Māori and Pacific three to 45 year olds from lower socioeconomic areas have the highest rate of ARF. A targeted approach to sore throat management is required, as outlined below, to reflect this difference in risk (panel consensus D).

### **Patients under three years of age:**

There has been little research on the diagnosis and management of GAS pharyngitis in children under the age of three years internationally. The few studies available are weak and inconclusive, hampered by the fact that the symptoms of upper respiratory streptococcal infection are difficult to assess in infants.<sup>44-55</sup> Rheumatic fever is rare in this age group in New Zealand. In 2003 there were two cases in the four and under age bracket.<sup>36</sup>

<b>Recommendation:</b>	Insufficient evidence to make any recommendations currently
<b>Recommendation grade:</b>	D
<b>Evidence level:</b>	Insufficient evidence

### **Patients aged three to 45 years:**

The peak incidence of rheumatic fever is among school-aged children and there are few new cases or recurrences over the age of 30 years.<sup>56-58</sup> Most published studies concern the management of this age group (refer to [Question 1](#)).

<b>Recommendation:</b>	Treat patients with pharyngitis aged three to 45 years as per the sore throat management algorithm on <a href="#">page 14</a>
<b>Recommendation grade:</b>	B, for the use of modified Centor criteria in three to 45 year olds in general. D, for the use of this specific algorithm in the New Zealand context, as no trials held to date
<b>Evidence level:</b>	II, for the use of modified Centor criteria in three to 45 year olds in general

### **Patients aged over 45 years:**

The modified Centor criteria<sup>14</sup> in [Table 5](#), recognises the low risk of episodes of rheumatic fever in this age group. The scoring system is as follows:

Score 0-1: No further testing, no antibiotics

Score 2-3: Culture all, treat positive GAS cultures only  
 Score 4+: Treat empirically with antibiotics, and/or take throat culture.

<b>Recommendation:</b>	Older patients are at a reduced risk of rheumatic fever. This is reflected in the scoring system. Use the modified criteria to assess and treat over 45 year old patients
<b>Recommendation grade:</b>	B, for use for modified Centor criteria in over 45 year old patients
<b>Evidence level:</b>	II, for use for modified Centor criteria in over 45 year old patients

**Patients at high risk for acquiring ARF:**

International research on genetic susceptibility has been inconclusive.<sup>59,60</sup> Clusters in families<sup>61</sup> and army barracks<sup>8</sup> are well recognised. Crowding and poverty may have an impact on the risk of rheumatic fever acquisition (discussed in **Question 20**). In New Zealand, Māori and Pacific peoples make up the majority of those diagnosed with ARF. Most are aged three to 45 years and live in lower-income areas of the North Island, including Northland, Bay of Plenty, Rotorua, Waikato, Hawke’s Bay, Porirua, parts of Auckland and Gisborne. Statistics from 2003 are representative of recent years, as detailed below. Refer to the rheumatic fever at-risk areas in **Appendix C** and **D**.

**Table 7. Notified Rheumatic Fever Cases in New Zealand 2003 (Initial Cases & Recurrences)**

ETHNICITY	NUMBER OF CASES OF RHEUMATIC FEVER (TOTALS)	RATE PER 100,000 POPULATION
European	4	0.2
Māori	70	13.3
Pacific peoples	58	29.0
Other ethnicity	6	2.4
Unknown	5	-
Total-initial cases	141	3.8
Total-recurrences	2	0.1

**Source:** Adapted from Table 33 and page 32. Rheumatic fever cases in New Zealand 2003. From: Institute of Environmental Sciences and Research Ltd. Notifiable and other diseases in New Zealand, Annual Report 2003. Wellington: Ministry of Health.<sup>36</sup> Downloaded from: [http://www.surv\\_esc.cri.nz/PDF\\_surveillance/AnnSurvRpt/2003AnnualSurvRpt.pdf](http://www.surv_esc.cri.nz/PDF_surveillance/AnnSurvRpt/2003AnnualSurvRpt.pdf)

The Ministry of Health data relies on timely notifications of rheumatic fever cases. It is of concern that notifications to the Ministry of Health of new cases have fallen below rates of ARF hospital admissions.<sup>7,58</sup>

Rheumatic fever has had an inequitable, and significant, impact on Māori and Pacific peoples. The morbidity and mortality associated with ARF and chronic rheumatic heart disease may reduce educational and employment opportunities, impact on family and community life, increase dependence on welfare and shorten lives. ARF is predominately a disease of children and adolescents. The less than 20 age group currently make up the largest age group for Māori. By 2021, Māori will make up 28% of this age group in New Zealand. The highest incidence of ARF in New Zealand is among Pacific young people, approximately 60% of whom were born in this country. The youth of New Zealand are crucial for the nation’s future prosperity. It is unacceptable that the Māori and Pacific youth of New Zealand carry a third-world burden of this preventable disease. The appropriate diagnosis and management of sore throats in these groups is therefore critical. The Māori whakatauki (proverb) chosen for this guideline reflects this:

***he korokoro ora he manawa ora, mo tatou katoa  
 a healthy throat, a healthy heart for us all***

Lance O’Sullivan 2006.

**Recommendation:** Those in high rheumatic fever-risk households (Māori or Pacific and living in a lower socioeconomic area) or with a family history of ARF in first degree relatives, may be swabbed whatever the age, to prevent streptococcal pharyngitis in the individual and it spreading to the household (see sore throat algorithm, [page 14](#))  
See [Appendix C](#) and [D](#) for high-risk rheumatic fever areas

**Recommendation grade:** D, expert opinion only, from panel consensus

**Evidence level:** No evidence available

### **Question 3. Which test should be done to diagnose GAS pharyngitis?**

The current gold standard for the diagnosis of GAS pharyngitis is a rayon-tipped throat culture swab, taken by sampling the tonsils and back of the throat, carefully avoiding the tongue and other areas of the oral cavity to minimise contamination with oropharyngeal flora. The swab is then placed in a tube containing a transport medium, and sent to the laboratory. In cases of uncomplicated pharyngitis, it is then inoculated on to a 5% sheep blood agar plate. In certain other circumstances, laboratory staff may utilise other types of agar for throat swabs. Correct swabbing technique is summarised in [Appendix G](#).

In general, it is recommended that a throat swab be sent to the laboratory preferably within two hours, but a delay of up to 24 hours before processing is acceptable.<sup>62</sup>

Martin et al, in a randomised controlled trial (RCT) compared delayed and immediate transfer of throat swabs onto culture plates and the extraction of group A streptococci.<sup>63</sup> Delayed plating was defined as 'after four days in the dark at room temperature' and immediate plating as 'within four hours on swabbing'. These results showed that delayed plating had a marginal superiority in GAS retrieval ( $p=0.0523$ ) over immediate plating. In the delayed plating setting, the result was not influenced significantly by the swab type (plain or serum coated swab) or whether these was silica gel present in the swab tube. A plain throat swab, with no silica gel in the tube, plated within four hours, was the least likely to lead to the isolation of GAS.<sup>63</sup>

In terms of recovering beta-haemolytic streptococci in tropical conditions, McDonald et al found that optimal results were obtained from directly inoculating culture media followed by cold-box transport (plating method) or sealing the swab in a bag with a silica gel dessicant and cold-box transport (dessicant method).<sup>64</sup> These two were superior to transporting swabs at ambient temperature and humidity, when paired throat swabs were compared.

Rapid tests, which can be performed by clinical staff at the time the patient presents and which give a result inside approximately ten minutes, are not currently funded in New Zealand. The rapid test sensitivity and specificity results vary significantly from study to study.<sup>65</sup> At this time, rapid tests are not considered consistent enough to be relied upon as the sole diagnostic test. Culture of throat swabs continues to be recommended as a backup particularly for negative rapid tests, at least in the United States.<sup>10,66</sup>

**Recommendation:** Culture of throat swabs is recommended to confirm diagnosis of GAS pharyngitis in New Zealand. Swabs should ideally be sent to the laboratory within two hours but a delay of several days does not seem to be detrimental

**Recommendation grade:** B

**Evidence level:** II

#### Question 4. Are two throat swabs more accurate than one?

There are no systematic reviews and only one randomised controlled trial found which addressed this issue. Ezike et al studied 373 children with pharyngitis presenting to a paediatric emergency department. Children were randomised to have either one or two throat swabs taken. All swabs were cultured in addition to being tested using a rapid diagnostic test. Positive culture rates were approximately 42% and did not vary between one or two swabs.<sup>67</sup>

<b>Recommendation:</b>	Current recommendations internationally and within New Zealand are for a single throat swab to be taken and there is no evidence this should change
<b>Recommendation grade:</b>	B
<b>Evidence level:</b>	II-I

#### Question 5. Which antibiotic should be used for treating GAS pharyngitis and for how long?

Group A streptococci worldwide remain penicillin-sensitive. Although up to 2.6% of streptococcal isolates in US studies were found to be macrolide-resistant,<sup>68</sup> in New Zealand erythromycin resistance is rare.

**Table 8. Group A Streptococcus Sensitivities 2004**

ANTIBIOTIC	GROUP A STREPTOCOCCUS	
	% Resistant to antibiotic	Numbers tested
Erythromycin	0.9%	6,721
Penicillin	0%	12,492

Source: Environmental Sciences and Research Ltd website: <http://www.esr.cri.nz><sup>69</sup>

Both national and international recommendations continue to be for the use of narrow-spectrum antibiotics.<sup>10,70</sup> Penicillin remains the treatment of choice because of its proven efficacy, safety, narrow spectrum and low cost.<sup>12,66,71-73</sup> Erythromycin is a suitable alternative for reliably documented penicillin allergies.<sup>74</sup> The following Infectious Disease Society of America (IDSA) Guidelines have been adapted for New Zealand use.

**Table 9. Recommendations for Standard Antibiotic Regimes for GAS Pharyngitis**

ANTIBIOTIC	ROUTE	DOSE	DURATION *	IDSA EVIDENCE RATING (see Table 2)
Penicillin V **	PO	Children: 250mg bd or tds	10 days	A-II
	PO	Adolescents and Adults: 250mg tds or qid	10 days	A-II
	PO	Adolescents and Adults: 500mg bd	10 days	C-III
Benzathine penicillin G	IM	Children: 600,000U	Single dose	A-II ***
	IM	Adults: 1,200,000U	Single dose	A-II #
<b>For reliably documented penicillin allergies:</b>				
Erythromycin	PO	Varies with formulation §	10 days	A-II
First-generation cephalosporin ‡	PO	Varies with agent	10 days	A-II

Source: Adapted from Table 4, Bisno et al. Clinical Infectious Diseases. 2002; 35:113-125. University of Chicago.<sup>10</sup> © 2002 by the Infectious Diseases Society of America. All rights reserved.

