

Worldwide Comparison of Treatment Guidelines for Sore Throat

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Abstract

Sore throat (acute pharyngitis) is globally one of the most frequent reasons for seeking healthcare. Its etiology is mostly viral. In 15-30% of cases, group A streptococci (GAS) are detected, which may cause acute rheumatic fever. We have done a worldwide systematic review to compare diagnostic and therapeutic guidelines across countries and regions. Previous reviews of sore throat guidelines were limited to specific regions and/or language; this is the first global review. Searches were performed in MEDLINE, EMBASE and COCHRANE (key words: sore throat, pharyngitis, tonsillitis or pharyngotonsillitis, and management, guidance, guideline or recommendation) and on the web sites of major health authorities and associated institutions from Africa, Asia, Europe, Middle East, North America, Oceania and South America. Thirty-six guidelines were identified from 26 countries. Most common are recommendations relying on the symptom- and age-based Centor or McIsaac scores. However, antibiotic treatment may be based on other symptomatic criteria; in the most extreme approach just sore throat in children. The recommendation of GAS-specific diagnostic tests is mainly limited to countries where such tests are readily available, although some countries choose not to use them. Penicillins are consistently recommended as first-line antibiotics. By contrast, guidance for symptomatic treatment is variable and mostly sparse or missing. African countries without sore throat guidelines and Asian countries bypassing them are afflicted by rising antibiotic resistance. The availability of sore throat guidelines varies considerably by region and country. Moreover, important divergence is found among the guidelines regarding diagnostic and treatment criteria. This may be explained by the historical background or adoption of external guidelines, rather than the local incidences of GAS infections or acute rheumatic fever. Absence of recommendations on symptomatic treatment in many guidelines is concerning, and raises issues about antimicrobial stewardship, as this is the mainstay of sore throat management, rather than antibiotics.

REVIEW CRITERIA

Searches for guidelines were performed in the COCHRANE Library (Systematic Reviews), EMBASE (entire database) and PUBMED (all databases, including MEDLINE), using the search terms, criteria and cut-offs defined in the manuscript. Further guideline searches were performed on the internet, with the Google search engine using the specified English search terms, and their translations in Arabic, Chinese, French, German, Portuguese, Russian and Spanish, as well as on the websites of the major health authorities and associated institutions of all regions worldwide.

Only guidelines that provided recommendations for the diagnosis and the treatment of sore throat (acute pharyngitis) in general were considered and included. For Europe and the USA, where large numbers of

guidelines are available, the most recent and representative published guidelines supported by the major national or regional health care organizations were selected.

MESSAGE FOR THE CLINIC

Sore throat is one of the commonest reasons for using antibiotics worldwide, although most cases are viral.

There are major discrepancies across the guidelines, which are often not adapted to the actual, local incidence of group A streptococcus pharyngitis and its complications. Most guidelines do not provide any advice on symptomatic treatment.

These issues are of clinical concern as they may cause unnecessary suffering of patients and drive the ineffective use of antibiotics.

MAIN BODY OF THE MANUSCRIPT

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INTRODUCTION

Sore throat (acute pharyngitis) is prevalent worldwide and one of the most frequent complaints in children and adults requiring healthcare.¹⁻³ The etiology of sore throat is in 70-95% of cases viral.⁴ Rhinovirus, coronavirus and adenovirus account for at least 30% of all cases, while influenza or parainfluenza viruses are found in about 4%.⁵ Other viral pathogens in children and adults include Epstein-Barr virus, enteroviruses, respiratory syncytial virus, herpes viruses, cytomegalovirus and human immunodeficiency virus.^{1, 3}

