In the name of God

CLINICAL PRACTICE GUIDELINES

MANAGEMENT OF SORE THROAT

Professor Alborzi Clinical Microbiology Research Center

Shiraz University of Medical Sciences

2014

Statement of Intent

These guidelines are meant to be a guide for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily ensure the best outcome in every case. Every health care provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

Review of the Guideline

This guideline was issued in October 2014 and will be reviewed in November 2016 or sooner if new evidence becomes available

Professor Alborzi Clinical Microbiology research center

Namazi Teaching Hospital

Shiraz University of Medical Sciences

Shiraz, Iran

Available on the following website: http:// www.alborzicmrc.sums.ac.ir

Preface

Sore throat is inevitably one of the most common symptoms experienced by people at one time or another. As there are many causes of sore throats, it is important that the medical practitioner be familiar with the possibilities so that the best evidence-based treatment can be offered to the patient. As infective etiologies of sore throat are arguably among the most common causes of sore throat and with widespread injudicious antimicrobial therapy for sore throat in the community, there is a danger of increasing antimicrobial resistance and untoward side effects of therapy. Furthermore, accurate clinical diagnosis of the most common infective pathogen for sore throat, i.e. Group A Streptococcus, is often difficult to establish. Diagnostic facilities for accurate detection of this particular organism are often lacking and results are often delayed in most ambulatory practices, compounding the difficulties in accurate diagnosis and appropriate management. It is with this multi-faceted background that this clinical practice guideline (CPG) on the management of sore throat is developed, with unique reference to Group A Streptococcal pharyngitis because it is the most common bacterial cause of sore throat where treatment is indicated. It is hoped that this CPG will be able to address some of these issues and meet the needs of the medical practitioner towards managing this common symptom. This guideline was originally developed by Dr Tan Kah Kee and his co-workers in Kuala Lumpur, Malaysia. Ministry of Health Malaysia, the Academy of Medicine Malaysia, the Malaysian Society of Infectious Diseases & Chemotherapy and Pharmacia Malaysia supported the development and the publishing of the original Guideline in 2003. The original guideline is available on the following websites: http:// www.moh.gov.my/medical/htm : http://www.acadmed.org.my. We mainly changed “algorithm for the management of sore throat” according to our practical situation in Iran. Also, we update the content according to “Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012

Update by the Infectious Diseases Society of America" and "University of Michigan Health System (UMHS) Pharyngitis Guideline, published May 2013". I acknowledge Dr Abdolvahab Alborzi, Dr Mohammad Rahim Kadivar and Dr Anahita Sanaei for their invaluable comments. My thanks also go to Dr Zahra Jafarpour for her help with the organization of the guideline and finally I appreciate Hassan Khajehei for linguistic editing. This guideline was revised and published in Professor Alborzi Clinical Microbiology Research Center.

Gholamreza Pouladfar M.D.

Pediatric Infectious Diseases Specialist

Professor Alborzi Clinical Microbiology research center

Shiraz University of Medical Sciences

GUIDELINE DEVELOPMENT AND OBJECTIVES

Guideline Development

Sore throat is a very common symptom in both children and adults, caused by many etiologies including infections due to bacterial and viral pathogens. It is also a common cause of presentation to medical practitioners. Sore throat is a frequent indication of antibiotic prescription in the community, resulting in significant healthcare costs and may potentially contribute to increasing antimicrobial resistance with widespread and inappropriate use of antibiotics. Sore throat in this guideline refers to both tonsillitis and pharyngitis or both, occurring in the context of infection.

Objectives

The main aim of the guideline is to present evidence based recommendations to assist medical practitioners in providing a rational approach in the management of sore throat and also would highlight the need for rational and judicious use of antibiotics in its management.

Clinical Question

The clinical question of this guideline is what the rational approach to the management of sore throat in the community is.

Target Population

These guidelines are to be applied to both paediatric and adult patients from the community with complaints of sore throat.

Target Group

These guidelines are developed for all health care professionals involved in the diagnosis and management of cases with sore throat.