- \* Although shorter courses of azithromycin and some cephalosporins have been reported to be effective for treating GAS upper respiratory tract infections, evidence is not sufficient to recommend these shorter courses for routine therapy at this time<sup>75-80</sup>
- \*\* Amoxycillin is often used in place of oral penicillin V for young children, efficacy appears to be equal. The choice is primarily related to acceptance of the taste of the suspension
- \*\*\* For patients under 27kg
- # Long-acting penicillin in differing forms has been used.<sup>81-83</sup> In New Zealand, only benzathine penicillin pre-packaged as 1.2 megaunits is available
- § In New Zealand, erythromycin is available as erythromycin ethyl succinate, erythromycin lactobionate and erythromycin stearate. Only succinate and lactobionate are fully subsidised
- ‡ These agents should not be used to treat patients with immediate-type hypersensitivity to beta-lactam antibiotics.

#### **The use of once-daily amoxycillin:**

Four randomised controlled trials (RCTs) have assessed once-daily amoxycillin as an alternative to penicillin V (see [Appendix H](#)). In these studies, eradication of streptococci from the throat was found to be equivalent to penicillin and the amoxycillin was well tolerated. Its absorption is not affected by food.<sup>84-86</sup> The taste of amoxycillin suspension is relatively palatable.<sup>87</sup> Clegg et al, comparing once to twice-daily amoxycillin, found the bacteriological failure rates were similar.<sup>88</sup>

#### **The use of amoxycillin in sore throats:**

Amoxycillin should not be used if infectious mononucleosis (IMN) (Epstein-Barr Virus [EBV]) is considered a possible differential diagnosis, as a rash may occur.<sup>86,89,90</sup> With EBV infection the rate of rash in reaction to amoxycillin may be 70-100%. In a small study of four IMN patients with amoxycillin-induced exanthema, Renn et al conducted skin tests and lymphocyte transformation testing (LTT), concluding that real sensitisation to amoxycillin could occur in this setting.<sup>91</sup> If a rash to amoxycillin is non-pruritic, maculopapular, and seen in a patient with IMN, then it is probable that subsequent penicillins are generally tolerated.<sup>92,93</sup> This type of rash is generally not immunoglobulin E (IgE) mediated. Although there may be a risk of recurrence of similar rash and there is likely some other underlying immunologic mechanism, there is not an increased risk of severe allergic reaction to subsequent courses.

If there was an urticarial rash or other features suggesting an IgE mediated mechanism then, even if a patient had IMN, evaluation for drug allergy should be undertaken prior to considering further courses of penicillin-based antibiotics.

#### **Duration of antibiotic treatment:**

Early studies in the treatment of streptococcal pharyngitis to prevent rheumatic fever used injectable long-acting penicillin. Failure to prevent rheumatic fever was found to equate with failure to eradicate GAS from the throat.<sup>40</sup> A ten-day treatment course of oral penicillin was found to be as effective as a single dose of IM benzathine penicillin. Recent studies have shown that ten days of oral penicillin are more likely than shorter courses to eradicate GAS.<sup>94,95</sup> The New Zealand recommendation therefore remains for ten days of treatment, or a single dose of IM benzathine penicillin.

<b>Recommendation:</b>	The recommendations for the treatment of GAS pharyngitis in New Zealand are outlined in the sore throat management algorithm <a href="#">Page 14</a> . This is shown below:
<b>Recommendation grade:</b>	A, based on meta analyses
<b>Evidence level:</b>	I

**Table 3. Routine Antibiotics**

Standard treatment of GAS positive pharyngitis for patient's first or second case of GAS pharyngitis in three month period.

ANTIBIOTIC	ROUTE	DOSE	DURATION
<b>Penicillin V</b> Give as first choice Give on empty stomach	PO	Children: 20mg/kg/day in 2-3 divided doses Maximum 500mg 3 times daily (250mg 3 times daily for smaller children)  Adults: 500mg twice daily	10 days
<b>Erythromycin Ethyl Succinate (EES)</b> Give if allergy to penicillin reliably documented	PO	Children: 40mg/kg/day in 2-4 divided doses Maximum 1g/day  Adults: 400mg twice daily	10 days
<b>Benzathine Penicillin G (BPG)</b> Give if compliance with 10 day regime likely to be a problem	IM	Children <20kg: 600,000 U once only Adults and children >20kg: 1,200,000 U once only	Single dose
<b>Amoxicillin</b> Useful alternative as can be given with food, may improve compliance	PO	Weight <30kg: 750mg once daily Weight >30kg: 1500mg once daily	10 days

Twice daily dosing of penicillin has been found to be equivalent to more frequent regimes, see [Question 12](#).<sup>96</sup>

<b>Recommendation:</b>	There is limited data from RCT's to support once-a-day amoxicillin
<b>Recommendation grade:</b>	B
<b>Evidence level:</b>	II

Cephalosporins are not recommended as it appears all cephalosporins have the potential to cause an increase in multi-drug resistant organisms, in particular, extended spectrum beta lactamases (ESBL).

## Question 6. Should GAS culture-positive pharyngitis patients be isolated?

The American Academy of Pediatrics<sup>12</sup> recommends keeping children out of school and day care for 24 hours after the initiation of appropriate therapy.<sup>97</sup> Snellman et al found that 17 out of 47 children (36.2%) with GAS pharyngitis still had a positive throat culture the morning after beginning antibiotic therapy. Of the 17 children, eight received oral erythromycin, four received IM penicillin and five were given oral penicillin. Snellman et al recommends that children be kept at home until they completed a full 24 hours of antibiotics before returning to school or day care.<sup>97</sup> The New Zealand Ministry of Health also recommends exclusion from school or day care for the first 24 hours of antibiotic treatment.<sup>98,99</sup>

<b>Recommendation:</b>	Children should be kept out of school/day care for 24 hours after antibiotics are begun, if at all possible
<b>Recommendation grade:</b>	C
<b>Evidence level:</b>	IV

## Question 7. How should treatment failure and/or the recurrence of GAS pharyngitis be managed?

Recurrences, defined as the patient's third or further episode of GAS pharyngitis in a three month period, can be treated using the Infectious Diseases Society of America guidelines (2002)<sup>10</sup> as shown below. Important considerations are re-infection of the patient from a family or household source or poor compliance with treatment. It may be possible to improve the latter by using once-daily oral amoxycillin or a single dose of IM benzathine penicillin. Treatment failure can be defined as the recurrence of the same serotype of GAS pharyngitis accompanied by a corresponding rise in serial streptococcal serology.

Household contacts of patients experiencing recurrences should be assessed as per the household sore throat management algorithm on [page 15](#).

**Table 4. Recurrent Antibiotics**

Recommendations for treatment of symptomatic persons with multiple, recurrent, episodes of GAS proven by culture or rapid antigen testing<sup>10</sup>

ANTIBIOTIC	REGIMEN	DURATION	RATING <sup>§</sup>
<b>Oral</b>			
Clindamycin	Children: 20-30mg/kg/day in 3 divided doses	10 days	B-II
	Adults: 600mg/day in 2-4 divided doses*	10 days	B-III
Amoxycillin; clavulanic acid	Children: 40mg/kg/day in 3 equally divided doses***	10 days	B-II
	Adults: 500mg twice daily	10 days	B-III
<b>Parenteral with or without oral</b>			
Benzathine penicillin G	For IM dosages, see <a href="#">Table 3</a> , or refer to IDSA guidelines <sup>#</sup>	1 dose	B-II
Benzathine penicillin G with rifampicin	For IM dosages, see <a href="#">Table 3</a> , or refer to IDSA guidelines <sup>#</sup>	4 days	
	Rifampicin: 20mg/kg/day orally in 2 divided doses		

**Source:** Modified from Table five, Bisno et al. Clinical Infectious Diseases. 2002; 35:113-125. University of Chicago.<sup>10</sup> ©2002 by the Infectious Diseases Society of America. All rights reserved.

Macrolides (e.g. erythromycin) and cephalosporins are not included in the table, because there is insufficient data to support their efficacy in this specific circumstance.

\* Adult doses are extrapolated from data for children. Use of this drug for this indication has not been studied in adults. Further references on clindamycin available from Tanz RR et al. 1991<sup>15</sup> and Orling A et al. 1994<sup>16</sup>

\*\* Maximum dose, 750mg of amoxicillin per day

\*\*\*Refers to amoxicillin component. Note that the amount of clavulanic acid may vary between formulations. Further reference from Kaplan and Johnson 1988<sup>17</sup>

# Treatment with benzathine penicillin G is useful for patients in whom compliance with previous courses of oral antimicrobials is in question. Addition of rifampicin to benzathine penicillin G may be beneficial for eradication of streptococci from the pharynx.<sup>18</sup> It has also been reported that addition of rifampicin (20mg/kg/day, once daily) during the final four days of a ten day course of oral penicillin V may achieve high rates of eradication.<sup>19</sup> The maximum daily dose of rifampicin is 600mg; rifampicin is relatively contraindicated for pregnant women

§ Refer to the IDSA evidence rating on [Table 2](#).

<b>Evidence level:</b>	As per the IDSA rating in <a href="#">Table 2</a>
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## **Question 8. How should asymptomatic pharyngeal carriers of GAS be managed?**

Treatment is **not** recommended for asymptomatic GAS carriers **except** in certain specific situations, as defined by the American Academy of Pediatrics,<sup>12</sup>

- an outbreak of rheumatic fever or post streptococcal glomerulonephritis
- an outbreak of GAS in a closed or semi-closed community
- where a family history of ARF exists
- when multiple episodes of documented symptomatic GAS pharyngitis continue to occur within a family during a period of many weeks despite appropriate treatment (see [Question 7](#))
- when a family is anxious about GAS infection
- when tonsillectomy is being considered only because of chronic GAS carriage.<sup>12</sup>

Similarly the Infectious Diseases Society of America (IDSA) guidelines recommend against the routine culture of throat swab specimens from, or treatment of, asymptomatic household contacts of patients with GAS pharyngitis, except in situations where there is increased risk of frequent infections or of non-suppurative streptococcal sequelae (IDSA level of evidence B-III, see [Table 2](#)).<sup>10</sup>

<b>Recommendations:</b>	Do not treat asymptomatic GAS carriers unless they meet one or more of the criteria listed above. If treatment is required, treat as per <a href="#">Table 3</a> , usual or routine antibiotics, unless this is the patients' third or more cases of GAS pharyngitis within three months, in which case use <a href="#">Table 4</a>
<b>Recommendation grade:</b>	D, for when to treat GAS carriers
<b>Evidence level:</b>	Insufficient evidence for when to treat GAS carriers

**Question 9. In patients with or without GAS pharyngitis, do antibiotics shorten symptoms of sore throat on day three and at one week (days six to eight)?**

Data for this section comes from a Cochrane Review by Del Mar et al on antibiotics for sore throat.<sup>39</sup> A total of 27 studies were found which assessed antibiotics against controls in pharyngitis, 18 double-blinded and three single-blinded. Most of the studies were in adults. Some of the studies were not placebo controlled and do not consider the possible placebo effect of treatment on throat pain (see [Appendix I](#)).