In approximately 15-30% of all cases with sore throat (5-15% in adults, 20-30% in children), *Streptococcus pyogenes* (group A streptococcus, GAS) is detected.⁶⁻⁸ These numbers, however, also include healthy carriers and false positive test results (see below). GAS has been associated with acute rheumatic fever (ARF), which may lead to rheumatic heart disease (RHD).^{9, 10} While similar proportions of GAS infection are reported in different regions,⁶⁻⁸ the incidence of ARF varies greatly; in most industrialized nations it is 100-200 times lower than in developing countries.¹¹ Less frequent bacterial causes of sore throat include group C or G streptococci (about 5%), chlamydia, mycoplasma, *Arcanobacterium haemolyticum*, *Neisseria gonorrhoeae* and *Corynebacterium diphtheriae* (all <1%).^{5, 1, 3}

The clinical distinction between GAS pharyngitis (scarlet fever) and acute pharyngitis caused by viral or other pathogens is notoriously difficult.¹² Clinical scores have been developed to identify GAS infection, such as the Centor score for adults¹³ and the modified / McIsaac Centor score for children and adults¹⁴. In the original Centor score, one point is given for each history of fever (>38° C), tonsillar exudates, tender anterior adenopathy, and absence of cough.¹³ In the modified Centor score, one point is added to the original score for age 3-14 years, whereas one point is subtracted for age [?]45 years.¹⁴ Throat swab cultures are considered the gold standard for diagnosing GAS infection.^{7, 15} As the results of cultures are not available before 1-2 days, rapid antigen detection tests (RADT) have been developed to identify GAS.^{16, 17} However, false positive RADT results have been reported in about 5% of children¹⁸ and up to 15% of adults with acute pharyngitis.¹⁹ The addition of polymerase chain reaction (PCR) tests may increase sensitivity and specificity, with relatively rapid turnaround times.¹⁵ Yet neither RADT nor PCR or cultures can distinguish between GAS pharyngitis and GAS carriers with viral pharyngitis. The asymptomatic carriage rate of GAS is estimated around 6-11% of the patient population.²⁰

The majority of adult and pediatric cases of sore throat, in particular those with viral infections that are self-limiting, do not require antibiotic treatment, but are amenable to systemic and/or local symptomatic

treatments for pain, inflammation and fever.^{14, 21} In bacterial throat infections, antibiotics may shorten the duration of symptoms by about a day and reduce the risk of ARF by about two thirds in communities where this complication is common.²²

Based on this etiological background and the different diagnostic tools and treatments, various guidelines have been developed around the world, to diagnose and treat sore throat. We have performed a systematic search to compare such guidelines across countries and regions, identify significant differences and discuss reasons for the major discrepancies.

METHODS

Searches for guidelines were performed in COCHRANE Library (Systematic Reviews), EMBASE (entire database), PUBMED (all databases, including MEDLINE) and on the internet, using the the following search terms and specifications.

COCHRANE Library: sore throat or pharyngitis or tonsillitis or pharyngotonsillitis from January 2010 through 19 May 2020 (67 items).

EMBASE: (sore throat or pharyngitis or tonsillitis or pharyngotonsillitis) and (management or guidance or guideline(s) or recommendation(s) in Title from 2010 through 19 May 2020 (130 items).

PUBMED (MEDLINE): (sore throat or pharyngitis or tonsillitis or pharyngotonsillitis) and (management or guidance or guideline(s) or recommendation(s) in Title from 01 January 2010 through 19 May 2020 (108 items).

Internet searches were performed up to 19 May 2020 with the GOOGLE search engine, using the English search terms of the literature searches and translations of SORE THROAT, ACUTE PHARYNGITIS and GUIDELINE in Arabic, Chinese, French, German, Portuguese, Russian and Spanish, as well as searches of the websites of the major health authorities and associated institutions of all the regions shown in Table 1. For the retrieval and analysis of guidelines published in other languages than English, French, German, Portuguese or Spanish, translations by GOOGLE TRANSLATE and YANDEX TRANSLATE were used.

Only guidelines that provided recommendations for the diagnosis and the treatment of sore throat (acute pharyngitis) in general were considered. For the Western countries, in particular Europe and the United States of America (USA), where large numbers of guidelines are available, the most recent and representative published guidelines supported by the major national or regional health care organizations were selected.

