



SPANISH ASSOCIATION OF PAEDIATRICS

Diagnosis and treatment of acute tonsillopharyngitis. Consensus document update[☆]



Roi Piñeiro Pérez^{a,e,*}, Fernando Álvez González^a, Fernando Baquero-Artigao^a, Marta Cruz Cañete^a, Josep de la Flor i Bru^d, Ana Fernández Landaluze^b, César García Vera^c, Francisco Hijano Bandera^c, Carlos Pérez Cánovas^b, Juan Carlos Silva Rico^d, Collaborative Group on Acute Tonsillopharyngitis in Paediatrics¹, Santiago Alfayate Miguélez, Josefa Ares Álvarez, Alicia Berghezan Suárez, Ana María Borrull Senra, Gonzalo Cabrera Roca, Cristina Calvo Rey, Begoña Carazo Gallego, María José Cilleruelo Ortega, Antonio Conejo Fernández, Javier López Ávila, Pilar Lupiani Castellanos, eticia Martínez Campos, Jorge Sotoca Fernández

^a Sociedad Española de Infectología Pediátrica (SEIP)

^b Sociedad Española de Urgencias de Pediatría (SEUP)

^c Asociación Española de Pediatría de Atención Primaria (AEPap)

^d Sociedad Española de Pediatría Extrahospitalaria y Atención Primaria (SEPEAP)

^e Comité de Medicamentos de la Asociación Española de Pediatría (CM-AEP)

Received 27 April 2020; accepted 12 May 2020

Available online 27 August 2020

KEYWORDS

Appropriateness;
Antibiotics;
Diagnosis;
Consensus document;
Streptococcus;
Tonsillopharyngitis;

Abstract An update of the Spanish consensus document on the diagnosis and treatment of acute tonsillopharyngitis in 2011 is presented. Clinical scores should not be used to prescribe antibiotics, unless microbiological tests are not available or there is a child at risk of rheumatic fever. There is no score better than those set out in the previous consensus. Microbiological tests are recommended in proposed cases, regardless of the result of the scores. Penicillin is the treatment of choice, prescribed twice a day for 10 days. Amoxicillin is the first alternative, prescribed once or twice a day for the same time. First-generation cephalosporins are the treatment of choice in children with non-immediate reaction to penicillin or amoxicillin. Josamycin

[☆] Please cite this article as: Piñeiro Pérez R, Álvez González F, Baquero-Artigao F, Cruz Cañete M, de la Flor i Bru J, Fernández Landaluze A, et al. Actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda. An Pediatr (Barc). 2020. <https://doi.org/10.1016/j.anpedi.2020.05.004>

* Corresponding author.

E-mail address: roi.pineiro@hgvillalba.es (R. Piñeiro Pérez).

¹ Details the members of Collaborative Group on Acute Tonsillopharyngitis in Paediatrics in Appendix A.

Children;
Streptococcus
pyogenes;
 Treatment;
 Rational use

PALABRAS CLAVE

Adecuación;
 Antibióticos;
 Diagnóstico;
 Documento de
 consenso;
 Estreptococo;
 Faringoamigdalitis;
 Niños;
Streptococcus
pyogenes;
 Tratamiento;
 Uso racional

and midecamycin are the best options for children with immediate penicillin allergic reactions, when non-beta-lactam antibiotics should be used. In microbiological treatment failure, and in streptococcal carriers, the treatments proposed in the previous consensus are still applicable. © 2020 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda

Resumen Se presenta una actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda, publicado en 2011. Las escalas de predicción clínica no deben ser utilizadas para iniciar antibioterapia, salvo que las pruebas microbiológicas no estén disponibles o exista riesgo de fiebre reumática. No existe ninguna escala que sea mejor que las expuestas en el consenso previo. Se proponen casos en los que se recomienda realizar pruebas microbiológicas, con independencia de los resultados de las escalas. El tratamiento de elección de la faringoamigdalitis estreptocócica es penicilina en dos dosis diarias y durante diez días. Amoxicilina, en una o dos dosis diarias y durante el mismo tiempo, es la primera alternativa terapéutica. Las cefalosporinas de primera generación son el tratamiento de elección en niños con reacción retardada no grave a penicilina o amoxicilina. En reacciones alérgicas inmediatas deben utilizarse antibióticos no betalactámicos, siendo josamicina y diacetil-midecamicina las mejores opciones. En el fracaso terapéutico bacteriológico, y en el estado de portador, los tratamientos planteados en el consenso previo siguen siendo válidos.

© 2020 Asociación Española de Pediatría. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Between 2009 and 2011, the Working Group on Infections Managed at the Outpatient Level of the Sociedad Española de Infectología Pediátrica (Spanish Society of Paediatric Infectious Disease, SEIP) coordinated the development of a consensus document on the diagnosis and treatment of acute tonsillopharyngitis¹ with participation of the Sociedad Española de Urgencias de Pediatría (Spanish Society of Paediatric Emergency Medicine, SEUP), the Asociación Española de Pediatría de Atención Primaria (Spanish Society of Primary Care Paediatrics, AEPap) and the Sociedad Española de Pediatría Extrahospitalaria y Atención Primaria (Spanish Society of Outpatient and Primary Care Paediatrics, SEPEAP). This document had considerable impact and was one of the most-read articles in the history of *Anales de Pediatría* (more than 66 000 visits as of April 2020).