**Does treating GAS positive pharyngitis with antibiotics make a difference to throat pain at day three and days six to eight?**

**At day three:**

Del Mar et al found 11 studies which examined patients with pharyngitis who all had GAS positive throat swabs. Two studies did not use placebos. Giving antibiotics to patients with GAS positive pharyngitis reduced pain by 28% on day 3 (see [Appendix I](#)).<sup>39</sup>

**At one week (six to eight days):**

In Del Mar et al's Cochrane analysis, there were six studies of GAS positive patients at one week. There were no placebos in two of the trials. Treatment with antibiotics, compared to no treatment, resulted in a 23% reduction in throat pain (see [Appendix I](#)).<sup>39</sup>

**Does treating GAS negative pharyngitis with antibiotics make any difference to throat pain at day three and days six to eight?**

**At day three:**

Del Mar et al found six studies which looked at throat pain on day three in patients with pharyngitis who all had GAS negative throat swabs. All used placebos. Reported throat pain was reduced by half in GAS negative patients treated with antibiotics, despite the negative throat swabs (see [Appendix I](#)).<sup>39</sup>

**At days six to eight:**

In the Del Mar et al analysis, five studies were found which examined the symptom of sore throat at one week (six to eight days) in patients with pharyngitis who were GAS negative. The studies were all placebo-controlled. In negative GAS swab patients, antibiotic treatment did not make a significant difference to throat pain at one week (see [Appendix I](#)).<sup>39</sup>

<b>Recommendation:</b>	There is insufficient data to draw conclusions about antibiotic limiting symptoms of pharyngitis in children. In adults, the symptom of throat pain in GAS positive pharyngitis is improved by antibiotics
<b>Recommendation grade:</b>	A
<b>Evidence level:</b>	I

## **Question 10. Does treating pharyngitis with antibiotics reduce the suppurative complications of GAS pharyngitis (acute otitis media and quinsy)?**

Data for this section comes from a Cochrane Review on antibiotics for sore throat.<sup>39</sup> A total of 27 studies were found which assessed antibiotics against controls in pharyngitis (pharyngitis in general, not specifically GAS pharyngitis). Eighteen were double-blinded and three were single-blinded. Most of the studies were in adults (see [Appendix I](#)).<sup>39</sup>

### **Does treating pharyngitis with antibiotics reduce the incidence of acute otitis media (by clinical diagnosis) occurring within 14 days?**

Del Mar et al found 11 RCTs which looked at this issue, nine were placebo-controlled. Overall, antibiotics reduced the rate of clinically suspected acute otitis media following pharyngitis by about 23% (see [Appendix I](#)).<sup>39</sup>

### **Does treating pharyngitis with antibiotics reduce the incidence of quinsy (by clinical diagnosis) occurring within 2 months?**

Eight RCTs were found by Del Mar et al; in six the patients were given placebos. A potential benefit for antibiotic treatment (16% reduction) in preventing clinically suspected quinsy was demonstrated (see [Appendix I](#)).<sup>39</sup>

<b>Recommendation:</b>	Treating pharyngitis with antibiotics reduces acute otitis media and quinsy
<b>Recommendation grade:</b>	A
<b>Evidence level:</b>	I

## **Question 11. Do antibiotics reduce the incidence of non-suppurative complications of GAS pharyngitis (acute post streptococcal glomerulonephritis [APSGN] and ARF)?**

Data for this section comes once more from a Cochrane Review.<sup>39</sup> A total of 27 studies were found which assessed antibiotics against controls in pharyngitis. Eighteen were double-blinded and three were single-blinded. Most of the studies were in adults (see [Appendix I](#)).<sup>39</sup>

### **Does treating pharyngitis with antibiotics reduce the incidence of acute post streptococcal glomerulonephritis (APSGN) within one month?**

Del Mar et al reviewed ten RCTs, four were placebo-controlled. Only six studies looked at APSGN as an end point. Two cases of APSGN occurred, both in the control groups. Due to the small numbers involved, he concluded that there was insufficient data to find a benefit for antibiotics in sore throat management to reduce the incidence of APSGN (see [Appendix I](#)).<sup>39</sup>

### **Does treating pharyngitis with antibiotics reduce the incidence of ARF (within two months)?**

Fourteen RCTs were analysed by Del Mar et al, eight using placebos. Overall the incidence of ARF was reduced to 27% of that in the placebo groups (see [Appendix I](#)).<sup>39</sup>

<b>Recommendations:</b>	Treating pharyngitis with antibiotics reduces the rate of ARF, but there is insufficient evidence regarding acute post streptococcal glomerulonephritis
<b>Recommendation grade:</b>	A
<b>Evidence level:</b>	I

## Question 12. Which measures improve adherence to antibiotic courses (prescribed for GAS pharyngitis)?

### Verbal/written interventions, including telephone calls:

A Cochrane review looked at interventions for enhancing medication adherence.<sup>100</sup> Three of the RCT studies are relevant to compliance with antibiotic treatment.<sup>101-103</sup> Overall, statistically significant improvements in medication adherence (31 of 67 studies) and treatment outcomes (22 of 67 studies) occurred no matter what the intervention.

An RCT in 2004 found that a telephone call four to five days into treatment increased antibiotic compliance from 54% to 78% among patients over 18 years old who attended a Spanish health clinic with pharyngitis.<sup>104</sup>

### Reducing the number of antibiotic doses per day:

Pichichero estimated the failure rate of oral penicillin in eradicating GAS from the throat was ten to 25% and believed that at least some of this was due to poor compliance.<sup>105-114</sup> Simplifying medication regimes may increase compliance and the rate of eradication. Lan et al found twice-daily dosing of oral penicillin to be as effective as more frequent regimes and the cure rates with once-daily dosing only 12% lower than more frequent penicillin dosing.<sup>96</sup> There is some evidence that once-daily dosage of amoxicillin is as effective as standard oral penicillin regimes.<sup>84-86</sup> Compliance with amoxicillin therapy may also be greater than with oral penicillin therapy, because amoxicillin need not be taken on an empty stomach.

### Shortening courses of oral antibiotics:

When compared to the standard ten day oral regime, shorter courses of penicillin have been shown to be less effective in achieving bacterial eradication.<sup>115</sup> Refer to [Question 5](#) for further discussion of antibiotics and amoxicillin.

However, Pichichero in a meta-analysis of oral antibiotic treatment for tonsillopharyngitis found six days of amoxicillin, four to five days of various cephalosporins and five days of azithromycin were reasonable alternatives to ten days of oral penicillin, in terms of bacteriologic eradication and clinical cure.<sup>105</sup>

**Recommendations:** Ten days of oral penicillin twice daily is the gold standard for treating GAS pharyngitis. Once daily oral amoxicillin is a reasonable alternative, as is IM benzathine penicillin. Evidence for shorter regimes remains insufficient, nor is there sufficient evidence to make firm recommendations on clinical measures to increase compliance

	Evidence level:	Recommendation grade:
Ten days twice-daily penicillin regimes	I	A
Ten days once-daily oral amoxicillin	III	B
Telephone support for compliance with antibiotics	III	B

## Question 13. Do recurrent sore throats increase the risk of a patient progressing to ARF?

There is insufficient published data to answer this question with any degree of certainty. See [Appendix J](#) for studies listing sore throat episodes and rheumatic fever.<sup>116,117</sup>

<b>Recommendation:</b>	The writing group consensus is that recurrent GAS sore throats may increase the likelihood of developing ARF. Attempt to eradicate GAS recommended in high-rheumatic fever risk groups. High risk patients are Māori or Pacific peoples, those aged three to 45 years, and those with a past history of rheumatic fever. Living in a lower socioeconomic area of the North Island is also a risk factor (see <a href="#">Appendix C</a> and <a href="#">D</a> )
<b>Recommendation grade:</b>	D, writing group consensus
<b>Evidence level:</b>	Insufficient evidence

**Question 14. Does delay in the availability of the throat culture result (up to nine days) increase the risk of the development of ARF?**

Studies in the US military have shown that primary preventative treatment with penicillin is effective even if started as late as nine days after the infection develops.<sup>118</sup>

<b>Recommendation:</b>	Treatment of streptococcal pharyngitis can be delayed until culture results are available as rheumatic fever is unlikely to occur up to nine days after the first symptoms of pharyngitis
<b>Recommendation grade:</b>	B
<b>Evidence level:</b>	III

**Question 15. Is seasonal prophylaxis for recurrent streptococcal pharyngitis useful?**

There is limited evidence from two RCTs that this may be effective in a circumscribed community.<sup>119,120</sup> These studies are summarised below.