RESULTS

Geographic origin and selection of the guidelines

A total of 36 guidelines from 26 countries were identified. Table 1 gives an overview of these guidelines by region and country; Figure 1 shows their origin on a world map. The highest number of guidelines were published in Europe; in addition to a European guideline,²³ a selection of the most recent and relevant published guidelines from Central (Germany),²⁴ Eastern (Russian Federation),²⁵ Northern (Netherlands²⁶ and Sweden²⁷), Southern (Italy²⁸ and Spain²⁹) and Western countries (France³⁰ and United Kingdom³¹) were included. Out of a large number, the most recent and relevant published guidelines were selected from North America, including Canada,³² Mexico^{33, 34} and the USA.³⁵⁻³⁷ and Asia, i.e. China^{38, 39} (with Hong Kong⁸), India,⁴⁰ Japan,⁴¹ Malaysia,⁴² and Thailand.⁴³ Regarding the Middle East, the principal recommendations were found from Iran,^{44, 45} Israel,⁴⁶ Saudi Arabia,⁴⁷ and Turkey.⁴⁸ For South America, recommendations from Argentina⁴⁹ and Brazil^{6, 50} were included, in addition to a Latin American guideline.⁵¹ Guidance from the African continent was scarce; only two relevant, recent guidelines, one from Egypt⁵² and one

from South Africa,⁵³ were included. Notably, there was no guideline for the management of sore throat in Nigeria,⁵⁴ Africa's most populated country. Two relevant guidelines were found for the Oceanian countries, one from Australia⁵⁵ and one from New Zealand.⁵⁶

Clinical diagnosis of acute pharyngitis

Although not all cases of sore throat are actually acute pharyngitis,^{57, 58} the terms are commonly used as synonyms. Acute pharyngitis is hallmarked by the acute onset of throat pain, typically with odynophagia, and signs of pharyngeal inflammation, e.g. erythema.^{59, 60} Beyond clinical history and clinical examination, environmental and epidemiologic factors should be considered in the clinical differential diagnosis of sore throat.⁶¹ However, none of the retrieved guidelines provides information to distinguish acute pharyngitis from other conditions. Instead, most guidelines discuss criteria of seriousness, bacterial origin or GAS infection, to support the decision about antibiotic treatment.

Recommendations for antibiotic treatment

All the retrieved guidances provide criteria for antibiotic treatment, except one review of Chinese medicinal herbs for sore throat.³⁸ With regards to antibiotic treatment, three groups of recommendations can be distinguished: 1) only clinical criteria, not based on the Centor score (or similar); 2) only clinical criteria, based on Centor score (or similar); 3) criteria including laboratory tests. These groups were strongly clustered according to regions. Thus, all African guidelines are based solely on clinical criteria, including neither the Centor score, nor laboratory tests.^{62, 52, 53} By contrast, all European and North American guidelines recommend RADT, pending on clinical signs and symptoms mostly including the Centor score, with the exception of the recommendations from the Netherlands,²⁶ the United Kingdom³¹ and Mexico.³⁴ While the latter two rely on the Centor score only, the Dutch guideline considers the distinction of viral and bacterial acute pharyngitis as usually irrelevant, given the low incidence of GAS in the Netherlands.²⁶ A mixed picture emerges from Asia (except China) and the Middle East, where the richest countries, such as Japan,⁴¹ Israel⁴⁶ and Saudi Arabia⁴⁷, but also Malaysia⁴² and a recent recommendation from Iran,⁴⁵ include RADT in their guidelines, while the other countries, and an earlier Iranian guideline,⁴⁴ recommend treatment according to clinical criteria, with^{48, 40} or without^{43, 44} using the Centor score. In China, the Special Administrative Region of Hong Kong recommends RADT,⁸ whereas Chinese National guidelines endorse antibiotic treatment based on clinical signs and symptoms only.³⁹ Regarding Oceania, antibiotic treatment for sore throat is based on the Centor score in Australia,⁵⁵ but on age, ethnic origin and socioeconomic circumstances in New Zealand.⁵⁶