As 9 years have passed since its publication, the Working Group considered that an update was advisable, subjecting 10 questions and answers on the most relevant aspects that may have changed in the past few years to a consensus process. To do so, it formed a new group of experts with participation of the same associations involved the first consensus and the addition of the Committee on Medicines of the Asociación Española de Pediatría (Spanish Association of Pediatrics, AEP). After performing a literature search and reviewing the selected articles, we present recommendations based on our findings. We evaluated the quality of evidence and strength of the recommendations by means of the Infectious Diseases Society of America-United States

Table 1 Infectious Diseases Society of America-United States Public Health Service Grading System for Ranking Recommendations in Clinical Guidelines.

Strength of recommendation

- A. → Good evidence to support a recommendation for or against use
- B. → Moderate evidence to support a recommendation for or against use
- C. → Poor evidence to support a recommendation for or against use

Quality of evidence

- I. → Evidence from ≥ 1 properly randomised, 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 from uncontrolled experiments
- III. → Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Public Health Service Grading System for Ranking Recommendations in Clinical Guidelines (Table 1). In addition, each recommendation was subjected to a vote by every member of the group, as has been done in the development of other consensus documents in Spain.²

Table 2 Clinical scores used to predict involvement of group A beta-haemolytic streptococcus (GABHS).

Clinical criteria	Centor	Mclsaac	FeverPAIN
Fever > 38 °C	+1	+1	+1
Absence of cough	+1	+1	
Absence of cough or coryza			+1
Tonsillar exudate	+1		+1
Tonsillar swelling or exudate		+1	
Moderate to severe tonsillar swelling			+1
Tender lateral cervical nodes	+1	+1	
Age			
• 3- < 15 years		+1	
• 15- < 45 years		0	
• ≥ 45 years		-1	
Attended rapidly (≤ 3 days)			+1
Estimated probability of culture positive for GABHS	Score	Score	Score
	0: 2.5%	0: 1–2.5%	0–1: 13–18%
	1: 6–6.9%	1: 5–10%	2–3: 34–40%
	2: 14.1–16.6%	2: 11–17%	4–5: 62–65%
	3: 30.1–34.1%	3: 28–35%	
	4: 55.7 %	≥ 4: 51–53%	

Clinical questions

Question 1. Is there a new clinical prediction rule that is better than the previous ones?

Clinical prediction rules have been developed for diagnosis of acute tonsillopharyngitis (ATP) to calculate the probability of a streptococcal aetiology. The best known among them are the Centor, Mclsaac and FeverPAIN scales (Table 2).^{3–6}

The 2018 NICE guideline considered the FeverPAIN and Centor scoring systems comparable for the purpose of assessing patients with sore throat.⁷ In the best-case scenario, 65% of patients that get the maximum score have streptococcal ATP, so these scores should only be used to determine eligibility for microbiological testing.

A Centor score of 3 or greater is associated with a probability of streptococcal aetiology of 30% to 56%. The Centor criteria modified by Mclsaac, recommended in the previous consensus,¹ offers a similar sensitivity. It includes consideration of tonsillar exudate and one item concerning the age of the patient, which is less relevant in the paediatric population, as use of clinical prediction rules is not recommended in children aged less than 3 years.

The estimated probability of culture positive to group A beta-haemolytic streptococcus (GABHS)⁸ is similar for all three scales, as can be seen in Table 2. The group of experts considered that no new clinical prediction rules better than those that were already available and reviewed in the previous consensus.¹ Further down in the document, we propose a pathway to identify patients in who microbiological testing is indicated.

Question 2. Do these clinical prediction rules suffice to support the decision to initiate empirical antibiotherapy without prior performance of microbiological tests?

Isolated signs and symptoms correspond to very low positive likelihood ratios (LR+) (values < 5 have a very low impact on the probability of disease). In decreasing order, the LR+ for specific manifestations is^{6,9,10}: scarlatiniform rash, 4.7; palatal petechiae, 1.8; tonsillar or pharyngeal exudate, 1.6; cervical lymphadenopathy, 1.6; tonsillar swelling/redness, 1.3. Furthermore, grouping them to form scales does not achieve a significant improvement⁶ (LR+ of 2.5 for 5 Mclsaac criteria and 1.7 for 3–4 Centor criteria).

Clinical prediction rules should be used to make the decision whether to initiate empirical antibiotherapy only if diagnostic tests are not available or in patients at risk of developing rheumatic fever. There is evidence that without microbiological testing, and based on clinical features alone, experienced professionals misdiagnose streptococcal ATP in as many as 20%–25% of patients.¹¹

Exceptionally,⁷ the NICE guideline continues to recommend immediate or back-up antibiotic prescription in patients with a FeverPAIN score of 4 or 5 or a Centor score of 3–4. However, the probability of a streptococcal aetiology in patients with ATP with the maximum score in either prediction rule is of less than 66%. In the best-case scenario, prescribing antibiotherapy based on these rules would lead to inappropriate treatment in 1 out of 3 children. Therefore, nearly all paediatric guidelines in developed countries recommend against using clinical scoring systems to decide on the use of antibiotherapy.