**Table 10. Studies on Seasonal Prophylaxis for Pharyngitis**

STUDY	PATIENTS	INTERVENTION	OUTCOME IN CONTROLS	OUTCOME IN TREATMENT GROUP
Aksit S et al. 1998 <sup>119</sup>	160 children aged 4-11 years, in Turkey, who had 2+ episodes of GAS pharyngitis during 4 month period in 1995	RCT. <b>Treatment group:</b> 80 patients given IM benzathine penicillin G every 3 weeks. <b>Control group:</b> 80 controls not given any medication. 4 month observation period for results	244 episodes of GAS pharyngitis. 5 control patients excluded for poor compliance	16 episodes of GAS pharyngitis. 2 patients excluded for poor compliance
Mora R et al. 2003 <sup>120</sup>	180 children aged 4-14 years, who had 3+ episodes of tonsillitis in the previous year	RCT. <b>Treatment group:</b> 90 patients given cefpodoxime 100mg po bd for 6 days a month for 6 months. <b>Control group:</b> 90 control patients given placebo medication at the same dosage and duration. Patients followed for 12 months	At 12 months: 86.4 episodes of tonsillopharyngitis, and 86.4 episodes of non-complete eradication or re-infection with GAS (on pharyngeal swab)	At 12 months: 11.6 episodes of tonsillopharyngitis, and 20 episodes of non-complete eradication or re-infection with GAS (on pharyngeal swab)

<b>Recommendation:</b>	No recommendation is possible regarding seasonal prophylaxis
<b>Recommendation grade:</b>	D, insufficient evidence to make a judgment
<b>Evidence level:</b>	Insufficient evidence to make a judgment

### **Question 16. Does having a smoker in the house make GAS throat infection more likely?**

There is insufficient published evidence to answer this question. A single Indian study found a link between the presence of a tobacco smoker in the household and the incidence of GAS pharyngitis in the children.<sup>121</sup> Evidence exists that the incidence of other respiratory illnesses, including meningococcal disease, is increased by the presence of smokers.<sup>122,123</sup>

<b>Recommendation:</b>	The writing group consensus is that streptococcal pharyngitis, like other respiratory illnesses, is likely to be exacerbated by smoking within the household and recommends cessation of smoking or smoking outdoors
<b>Recommendation grade:</b>	D, writing group consensus
<b>Evidence level:</b>	Insufficient evidence

### **Question 17. Is there a vaccine available for the control of GAS disease?**

No GAS streptococcal vaccine has been marketed to date. However, recent clinical trials have been promising.<sup>124</sup>

<b>Recommendation:</b>	No recommendations are available to be made, as possible vaccines are still under development
<b>Recommendation grade:</b>	D
<b>Evidence level:</b>	Insufficient evidence

### **Question 18. Should throat swabs be repeated after antibiotic course has ceased?**

A follow-up throat swab following an adequate course of treatment for GAS pharyngitis is not usually recommended.<sup>10</sup>

The IDSA<sup>10</sup> recommends the following patients in special situations be routinely swabbed after completing their antibiotic courses for GAS pharyngitis:

- Those with a history of rheumatic fever
- Those who develop GAS pharyngitis during outbreaks of acute rheumatic fever or post streptococcal glomerulonephritis
- Those who develop GAS pharyngitis during outbreaks in a closed or partially closed community
- Where there is recurrent GAS pharyngitis within families (IDSA evidence level B-III).<sup>10, 73, 125</sup>

In New Zealand, patients who remain symptomatic after completing their full course of antibiotics, should have throat swabs repeated to exclude other causes<sup>126</sup> (writing group consensus).

The majority of asymptomatic patients who continue to have positive swabs post-antibiotic treatment are carriers.<sup>125,127</sup>

**Recommendation and recommendation grade:**

Do NOT swab patients after they complete antibiotics for GAS pharyngitis (IDSA evidence level A-II), **unless:**

- The patient has a history of rheumatic fever and is not receiving prophylactic IM penicillin
- The patient develops GAS pharyngitis during an outbreak of acute rheumatic fever **or** post streptococcal glomerulonephritis
- The patient developed GAS pharyngitis during outbreaks in a closed or partially closed community
- There is recurrent GAS pharyngitis within the family/household (IDSA evidence level B-III)
- The patient remains symptomatic after completing their full course of antibiotics.

**Evidence level:** As above. See **Table 2** for explanation of IDSA evidence ratings system

## **Question 19. Is there a role for tonsillectomy in recurrent pharyngitis?**

This area has not been well addressed in the literature. The most useful reviews were a Cochrane Review<sup>128</sup> and one in Clinical Evidence online,<sup>129</sup> available from: <http://www.clinicalevidence.com>. The numbers of children involved were small (665 in total) and no studies were in adults.

Of concern is that the three key RCT studies were all by the same author<sup>130-132</sup> with one remaining an abstract only.<sup>131</sup> The reviews found that there was insufficient evidence to form conclusions about tonsillectomy versus medical management in recurrent pharyngitis.

A recent meta-analysis by van Staaij et al<sup>133</sup> had less stringent inclusion criteria for the studies and looked at tonsillectomy with or without adenoidectomy in children under 18 years of age. Six RCTs and seven trials, which were not randomised, were analysed. Overall there was no clear consensus on when tonsillectomy is beneficial in children and no data for adults.

**Recommendation:** For adults or children with recurrent pharyngitis, the writing group is unable to make a recommendation on the indications for tonsillectomy

**Recommendation grade:** D

**Evidence level:** Insufficient evidence

## **Question 20. Which factors lead to the spread of GAS pharyngitis?**

There has been some research on several factors, namely; droplet spread, crowding and number of people in the home, fomites, hygienic measures, poverty and the presence of young children within the household. Where there have been studies, they are mostly descriptive and not of high quality.

### **Is GAS droplet spread?**

Group A streptococcus is a respiratory pathogen and thought to spread through droplets of salivary or nasal secretions or occasionally through food preparation<sup>134</sup> or via water.<sup>135</sup>

### **Do fomites (dust/clothing/bedding) have a role in the spread of GAS?**

Although this area has not been extensively researched, current thinking is that GAS is not significantly spread through contaminated fomites such as dust, bedding and furnishings.<sup>135,136</sup> In two key experimental studies, Perry et al did not find any evidence that dust or GAS-contaminated blankets spread GAS pharyngitis.<sup>137,138</sup> Falck et al, in a case-control study also found that hygienic measures, such as changing toothbrushes and washing bedclothes, made no difference to the recurrence of GAS sore throat.<sup>139</sup> These studies are summarised in [Appendix K](#).

### **Does crowding/number of people in the household affect the spread of GAS pharyngitis?**

Most of this information comes from observational, retrospective studies looking at ARF. The crowding in the house and/or bed literature and its relationship to rheumatic fever incidence has been summarised by McNicholas.<sup>140</sup> McNicholas analysed nine key studies, including those in crowded military settings, a key Bristol study<sup>141</sup> and a study in a New Zealand setting.<sup>31</sup> A clear link was found between overcrowding and rheumatic fever incidence, independent of socioeconomic variables.

A subsequent Indian study found a small increase in incidence of GAS pharyngitis per child-year, when children lived in more crowded homes. They also found a peak during the rainy and winter seasons, when children tended to cluster indoors.<sup>121</sup>

Lindbaek et al, in a Norwegian study, found households with four or more members were more likely to have GAS spread.<sup>142</sup>

In a community outbreak of rheumatic fever in the United States in the late 1980s, cases were associated with larger families, but not lower socioeconomic status.<sup>143</sup>

### **Does having young children in the household influence the spread of GAS pharyngitis?**

This is not well addressed in the literature. Lindbaek et al's study found the strongest predictor of GAS pharyngitis spread was having children less than 16 years of age in the household. All 30 of the households where the spread occurred had children under the age of 16 years. There were no cases of GAS pharyngitis spreading, where all members of the household were aged 16 years and over.<sup>142</sup> Powers and Boisvert have pointed out that children with streptococcal infections are important reservoirs of contagion, as they require close contact in their care.<sup>144</sup> However, Nandi et al in their household study of 536 children (see above) found the number of children in a family (one to five children) did not make a significant difference in the number of cases of GAS pharyngitis.<sup>121</sup>

### **What is the chance of GAS pharyngitis spreading within a household, and how should households with GAS pharyngitis be managed?**

Four key studies were found which looked at this topic.

Lindbaek et al found 30 out of 110 households (27%) had one or more new cases of GAS tonsillitis after an initial case (40 new infections). Lindbaek et al treated GAS pharyngitis with five days of penicillin.<sup>142</sup>

Breese et al found half to quarter of sibling contacts developed a form of streptococcal infection during the study period although less than one in 20 parents did. Breese et al did not look solely at pharyngitis for those statistics: pharyngitis, tonsillitis, scarlet fever, otitis media and cervical adenitis were all counted. When analysing streptococcal pharyngitis and tonsillitis alone, the attack rate in siblings was 96 out of 496 (19.4%). Breese et al treated GAS pharyngitis with 600,000 units of IM benzathine penicillin G.<sup>145</sup>

Falck et al investigated 114 patients and their families, 305 possible exposed people and found 95 (31%) were infected with GAS pharyngitis within a month. Falck et al treated GAS pharyngitis with five days of phenoxymethyl penicillin. Falck et al proposed that most GAS treatment failures depended on ping-pong reinfection from family members with the same T and RFLP type as the index case and recommended further studies.<sup>146</sup>

Poku estimated the probability of one person aged up to 16 contracting GAS, positive on throat swab, in one month was 0.05-0.06, i.e. in a household with five susceptible people, the risk of one person becoming infected with GAS was  $1-0.94^{**5}$  (27%).<sup>147</sup>

From the above studies, the rate of spread seems to be about 30% per household, or five to six percent chance per at-risk person in the household per month, although the numbers are small. It is not possible

to draw significant conclusions on the likelihood of spread to any particular age group, but adults seemed to be at a lower risk of spread in general.

No trials were found (with intervention and control groups, regardless of randomisation) where the treatment or not of households with GAS pharyngitis has been looked at.

The American Academy of Pediatrics<sup>12</sup> does not recommend asymptomatic GAS carrier treatment except in certain situations, including in situations where multiple episodes of documented symptomatic GAS pharyngitis continues within a family during a period of many weeks despite appropriate treatment (refer to [Question 8](#) for more detail).

Similarly, the IDSA guidelines recommend against routine culture of asymptomatic household contacts of patients with GAS pharyngitis, except in situations where there is increased risk of frequent infections or of non-suppurative streptococcal sequelae (IDSA evidence level B-III).<sup>10</sup> See [Table 2](#) for IDSA ratings and [Question 8](#) for more detail).

Although the literature is weak, if the true rate of symptomatic GAS pharyngitis cross infection within households is potentially between 19-50%, this is a problem in New Zealand with its rate of rheumatic fever being high by world standards. The rate in New Zealand is 3.8 per 100,000 (see [Table 7](#))<sup>36</sup> and the burden of rheumatic fever is inequitably borne by Māori and Pacific peoples, and in lower socioeconomic parts of the country. Based on the American Academy of Pediatrics (Red Book) and IDSA guidelines it is recommended that GAS pharyngitis be re-instated as a disease notifiable to the Ministry of Health (as rheumatic fever is currently). This would facilitate the follow up of outbreaks of three or more cases of GAS pharyngitis per household per three month period, and allow RF at-risk households to be screened for GAS pharyngitis, thereby reducing the rate of subsequent rheumatic fever. There is inadequate information at this stage to determine if any age groups in particular should be screened within households.

