

ISKRA guidelines on sore throat: diagnostic and therapeutic approach – Croatian national guidelines

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1.0 Introduction

Sore throat is a very common symptom for which patients often seek medical attention, however, only a small number of these complaints demand antimicrobial treatment. Sore throat, especially long-term, can be the consequence of repeated clearing of the throat or dry air and smoke inhalation. In case of sore throat with infectious etiology, viruses are, in the majority of cases, the most common pathogens.

The most significant cause of bacterial sore throat is group A beta-hemolytic Streptococcus (GABHS) causing 5-15% of acute sore throats.¹ Though rarely, some other bacteria may also cause sore throat, however, for everyday practice GABHS is the most significant causative pathogen, so that the term „bacterial“ or „streptococcal“ throat infection in this text refers to inflammations caused by this bacteria.

Although infections caused by group A streptococcus (GAS) are self-limiting, antibiotic treatment is recommended since it shortens the duration of illness in severe clinical presentations and decreases the possibility for the occurrence of rheumatic fever for 10-25%.^{2,3} (Ia, A)

Today, the incidence of rheumatic fever in developed countries is extremely rare, not because of wide use of antibiotics, but because of improved hygienic conditions and better population nutrition^{4,5,6,7} (III, C) as well as changes in pathogenic streptococcal characteristics.^{7,8,9} (III, C)

Therefore, the use of antibiotics in developed countries has a small effect on the incidence of rheumatic fever. Antibiotics also have a negligible effect on the prevention of post-streptococcal glomerulonephritis^{10,11,12,13,14,15,16} (IIa, B).

Since excessive use of antibiotics can have unwanted side effects for individual and the community, the aim of these guidelines is to help differentiate clinical presentation of severe streptococcal infection, where antibiotics are justified, from numerous other sore throat episodes where antibiotics will have no significant effect on the course of disease, but will contribute to development of bacterial resistance to antibiotics.

The aim of these guidelines is to define optimal therapy for streptococcal sore throat and reasonable indications for tonsillectomy.

Some national guidelines, when deciding on antibiotic administration in acute sore throat, mostly observe the severity of clinical presentation (Netherlands, Scotland)^{17,18} while for some countries the basic criteria is pharyngeal culture for GABHS (Finland)¹⁹ or the use of rapid test for GABHS (USA).²⁰ These guidelines will present expert opinion on important clinical, epidemiologic and diagnostic criteria, and define indications and recommendations for the treatment and prevention of streptococcal sore throat.

The recommendations are intended for physicians that care for patients with sore throat that do not require hospitalization. Indications for hospitalization are inability to take food and fluid through mouth, suspected localized purulent process (peritonsillar abscess, retropharyngeal abscess) and the need for parenteral antibiotic therapy. These recommendations refer to patients of all ages. Immunosuppressed patients are not included in this guideline.

Guidelines refer to acute sore throat lasting not longer than 14 days and do not include recommendations for sore throat caused by trauma, foreign body, allergy or tumor.

The use of these guidelines does not ensure treatment success in every patient. The approach to each patient should be individual. Physicians are expected to use these guidelines as a basis for their practice. In exceptional cases, arguments for deviations from these guidelines should be noted in the patients' files.

2.0 Development of the guideline

2.1 The need for national guidelines – ISKRA initiative

The Interdisciplinary Section for Antibiotic Resistance Control (ISKRA) of the Croatian Ministry of Health and Social Welfare has initiated the development of national guidelines on a series of topics where antimicrobial therapy plays an important role in the treatment of patients. The aim of this initiative is to provide optimal treatment options for patients with infectious diseases, promote rational use of antibiotics and develop strategies for infection prevention and control of the spread of resistant bacteria. These guidelines are in line with the Croatian strategy for antibiotic resistance control issued by the Croatian Ministry of Health and Social Welfare and the European Union Council Recommendation (2002/77/EC). When deciding on antibiotic therapy options, data from the Croatian Committee for Antibiotic Resistance Surveillance of the Croatian Academy of Medical Sciences were taken into consideration. The guidelines have been established based on the AGREE (Appraisal of Guidelines for Research and Evaluation) methodology.²¹

2.2 The guideline Working Group

The Ministry of Health and Social Welfare of the Republic of Croatia has appointed the following representatives of professional societies or institutions members of the Working Group (WG) for the development of **guidelines on sore throat: diagnostic and therapeutic approach-Croatian national guidelines:**

Members of the Sore Throat Working Group (in alphabetical order):

T. Baudoin, Chair, Croatian Society for Otolaryngology and Head and Neck Surgery

M. Abram, Croatian Committee for Antibiotic Resistance Surveillance of the Croatian Academy of Medical Sciences
 D. Bejuk, Croatian Society for Medical Microbiology
 Z. Grgurev, Croatian Society for Family Medicine
 S. Mimica Matanović, Croatian Society for Clinical Pharmacology
 D. Puževski, Croatian Pediatric Society
 A. Tambić Andrašević, Reference Center for Antibiotic Resistance Surveillance
 G. Tešović, Croatian Society for Infectious Diseases
 D. Vukelić, Croatian Society for Chemotherapy

2.3 Literature review, evidence statements and grades of recommendations

2.3.1 Literature review

The evidence supporting these guidelines are based on a systematic review of the literature. For the initial evidence search the WG has used the existing Scottish,¹⁸ American,^{10, 20} Finnish,¹⁹ and Dutch¹⁷ clinical guidelines for diagnosis and therapy of sore throat caused by GABHS.