LEVELS OF EVIDENCE SCALE

I Evidence obtained from at least one properly randomized controlled trial

II-1 Evidence obtained from well-designed controlled trials without randomization

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence

III Opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees

SOURCE: U.S. / CANADIAN PREVENTIVE SERVICES TASK FORCE

TABLE OF CONTENTS

1. SUMMARY

1.1. Summary and algorithm for management of sore throat (in Persian)

۱.۱. خلاصه

اهداف

- به حداقل رساندن خطر بروز تب رماتیسمی و عوارض چرکی

-استفاده از یافته های بالینی برای تعیین احتمال وجود "گلودرد استرپتوکوکی گروه آ" (به اختصار گلودرد استرپتوکوکی ذکر می شود.)

- کاهش استفاده بی ملاحظه و کم دقت از آنتی بیوتیکها و به حداقل رساندن عوارض دارویی و مقاومت دارویی باکتریها

نکات کلیدی

اصول عمومی

- پاتوژنهای ویروسی عامل گلودرد اکثر بیماران هستند که شامل ۹۰٪ موارد در بزرگسالان و ۷۰٪ در کودکان می شوند.

- کاهش خطر بروز تب روماتیسمی حاد (ARF) هدف اصلی تشخیص و درمان گلودرد استرپتوکوکی می باشد.

- درمان سریع گلودرد استرپتوکوکی می تواند دوره علامت دار بودن بیماری را از ۳-۷ روز به ۱-۳ روز کاهش دهد و دوره مسری بودن عفونت را کاهش می دهد.

تشخیص

- بیمارانی که در خطر بسیار کم "گلودرد استرپتوکوکی" هستند، با استفاده از "الگوریتم یافته های بالینی" قابل تشخیص هستند.

- در بیمار مبتلا به گلودرد وجود علایمی شامل عطسه، سرفه، آبریزش بینی، خشونت صدا، اسهال، التهاب ملتحمه چشم و زخمهای کوچک قسمت خلفی حفره دهانی در ناحیه گلو به شدت مطرح کننده تشخیص عفونت با پاتوژنهای ویروسی می باشند. در بیماران دارای این علایم احتمال "گلودرد استرپتوکوکی" غیر محتمل است بنابراین ضمن اینکه نیاز به اقدامات تشخیصی نیست، نبایستی آنتی بیوتیک برای درمان گلو درد استرپتوکوکی تجویز شود (گروه یک در الگوریتم تشخیصی).

- در بیمار مبتلا به گلودرد که علایمی دال بر عفونت ویروسی ندارد (علایم گروه یک در الگوریتم تشخیصی)، وجود مجموعه علایم و نشانه هایی شامل تب، لنفادنوپاتی حساس در ناحیه قدامی گردن و گلوی ملتهب با لوزه متورم دارای اگزودا، مطرح کننده تشخیص گلودرد استرپتوکوکی هستند. در بیماران با سن ۳ تا ۱۵ سال که احتمال "گلودرد استرپتوکوکی" زیادتر است، می توان بدون انجام اقدامات تشخیصی بیمار را با تشخیص احتمالی "گلودرد استرپتوکوکی" درمان کرد (گروه دو در الگوریتم تشخیصی). بیماران با سن بیش از ۱۵ سال که احتمال گلودرد استرپتوکوکی کمتر است، در صورت امکان "آزمایش سریع تعیین آنتی ژن" (RADT) یا کشت گلو انجام شود و اگر نتیجه آزمایش نشانگر گلودرد استرپتوکوکی بود، درمان انجام شود . در صورتی که موانعی برای انجام آزمایش وجود داشته باشد شامل در دسترس نبودن آزمایش، قیمت بالا و یا عدم مراجعه مجدد بیمار، در این بیماران نیز توصیه می شود با تشخیص احتمالی "گلودرد استرپتوکوکی" درمان انجام شود. در کودکان زیر سه سال با توجه به نادر بودن گلو درد استرپتوکوکی و همچنین بروز تب رومانیسمی، توصیه نمی شود آنتی بیوتیک برای ئرمان گلو درد استرپتکوکی تجویز شود.

- در بیماران مبتلا به گلودرد که **نه** علایمی دال بر عفونت ویروسی دارند (علایم گروه یک در الگوریتم تشخیصی) و **نه** مجموعه علایم و نشانه های دال بر "گلودرد استرپتوکوکی" را دارند (گروه دو در الگوریتم تشخیصی)، برای تشخیص گلودرد چرکی نیاز به تایید آزمایشگاهی شامل "آزمایش سریع تعیین آنتی ژن" (RADT) و کشت گلو بر طبق الگوریتم تشخیصی می باشد (گروه سوم در الگوریتم تشخیصی).