### **Is poverty a factor in the spread of GAS pharyngitis?**

There is little information on this topic. Research tends to focus on ARF and poverty rather than GAS pharyngitis itself and the studies are observational and of poor quality. Najeeb, in a report for the World Health Organisation (WHO) on rheumatic fever in developing countries, argues that ARF is 'basically a socioeconomic disease'.<sup>148</sup> The report states that it has declined in developed countries, with the exception of pockets in city slums, due to medical and non-medical factors, including improvements in socioeconomic conditions. Furthermore, it is not the poverty per se, but the manifestation of poverty through overcrowding in substandard housing which is the cause of ARF.<sup>148</sup> Bhave et al in Bombay, India, found poorer children were more likely to have higher Antistreptolysin O (ASO) titres and were more likely to have rheumatic heart disease.<sup>149</sup>

Nandi et al's study did not detect a difference in socioeconomic status in the incidence of GAS pharyngitis in households, although the study was conducted in a slum community where there were 'no major difference in socioeconomic status between households'.<sup>121</sup>

#### **Recommendation:**

Addressing the socioeconomic factors which may contribute to the spread of GAS in the community, such as household crowding, is likely to reduce the incidence of ARF. However, adequate medical intervention in GAS pharyngitis is likely to have a major role in overriding the effect of socioeconomic factors (Lennon unpublished RCT data)<sup>41-43</sup>

The writing group recommends, where three or more cases of confirmed GAS pharyngitis occur in a household, that the household be screened and all those GAS positive on throat swab (regardless of symptoms) be treated with antibiotics

**Recommendation grade:** D, expert opinion for the second recommendation

**Evidence level:** Expert opinion

## [7. Implementation of the Guideline]

### Driving forces

Reducing the incidence of rheumatic fever, a preventable chronic disease, has driven this guideline. About a third of rheumatic fever patients in current times will present with moderate or severe heart disease, and ten to twenty percent of patients will continue to have severe chronic heart disease and require intensive medical or surgical management for their shortened lifetimes. The burden of rheumatic fever is inequitably borne by Māori and Pacific peoples, especially children and youth. Rheumatic fever is a disease which New Zealand, unlike other westernised countries, has failed to control.

### Restraining forces

The following challenges will need to be met:

- Perception by many children, young people, parents and caregivers that sore throats are a minor ailment and do not have sequelae
- Barriers to primary care services and diagnostic tests
- Lack of knowledge by health professionals and lay public alike that rheumatic fever and rheumatic heart disease are preventable
- The need to wait until swab results are known before antibiotics are prescribed, therefore requiring more than one health care visit
- The cost of doctor visits and antibiotics for patients aged over six years
- The difficulty in completing a ten day course of antibiotics and patient dislike of intramuscular benzathine penicillin injections
- Avoiding unnecessary antibiotic prescribing in low ARF-risk patients
- Poorer socioeconomic circumstances (including a lack of transport or telephone) which may contribute to untreated sore throats and thus rheumatic fever
- Cost and complexity of investigation of families and household members in association with a case of recurrent GAS pharyngitis in a high risk population
- Streptococcal disease other than rheumatic fever is no longer a notifiable disease
- A lack of funding in New Zealand for rapid streptococcal throat swab diagnostic tests, and need for consideration of their effectiveness
- Other unknown factors.

### Consultation

Relevant consumer groups and community organisations including Te Hotu Manawa Māori and Pacific Islands Heartbeat Programme were consulted and reviewed the guideline. Prior to the Auckland school-based randomised-controlled trial for the prevention of rheumatic fever (2006 Lennon unpublished data), in 1996 there was consultation at St Stephen's church in Otara and Te Puea marae in Mangere regarding possible venues for sore throat clinics. The community feedback at that time backed schools as the preferred option. Both communities called for more information on rheumatic fever prevention and the consequences of rheumatic fever.

### Suggested implementation strategies

- Re-instate GAS pharyngitis as a notifiable disease, to catch three or more cases in three months in a household. In a transient population or one where patients from a household see doctors in different hospitals or practices, this is likely to be the only practical option
- Where there are three or more cases of GAS pharyngitis in a household within a three month period, community or public health nurses would need to take throat swabs from the entire household (see sore throat management algorithm, [page 14](#)), as well as from all rheumatic fever case families
- Raise awareness of rheumatic fever as a preventable disease in high-risk populations, through:
  - Development of health promotion materials, such as pamphlets, DVDs, videos, posters, appropriate for those at highest risk
  - Health promotion in schools in high-risk areas

- Educating community and family groups in high-risk areas (whānau, iwi, marae and church groups and other appropriate vehicles)
- Ensuring funding for training of primary care persons to implement this guideline.
- Consider implementation strategies, e.g. schools, marae or church clinics, to highlight sore throats for diagnosis and treatment, overcoming some of the above restraining forces. As stated above, school clinics have been preferred by two South Auckland communities, and have been studied in the New Zealand context (Diana Lennon unpublished 2006)
- Dissemination of this guideline through the National Heart Foundation of New Zealand and its website, relevant professional organisations and members of the writing group.

This guideline is available to download online at: <http://www.heartfoundation.org.nz> .

### **Measuring effectiveness/outcomes**

Although there may be confounding variables, the primary outcome of the institution of this guideline ought to be the reduction in the incidence of ARF, particularly in targeted high-risk groups. Rheumatic fever is a notifiable disease and the incidence is monitored by the Ministry of Health in New Zealand.

### **Economic analysis**

An economic analysis is due for completion later in 2008 and will be published separately.

## 8. Appendices

### Appendix A: Microbial causes of acute pharyngitis

Table 11. Microbial Causes of Acute Pharyngitis:

PATHOGEN	SYNDROME / DISEASE	ESTIMATED PERCENTAGE OF CASES OF PHARYNGITIS, IN ALL AGE GROUPS
<b>Viral</b>		%
Rhinovirus (100 types and 1 subtype)	Common cold	20
Coronavirus (3 or more types)	Common cold, SARS	>=5
Adenovirus (types 3, 4, 7, 14, 21)	Pharyngoconjunctival fever, ARD	5
Herpes simplex virus (types 1 and 2)	Gingivitis, stomatitis, pharyngitis	4
Parainfluenza virus (types 1-4)	Common cold, croup	2
Influenza virus (types A and B)	Influenza	2
Cocksackievirus A (types 2, 4-6, 8, 10)	Herpangina	<1
Epstein-Barr virus	Infectious mononucleosis	<1
Cytomegalovirus	Infectious mononucleosis	<1
HIV-1	Primary HIV infection	<1
<b>Bacterial</b>		
Streptococcus pyogenes (group A beta haemolytic streptococci)	Pharyngitis/tonsillitis, scarlet fever	15-30
Group C and G beta haemolytic streptococci	Pharyngitis/tonsillitis	5-10
Mixed aerobic/anaerobic infection	Gingivitis (Vincent's angina)	<1
	Peritonsillitis/peritonsillar abscess (quinsy)	<1
Neisseria gonorrhoeae	Pharyngitis	<1
Corynebacterium diphtheriae	Diphtheria	>=1
Corynebacterium ulcerans	Pharyngitis, diphtheria	<1
Arcanobacterium haemolyticum (Corynebacterium haemolyticum)	Pharyngitis, scarlatiniform rash	<1
Yersinia enterocolitica	Pharyngitis, enterocolitis	<1
Treponema pallidum	Secondary syphilis	<1
Francisella tularensis	Oropharyngeal tularemia	<1
<b>Chlamydial</b>		
Chlamydia pneumoniae	Pneumonia/bronchitis/pharyngitis	Unknown
<b>Mycoplasma</b>		
Mycoplasma pneumoniae	Pneumonia/bronchitis/pharyngitis	<1
Mycoplasma hominis (type 1)	Pharyngitis in volunteers	Unknown
<b>Unknown</b>		30

Source: Modified from table 51-1. This table was published in: Bisno A. Pharyngitis. In: Mandell GL, Bennett JE, Dolin R (Eds), Mandell, Douglas & Bennett's Principles and Practice of Infectious Diseases, 6<sup>th</sup> ed, 2004. Philadelphia, USA: Elsevier Churchill Livingstone. 2004; 1: 752-758.<sup>31</sup> Copyright Elsevier (2007)

## Appendix B: Guideline development process

- Relevant literature regarding sore throats and ARF was identified using computerised databases described below, primarily Pubmed. Publications were limited to those in the English language. Articles found through this methodology were then searched for relevant information and further articles identified through bibliographic references. A substantial physical library of sore throat and ARF references held at the School of Population Health was also reviewed for key articles
- Sore throat guidelines prepared by the Infectious Diseases Society of America,<sup>10</sup> the American Academy of Family Physicians and The American College of Physicians,<sup>11</sup> the 2003 Report of the Committee on Infectious Diseases by the American Academy of Pediatrics<sup>66</sup> and McIsaac's GAS pharyngitis criteria (based on (Centor et al. 1981;<sup>13</sup> McIsaac et al. 2004<sup>14</sup>) were reviewed
- In 2004, a steering group met to agree that guidelines for rheumatic fever should be developed. In 2005 a similar group met agreeing that guidelines should be drawn up for ARF for New Zealand including secondary prophylaxis, sore throat management and primary prevention in addition to diagnosis and treatment
- A writing group formed for the sore throat management guideline. Selected individuals drafted the guideline which was then reviewed by all members of the writing group with experience in ARF and/or sore throat management and their suggestions were incorporated into a second draft
- The revised draft was widely distributed to a range of stakeholders who were then invited to comment
- The stakeholders reviewed the draft and reached consensus on areas of disagreement
- Comments were then incorporated to a final draft which was endorsed by the stakeholders.