Also the following databases were searched without publication date limit: Medline, Evidence Based Medicine Reviews, and Cochrane Database of Systematic Reviews. For literature search, the following key words were used: sore throat, group A streptococcus, diagnosis, treatment.

Local antibiotic resistance data were obtained from the Committee for Antibiotic Resistance Surveillance of the Croatian Academy of Medical Sciences.²²

2.3.2 Level of evidence

Levels of evidence, according to US Agency for Health Care Policy and Research²³

Level	Type of evidence
Ia	Evidence obtained from meta-analysis of randomized trials
Ib	Evidence obtained from at least one randomized trial
IIa	Evidence obtained from at least one well-designed controlled study without randomization
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports
IV	Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities

2.3.3 Grade of recommendations

Grades of guideline recommendations, modified according to the US Agency for Health Care Policy and Research²³

Grade	Nature of recommendations
A	Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial
B	Based on well-conducted clinical studies, but without randomized clinical studies
C	Made despite the absence of directly applicable clinical studies of good quality

2.4 Consultation and peer review

2.4.1 Professional societies and institutions supporting the guidelines

Professional society presidents, heads of reference centers and institutions listed under section 2.2 were first asked to delegate one of their members into the Working Group for guideline development. The Working Group produced a draft version of the guideline that represented a Working Group consensus document. The presidents and heads of the respected societies and institutions were asked to inform all their members that a draft version of the guideline is available for comments on the ISKRA web site: <http://iskra.bfm.hr/> for a period of two months. General practitioners were also informed about the guidelines through a network of health center representatives and were also asked to give comments. The Working Group has analyzed all comments received on the proposed guidelines before adopting the final version of the document.

2.4.2 Piloting of the guidelines

During the two-month piloting period the guidelines were used in everyday practice by five to ten specialists in pediatrics, infectious diseases, otolaryngology and 47 general practitioners. Physicians that used the guidelines in the pilot stage were asked to register their observations by filling in a predefined questionnaire with questions related to the feasibility of the guideline. Working group members considered all obtained suggestions and comments before adopting the final version of the guidelines.

2.4.3 International consultants

As a part of the MATRA project “Antibiotic resistance surveillance in human medicine”, the assistance of international consultants was available throughout the guideline development. The project was financially supported by the Dutch government and was carried out by the Reference Center for Antibiotic Resistance Surveillance of the Croatian Ministry for Health and Social Welfare. International consultants from the Netherlands Working Party on Antibiotic Policy (SWAB), Trnava University and the Dutch Family Medicine Society were involved in the development

of the guidelines. International consultants have supported this initiative through a series of workshops on guideline writing and personal contacts with members of the Working Group.

2.4.4 ISKRA Board

The final version of the guideline was reviewed and accepted by the ISKRA board.

Members of the ISKRA board are:

A. Tambić Andrašević, Chair of ISKRA, Reference Center for Antibiotic Resistance Surveillance

V. Stamenić, Ministry of Health and Social Welfare of the Republic of Croatia

B. Aleraj, Reference Center for Epidemiology

Lj. Betica Radić, Croatian Society for Infectious Diseases

I. Francetić, Reference Center for Clinical Pharmacology

S. Kalenić, Reference Center for Nosocomial Infections

I. Kosalec, Ministry of Science, Education and Sports of the Republic of Croatia

Z. Lončar, Medius - Association for Human Rights in Medicine and Health Care

V. Mađarić, Croatian Society for Chemotherapy

Lj. Maltar, Ministry of Agriculture, Fisheries and Rural Development of the Republic of Croatia

M. Jakševac Mikša, Croatian Pharmaceutical Society

M. Payerl Pal, Croatian Committee for Antibiotic Resistance Surveillance

T. Strbad, Croatian Institute for Health Insurance

J. Škrilin, Croatian Society for Medical Microbiology and Parasitology

V. Vlahović-Palčevski, Croatian Society for Clinical Pharmacology

M. Vrca Botica, Croatian Society for Family Medicine

2.5 Updating guidelines

Guidelines will be updated every five years or sooner if there is a significant reason for it (e.g. increased resistance rates, new antibiotics).

3.0 Diagnosis of sore throat

The symptoms of streptococcal and viral sore throat often overlap, although there are symptoms that are more characteristic for streptococcal inflammation and symptoms more specific for viral inflammation.