Table 3 Cases in which microbiological tests should be ordered in the opinion of the group of experts.

- Children aged more than 3 years with clinical manifestations consistent with ATP in absence of symptoms suggestive of viral infection: rhinitis, stridor, vesicles, palate sores, etc. Quality of evidence: I. Strength of recommendation supporting use: A
- Children aged less than 3 years with clinical manifestations consistent with ATP and close contact with individuals with confirmed ATP caused by GABHS or with ATP with a presentation highly suggestive of a streptococcal aetiology, such as scarlatiniform rash or strep throat symptoms. Quality of evidence: II. Strength of recommendation supporting use: A
- Suspected ARF or APSGN. ATP in patients with ARF and household contacts. Household contacts with recent diagnosis of APSGN. Quality of evidence: II. Strength of recommendation supporting use: B
- ATP and high incidence of invasive streptococcal disease. Contact with patients with invasive streptococcal disease. Quality of evidence: II. Strength of recommendation supporting use: B
- Presence of household contacts with ATP in case of recurrent transmission in the family. Quality of evidence: II. Strength of recommendation supporting use: A

APSGN, acute poststreptococcal glomerulonephritis; ARF, acute rheumatic fever; ATP, acute tonsillopharyngitis; GABHS, group A beta-haemolytic streptococcus.

In conclusion, in children and adolescents, clinical prediction rules for identification of streptococcal ATP are not sensitive or specific enough to eliminate the need of microbiological testing and should not ever be the sole reason to initiate empirical antibiotherapy.

Question 3. Do these clinical prediction rules suffice to select patients eligible for microbiological testing?

The studies that support some of the most widely-used scales have methodological limitations that call their results into question.^{3,4,12} Other studies have found inconsistencies between higher scores in these scales and positive results in microbiological tests.^{13,14} For these reasons, based on the available evidence, it is not possible to draw definitive conclusions about the usefulness of clinical prediction rules for selection of patients for microbiological testing.

Table 3 shows the cases in which the group of experts recommends ordering microbiological tests, supported by evidence of varying quality.

Question 4. Are there new microbiological tests for diagnosis of streptococcal tonsillopharyngitis?

At present, different molecular tests are available: nucleic acid probe assays, polymerase chain reaction (PCR) and fluorescence in situ hybridization for detection of DNA sequences specific to GABHS.¹⁵ These methods allow iden-

tification even if only a small amount of the target sequence is available for amplification.¹⁶

In recent years, the United States Food and Drug Administration has approved low-complexity molecular tests that can be performed at the bedside by staff without specialised training, with turnaround times of less than 30 min and with a lower risk of contamination than previously existing tests that were more complicated.¹⁷

Given their high sensitivity and specificity compared to culture¹⁸ (sensitivity, 93% with a 95% confidence interval [CI] of 89%–96%; specificity, 99% with a 95% CI of 98%–100%), some hospitals have introduced them as the initial test for diagnosis of GABHS or as a confirmation test when the streptococcal antigen detection test is negative.¹⁷

As a counterbalance to all these advantages, we ought to mention two potential drawbacks. The first is the risk of overdiagnosis in patients that are only carriers, which ought to be minimised by careful selection of patients for testing, as is also the case for testing by means of a rapid antigen detection test (RADT) and throat swab culture.^{16,19} The second is the high cost of these tests compared to other microbiological tests, so prior to the introduction of these methods, pharmacoeconomic studies should be carried out in different clinical settings, as well as studies analysing of the clinical benefits of their implementation.^{16,17,19}

Question 5. Should penicillin and amoxicillin continue to be considered first-line treatments for streptococcal tonsillopharyngitis?

For more than 50 years, GABHS has been universally susceptible to beta-lactam agents.^{20,21}

Oral penicillin (phenoxymethylpenicillin potassium and potassium phenoxymethylpenicillin-benzathine) is the first-line antibiotic treatment for streptococcal ATP, and amoxicillin is the first alternative. These drugs are safe and effective and meet the current goals of treatment: to achieve rapid clinical improvement, shorten the contagious period and prevent already infrequent complications. Other advantages are their narrow spectrum, good bioavailability and low cost.^{7,20–23} Some authors of the present document consider that both penicillin and amoxicillin should be considered first-line therapies.