- در بیماران مبتلا به گلودرد که در گروه سوم الگوریتم تشخیصی هستند، در صورتی که موانعی برای انجام تایید آزمایشگاهی وجود داشته باشد تصمیم گیری بر اساس سن بیمار خواهد بود. در صورتی که سن بیمارسه سال یا بیشتر باشد، توصیه می گردد برای پیش گیری از خطر بروز تب روماتیسمی آنتی بیوتیک برای درمان "گلودرد استرپتوکوکی" تجویز شود. در صورتی که سن بیمارکمتر از سه سال است، بروز "گلو درد استرپتوکوکی" و تب رماتیسمی در این سنین نادر هستند بنابراین نیازی به تجویز آنتی بیوتیک برای درمان گلودرد استرپتوکوکی نیست و تنها اقدامات حمایتی و پیگیری درمانگاهی بیمار تا قطع تب مورد نیاز است چراکه است.

درمان

- "پنی سیلین وی" داروی انتخابی در بیمارانی است که می توانند قرص مصرف نمایند و اطمینان از کامل نمودن دوره درمان در آنها وجود دارد.

- در صورت استفاده ازداروهای سوسپانسیون، "پنی سیلین وی" یا آموکسی سیلین توصیه می شود. تجویز آموکسی سیلین به علت مزه بهتر در برخی کودکان بیشتر توصیه می شود.

- آموکسی سیلین به صورت تک دوز روزانه (به میزان یک گرم در روز برای بزرکسالان و ۵۰ میلی گرم به ازا هر کیلوگرم برای کودکان زیر ۳۰ کیلوگرم) به مدت ۱۰ روز به اندازه "پنی سیلین وی" یا آموکسی سیلین در چند دوز منقسم در روز به مدت ۱۰ روز موثر است.

- تجویز بنزاتین پنی سیلین تزریقی به صورت تک دوز در صورتی که اطمینان از کامل کردن دوره درمان خوراکی وجود ندارد، توصیه می شود اما تزریق آن دردناک است.

- در صورت سابقه آلرژی به پنی سیلین، تجویز سفالوسپورین نسل یک (سفالکسین) توصیه می شود در صورتی که آلرژی نوع پرحساسیتی نوع یک (آنافیلاکسی، کهیر و لارنگواسپاسم) نباشد.

- در صورت سابقه آلرژی به پنی سیلین، کلیندامایسین خوراکی داروی جایگزین است در صورتی که آلرژی "پرحساسیتی نوع یک" (آنافیلاکسی، کهیر و لارنگواسپاسم) باشد و یا بیمار نتواند سفالکسین مصرف نماید.