The Agree instrument ([www.agreecollaboration.org](http://www.agreecollaboration.org)) available through the NZ Guidelines Group website, via the link:

<http://www.nzgg.org.nz/index.cfm?fuseaction=evidence&fusesubaction=article&documentid=11&articleID=9> ) was applied to the 3 main guidelines used as a basis for the document, by two members of the writing group (MK and DL). The three guidelines were:

- Infectious Diseases Society of America<sup>10</sup>
- The American Academy of Family Physicians and The American College of Physicians<sup>11</sup>
- The 2006 Report of the Committee on Infectious Diseases by the American Academy of Pediatrics.<sup>12</sup>

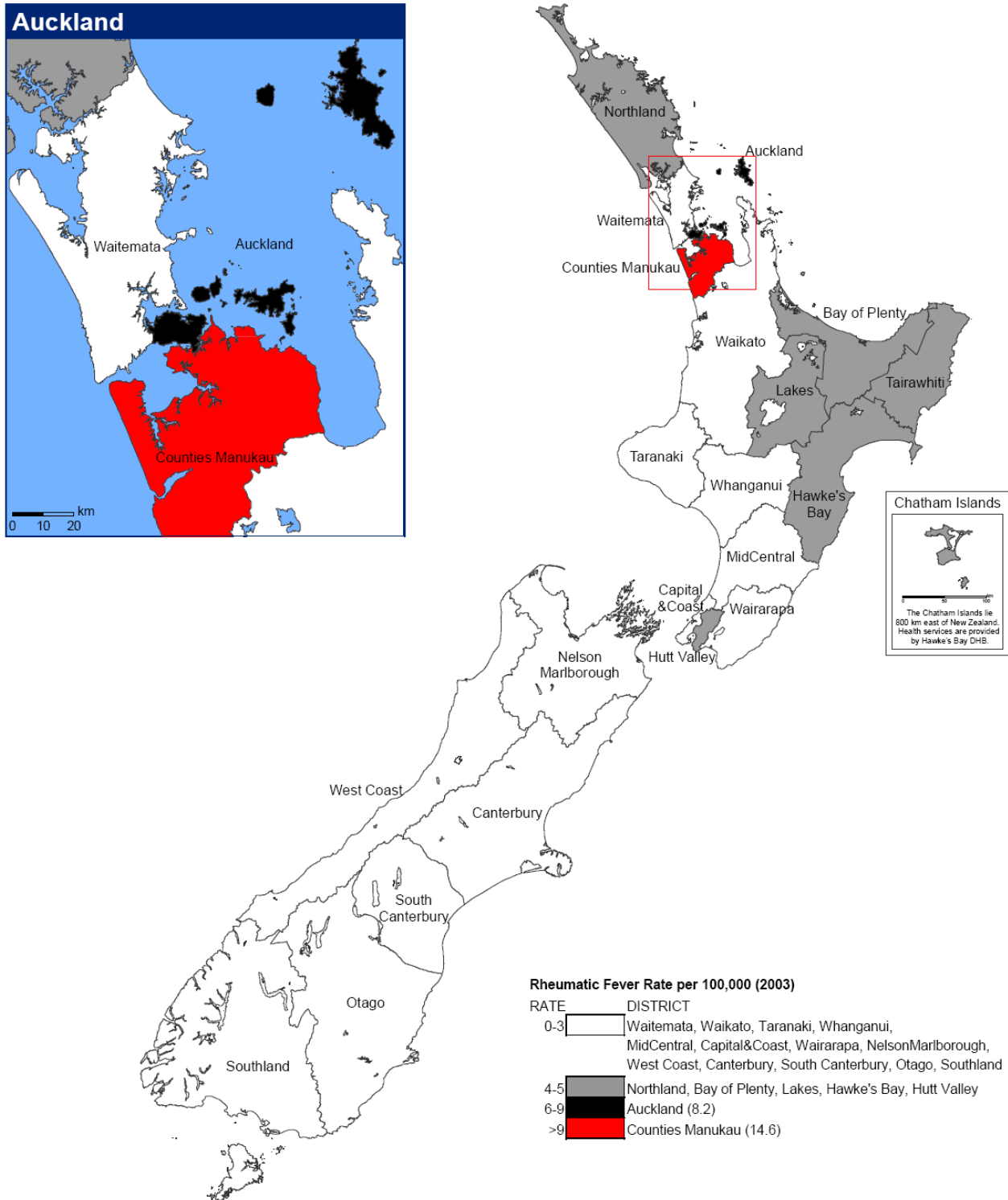
Scores are listed in [Table 12](#).

**Table 12. Quality of the Three Guidelines Used as a Basis for the Sore Throat Guideline**

QUESTION NUMBER (FROM AGREE INSTRUMENT)	INFECTIOUS DISEASES SOCIETY OF AMERICA (2002) <sup>10</sup> SCORE OUT OF MAXIMUM OF 4 FOR EACH QUESTION (1 = STRONGLY DISAGREE, 4 = STRONGLY AGREE - HIGH SCORE MOST DESIRABLE)	COOPER (2001) <sup>11</sup> SCORE OUT OF MAXIMUM OF 4	AMERICAN ACADEMY OF PEDIATRICS (2006) <sup>12</sup> SCORE, OUT OF MAXIMUM OF 4
1	4	4	4
2	4	4	4
3	4	4	4
4	4	4	4
5	0	1	1
6	3	4	4
7	3	1	4
8	3	4	1
9	3	4	1
10	4	4	1
11	4	3	4
12	4	3	1
13	1	4	4
14	3	1	4
15	4	3	4
16	4	2	4
17	4	3	4
18	4	2	4
19	2	4	1
20	2	3	3
21	4	1	1
22	2	4	1
23	1	4	1
Total score (from maximum of 92)	72	71	64
Quality recommendation:	Strongly recommend	Strongly recommend	Strongly recommend

A full description of the guideline development process for this guideline is available to download from URL: <http://www.heartfoundation.org.nz>

## Appendix C: Rheumatic fever incidence in New Zealand per District Health Board



Source: Public Health Intelligence, Ministry of Health. 06/06/2007

## Appendix D: Areas of New Zealand with high incidences of rheumatic fever

Table 13. Areas of New Zealand with High Incidences of Rheumatic Fever

LOWER SOCIOECONOMIC REGIONS WITHIN:
Northland
Auckland
Waikato
Bay of Plenty/Rotorua
Gisborne
Hawke's Bay
Wellington area

## Appendix E: Incidence of ARF in children and adolescents in studies published since 1990

**Table 14. Incidence of ARF in Children and Adolescents in Studies Published Since 1990**

STUDY	PLACE	YEAR	POPULATION SUB-GROUP	AGE (YEARS)	ARF INCIDENCE (PER 100 000 PER YEAR)
Cernay J et al. Incidence of rheumatic fever in Slovakia during the last 20 years. Cesk Pediatr. 1993; 48: 79-83.	Slovakia	1990-91		0-14	0.7
Lopez R. RF/RHD: comprehensive programme for prevention. Pinar de Rio, Cuba, 1986-96 (primary and secondary prevention). Havana: University of Cuba, 2000.	Cuba	1996		5-14	2.7
Noah PK. Trends in acute rheumatic fever: the Barbados experience. J Trop Pediatr, 1994; 40: 94-96.	Barbados	1986-90		0-19	8
Lennon D. Rheumatic fever, a preventable disease? The New Zealand experience. In: Martin DR, Tagg JR, eds. Streptococci and streptococcal diseases; entering the new millennium. Porirua: Institute of Environmental Science and Research. 2000: 503-512.	New Zealand	1982-97	European descent	5-15	<10
Kermani S, Berah H. La situation epidemiologique du RAA en Algerie depuis 1990. Algiers: Algerian Ministry of Health, Department of Epidemiology (National Program for the Prevention and Control of RF), 2001.	Algeria	1997-2000		4-19	11.1 (1997) 6.2 (2000)
Eltohami EA et L. Acute rheumatic fever in an Arabian Gulf country: effect of climate, advantageous socioeconomic conditions, and access to medical care. Angiology. 1997; 48: 481-489.	Qatar	1984-94		4-14	11.2
Eshel G et al. Chorea as a manifestation of rheumatic fever: a 30-year survey (1960-90). Eur J Pediatr. 1993; 152: 645-646.	Israel	1980-90		5-15	15.5
Carp C. WHO/WHF/UNESCO joint consultation on RF/RHD prevention: a progress report of activities for Romania. Bucharest: Illescu Institute of Cardiology. 1999: 1-12.	Romania	1999		5-15	16.5

Baker M et al. The comparative epidemiology of post streptococcal diseases in New Zealand: acute rheumatic fever and acute glomerulonephritis, In Streptococci and streptococcal diseases: entering the new millennium. Porirua: Institute of Environmental Science and Research. 2000: 545-547.	New Zealand	1988-97	All	5-14	16.7
Folomeeva OM, Benevolenskaia LI. Rheumatism in the Russian Federation: statistic and reality. Vestn Ross Akad Med Nauk. 1996; 11: 21-24.	Russia	1994		children	18
Omar A. Pattern of acute rheumatic fever in a local teaching hospital. Med J Malaysia. 1995; 50: 125-130.	Kuala Lumpur	1981-90		children	21.2
Kechrid A et al. Acute rheumatic fever in Tunisia: serotypes of group A streptococci associated with rheumatic fever. Adv Exp Med Biol. 1997; 418: 121-123.	Tunisia	1990		4-14	30
Hasab AA et al. Rheumatic heart disease among Omani school children. East Mediterr Health J. 1997; 3: 17-23.	Oman	1997		6-18	40
Lennon D. Rheumatic fever, a preventable disease? The New Zealand experience. In: Martin DR, Tagg JR, eds. Streptococci and streptococcal diseases; entering the new millennium. Porirua: Institute of Environmental Science and Research. 2000: 503-512.	New Zealand	1982-97	Māori	5-15	40-80
Kayemba Kay's KS, Dupuis E. Acute rheumatic fever is still active in Martinique: epidemiological and clinical study of 34 cases observed during the 1987-1991 period. Pediatrie. 1993; 48: 823-827.	Martinique	1987-91		5-14	53
Padmavati S. Rheumatic fever and rheumatic heart disease in India at the turn of the century. Indian Heart J. 2001; 53: 35-37.	India	1984-95		5-14	54
Lopez ESL. Fiebre rheumatica en el quinquenio 1994-1999 en dos hospitales en San Luis Potosí y en México DF. Archivos Cardiol Mex. 2001; 71: 127-135.	Mexico	1994-99		5-14	70

Lennon D. Rheumatic fever, a preventable disease? The New Zealand experience. In: Martin DR, Tagg JR, eds. Streptococci and streptococcal diseases; entering the new millennium. Porirua: Institute of Environmental Science and Research. 2000: 503-512.	New Zealand	1982-97	Pacific Island peoples	5-15	80-100
Australian Institute of Health and Welfare: Field B. Rheumatic heart disease: all but forgotten in Australia except among Aboriginal and Torres Strait Islander peoples. Canberra: AIHW, 2004.	Australia	1989-2002	Aboriginal	5-14	245-351
Meira ZMA. Prevalence of rheumatic fever in children from a public high school in Belo Horizonte, Brazil. Arq Bras Cardiol. 1995; 65: 331-334.	Brazil	1992		10-20	360
Richmond P, Harris L. Rheumatic fever in the Kimberley region of Western Australia. J Trop Pediatr. 1998; 44: 148-152.	Australia	1988-92	Aboriginal	5-14	375
Carapetis Jr et al. Cumulative incidence of rheumatic fever in an endemic region: a guide to the susceptibility of the population? Epidemiol Infect. 2000; 124: 239-244.			Aboriginal	5-14	508