A recent Cochrane review²³ did not find evidence of differences in symptom resolution when comparing penicillin and amoxicillin with cephalosporins and macrolides. The superiority of cephalosporins (with a broader spectrum and higher cost) in achieving a cure and reducing the incidence of recurrence was not statistically significant and required a high number needed to treat to benefit (NNTB, the number of patients that need to be treated to observe any additional benefit). Azithromycin allows shorter courses of treatment, but there is variability in the rate of antimicrobial resistance and its use could induce the development of antimicrobial resistances in other colonising bacteria, such as *Streptococcus pneumoniae*.^{22,23}

In young children, some paediatricians prefer to use amoxicillin rather than phenoxymethylpenicillin because it does not require fasting and it is available as a suspension with a pleasant taste.^{21,23,24} Phenoxymethylpenicillin-benzathine is also available as a suspension in Spain, which

is more palatable and offers a better pharmacokinetic profile compared to the potassium salt form. Intramuscular injection of a single dose of penicillin is painful and thus reserved for cases in which oral administration is not possible or there is concern regarding adherence to treatment. ¹

Question 6. Does the recommendation to administer a schedule with 1 or 2 doses per day hold?

In 1953, the American Heart Association (AHA) recommended a 10-day course of penicillin given in 3–4 doses a day. Since then, most studies have aimed to improve adherence to treatment.

The 2-dose per day schedule for penicillin was first proposed in 1995, when the statement of the AHA was updated. A review and meta-analysis conducted in 2000 concluded that a 2-dose per day schedule was as effective as schedules with more frequent doses. However, the schedule consisting of a single daily dose of oral penicillin has exhibited a lower efficacy. ²⁵

The greater palatability of oral amoxicillin in suspension has led to a greater use of this drug compared to penicillin in clinical practice in some countries. Due to its longer half life, studies have been conducted to assess its effectiveness when administered a single daily dose. The first randomised trials in the 1990s found a similar effectiveness on comparing a single daily dose of amoxicillin with administration of 3–4 doses a day of penicillin. ^{26,27} Later studies have found that regimens with a single daily dose or with 2 doses a day of amoxicillin were equally efficacious. ^{28,29}

Question 7. Does the recommended duration of treatment of 10 days hold?

The recommended duration of oral penicillin and oral amoxicillin courses is 10 days. ^{7,15,21,24,30} This length is preferred compared to a shorter course of 7 or fewer days in pursuit of the traditional goals of achieving maximum eradication of GABHS and preventing rheumatic fever. ¹⁵ In developed countries, given the very low incidence of rheumatic fever, the objectives of treatment are different, as previously described. ^{1,21}

There is evidence that the risk of complications is associated with the persistence of the bacterium in the pharynx, but no treatment achieves eradication in 100% of cases, although lack of eradication does not mean the treatment has failed. The residual strains are strains lacking protein M, which are more likely to colonise the mucosa than damage adjacent tissues. ²¹ Such evidence prompted the proposal of shorter courses of treatment, but studies that assessed the efficacy of courses of different antibiotic agents lasting 7 or fewer days yielded heterogeneous results. ³⁰ Thus, we conclude that the evidence available at present is insufficient to recommend courses shorter than 10 days. ^{7,30} On the other hand, the evidence in support of the traditional 10-day course is also not rigorous, so some guidelines, taking into account the potential development of antimicrobial resistance, propose shorter courses of 5–7 days, ^{31–33} which implementation might be appropriate depending on

the circumstances, for instance, if eradication is not a priority.

The recommended length of treatment with first-generation cephalosporins is also 10 days, although 5-day courses have been proven to be equally efficacious in resolving symptoms and eradicating the pathogen. This could be an alternative in patients with poor adherence. ^{15,24} The recommended duration of treatment with clarithromycin, josamycin, diacetyl-midecamycin and clindamycin is also 10 days. When it comes to azithromycin, in the few cases in which it is indicated, the recommended course is 3 days at higher doses (20 mg/kg/day) to try to prevent the risk of selection of macrolide-resistant strains. ^{1,15,21,24}

Question 8. Do the recommendations regarding treatment in patients allergic to penicillin hold?

Oral first-generation cephalosporins are the drug of choice for children with non-severe delayed hypersensitivity reactions to penicillin or amoxicillin. ^{1,22,24,34} The risk of cross-reactivity between penicillin or amoxicillin and first-generation cephalosporins is low ($\leq 1\%$). ³⁴ Most guidelines currently recommend cefadroxil on account of its narrower spectrum, excellent tolerability and good bioavailability. ^{1,22,24}

In case of immediate Ig-E-mediated hypersensitivity reactions and severe delayed reactions (such as Stevens-Johnson syndrome or toxic epidermal necrolysis), patients should be given non-beta-lactam antibiotics. ^{1,22,24,34,35}

The current rate of macrolide resistance of GABHS in Spain is less than 10%, although there has been an increase in the frequency of strains with an MLS phenotype, characterised by cross-resistance to all macrolides and clindamycin. ³⁶ Isolates with the M phenotype (resistance to 14- and 15-membered macrolides only) amount to 50% of resistant isolates. ³⁶ Notwithstanding, the best option for allergic patients continues to be the use of 16-membered macrolides, such as josamycin y diacetyl-midecamycin and, as a possible alternative, clindamycin, although the latter is not commercially available in the form of suspension and is not as well tolerated. ³⁴ It is important to collect samples for culture in all allergic patients due to the possibility of treatment failure in case of macrolide-resistant strains with an MLS phenotype. In such cases, the treatment must always be guided by the results of antimicrobial susceptibility testing. ¹

Question 9. Do the indications and therapeutic options proposed in case of failure of first-line treatment or carrier status hold?