According to American standards, in case of clinical doubt, pharyngeal culture for GABHS or rapid streptococcal antigen test should be used.²⁰ In order to objectivise clinical picture of streptococcal sore throat, the decision on antibiotic use and bacteriological testing is based on four criteria according to Centor.²⁴ (IIa,B)

In West European countries, the decision on antibiotic use is based exclusively on the assessment of the severity of clinical picture and anamnestic data.^{17, 18} Experts from these countries believe that not even mild streptococcal infections should be treated with antibiotics, since they have a self-limiting course and there is a minimal

risk for post-streptococcal sequelae in developed countries today. In the Netherlands, it is estimated that the incidence of rheumatic fever and post-streptococcal glomerulonephritis is below 1:100 000 inhabitants per year.²⁵ Such approach supports the fact that neither culture nor rapid streptococcal antigen test have a 100% sensitivity nor specificity. Asymptomatic carrier state of GAS can be recorded in up to 40% of healthy individuals^{26,27,28,29} which decreases the specificity of GAS finding in cases of mild clinical picture of acute sore throat.

In Croatia the incidence of acute rheumatic fever today is also very low. In the last 10 years, eight children with acute rheumatic fever were treated at the Rheumatology Department of the Pediatric Clinic, Clinical Hospital Centre Šalata, where the majority of children with such diagnosis are hospitalized (oral communication).

The Sore Throat Working Group considers these guidelines a helping tool in clinicians` everyday practice for differentiation of viral from severe streptococcal infections, and in reaching decisions whether to administer antibiotic or not.

3.1 Clinical diagnosis

The most reliable clinical symptoms that can lead to the diagnosis of streptococcal pharyngitis in adults and in children are the symptoms described by Centor.²⁴ (IIa,B) These are the following:

- Temperature >38°C
- Tonsillar exudate
- Enlarged and painful anterior cervical lymph nodes
- Absence of cough and catarrhal symptoms

Every symptom is marked by one point and depending on the total score (0-4), clinical diagnosis of streptococcal sore throat can be assessed.

Regarding the probability for streptococcal pharyngitis diagnosis, patients are divided into 3 groups, based on clinical criteria:

- 1/ Patients that have high probability for streptococcal pharyngitis (4 points)
- 2/ Patients that have moderate probability for streptococcal pharyngitis (2-3 points)
- 3/ Patients that have low probability for streptococcal pharyngitis (0-1 point)

Sensitivity and specificity of clinical diagnosis of streptococcal pharyngitis is estimated to 55-75%, hence the reason to complement clinical diagnosis with bacteriologic confirmation.³⁰ (IIb, B)

In estimated clinical diagnosis based on 3 or 4 clinical criteria in adults, positive predictive value is 40 – 60%.¹⁰ This number shows that clinical diagnosis of sore throat is overestimated and that patients with sore throat of different etiology are also included among those patients with 3 or 4 points according to Centor – these are falsely positive estimations.¹⁰ (IV, C)

In patients with sore throat having 1 or 0 clinical criteria, negative predictive value is 80%. This number shows that in the absence of specific clinical symptoms, identification of non-streptococcal pharyngitis is more precise – small number of falsely negative estimations.¹⁰ (IV, C)

These findings suggest that clinical scoring system is helpful in identifying patients who do not need antibiotics but is not precise enough to identify patients with true streptococcal infection.

The sore throat working group recommends:

- For patients with Centor **score 0-1**: no antibiotic therapy, no bacteriology testing
- For patients with Centor **score 2-4**: bacteriology testing (rapid test or culture), antibiotics if bacteriology tests positive*

* in severe clinical pictures antibiotics may be prescribed even before the culture results are known. However, upon the arrival of a negative bacteriological finding antibiotics should be withdrawn!

Apart from these basic criteria, the decision on antibiotic use should take into consideration the following data:

- Age 3-14 years
(Streptococcal infections are more common in children than in adults. The risk for development of rheumatic fever after uncured streptococcal infection in adults is extremely low)
- Close exposition to GABHS
- Scarletiform rash

Antibiotics should be used in case of acute sore throat regardless of the Centor criteria in case of:

- Very severe general condition
- Suspected peritonsillar infiltrate or abscess
- Rheumatic fever in personal or family history

Immunodeficient patients are not included in these guidelines.

If sore throat, elevated temperature and weakness last longer than 7 days, infectious mononucleosis should be suspected. In infectious mononucleosis, apart from lymphadenopathy, spleen and liver are generally enlarged. Blood count with the presence of $\geq 20\%$ atypical lymphocytes indicates diagnosis. In unclear cases, serological testing for infectious mononucleosis can be performed, that would confirm the diagnosis.

3.2 Microbiology testing

Microbiologic analysis of a throat swab includes rapid streptococcal antigen test and/or cultivation on blood agar, which is considered to be the golden standard in confirmation of clinical diagnosis of acute pharyngitis caused by group A streptococcus. The sensitivity of properly collected and cultivated throat swab is 90-95%.³¹ (III, C)

The specificity of rapid streptococcal antigen test is high (>90%), so either positive result acquired by rapid streptococcal antigen test or cultivation is sufficient for making the diagnosis and starting antibiotic treatment.³¹ (III, C)

Negative rapid streptococcal antigen test in children and adolescents needs to be certified by cultivation, in order to avoid possible oversight due to falsely negative results, which can be expected in lower sensitivity antigen tests.^{32,33} (IIb, B)

In case of negative rapid streptococcal antigen test in adults, it is not necessary to confirm negative result by culture, due to different epidemiological characteristics in adults (low incidence of streptococcal infections and low risk for rheumatic fever).