**Source:** Adapted from Table 1. Reprinted from The Lancet. Vol 366, Carapetis JR et al. Acute Rheumatic Fever, 155-168. Copyright 2007, with permission from Elsevier.<sup>151</sup>

**United States statistics:** In the United States in 1977, the crude death rate from rheumatic fever was less than 1 per 100,000 of the population (from figure 7).<sup>152</sup>

## Appendix F: Differential diagnosis of pharyngitis

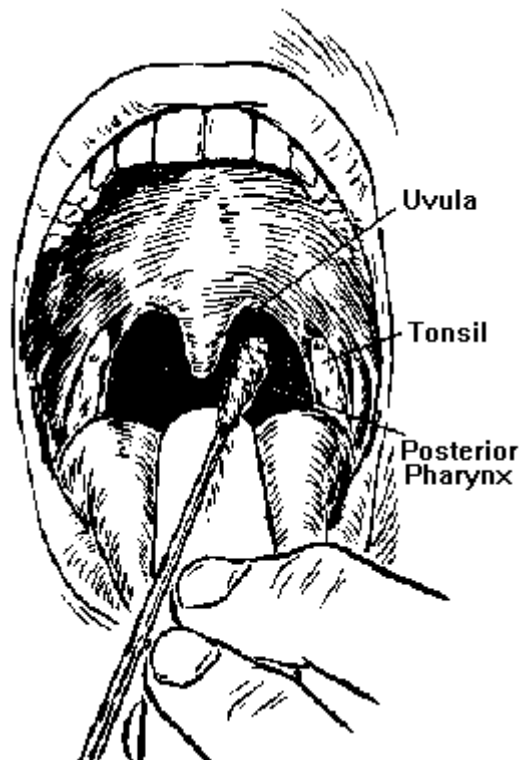
Table 15. Differential Diagnosis of Pharyngitis

CLINICAL AND EPIDEMIOLOGICAL FINDINGS AND DIAGNOSIS OF PHARYNGITIS DUE TO GROUP A BETA-HEMOLYTIC STREPTOCOCCI (GAS)
<b>Features Suggestive of GAS Aetiology</b>
Sudden onset Sore throat Fever Headache Nausea, vomiting, abdominal pain Inflammation of pharynx and tonsils Patchy, discrete exudate Tender, enlarged anterior cervical nodes Age 5-15 years Presentation in winter or early spring* History of exposure Rash consistent with scarlet fever
<b>Features Suggestive of Viral Aetiology</b>
Conjunctivitis Coryza Cough Diarrhoea Rash consistent with viral exanthema or mucosal enanthem

**Source:** Modified from Table 3, p 117, from IDSA guidelines.<sup>10</sup> ©2002 by the Infectious Diseases Society of America. All rights reserved.

\* In the USA. In Auckland, there is no seasonal peak for GAS pharyngitis (Lennon, unpublished data, 2006), and no data for more southern New Zealand climates.

## Appendix G: Throat swab technique



### Technique:

Ask the culturee to open the mouth widely and say a long "ah". The tongue should be gently depressed with a sterile tongue blade. The swab is then gently passed over the tongue and into the posterior pharynx. The mucosa behind the uvula and between the tonsils should then be gently swabbed with a back-and-forth motion.<sup>153</sup>

The tongue should be depressed and the throat adequately exposed and illuminated. Routinely the swab should be rubbed over each tonsillar area and the posterior pharynx. Any area exhibiting exudate should also be touched. Care should be taken to avoid contaminating the swab by touching the tongue and lips.<sup>154</sup>

**Source:** Diagram and related text reprinted with permission from Johnson 2007.<sup>153</sup>  
<http://web.indstate.edu/thcme/micro/samp-lab.html>

## Appendix H: Once-Daily amoxicillin studies

Table 16. Once-Daily Amoxicillin Studies

NAME	STUDY TYPE	PATIENTS	INTERVENTION	END POINTS	SERO-TYPING
Shvartzman et al. 1993 <sup>84</sup>	RCT	5 family practices, 393 patients with sore throat, 157 patients aged over 3 yrs. Positive GAS throat swab (blood agar)	82 patients in <b>penicillin arm</b> : 250mg po 3-4 x day for 10 days  75 patients in <b>amoxicillin arm</b> : (3 transferred to penicillin arm). 50mg/kg po daily for children, adults 750mg for 10 days  Compliance assessed by telephone interview and follow-up visits (it is unclear how compliance was assessed)	<b>Eradication:</b> <b>Amoxicillin:</b> 0/75 had positive throat cultures on day 14  <b>Penicillin:</b> 5/82 had positive throat cultures on day 14  <b>Symptoms:</b> pre and post treatment to day 10 were recorded; there was no significant difference between the two groups in terms of clinical response (fever, headache, malaise, sore throat)	No M subtyping. No serology to identify streptococcal carriers
Feder Jr, et al. 1999 <sup>86</sup>	RCT	152 children aged 4-18 years presenting to private practice with GAS pharyngitis	73 children in <b>penicillin V arm</b> : 250mg po tds for 10 days  79 in <b>amoxicillin arm</b> : 750mg po daily for 10 days  Compliance assessed by having parents perform dipstick on patient's urine on day 7 and mailed in the strip	<b>Eradication</b> at day 14-21 by throat culture: <b>Amoxicillin:</b> 4/79 (5%) had treatment failure (same M type), 9 (11%) had new M type of GAS.  <b>Penicillin:</b> 8/73 (11%) had same M type GAS (treatment failure), 7 (10%) had new M type.  <b>Symptoms:</b> no significant difference between two groups in signs and symptoms (fever, tonsillar exudate, cervical lymphadenitis, throat pain) at 18-24 hour follow up after treatment began	M typing done. No serology to identify streptococcal carriers

Lennon D (submitted 2006) <sup>85</sup>	RCT	254 children aged 5-12 years, diagnosed at a school clinic as positive for GAS on throat culture	<p>176 children in <b>penicillin V arm</b>: 500mg po bd, or 250mg if weight ≤20 kg for 10 days</p> <p>178 children in <b>amoxycillin arm</b>: 1500mg po daily or 750mg po daily if weight ≤30kg for 10 days</p> <p>Compliance assessed by directly observed therapy on week days at school, and a diary to be filled in on the weekends</p>	<p><b>Symptoms &amp; eradication:</b>  <b>Eradication</b> at day 12-16 by throat culture:  <b>Penicillin</b>: 7/159 (4.4%) had same M type, 12 (7.6%) had clinical relapse and 3 (1.9%) had new M type GAS.  <b>Amoxycillin</b>: 8/158 (5.1%) had same M type, 12 (7.6%) had clinical relapse and 2 (1.3%) had new M type GAS.</p> <p><b>Symptoms</b> at visit 2 (after 3-6 days of treatment), sore throat, tonsillar exudate, and tender lymph nodes were assessed. There was no difference between the two groups</p>	M typing done. No serology to identify streptococcal carriers
Clegg HW 2006 <sup>88</sup>	RCT	Children 3-18 years, with signs and symptoms of GAS pharyngitis, and positive rapid test for GAS. In 2001-03, of 2,139 potential patients, 652 enrolled, 326 into each arm. Both groups comparable with respect to demographic and clinical characteristics, except that the under 40kg children in both groups were more likely to have a rash on initial presentation, 33/326 (10%) in total, (p=0.015 for od group, p=0.074 for bd group). Investigators blinded	<p>Randomised into once-daily or twice-daily amoxycillin, for 10 days.</p> <p><b>Once daily amoxycillin</b>: 750mg po od for &lt;40kg patients, 1000mg po od for patients &gt;40 kg</p> <p><b>Twice daily amoxycillin</b>: 375mg po bd for &lt;40kg patients, or 500mg po bd for &gt;40kg patients</p> <p>Failure rates determined by positive GAS rapid test at visit 2 (day 14-21 after treatment begun) and visit 3 (day 28-35). Compliance: medication inspected and daily medication log books (filled in by parents) inspected on visit 2</p>	<p><b>Bacteriological treatment failure:</b>  <b>Amoxycillin od</b>: 59/294 who came to visit 2 had same M type, (20.1%). Intention to treat analysis: 108/326 (33%)  <b>Amoxycillin bd</b>: 46/296 who returned for visit 2 had same M type, (15.5%). Intention to treat analysis: 109/326 (33%)  EFFECT SIZE: Difference: 4.53%, (90% CI, 0.6-9.7)</p> <p><b>Clinical recurrence:</b> Symptomatic patients with positive GAS rapid tests:  <b>Amoxycillin od</b>: 29/294 (10%)  <b>Amoxycillin bd</b>: 23/296 (8%)</p> <p><b>Side effects:</b> with any adverse event after day 3 (returning with log at visit 2):  <b>Amoxycillin od</b>: 45/271 (17%)  <b>Amoxycillin bd</b>: 39/270 (14%)  (broken down into categories, abdominal pain most common followed by diarrhoea, same % in both od and bd groups)</p> <p>Physician-diagnosed allergic reactions seen in 0.9% of patients (6/635), each had diffuse urticaria or erythema multiforme on days 2-10, mean 7 days. 5 patients were in bd group and 1 in od group</p>	M typing done. No serology to identify streptococcal carriers

## Appendix I: Statistics for Clinical Questions No. 9, 10 & 11

Del Mar et al Cochrane review: 27 studies which compared antibiotics against controls in pharyngitis, 18 double-blinded, 3-single blinded. Most of the studies were in adults. Further details on quality of studies can be found in the review.<sup>39</sup>

**Table 17. Statistics for Clinical Questions (No. 9, 10 & 11) Treatment and Symptoms of Pharyngitis, Treatment and Suppurative and Nonsuppurative Sequelae**