At present, there is still agreement that failure to eradicate the bacterial pathogen and carrier status entail a minimal risk of complication or contagion. ¹ Therefore, initiation of antibiotherapy is not recommended except in the specific cases defined in the previous consensus document. ^{1,24,37,38} In fact, in order to prevent inaccurate diagnosis and inappropriate treatment, we hold the recommendation against performance of microbiological tests in asymptomatic children and against testing to confirm eradication of GABHS in treated children as long as the clinical

Table 4 Indications for treatment of cases with failed antimicrobial treatment and GABHS carrier status.

- a) History of rheumatic fever in patient or household contacts
- b) Recurrent episodes of ATP due to GABHS in the household
- c) Invasive disease by GABHS in patient or household contacts
- d) Carriers that lived in lock-down facilities or with immunocompromised individuals
- e) When performance of tonsillectomy is being considered as a last resort

ATP, acute tonsillopharyngitis; GABHS, group A beta-haemolytic streptococcus.

outcome is favourable and the risk factors ^{1,24} detailed in [Table 4](#) do not apply.

In the rare cases that require treatment, the evidence is still insufficient to support a specific regimen. ²⁴ Nevertheless, there is agreement that the selected agent should have activity against beta-lactamase-producing bacteria, ²⁴ a strategy based on a number of studies that found that it achieved a higher rate of GABHS eradication. The alternatives proposed in the previous consensus ¹ continue to be valid, with the strongest recommendations currently corresponding to clindamycin (BII), phenoxymethylpenicillin with rifampicin (BII) and amoxicillin/clavulanic acid (CIII). ²⁴

Question 10. What is the recommended approach for diagnosis and management in children aged less than 3 years?

The prevalence tonsillopharyngitis caused by GABHS in children aged less than 3 years is 10%–14%. ^{22,35,39,40} Infection by GABHS in this age group is suspected taking into account that clinical manifestations are less specific compared to older children, with the usual presentation including swelling of the tonsils and pharynx, persistent mucopurulent nasal discharge, moderate fever, loss of appetite, enlargement of submaxillary lymph nodes and in some cases sores in the nostrils and nostrils and otitis media. These forms of disease are referred to as *strep throat*, *streptococcal fever* or *streptococcal pharyngitis*. ^{15,24} These patients usually have older siblings or contact with children with infection by GABHS through a childcare centre. ²²

In case of streptococcal infection, the yield of rapid tests and culture is lower, so if these tests are indicated, we recommend obtaining both nasal and throat samples. In case of a scarlatiniform rash or known presence of streptococcal pharyngitis in the environment of the child, a RADT in a tonsillar exudate sample alone is useful.

The incidence of complications of invasive disease is low, but higher in early childhood. ^{39,40} Rheumatic fever is rare in developed countries in children aged less than 3 years, before the immune system has fully matured.

In case antibiotherapy is initiated, we recommend the same selection of antibiotic agents, dosage and duration as in older children.

Conclusions and summary of recommendations

Recommendation 1. There is no new clinical prediction rule to determine eligibility for a rapid test for detection of GABHS that performs better than those previously known and discussed in the previous consensus document. Quality of evidence: III. Strength of recommendation supporting use: C. Vote: 23 agreed, 0 abstained, 0 disagreed. Consensus, 100%.

Recommendation 2. Clinical prediction rules should not be used to make the decision to initiate empirical antibiotic therapy unless microbiological testing is not available or there is risk of rheumatic fever. Quality of evidence: I. Strength of recommendation against use: A. Vote: 23 agreed, 0 abstained, 0 disagreed. Consensus, 100%.

Recommendation 3. The group of experts proposes situations in which microbiological tests should be performed regardless of clinical prediction scores. Varying quality of evidence. See [Table 3](#). Vote: 19 agreed, 3 abstained (JFB, GCR and MCO), 1 disagreed (AFL). Consensus, 83%.

Recommendation 4. Molecular tests can be used for diagnosis of streptococcal pharyngitis, but we do not recommend their routine use at this time. Quality of evidence: II. Strength of recommendation against use: A. Vote: 23 agreed, 0 abstained, 0 disagreed. Consensus, 100%.

Recommendation 5. We recommend a daily dose of penicillin for 10 days for first-line treatment of streptococcal pharyngitis. Amoxicillin, given in 1 or 2 doses a day for the same duration, is the first alternative. Quality of evidence: II Strength of recommendation supporting use: A. Vote: 22 agreed, 1 abstained (RPP), 0 disagreed. Consensus, 96%. Some authors consider that both penicillin and amoxicillin should be considered for first-line treatment. There are also authors that propose shorter courses in specific situations.

Recommendation 6. First-generation cephalosporins are the drugs of choice in children that exhibit non-severe, delayed hypersensitivity reactions to penicillin or amoxicillin. In case of immediate hypersensitivity reaction, a non-beta-lactam antibiotic agent should be used, and the best options are josamycin and diacetyl-midecamycin. Quality of evidence: II Strength of recommendation supporting use: B. Vote: 23 agreed, 0 abstained, 0 disagreed. Consensus, 100%.