In some patients, GAS remains present in the upper respiratory tract after completing a course of antimicrobial therapy.^{34,35} (IIb,B)

GAS carrier state should not be treated with antibiotics and therefore a follow-up culture of throat swabs should not be routinely done in asymptomatic patients who have completed a course of therapy for GAS.

Carrier state, however, should be eradicated in patients with a history of rheumatic fever, in rheumatic fever or streptococcal glomerulonephritis epidemics or situations when it is documented that streptococcal infection is perpetually transferred from one family member to the other.²⁰

4.0 Therapy of sore throat

4.1 Symptomatic therapy of sore throat

In the majority of cases, symptomatic treatment and resting is sufficient for the treatment of acute sore throat. It should be explained to the patient that the pathogen is most probably a virus and that in such infections, antibiotics are not useful. Only in cases with proved streptococcal etiology, apart from symptomatic, antibiotic therapy is also necessary.

The drug of choice in symptomatic therapy is analgoantipyretic paracetamol.¹⁸ Paracetamol is usually administered 4 times a day, and exceptionally it can be given 6 times. Total daily dose of paracetamol in children should not exceed 90 mg/kg due to a potential drug hepatotoxicity.

In symptomatic therapy, non-steroidal anti-inflammatory drugs (NSAID) can also be used. Acetylsalicylic acid can be used in adults but not in children younger than 12 years of age.

Throat gargles with warm salty water (1/4 kitchen spoon diluted in 2 dL water), sage tea or antiseptic fluid (hexetidine) can be recommended to adult patients. Pastilles with local anesthetics can also be recommended to adults, as well as older children.

4.2 Antimicrobial treatment of sore throat

4.2.1 Acute sore throat caused by GAS

Antibiotic therapy should be prescribed to symptomatic patients with bacteriological confirmation of GAS infection by culture or rapid antigen test (see appendix 1, chapter 7.0).

In patients who are severely ill, suspected of having a peritonsillar infiltrate or abscess or with a history of rheumatic fever, antibiotics should be prescribed regardless of bacteriological finding of GAS. Severe clinical picture includes intense sore throat, difficulties in swallowing, severe malaise and high fever.

When there is no possibility for microbiological testing, antibiotics should be prescribed in case of:

- reasonable doubt for GAS infection which includes the presence of three to four Centor criteria
- severe throat infection (intense sore throat, swallowing complaints, severe malaise, high fever)
- peritonsillar infiltrate or abscess
- increased risk for complications (rheumatic fever in medical history, sensitive patients living in closed communities during an established streptococcal epidemic).

Whenever possible, suspected streptococcal infection should be confirmed by microbiological testing in order to prevent unnecessary use of antibiotics and the development of bacterial resistance in normal microbiota of the patient and his surroundings.

Absolute efficacy of antibiotic treatment of tonsillopharyngitis caused by GAS is moderate. With antibiotic therapy, the symptoms of bacterial tonsillopharyngitis are shortened for approximately one day. In developed countries with higher living standard, the effect of antibiotics on the incidence of suppurative and non-suppurative complications of infections caused by GAS is minimal.^{36,37,38,39} (Ia, A)

Penicillin is the drug of choice for the treatment of streptococcal tonsillopharyngitis because of its narrow spectrum, proved efficacy, low incidence of adverse effects and affordable price. Per oral treatment with penicillin V should be conducted for 10 days.^{40,41} (Ia, A)

In adults, recommended dose is 1.500,000 i.u. three times daily⁴² (Ib, A), and in children 40.000-80.000 i.u./kg (25-50 mg/kg) daily, divided in three doses.^{43,44,45,46,47} (Ib, A)

In case of poor patient compliance, benzathine penicillin G (Extencillin®) can be administered in a single dose of 1.200,000 i.u. for adult patients.⁴⁸

In children up to 27 kg of body weight, a single dose of 600.000 i.u. should be applied, and for children above 27 kg, 1,200.000 i.u. in a single dose.^{48,49} (Table 1)

Table 1. Therapy of sore throat caused by group A streptococcus

children	duration
penicillin V 40.000-80.000 IU/kg (25-50 mg/kg) divided into 3 doses	10 days
or	
benzathine penicillin G (Extencillin®) 600 000 IU IM ≤ 27 kg*	single dose
benzathine penicillin G (Extencillin®) 1 200 000 IU IM > 27kg*	
adults	duration
penicillin V 1,500.000 IU every 8 hours	10 days
or	
benzathine penicillin G (Extencillin®) 1,200.000 IU *	single dose

*and other preparations of depot benzylpenicillin in appropriate doses

In case of hypersensitivity to penicillin, the drug of choice is azithromycin. Azithromycin dose for the treatment of streptococcal pharyngitis in children is higher than for other indications and amounts to a total of 60 mg/kg: can be given as 20 mg/kg daily for 3 days or 12 mg/kg for 5 days. ^{41,50} (Ib, A)