OUTCOME	INTERVENTION	NO. OF RCTS	NO. OF PTS IN TREATMENT ARM	NO. OF PTS IN CONTROL ARM	OUTCOME IN TREATMENT ARM	OUTCOME IN CONTROL ARM	OR	P VALUE	95% CI
Symptom of sore throat pain on day 3 in patients with pharyngitis and GAS positive throat swabs	<b>Treatment arm:</b> given antibiotics. <b>Control arm:</b> not given antibiotics. 9 RCTs gave placebos	11	1,073	766	471/1,073	544/766	0.28	p <0.00001	0.23-0.34
Symptom of sore throat pain at one week (day 6-8) in patients with pharyngitis and GAS positive throat swabs	<b>Treatment arm:</b> given antibiotics. <b>Control arm:</b> not given antibiotics, 5 RCTs gave placebos	6	650	467	22/650	57/467	0.23	p <0.00001	0.14-0.37
Symptom of sore throat pain at day 3, in patients with pharyngitis and GAS negative throat swabs	<b>Treatment arm:</b> given antibiotics. <b>Control arm:</b> not given antibiotics, all given placebos	6	458	278	262/458	202/278	0.48	p <0.0001	0.35-0.67
Symptom of sore throat pain at one week (6-8) in patients with pharyngitis and GAS negative throat swabs	<b>Treatment arm:</b> given antibiotics. <b>Control arm:</b> not given antibiotics, all given placebos	5	315	226	42/315	43/226	0.67	p=0.12	0.40-1.11

Treatment of pharyngitis with antibiotics and outcome of acute otitis media (by clinical diagnosis) within 14 days	<b>Treatment arm:</b> given antibiotics. <b>Control arm:</b> not given antibiotics, 9 trials used placebos	11	2,325	1,435	11/2,325	28/1,435	0.23	p < 0.0001	0.12-0.44
Treatment of pharyngitis with antibiotics and outcome of quinsy (by clinical diagnosis) within 2 months	<b>Treatment arm:</b> given antibiotics <b>Control arm:</b> not given antibiotics, 6 trials gave placebos	8	1,438	995	2/1,438	23/995	0.16	p < 0.0001	0.07-0.35
Treatment of pharyngitis with antibiotics and outcome of acute post streptococcal glomerulonephritis within 1 month	<b>Treatment arm:</b> given antibiotics. <b>Control arm:</b> not given antibiotics, 5 studies used placebos	10	2,927	2,220	0/2,927	2/2,220	0.07	p = 0.08	0.00-1.32
Treatment of pharyngitis with antibiotics and outcome of acute rheumatic fever within 2 months	<b>Treatment arm:</b> given antibiotics. <b>Control arm:</b> not given antibiotics, 8 trials used placebos, 6 trials had no placebos	14	4,332	3,843	22/4,332	84/3,843	0.27	p < 0.00001	0.18-0.41

Source: Data adapted from Del Mar Cochrane review.<sup>39</sup>

## Appendix J: Studies listing sore throat episodes and rheumatic fever

Table 18. Studies Listing Sore Throat Episodes and Rheumatic Fever

STUDY	PLACE	STUDY GROUP	NUMBER OF SORE THROATS	RESULTS	RR OF RHEUMATIC FEVER WITH THE FREQUENT SORE THROATS	P VALUE	CI
Adanja B et al. 1988 <sup>116</sup>	Yugoslavia	Case-control. 148 patients with first attack of rheumatic fever compared to 444 controls from the same neighbourhood	'Frequent' sore throat (not defined)	52.0% of rheumatic fever patients had a history of frequent sore throat, compared to 34.2% of controls	2.01	p= 0.00018	1.41-2.89 (% CI unstated)
Lennon D (un-published data)	South Auckland, New Zealand	RCT. 24,000 school-children, half in treatment schools (with GAS pharyngitis clinics), half controls (no school clinics), followed for 4 years	In 1998, 50 throat swabs in children with pharyngitis were positive for GAS per 100 children per school year (in 24 schools).  In children diagnosed with rheumatic fever, rate of sore throats was 1.13 per year.  In children without rheumatic fever, rate of sore throats was 1.43 per year	Incidence of ARF: 60 per 100,000 in control group (without school clinics)			
Vlajinac H et al. 1991 <sup>117</sup>	Yugoslavia	Case-control. 148 cases with a first attack of rheumatic fever satisfying Jones criteria, which were home at time of survey. Three healthy controls matched for each rheumatic fever patient	2 or more sore throats per year	Patients with 2 or more sore throats per year were 2.26 times more likely to get rheumatic fever than patients who had one or less	2.26	p= 0.000	95% CI, 1.49-3.39

## Appendix K: Studies involving fomites in the spread of GAS

Table 19. Studies Involving Fomites in the Spread of GAS

STUDY	PATIENTS	INTERVENTION	RESULT
Perry WD et al. 1957A <sup>137</sup>	37 airmen, 8 volunteers (laboratory staff and jail inmates), all involved in the intervention. Wyoming, USA	Experimental study. 2 volunteers (staff) repeatedly exposed to dust contaminated with GAS in confined space. 6 volunteers (staff and jail inmates) directly inoculated by sprinkling dust on posterior oropharynx or forcibly blowing the sample into the posterior nasopharynx. 37 airmen lived in GAS dust-contaminated barracks. Nasal and oropharyngeal cultures were taken regularly, for up to 10 days. M typing was done	No infections resulted
Perry WD et al. 1957B <sup>138</sup>	85 airmen (intervention group), 177 airmen as controls. Wyoming, USA	Experimental case-control study. <b>Intervention group:</b> 85 airmen given blankets 'naturally contaminated' with during the winter of 1952. <b>Control group:</b> 177 airmen. Oropharyngeal and nasal cultures were taken, and a record of respiratory symptoms was kept. They were observed for 17-23 days. M typing was done	<b>Intervention group:</b> 6 GAS oropharyngeal infections (in 8,688 days exposed). 4 of those were of a different serotype than the GAS on the blankets, 2 were the same. <b>Control group:</b> 16 GAS oropharyngeal infections (in 16,021 days exposed). 14 of those were a different serotype than the GAS on the blankets, 2 were the same
Falck G et al. 1998 <sup>139</sup>	114 patients with GAS pharyngitis and 289 family members	Experimental case-control. 54 patients and their families were instructed to change their toothbrush, bed linen and wash children's toys. At 6-10 days, household members had nose throat swabs taken and samples were taken from pillowcases, floors, toothbrushes, children's dummies and toys. T typing was done. Followed for 28-35 days	Recurrence with the same T type was designated treatment failure, and assessed after 35 days. <b>Intervention group:</b> 17/46=37% had treatment failure. <b>Control group:</b> 10/39=26% had treatment failure

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## [10. Key Definitions]

**Case control study:** A study which involves identifying with the outcome of interest (cases) and control patients who do not have the same outcome and looking back to see if they had an exposure of interest.<sup>155</sup>

**Confidence interval (CI):** Quantifies uncertainty in measurement, usually uses 95% or 99%. A 95% CI is the range of values within which one can be 95% certain that the true value for the whole population lies.<sup>155</sup>

**Group A streptococcus (GAS):** Also known as *Streptococcus pyogenes*. Gram positive cocci producing beta haemolysis on blood agar.

**Meta-analysis:** A systematic review that uses quantitative methods to synthesize and summarise the results.<sup>155</sup>

**Odds ratio (OR):** The odds of having the target disorder in the experimental group, compared to the odds in favour of having the target disorder in the control group (in cohort studies or systematic reviews). Or the odds in favour of being exposed in participants with the target disorder divided by the odds in favour of being exposed in control participants (without the target disorder).<sup>155</sup>

**P value:** The probability a result could have occurred by chance. It is usually set at 0.05 by convention, which means there is a 5% probability that the effect occurred by chance. A p value of  $p > 0.05$  means the effect may have been due to chance, a p value of  $p < 0.05$  means the association between the exposure and the disease is considered statistically significant.<sup>156</sup>

**Pharyngitis:** Acute pharyngitis is an inflammatory syndrome of the pharynx caused by a variety of micro organisms. Most cases are of viral aetiology and occur as part of common colds and influenzal syndromes. The most important cause of bacterial pharyngitis is that due to group A beta haemolytic streptococci (*Streptococcus pyogenes*).<sup>21</sup>

**Post streptococcal glomerulonephritis:** An acute inflammatory disorder of the renal glomerulus characterised clinically by haematuria, oedema, hypertension and proteinuria, with evidence of an antecedent (usually group A) streptococcal infection of the pharynx or skin.

**Quinsy:** Peritonsillar abscess.

**Randomised controlled trial (RCT):** Clinical trial in which participants are randomly allocated into an experimental or into a control group and followed over time for the outcomes of interest.<sup>155</sup>

**Rheumatic fever:** Acute rheumatic fever (ARF) is a disease characterised by non-suppurative inflammatory lesions involving primarily the heart, joints, central nervous system, the skin and subcutaneous tissues. Permanent sequelae may result from cardiac involvement. Current opinion holds that all cases of ARF follow a group A streptococcal (GAS) upper respiratory tract infection, although the exact mechanism is unclear. ARF is diagnosed using the Jones Criteria<sup>157</sup> and adapted in New Zealand (and Australia) to permit echocardiography as a diagnostic criteria (see New Zealand Guidelines for Rheumatic Fever: 1. Diagnosis, Management and Secondary Prevention, available from: <http://www.heartfoundation.org.nz> ).

**Risk ratio (RR):** The ratio of risk in the treated group compared to the risk in the control group.<sup>155</sup>

**Sensitivity:** The proportion of people with the target disorder who have a positive test result.<sup>155</sup>

**Specificity:** The proportion of people without the target disorder who have a negative test result.<sup>155</sup>

**Systematic review:** A summary of medical literature that uses explicit methods to perform a comprehensive literature search and critical appraisal of individual studies and that uses appropriate statistical techniques to combine the valid studies.<sup>155</sup>

## [ 11. Glossary ]

<b>APSGN</b> .....	acute post streptococcal glomerulonephritis
<b>ARF</b> .....	acute rheumatic fever
<b>ASO</b> .....	antistreptolysin O
<b>BD</b> .....	twice a day
<b>BPG</b> .....	benzathine penicillin G
<b>EES</b> .....	erythromycin ethyl succinate
<b>EBV</b> .....	Epstein-Barr Virus
<b>ESBL</b> .....	extended spectrum beta lactamases
<b>GAS</b> .....	group A streptococcal
<b>IDSA</b> .....	Infectious Diseases Society of America
<b>IgE</b> .....	immunoglobulin E
<b>IMN</b> .....	infectious mononucleosis
<b>IM</b> .....	intramuscular
<b>LTT</b> .....	lymphocyte transformation testing
<b>OD</b> .....	once a day
<b>PO</b> .....	orally
<b>QID</b> .....	four times a day
<b>RCT</b> .....	randomised control trial
<b>RF</b> .....	rheumatic fever
<b>TDS</b> .....	three times a day
<b>WHO</b> .....	World Health Organisation

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