Recommendation 7. In case of failure of first-line treatment or carrier status, the therapeutic alternatives proposed in the previous consensus documents still hold. The quality of evidence varies depending on the treatment: clindamycin (BII), phenoxymethylpenicillin with rifampicin (BII), amoxicillin/clavulanic acid (CIII). Vote: 23 agreed, 0 abstained, 0 disagreed. Consensus, 100%.

Recommendation 8. In children aged less than 3 years, given the low incidence of streptococcal infection, microbiological testing for GABHS is not recommended, save in select cases. In case streptococcal infection is suspected, we recommend collection of 2 samples for the RADT: a nasal swab and a throat swab. Quality of evidence: II. Strength of recommendation supporting use: B. Vote: 22 agreed, 1 abstained (MCO), 0 disagreed. Consensus, 96%.

Table 5 Treatment of acute streptococcal tonsillopharyngitis.**Drug of choice:***Phenoxyethylpenicillin potassium or benzathine for 10 days*

- Weight < 27 kg: 250 mg every 12 h
- Weight ≥ 27 kg: 500 mg every 12 h

First alternative:*Amoxicillin for 10 days*

- 40–50 mg/kg/day every 12 or 24 h (maximum 500 mg every 12 h or 1 g every 24 h)

In case with non-adherence to oral treatment*Penicillin G benzathine, single deep intramuscular injection*

- Weight < 27 kg: 600 000 U
- Weight ≥ 27 kg: 1 200 000 U

Penicillin allergy (delayed reaction)*Cefadroxil for 10 days*

- 30 mg/kg/day every 12 h (maximum 2 g every 24 h)

Penicillin allergy (immediate or antibody/immune complex-mediated reaction)**Best choices:**

- Josamycin: 30–50 mg/kg/day, every 12 h for 10 days (maximum 1 g every 24 h)
- Diacetyl-midecamycin: 35–50 mg/kg/day, every 12 h for 10 days (maximum 1.8 g every 24 h)

Other options:

- Azithromycin 20 mg/kg/day every 24 h for 3 days (maximum 500 mg every 24 h)
- Clindamycin: 8–30 mg/kg/day every 6–8 h for 10 days (maximum 1.8 g every 24 h)

Proposed shorter courses^{39,40}*To consider in specific situations when eradication is not a priority. These proposed courses are not approved of by all authors*

- Penicillin or amoxicillin at the previously noted doses for 5–7 days

Table 6 Treatment of group A beta-haemolytic streptococcus carrier status.**Recommended regimens:***Clindamycin for 10 days*

- 8–30 mg/kg/day every 6–8 h for 10 days (maximum 1.8 g every 24 h)

Amoxicillin-clavulanic acid (4:1 ratio) for 10 days

- 40 mg/kg/day every 8 h (maximum 1.5 g every 24 h)

Phenoxyethylpenicillin for 10 days. Same doses given in Table 5

- Plus rifampicin in the last 4 days at a dose of 20 mg/kg/day every 12 h (maximum 600 mg every 24 h)

Alternatives:*Cefadroxil for 10 days*

- 30 mg/kg/day every 12 h (maximum 2 g every 24 h)
- Plus rifampicin in the last 4 days at a dose of 20 mg/kg/day every 12 h (maximum 600 mg every 24 h)

Azithromycin for 3 days

- 20 mg/kg/day every 24 h (maximum 500 mg every 24 h)

Tables 5 and 6 detail the updated antibiotic doses and schedules recommended for treatment of patients with streptococcal ATP and carriers.

Conflicts of interest

The authors have no conflicts of interest to declare.

Appendix A. Collaborative Group on Acute Tonsillopharyngitis in Paediatrics

Santiago Alfayate Miguélez (SEIP and AEPap).
 Josefa Ares Álvarez (SEIP and AEPap).
 Alicia Berghezán Suárez (SEIP and AEPap).
 Ana María Borrull Senra (SEIP and SEUP).
 Gonzalo Cabrera Roca (SEPEAP).
 Cristina Calvo Rey (SEIP and CM-AEP).
 Begoña Carazo Gallego (SEIP).
 María José Cilleruelo Ortega (SEIP).
 Antonio Conejo Fernández (SEIP).
 Javier López Ávila (SEPEAP).
 Pilar Lupiani Castellanos (AEPap).
 Leticia Martínez Campos (SEIP).
 Jorge Sotoca Fernández (SEUP).