With the exception of three guidances from China,³⁸ South Africa⁵³ and the USA,³⁵ all the sore throat guidelines give recommendations for antibiotic therapy. First-line treatment options are invariably penicillin-based medicines with treatment durations of 6 to 10 days for the oral treatments. Macrolides or cephalosporins are commonly recommended as second-line antibiotics; e.g. in case of penicillin allergy. While amoxicillin / clavulanate is infrequently recommended as second-line antibiotic in sore throat,^{33, 34} it is the most common treatment prescribed for sore throat in children in Nigeria, which has no national guideline.⁶³ In Italy, amoxicillin / clavulanate is the most commonly prescribed antibiotic in children,⁶⁴ although the guidelines recommend amoxicillin as first-line antibiotic for sore throat,²⁸ where its combination with clavulanic acid offers no therapeutic advantage.⁶⁴

Recommendations for other treatments

Whereas 33 out of the 36 guidelines provide recommendations regarding antibiotics, only 20 discuss other sore throat treatments. Of these 20 guidelines, 11 recommend paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) for the treatment of fever and pain, 4 recommend only NSAIDs,^{32, 46, 29, 25} 1 recommends only paracetamol,⁵² and 1 advises against the standard use of NSAIDs, because of their potential systemic side effects.²⁶ Furthermore, 4 guidelines recommend topical treatments such as lozenges, gargles or sprays for

analgesic treatment.^{42, 49, 34, 31} The review of Chinese medicinal herbs describes antiviral, anti-asthmatic, antitussive, and fever-relieving herbs as the basic elements of a traditional prescription for sore throat, detailing the therapeutic approaches for the different symptoms.³⁸

DISCUSSION

Several previous reviews have analyzed guidelines for the management of sore throat in children and adults.⁶⁵⁻⁶⁸ These reviews include guidelines published up to 2006,⁶⁵ 2010,⁶⁶ 2012,⁶⁸ and 2015 (date of latest reference),⁶⁷ respectively. The major limitations of these reviews are the restrictions to North American and European guidelines,⁶⁵⁻⁶⁷ to English language,^{67, 68} and to published literature.^{66, 67} To our knowledge, the present work is the first review of sore throat guidelines that has no geographic or linguistic restrictions, and includes guidelines not published in the literature. The fact that guidelines from either primary care or other fields of expertise were considered contributed to the diversity of the recommendations.

Major limitations of the present review are the restriction of literature searches to the last 10 years and the use of English as principal language for the internet searches, although limited internet searches were also performed in Arabic, Chinese, French, Russian, Spanish, German and Portuguese; the first six correspond to the official languages of the World Health Organization. Although guidelines in any language were considered, the search methods may have introduced a bias in favor of the Western industrialized countries, where guidelines tend to be published more frequently, both in the scientific literature and on the internet.

The review of the guidelines reveals important divergences regarding diagnostic and antibiotic treatment criteria in different countries. A large variety of clinical and/or laboratory criteria are proposed to identify and treat GAS infection. The reliance on merely clinical criteria in many of the recent guidelines is surprising, as few patients present the typical signs and symptoms of GAS pharyngitis described in the guidelines, and neither clinical history nor physical examination can differentiate between GAS infection and other causes of sore throat.⁶⁹ While lab tests may not be readily at hand in all regions (e.g. Africa), guidelines of many countries where the tests are available choose not to use them (e.g. several Middle East and Asian countries, Australia and New Zealand). Rather than by the availability of the lab tests, the large variability in the diagnostic criteria may be explained by the uncertainty of the scientific basis that underlies the different recommendations. In a well-documented ARF outbreak in the late 80ties in Utah (USA), half of the cases did not have any symptoms of sore throat, and swab tests were negative in a large proportion of the patients.^{70, 71} Furthermore, regarding the laboratory tests, neither RADT nor bacterial cultures can differentiate individuals with GAS pharyngitis from GAS carriers with intercurrent viral pharyngitis.³⁶