Because of better patient compliance and greater efficacy of higher individual doses of azithromycin, the working group has decided upon 20 mg/kg daily for 3 days. ⁵¹ (Ia, A) The recommended dose of azithromycin for adults is 500 mg daily for 3 days. ^{51,52} (Ia, A)

Although azithromycin is an attractive option because of single dosing, it should be avoided in the first line treatment because of fast development of group A streptococcus resistance to macrolides. ⁵³ (Ia, A)

In Croatia, the resistance of GAS to macrolides was 11% in 2007. ²²

The alternative option is to use clarithromycin. The recommended dose of clarithromycin for adults is 250 mg twice daily for 10 days, and for children 15 mg/kg/daily divided into 2 doses for 10 days. ^{54,55,56}

If hypersensitivity to penicillins is not anaphylactic, cephalosporins can also be used. 1st generation cephalosporins show higher cross reaction to penicillin than 2nd or 3rd generation cephalosporins. ⁵⁷ (Ia, A). Therefore, the working group has chosen 2nd or 3rd generation cephalosporins as the drug of choice in case of penicillin hypersensitivity. The recommended duration of treatment is 5-10 days, depending on the drug used. Some randomized controlled clinical trials have shown that 5 days cefuroxime axetil therapy is at least equally efficient, if not better, than the treatment with penicillin V lasting for 10 days. ^{52,58,59,60} (Ia, A)

Although the evidence on the efficacy of amoxicillin and cephalosporin in the treatment of streptococcal tonsillopharyngitis is indisputable, these drugs are not recommended as the first line treatment due to a wide spectrum of activity and possible development of resistance in the normal flora ^{40,48,53,61,62,63,64,65} (Ia, A) and in some cases higher price. (Table 2)

Table 2. Therapy of sore throat caused by group A streptococcus in case of hypersensitivity to penicillin

children	duration
azithromycin 20 mg/kg 1x per day	3 days
clarithromycin 15 mg/kg/daily divided into 2 doses	10 days
II or III generation cephalosporins	5-10 days depending on the preparation
adults	duration
azithromycin 500 mg 1x per day	3 days
clarithromycin 250 mg two times daily	10 days
II or III generation cephalosporins	5-10 days depending on the preparation

4.2.2 Recurrent episodes of sore throat caused by GAS

Taking throat swabs for GAS detection in asymptomatic patients after they have completed a course of antibiotic therapy should not be routinely performed. If a throat swab is taken for some reason anyway, finding GAS carriage in an asymptomatic patient should not be considered a relapse, but carrier state. Only patients that return with signs and symptoms of acute sore throat in the few weeks after completion of antibiotic therapy should be retested for GAS. If they are found positive for GAS again, there may be several explanations:

- poor compliance with antibiotic therapy instructions
- viral infection with concurrent GAS carriage
- reinfection with a new strain of GAS
- second episode caused by the original GAS strain

The second episode caused by the original GAS strain occurs very rarely, as well as reinfection with a new strain, and the most frequent explanation, especially in school-aged children and adolescents, is non-streptococcal infection in GAS carriers.^{20,35} (Ib,B)

However, these situations are difficult to distinguish in practice, and if clinical criteria correspond to streptococcal infection a patient should receive another course of antibiotic treatment.

Although there is no recorded resistance to penicillin in GAS yet, the therapy with oral penicillin may fail in some individuals due to unreliable absorption, or beta-lactam antibiotic may be inactivated at the site of infection by commensal mouth flora that produces beta-lactamases.^{66,67}

Because of this small, yet existing possibility for a relapse due to failed therapy, in recurrent streptococcal infections penicillin V or G are not recommended.

The working group has chosen a combination of amoxicillin and clavulanic acid, as the drug of choice for the treatment of recurrent GAS infections, 45 mg/kg divided into 2 doses in children, and 1g 2 times daily in adults.^{17,68} (Ib, A)

The alternative choice is clindamycin, 20 mg/kg divided into 3 doses in children, and 300 mg 3 times daily for adults. ^{68,69} (Ib, A) (Table 3)

For eradication of GAS in asymptomatic carriers (conducted only in well defined conditions, see chapter 3.2), the working group recommends clindamycin or azithromycin. ⁷⁰ (IIa, B) (Table 4)

Table 3. Therapy of recurrent episodes of streptococcal sore throat

children	duration
amoxicillin/clavulanic acid 45 mg/kg divided into 2 doses	10 days
or	
clindamycin 20 mg/kg divided into 3 doses	10 days
adults	duration
amoxicillin/clavulanic acid BID 1g 2 times daily	10 days
or	
clindamycin 300 mg 3 times daily	10 days

Table 4. Eradication of asymptomatic pharyngeal carriage of group A streptococcus

children and adults*	duration
clindamycin	10 days
or	
azithromycin	3 days

* doses are identical as for therapy, the choice of antibiotic depends on the isolated strain antibiogram

5.0 Tonsillectomy

Tonsillectomy is a surgical procedure that requires patient hospitalization. The procedure in children is conducted under general anesthesia, and in adults local anesthesia can also be used. The most common postoperative complication is haemorrhage (1-3%). Postoperative recovery lasts 14 days during which the patient is absent from school or work.