References

1. Piñeiro Pérez R, Hijano Bandera F, Álvez González F, Fernández Landaluce A, Silva Rico JC, Pérez Cánovas C, et al. Documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda. *An Pediatr (Barc)*. 2011;75:e1–342.e13.
2. Espín Jaime B, Díaz Martín JJ, Blesa Baviera LC, Claver Monzón A, Hernández Hernández A, García Burriel JI, et al. Alergia a las proteínas de leche de vaca no mediada por IgE: documento de consenso de la Sociedad Española de Gastroenterología, Hepatología y Nutrición Pediátrica (SEGHNP), la Asociación Española de Pediatría de Atención Primaria (AEPAP), la Sociedad Española de Pediatría Extrahospitalaria y Atención Primaria (SEPEAP) y la Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica (SEICAP). *An Pediatr (Barc)*. 2019;90:193.e1–11.
3. Centor RM, Witherspoon JM, Dalton HP, Brody CE, Link K. The diagnosis of strep throat in adults in the emergency room. *Med Decis Making*. 1981;1:239–46.
4. McIsaac WJ, Kellner JD, Aufricht P, Vanjaka A, Low DE. Empirical validation of guidelines for the management of pharyngitis in children and adults. *JAMA*. 2004; 291:1587–95. Erratum in. *JAMA*. 2005;294:2315–22.
5. Little P, Hobbs FD, Moore M, Mant D, Williamson I, McNulty C, et al. PRISM investigators. Primary care Streptococcal Management (PRISM) study: in vitro study, diagnostic cohorts and a pragmatic adaptive randomised controlled trial with nested qualitative study and cost-effectiveness study. *Health Technol Assess*. 2014;18:1–101.
6. Shaikh N, Swaminathan N, Hopper EG. Accuracy and precision of the signs and symptoms of streptococcal pharyngitis in children: a systematic review. *J Pediatr*. 2012;160:487–93.
7. NICE Guideline. Sore throat (acute): antimicrobial prescribing. January 2018. [Accessed 1 April 2020]. Available from: www.nice.org.uk/guidance/ng84.
8. Bercedo Sanz A, Cortés Rico O, García Vera C, Montón Álvarez JL. Faringoamigdalitis aguda en Pediatría. *Protocolos del GVR*