Comparing the guidelines from different regions, the most unexpected observation is that their differences in the antibiotic treatment criteria do generally not reflect the large variations in the risk of GAS infection and its complications across the world. While ARF and RHD have declined worldwide, they still remain major a cause of morbidity and mortality in some regions.^{9, 72} The African, South-East Asia and Western Pacific regions are most affected, accounting for 84% of all prevalent cases and 80% of all estimated deaths due to RHD globally in 2015.⁷³ Yet, with the exception of New Zealand,⁵⁶ the guidelines from Africa (Egypt), South-East Asia (India, Malaysia, Thailand) and Western Pacific (Australia, New Zealand) appear to mirror those of Europe and North America, where the incidence of ARF and the prevalence of RHD are about 100 times lower.^{11, 72} It might be argued that the systematic antibiotic treatment of sore throat has enabled reduction in the incidence of complications from GAS in the developed nations. If so, these guidelines would be particularly beneficial for the high risk countries. Yet, there is no evidence that the near disappearance of ARF and RHF in the industrialized countries, such as the United States of America, since the beginning of the last century was related to the wide use of antibiotics since the early 50ies.⁷¹

Based on the data from older trials, antibiotics can significantly reduce the incidence of ARF and other complications (including otitis media and tonsillar abscess), in patients with acute pharyngitis.²² However, in high-income countries, where not only the overall incidence of GAS infections is very low, but also the rates

of complications from the latter are reduced, the number needed to treat may exceed an acceptable limit.²² Any use of antibiotics, but especially widespread and excessive use, increases the risk of drug resistance.^{74, 75} Rising antimicrobial resistance threatens the national health care systems and economics, including those of the industrialized countries.^{75, 76} To prevent the unnecessary use of antibiotics, national and international treatment guidelines are of prime importance.⁷⁷ Whilst most prescribers in the USA and in Europe have easy access to antibiotic guidelines, many do not trust these guidelines.^{78, 79} Only a minority of physicians in the USA^{80, 81} and in many European countries^{82, 83} follow current guidelines to treat sore throat and prevent ARF. By contrast, effective implementation of appropriate guidelines was shown to improve general practitioners' adherence and reduce unnecessary and inappropriate use of antibiotics.^{84, 85}

In African countries where no national guidelines for the treatment of acute pharyngitis exist, such as Nigeria,⁵⁴ antibiotics are prescribed empirically for most patients presenting with sore throat.⁶³ Such practices may fuel deadly drug-resistant infections, such as bacterial pneumonia and diarrhea.⁸⁶ Today, a large proportion of salmonella infections have become resistant to the most widely available antibiotics in Nigeria⁸⁷ and Kenya.⁸⁸ In Asian countries where many people take antibiotics for infections without any prescription,^{89, 90} alarming levels of multidrug resistance have emerged.^{91, 92} Thus, rather than helping vulnerable populations plagued by life-threatening infections, such as HIV, tuberculosis and certain respiratory viruses, excessive and irrational uses of antibiotics seriously compound their health care issues.

Whereas well-targeted antibiotic treatments may prevent complications of GAS pharyngitis, their overall efficacy in reducing the duration of symptoms of sore throat is modest.^{93, 22} Analgesics and in particular NSAIDs are more effective than antibiotics to treat sore throat symptoms such as pain and fever.^{94, 93} Given the fact that symptomatic therapy represents the primary medical need for most patients,⁹⁵ it is striking that many guidelines only provide guidance for antibiotic treatment of sore throat. Furthermore, besides throat pain and fever, acute pharyngitis may present with a variety of symptoms, such as oral ulcers, difficulties in swallowing, hoarse voice, cough, rhinorrhoea, conjunctivitis, painful and swollen glands, skin rash, gastrointestinal symptoms and malaise^{69, 96} The only guidance, however, that discusses symptoms other than pain and fever is the review of Chinese traditional medicines.³⁸