To date there are no appropriate studies devised according to evidence based medicine (EBM) standards that would analyze the efficacy and justifiability of tonsillectomy in the treatment of recurrent tonsillitis. There are several older randomized controlled studies that show that tonsillectomy is superior to conservative treatment of recurrent acute tonsillitis in children, in a sense that the number of tonsillitis episodes after surgery is significantly smaller than in the control, non-surgically treated group of examinees. Although, when comparing the number of sick leave days due to sore throat, including postoperative recovery, the difference between these two groups is not so significant. ^{71,72,73,74} (Ib, A) There are no randomized control studies with adult examinees.

In spite of lacking EMS studies, there are studies that suggest the benefit of tonsillectomy in children, not only in decreased number of sore throat episodes, but also improved child`s general condition. ^{75,76} (IIa, B).

Therefore, the working group recommends tonsillectomy for indications listed in Chapter 5.1.

5.1 Indications for tonsillectomy in children and adults

Absolute indications

- sore throat caused by tonsillitis with the following criteria fulfilled:
 - 5 or more sore throat episodes per year
 - diagnostically confirmed tonsillitis with at least one of the following criteria: positive GAS swab, purulent tonsillar exudate, body temperature $\geq 38^{\circ}\text{C}$, lymphadenitis in the neck with at least one node ≥ 2 cm
 - sore throat episodes affect the patient's general condition and his normal everyday life functioning
 - duration of symptoms for at least a year
- complications of tonsillitis (peritonsillar abscess, sepsis)
- permanent respiratory tract obstruction
- obstructive sleep apnea syndrome
- suspected tonsillar malignancy

Relative indications

- occlusion disturbances
- chronic tonsillitis – if the patient suffers from chronic sore throat and bad breath and if the symptoms persist during the period of one year^{18,19}

Before reaching a decision for tonsillectomy, a six month monitoring period is recommended.¹⁸ Once the indication is established, the procedure should be performed as soon as possible in order to achieve successful result.¹⁸

6.0 Key messages

- **Sore throat diagnosis does not automatically imply antibiotic use**

Sore throat most frequently occurs as a part of a viral infection, and symptomatic therapy is most commonly sufficient. As a rule, the only bacterial pathogen with antibiotic indication is group A streptococcus. Other bacterial pathogens cause sore throat extremely rarely with recognizable clinical picture (diphtheria, Lemierre's disease) or with benign course (*Arcanobacterium haemolyticum*, non-A streptococci).

- **In patients with severe general condition, antibiotic should be administered regardless of bacteriological finding**

The sensitivity of properly collected throat swab is 90 -95%³¹, depending how it was collected, transported and whether the patient received any antibiotic therapy prior to pharyngeal swab.

Pharyngeal swab is collected from the surface of both tonsils (or tonsillar core), and posterior pharyngeal wall, without touching the tongue and oropharyngeal area. In uncooperative children it is sometimes difficult to obtain a representative sample.

Pharyngeal swab should be delivered immediately to microbiology laboratory or it can be stored at room temperature maximally up to 24 hours in transport medium, until transportation is possible.

Negative swab result with the presence of strongly expressed symptoms of bacterial inflammation does not exclude the possibility of streptococcal infection.

- **Antibiotics should not be administered in mild clinical pictures of sore throat only because of fear that unrecognized streptococcal infection can lead to post-streptococcal sequellae or severe clinical presentations**

Prevention of rheumatic fever and post-streptococcal glomerulonephritis

The prevention of rheumatic fever and post-streptococcal glomerulonephritis have traditionally been considered the main reasons for antibiotic treatment of sore throat. Since the 1950s, developed countries have recorded a decrease in the incidence rates of rheumatic fever, not because of wide use of antibiotics but because of improved living standards.^{4,5,6,7} Post-streptococcal glomerulonephritis is, also, extremely rare and the use of antibiotics does not affect the incidence of this complication.^{10,11,12,13,14,15,16} In the USA, during the 1980s, repeated localized epidemics of rheumatic fever were recorded.^{77,78}

In Croatia, the incidence of acute rheumatic fever is very low, and these guidelines are valid only for current situation in Croatia. In case of rheumatic fever epidemics, searching for GAS carriers and rheumatogenic or nephritogenic strain eradication is justified.

Prevention of peritonsillar abscess

The incidence of purulent complications of streptococcal infections is low regardless of whether antibiotics are administered or not.^{10,42,79,80} Antibiotics can prevent the development of peritonsillar abscess, however one retrospective study conducted on more than 30 000 patients and 71 patient with peritonsillar abscess has showed that 44% patients had clinical presentation of peritonsillar abscess at the very first visit to general practitioner. Out of the remaining 56%, in whom peritonsillar abscess was preceded by tonsillopharyngitis, 67% received appropriate antibiotic therapy prior to peritonsillar abscess development.⁸¹

Prevention of invasive streptococcal infections

Although epidemics of invasive streptococcal infections caused by virulent types (especially T1M1, T3M3) were announced in the 1990s, necrotizing fasciitis and toxic shock syndrome still occur rarely and sporadically and are rarely related to previous throat inflammation,⁸² (IV) and types that cause invasive infections differ from the types that commonly occur during throat inflammations.^{83,84,85,86,87} (IIb, B) GAS bacteremia is also very rarely related to throat inflammation.⁸⁸

- **Asymptomatic GAS carriers, as a rule, should not be sought nor treated**

Some persons remain streptococcal carriers even after completed antistreptococcal therapy. Since carrier state is not treated with antibiotics, it is unnecessary to collect control throat swabs after completed therapy.