- (publicación P-GVR10) [Accessed 1 April 2020]. Available from: www.aepap.org/gvr/protocolos.htm.
9. Ochoa Sangrador C, Andrés de Llano JM. Los signos y síntomas clínicos no son suficientemente válidos para diagnosticar la faringitis estreptocócica. *Evid Pediatr*. 2012;8:33.
 10. Le Marechal F, Martinot A, Duhamel A, Ptuvost I, Dubos F. Streptococcal pharyngitis in children: a meta-analysis of clinical decision rules and their clinical variables. *BMJ Open*. 2013;3, <http://dx.doi.org/10.1136/bmjopen-2012-001482>.
 11. Gerber MA, Shulman ST. Rapid diagnosis of pharyngitis caused by group A Streptococci. *Clin Microbiol Rev*. 2004;17:571–80.
 12. Fine AM, Nizet V, Mandl KD. Large-Scale validation of the Centor and Mc Isaac scores to predict Group A streptococcal pharyngitis. *Arch Intern Med*. 2012;172:847–52.
 13. Roggen I, van Berlaer G, Gordts F, Pierard D, Hubloue I. Centor criteria in children in a paediatric emergency department: for what is it worth? *BMJ Open*. 2013;3:e002712, <http://dx.doi.org/10.1136/bmjopen-2013-002712>.
 14. Vasudevan J, Mannu A, Ganavi G. Mc Isaac modification of Centor score in diagnosis of streptococcal pharyngitis and antibiotic sensitivity pattern of beta-hemolytic streptococci in Chennai, India. *Indina Pediatr*. 2019;56:49–52.
 15. Committee on Infectious Diseases, American Academy of Pediatrics, Group A streptococcal infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. *Red Book: 2018 Report of the Committee on Infectious Diseases*. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018. p. 748–62.
 16. Tanz RR, Zheng XT, Carter DM, Steele MC, Shulman ST. Caution Needed: Molecular Diagnosis of Pediatric Group A Streptococcal Pharyngitis. *J Pediatric Infect Dis Soc*. 2018;7:e145–7.
 17. Pritt BS, Patel R, Kirn TJ, Thomson RB. Point-counterpoint: A nucleic acid amplification test for *Streptococcus pyogenes* should replace antigen detection and culture for detection of bacterial pharyngitis. *J Clin Microbiol*. 2016;54:2413–9.
 18. Lean WL, Arnup S, Danchin M, Steer AC. Rapid diagnostic tests for group A streptococcal pharyngitis: a meta-analysis. *Pediatrics*. 2014;134:771–81.
 19. Rao A, Berg B, Quezada T, Fader R, Walker K, Tang S, et al. Diagnosis and antibiotic treatment of group A streptococcal pharyngitis in children in a primary care setting: impact of point-of-care polymerase chain reaction. *BMC Pediatr*. 2019;19:24.
 20. Pelucchi C, Grigoryan L, Galeone C, Esposito S, Huovinen P, Little P, Verheij T. Guideline for the management of acute sore throat. ESCMID Sore Throat Guideline Group. *Clin Microbiol Infect*. 2012;18:1–27.
 21. Wessels MR. Pharyngitis and Scarlet Fever. In: Ferretti JJ, Stevens DL, Fischetti VA, editors. *Streptococcus pyogenes: Basic Biology to Clinical Manifestations*. Oklahoma City (OK): University of Oklahoma Health Sciences Center; 2016. p. 705–22.
 22. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012;55:1279–82.
 23. Van Driel ML, De Sutter AI, Habraken H, Thorning S, Christiaens T. Different antibiotic treatments for group A streptococcal pharyngitis. *Cochrane Database Syst Rev*. 2016;9:CD004406, <http://dx.doi.org/10.1002/14651858.CD004406.pub4>.
 24. Pichichero ME [Accessed 1 April 2020]. Available from: www.uptodate.com/contents/treatment-and-prevention-of-streptococcal-pharyngitis, 2019.
 25. Lan AJ, Colford JM, Colford JM Jr. The impact of dosing frequency on the efficacy of 10-day penicillin or amoxicillin therapy for streptococcal tonsillopharyngitis: A meta-analysis. *Pediatrics*. 2000;105:E19.
 26. Shvartzman P, Tabenkin H, Rosentzwaig A, Dolginov F. Treatment of streptococcal pharyngitis with amoxicillin once a day. *BMJ*. 1993;306:1170–2.
 27. Feder HM Jr, Gerber MA, Randolph MF, Stelmach PS, Kaplan EL. Once-daily therapy for streptococcal pharyngitis with amoxicillin. *Pediatrics*. 1999;103:47–51.
 28. Clegg HW, Ryan AG, Dallas SD, Kaplan EL, Johnson DR, Norton HJ, et al. Treatment of streptococcal pharyngitis with once-daily compared with twice-daily amoxicillin: a noninferiority trial. *Pediatr Infect Dis J*. 2006;25:761–7.
 29. Lennon DR, Farrell E, Martin DR, Stewart JM. Once-daily amoxicillin versus twice-daily penicillin V in group A beta-hemolytic streptococcal pharyngitis. *Arch Dis Child*. 2008;93:474–8.
 30. Chiappini E, Principi N, Mansi N, Serra A, De Masi S, Camaioni A, et al. Italian Panel on the Management of Pharyngitis in Children. Management of acute pharyngitis in children: summary of the Italian National Institute of Health guidelines. *Clin Ther*. 2012;34:1442–58.
 31. Fernández-Cuesta Valcarce MA, Kirchscläger Nieto S. Faringitis aguda (v.4.0/2019) En Guía-ABE. Infecciones en Pediatría. Guía rápida para la selección del tratamiento antimicrobiano empírico [en línea] [actualizado 18 Jun 2019; Accessed 1 April 2020]. Available from: <http://www.guia-abe.es>.
 32. NICE Guideline. Sore throat (acute): antimicrobial prescribing. January 2018. [Accessed 1 April 2020]. Available from: www.nice.org.uk/guidance/ng84.
 33. Radetsky M. Hostage to history. The duration of antimicrobial treatment for acute streptococcal pharyngitis. *Pediatr Infect Dis J*. 2017;36:507–12.
 34. Baquero-Artigao F, Michavila A, Suárez-Rodríguez A, Hernandez A, Martínez-Campos L, Calvo C, Grupo Colaborador de Infecciones de Manejo Ambulatorio. Documento de consenso de la Sociedad Española de Infectología Pediátrica, Sociedad Española de Inmunología Clínica y Alergia Pediátricas, Asociación Española de Pediatría de Atención Primaria y Sociedad Española de Pediatría Extrahospitalaria y Atención Primaria sobre antibioterapia en alergia a penicilina o amoxicilina. *An Pediatr (Barc)*. 2017;86:99.e1–9.
 35. Campagna JD, Bond MC, Schabelman E, Hayes BD. The use of cephalosporins in penicillin-allergic patients: a literature review. *J Emerg Med*. 2012;42:612–20.
 36. Calle-Miguel L, Pérez-Méndez C, Miguel Martínez MD, Lombrana-Álvarez E, García-García E, Solís-Sánchez G. Cambios evolutivos en las tasas y fenotipos de resistencia de *Streptococcus pyogenes* en una población pediátrica de Asturias, España (2005-2015). *Rev Esp Quimioter*. 2017;30:90–5.
 37. Oliver J, Malliya Wadu E, Piersie N, Moreland NJ, Williamson DA, Baker MG. Group A Streptococcus pharyngitis and pharyngeal carriage: A meta-analysis. *PLoS Negl Trop Dis*. 2018;12:e0006335.
 38. Shaikh N, Leonard E, Martin JM. Prevalence of Streptococcal Pharyngitis and Streptococcal Carriage in Children: a Meta-analysis. *Pediatrics*. 2010;126:e557–64.
 39. Woods WA, Carter CT, Schlager TA. Detection of group A streptococci in children under 3 years of age with pharyngitis. *Pediatr Emerg Car*. 1999;15:338–40.
 40. Espadas Maciá D, Flor Macián EM, Borrás R, Poujois Gisbert S, Muñoz Bonet JI. Infección por estreptococo pyogenes en la edad pediátrica: desde faringoamigdalitis aguda a infecciones invasivas. *An Pediatr (Barc)*. 2018;88:75–81.