In conclusion, the important differences observed in the worldwide treatment guidelines for sore throat do not seem to have a rational basis. While the guidelines may reflect the historical background (such as the high prevalence of ARF in the USA during the 19th century) or the adoption of recommendations from external guidelines (e.g. by African, South-East Asia and Western Pacific countries), they have often not been adapted to the actual, present-day local incidence of GAS pharyngitis or its complications. Implementation of appropriate treatment guidelines can increase physicians' adherence and correct use of the available treatments. Although symptomatic treatments, rather than antibiotics, are the mainstay of the therapeutic management for sore throat, recommendations on symptomatic treatment are missing in many guidelines. This may cause unnecessary suffering and drive the ineffective use of antibiotics. As sore throat is one of the commonest reasons for using antibiotics worldwide, these omissions impede current international strategies to reduce antibiotic use as part of antimicrobial stewardship.^{87, 88}

TABLES AND FIGURES

Table 1 – Overview of worldwide treatment guidelines

Region	Issuer of guideline or backing organizations	Criteria for antibiotic therapy	Antibiotic treatments	Symptomatic treatments
Country				

Region	Issuer of guideline or backing organizations	Criteria for antibiotic therapy	Antibiotic treatments	Symptomatic treatments
Africa Egypt	Africa World Health Organization ⁵²	Africa [?] 2 of following: * Erythema * White or yellow exudate * Enlarged tender lymph node(s)	Africa Benzathine penicillin G injection	Africa Paracetamol
South Africa	University of Cape Town ⁵³	No cough (1) + No rhinorrhea (1) + tonsillar swelling (2) + tonsillar exudate (1) [?] 3 with tonsillar swelling	not specified	not specified
Asia China	Asia Cochrane review ³⁸	Asia not specified	Asia not specified	Asia Antiviral, anti-asthmatic, antitussive, and fever-relieving herbs
China	Chinese Medical Association ³⁹	Pharyngeal hyperemia, tonsillar swelling with purulent exudate, swollen and tender lymph nodes	Penicillin or first generation cephalosporins	Paracetamol; aspirin; ibuprofen
China (Hong Kong)	Centre for Health Protection ⁸	Treatment if modified Centor score ^{13, 14} [?] 4	Oral penicillin V or amoxicillin or cephalexin	not specified
India	University of Chennai ⁴⁰	Treatment if modified Centor score ^{13, 14} [?] 4	Penicillin	not specified
Japan	Ministry of Health ⁴¹	RADT if modified Centor score ^{13, 14} [?] 2 or if high risk for GAS infection	Amoxicillin for 10 days	not specified
Malaysia	Ministry of Health ⁴²	RADT based on modified Centor score ^{13, 14} , culture if modified Centor score ^{13, 14} [?] 2; culture or treatment if modified Centor score [?] 4	Ampicillin for 10 days or benzathine penicillin G injection; if allergies: erythromycin or clindamycin	Paracetamol; NSAIDs; lozenges or gargles

Region	Issuer of guideline or backing organizations	Criteria for antibiotic therapy	Antibiotic treatments	Symptomatic treatments
Thailand	Mahidol University Bangkok ⁴³	Treatment if [?] 3 of the following: * High fever in combination with sore throat * Purulent tonsillar exudate or swollen red tonsils * Enlarged, tender neck lymph nodes * No symptoms of colds, such as cough or sneezing	Penicillin V or amoxicillin	not specified
Europe European Union	Europe European Society of Clinical Microbiology and Infectious Diseases ²³	Europe RADT if Centor score or modified Centor score ^{13, 14} [?] 3	Europe Penicillin V, 2-3x daily for 10 days	Europe Ibuprofen; paracetamol
France	Haute Autorité de Santé ³⁰	RADT if modified Centor score ^{13, 14} [?] 2	Amoxicillin 1 g 2x daily for 6 days; if allergies, cefuroxime or josamycin	not specified
Germany	Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin ²⁴	Treatment if Centor score or modified Centor score ^{13, 14} [?] 3; RADT or culture only for intermediate scores	Penicillin; if allergy erythromycin	Paracetamol; ibuprofen
Italy	Italian Panel on the Management of Pharyngitis in Children ²⁸	RADT if modified Centor score ^{13, 14} [?] 2	Amoxicillin 50 mg/kg/d 2-3x daily for 10 days	Paracetamol; ibuprofen
Netherlands	Dutch College of General Practitioners ²⁶	Not specified; antibiotics almost never indicated	Penicillin; if peritonsillar infiltrate suspected: amoxicillin / clavulanic acid	NSAIDs not recommended as standard treatment