Throat swabs should not be collected from contacts of patients having a streptococcal throat infection. Carrier state in a patient's family is usual,²⁸ and should not be sought nor treated.

Rare exceptions are patients with a history of rheumatic fever, cases of repeated streptococcal infections within a family and rheumatic fever or streptococcal glomerulonephritis epidemics.

Streptococcal carriers are not under increased risk for the development of suppurative or non-suppurative complications of streptococcal infection.⁸⁹ (IV,C)

Streptococcal carriers do not transmit GAS to their close contacts, as patients in acute phase of streptococcal inflammation do.⁸⁹ (IV,C)

Streptococcal carrier state is much more difficult to eradicate with antibiotics than streptococcus during acute infection.^{67,88} (Ib, A)

The transmission of invasive GAS strain causing necrotizing fasciitis or toxic shock syndrome should be prevented, and carrier state should be treated in close contacts of patients suffering from invasive streptococcal infection. Patients with invasive streptococcal disease are not, however, the subject of these guidelines.

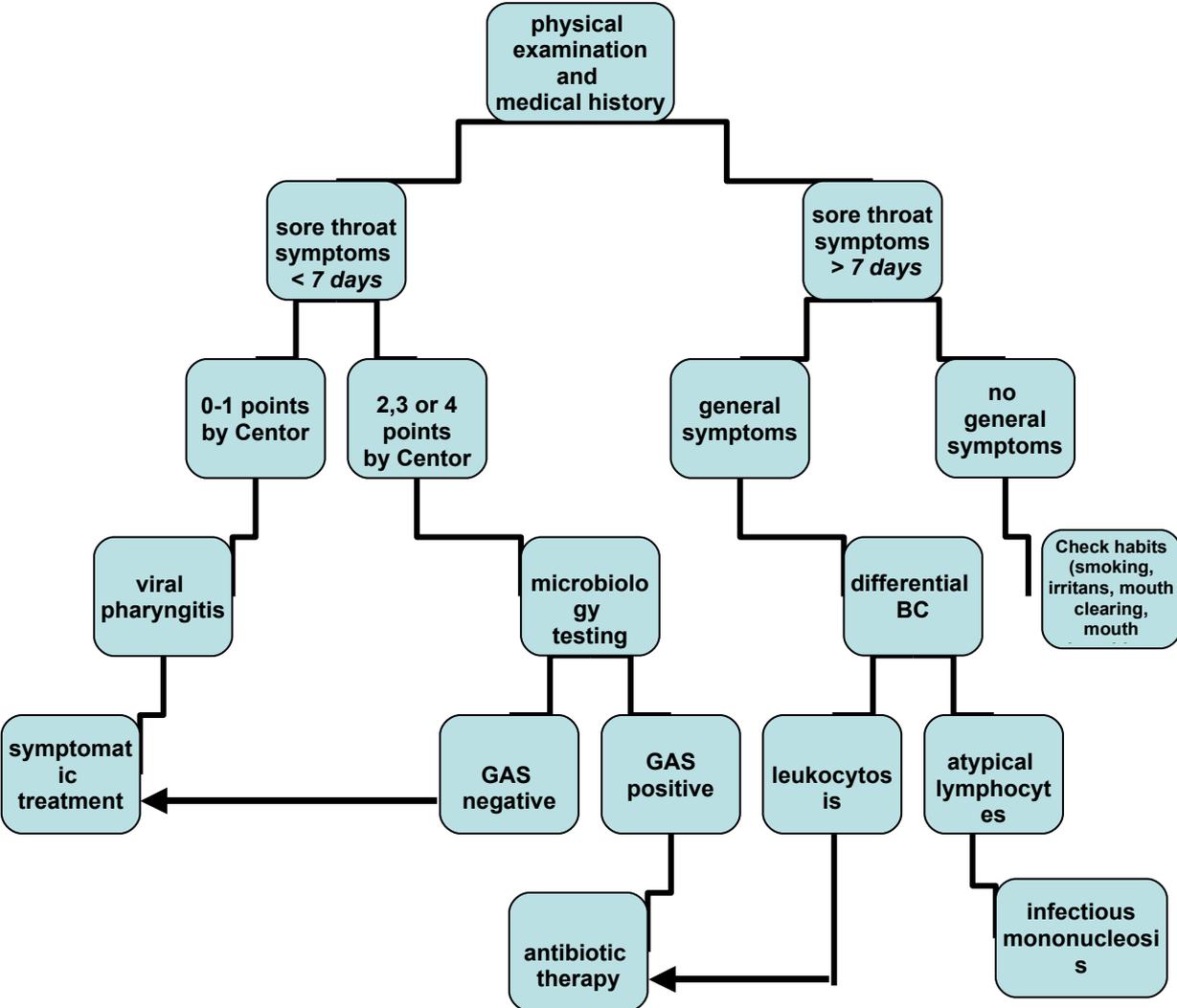
- **O-Antistreptolysin Titre (ASO) in sore throat diagnostics**