Region	Issuer of guideline or backing organizations	Criteria for antibiotic therapy	Antibiotic treatments	Symptomatic treatments
Russian Federation	Scientific Center of Children's Health ²⁵	RADT if signs of bacterial pharyngitis; confirmation by culture unless treatment is urgent	Penicillin or amoxicillin	NSAIDs; aspirin in adults
Spain	Sociedad Española de Medicina de Familia y Comunitaria, Grupo de Estudio de la Infección en Atención Primaria de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica, Sociedad Española de Médicos Generales y de Familia, Sociedad Española de Farmacia Familiar y Comunitaria, Sociedad Española de Médicos de Atención Primaria, Sociedad Española de Otorrinolaringología y Patología Cérvico-Facial ²⁹	Community outbreak, immunosuppression, previous ARF, severe symptoms; RADT or treatment if not available if Centor score ¹³ [?] ³	Penicillin V; alternatively penicillin G, amoxicillin or cefadroxil; if allergy josamycin or diacetyl-midecamycin	Ibuprofen; diclofenac; flurbiprofen
Sweden	Medicinal Products Agency ²⁷	RADT if Centor score ¹³ [?] ³	Penicillin V; if allergy clindamycin	Paracetamol; NSAIDs; aspirin
United Kingdom	National Institute for Health and Clinical Excellence ³¹	Treatment if Centor score ¹³ [?] ³ (or use FeverPAIN score)	Penicillin V; if allergy clarithromycin or erythromycin	Paracetamol; ibuprofen; medicated lozenges
Middle East Iran	Middle East Islamic Azad University ⁴⁴	Middle East Exudate plus enlarged tender cervical nodes	Middle East Benzathine penicillin G injection or amoxicillin	Middle East not specified

Region	Issuer of guideline or backing organizations	Criteria for antibiotic therapy	Antibiotic treatments	Symptomatic treatments
Iran	Iran University of Medical Science ⁴⁵	RADT followed by culture	Penicillin	not specified
Israel	Ben-Gurion University ⁴⁶	RADT in children and adolescents culture, if RADT negative, for acute pharyngitis except if viral features (e.g. rhinorrhea, cough, oral ulcers, hoarseness), following IDSA ⁹⁷	Penicillin V, amoxicillin or benzathine penicillin G; if allergy cephalixin, cefadroxil, clindamycin, azithromycin or clarithromycin ⁹⁷	Acetaminophen or NSAID; aspirin to be avoided in children ⁹⁷
Saudi Arabia	Ministry of Health ⁴⁷	Treatment if modified Centor score ^{13, 14} [?] 4; culture or RADT if score 2-3	Penicillin V 500 mg 2x daily for 10 days; if allergy cephalixin 500 mg 2x daily for 10 days	not specified
Turkey	Osmangazi University ⁴⁸	Treatment if Centor score ¹³ [?] 3	Penicillin and erythromycin	not specified
North America Canada	North America College of Family Physicians ³²	North America Treatment if Centor score ¹³ [?] 3; RADT if Centor score = 2	North America Penicillin V	North America NSAIDs
Mexico	Instituto Mexicano del Seguro Social ³³	Treatment if Ebell score ⁹⁸ 4-5; RADT if Ebell score 1-3	Benzathine penicillin G injection; if allergy macrolides; second line: amoxicillin / clavulanic acid	not specified
Mexico	Centro Nacional de Excelencia Tecnológica en Salud ³⁴	Treatment if modified Centor score ^{13, 14} [?] 4	Penicillin, clindamycin, amoxicillin / clavulanic acid, benzathine penicillin G, first generation cephalosporin	Paracetamol or ibuprofen; lidocain spray or solution for adults

Region	Issuer of guideline or backing organizations	Criteria for antibiotic therapy	Antibiotic treatments	Symptomatic treatments
USA	American Academy of Family Physicians ³⁵	Treatment if modified Centor score ^{13, 14} [?] 4; RADT if score 1-3	not specified	not specified
USA	American Heart Association ³⁶	RADT or culture if symptoms suggest GAS; no test if symptoms suggest viral infection	Penicillin V, amoxicillin or benzathine penicillin G; if allergy cephalixin, cefadroxil, clindamycin, azithromycin or clarithromycin	not specified
USA	Infectious Diseases Society of America ^{97, 37}	RADT, in children and adolescents culture if RADT negative, for acute pharyngitis except if viral features are present (e.g. like rhinorrhea, cough, oral ulcers, and/or hoarseness)	Penicillin V, amoxicillin or benzathine penicillin G; if allergy cephalixin, cefadroxil, clindamycin, azithromycin or clarithromycin	Paracetamol or NSAIDs; aspirin to be avoided in children
Oceania Australia	Oceania New South Wales Health ⁵⁵	Oceania Treatment if modified Centor score ^{13, 14} [?] 3; plus cultures optionally if score 3-4	Oceania Penicillin V 15 mg/kg/dose 12 hourly for 10 days; if allergy roxithromycin 4mg/kg/dose 12 hourly for 10 day	Oceania Paracetamol 15 mg/kg/dose ([?] 1 g) 4x daily for 1-2 days or ibuprofen 5 mg/kg/dose ([?] 400 mg) 3x daily for 1-2 days
New Zealand	Heart Foundation ⁵⁶	Culture and start treatment if [?] 2 of following: Maori or Pacific, age 3-35 years, crowded or low socioeconomic circumstances	Penicillin V or amoxicillin or benzathine penicillin G; if allergy roxithromycin or erythromycin	Paracetamol or NSAIDs; aspirin to be avoided in children
South America	South America	South America	South America	South America

Region	Issuer of guideline or backing organizations	Criteria for antibiotic therapy	Antibiotic treatments	Symptomatic treatments
Latin America	Asociación Panamericana de Infectología ⁵¹	Treatment if Centor score ¹³ [?] 3; RADT if score = 2	Penicillin V for 10 days or benzathine penicillin G; if allergy erythromycin	Analgesics; NSAIDs; supportive treatment
Argentina	Sociedad Argentina de Infectología, Sociedad Argentina de Pediatría, Sociedad Argentina de Medicina, Sociedad Argentina de Bacteriología, Micología y Parasitología Clínica ⁴⁹	Treatment if modified Centor score ^{13, 14} [?] 3; RADT if score 2-3	Penicillin 2x daily for 10 days, amoxicillin 1x daily for 10 days, if oral treatment not possible benzathine penicillin G; if allergy clarithromycin or clindamycin	NSAIDs; paracetamol; topical anesthetics
Brazil	Agência Nacional de Vigilância Sanitária ⁶	Clinical signs of bacterial pharyngotonsillitis	Benzathine penicillin G or penicillin V; if allergy erythromycin, azithromycin or clindamycin	not specified
Brazil	Associação Brasileira de Otorrinolaringologia e Cirurgia Cérvico-Facial ⁵⁰	Pharyngotonsillitis with aggravating clinical or epidemiological factors	Amoxicillin, cefuroxime, amoxicillin-clavulanate, or ceftriaxone	not specified

Abbreviations: ARF = acute rheumatic fever; NSAID = non-steroidal anti-inflammatory drug; penicillin G = benzylpenicillin; penicillin V = penicillin VK = phenoxymethyl-penicillin; RADT = rapid antigen detection test; USA = United States of America.

Figure 1 – Origin of worldwide treatment guidelines



Figure legend

Numbers refer to the guidelines that are listed in the REFERENCES and shown in Table 1 (regional guidelines: Europe;²³ Latin America⁵¹). Source of blanc world map: Wikimedia Commons.⁹⁹

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