Routine testing of O-antistreptolysin titre (ASO titre) aimed at diagnosing streptococcal sore throat is not recommended (IIa, B). The results of repeated ASO titre tests are available to clinician too late to have an impact on the choice of therapy.¹⁷ (IV,C). Individual ASO titre is neither sensitive nor specific enough for diagnosing streptococcal sore throat.⁹⁰

- **Viral throat infections are common in children and are not an indication for tonsillectomy**

The assumption that recurrent streptococcal tonsillitis can be prevented with tonsillectomy is justified; however, tonsillectomy shall not prevent recurrent sore throats caused by other pathogens. Before making the decision for tonsillectomy, the diagnosis of recurrent streptococcal tonsillitis has to be confirmed by medical history and local status.

7.0. Appendix 1 - Diagnosis and therapy of sore throat



8.0 Appendix 2 - Patient information sheet

<p>What causes sore throat?</p> <ul style="list-style-type: none"> ▪ in 85-90% of cases sore throat is caused by viruses ▪ leading bacterial pathogen is group A beta-haemolytic Streptococcus 	<p>How are upper respiratory tract infections transmitted and who is most frequently affected?</p> <ul style="list-style-type: none"> ▪ the most common route of transmission is by droplet i.e. during conversation, coughing or sneezing. For this reason, when coughing or sneezing, the mouth should be protected with a tissue and hands should be washed. If tissue is not available, sneezing into the sleeve may help (in order to least as possible contaminate the hands and surrounding areas). Frequent hand disinfection– alcohol rubbing or washing is the best protection from spreading the pathogens of sore throat infection. ▪ people of all age groups can suffer from sore throat, however it is most frequent in small children and younger adults ▪ adults may suffer from sore throat 2 – 3 times per years, small children even up to 6-7 times per year
<p>When to visit doctor?</p> <ul style="list-style-type: none"> ▪ is sore throat lasts longer than 7 days ▪ in case of abnormal course of disease (worsening of pain, weakness and/or difficulty swallowing after 4-7 days) ▪ in case of enlarged and painful lymph nodes in the neck ▪ difficulties in swallowing or opening mouth ▪ in case of malaise and limitations in performing everyday activities ▪ in case of body rash ▪ in case of a history of rheumatic fever ▪ in case of weak immune system 	<p>Treatment?</p> <p>The majority of sore throat episodes do not require antibiotic treatment since they are caused by viruses and antibiotics are not effective against viruses. The majority of sore throats are self-limiting infections. Symptomatic treatment is most commonly sufficient.</p> <p>It is recommended to:</p> <ul style="list-style-type: none"> ▪ drink enough fluid (tea) ▪ gargle (not swallow) warm salty water, sage tea or antiseptic fluids (hexetidine) ▪ in case of elevated temperature and poor general condition it is best to stay at home ▪ if the temperature is above 38 °C, an antipyretic can be used: for children: paracetamol (Lupocet syrup, Plicet syrup etc.) in doses as indicated in the instructions for use

	<p>(overuse is toxic!)</p> <p>for adults: paracetamol 1 pill 4 – 6 x daily, acetylsalicylic acid (Andol, Aspirin etc.) 1-2 pills every 4-6 hours (in children contraindicated!)</p> <ul style="list-style-type: none"> ▪ sucking pastilles as a sore throat relief – effective as an antiseptic, there are several types with additional active ingredients - menthol, etheric oils (peppermint, eucalyptus). Also, there are pastilles with local anesthetic (for pain relief) such as Angal, Strepsils plus, Septolete plus etc. ▪ avoid cigarette smoke
<p>Why excessive use of antibiotics is harmful?</p>	<ul style="list-style-type: none"> ▪ Antibiotics themselves, even when used for justified reasons, have side effects or cause adverse events (rash, nausea, diarrhea) and if not needed, should be avoided ▪ Antibiotics, apart from disease pathogens, also have an effect on the so called „good bacteria“ normally found in our organism (skin, intestine...) making them resistant to antibiotics. Such resistant bacteria live in our organism and are transmitted to other people though everyday contact in day-to-day situations. These resistant bacteria become visible only when they cause an infection, either in persons using antibiotics by themselves, or in persons who did not consume antibiotics by themselves but to whom resistant bacteria was transmitted through everyday contact with humans and surrounding. ▪ Antibiotics are the only medication with an effect on the entire community, and not only on individuals, because resistant bacterial are easily spread within the community. ▪ If antibiotics are spent on infections not caused by bacteria (e.g. common viral upper respiratory tract infections), we won't have these valuable drugs available for patients with severe bacterial infections.

	Bacteria resistant to all known antibiotics are so far scarce; however, they have been described as disease pathogens.
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10.0 Conflict of interest

None.

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