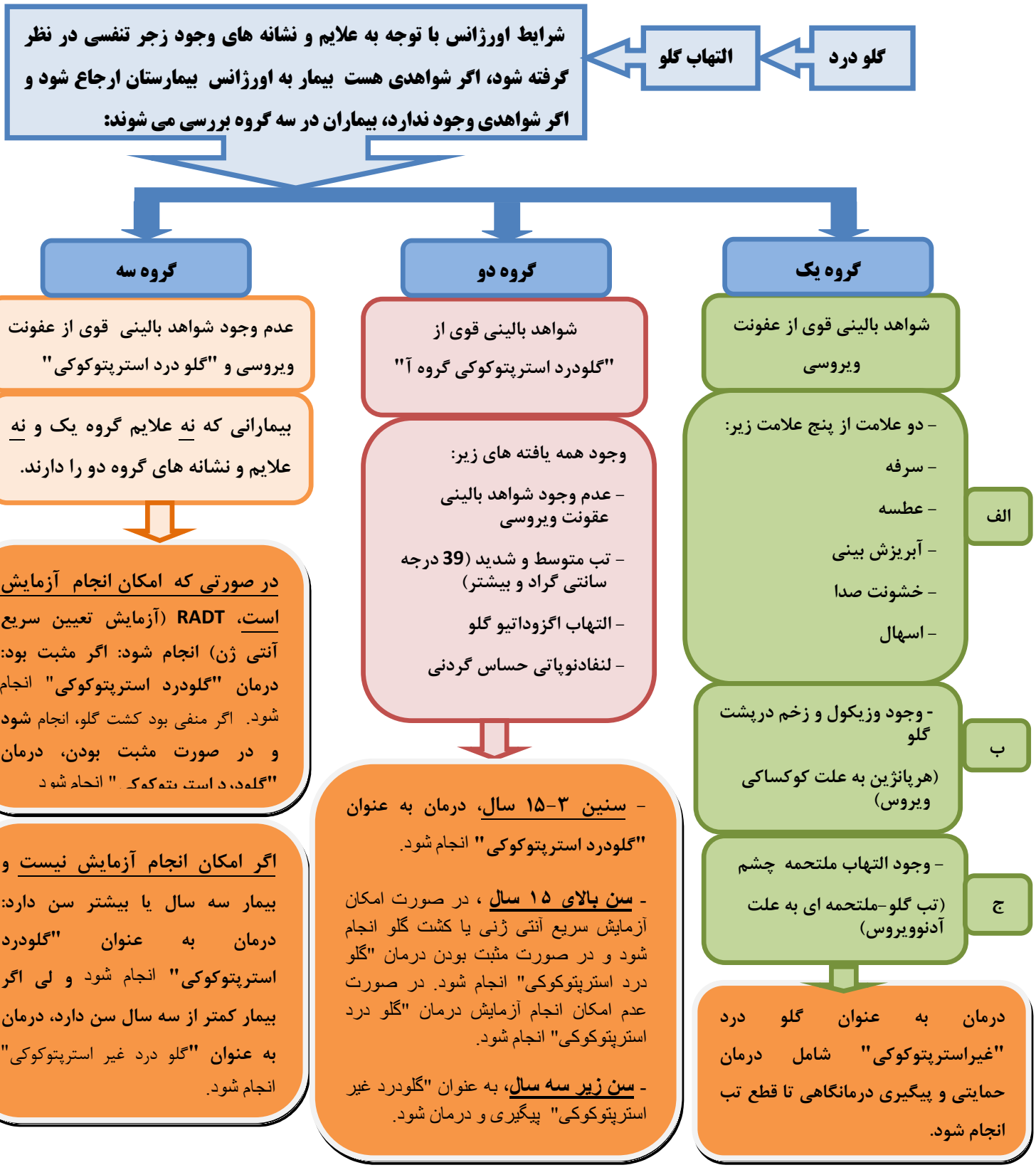
- یک داروی ماکرولید (اریترومایسین و کلاریترومایسن) و یا آزالید (آزیترومایسین) داروی جایگزین مورد قبول برای کلیندامایسین است (میزان مقاومت دارویی بین ۵-۴۰٪ گزارش شده است).

- درمان بایستی تا ۹ روز بعد از بروز علایم حاد بیماری شروع شود و به مدت ۱۰ روز ادامه یابد (غیر از آزیترومایسین که دوره ۵ روزه با دوز ۱۲ میلی گرم/کیلوگرم/روز مورد قبول است) تا "استرپتوکوک گروه آ" از گلو ریشه کن گردد و از تب روماتیسمی حاد پیشگیری شود.

- عدم پاسخ به درمان (بعد از ۴۸ ساعت) نشانگر بروز گلودرد به علل دیگر مانند گلودرد ویروسی، بروز عوارض چرکی مانند آبسه دورلوزه، درمان با آنتی بیوتیک نامناسب (مانند کوتریموکسازول)، درمان با دوز نامناسب دارو یا به مدت ناکافی، عدم پایبندی بیمار به مصرف دارو و یا وجود پاتوژنهای تولید کننده بتالاکتاماز در گلو به همراه "استرپتوکوک گروه آ" است. این موارد نیاز به بررسی مجدد دارند.

- کودکانی که مدت کوتاهی بعد از کامل نمودن رژیم خوراکی آنتی بیوتیک مبتلا به "عود گلو درد استرپتکوکی" می شوند، توصیه می شود یا با رژیم درمان خوراکی مشابه و یا با تزریق بنزاتین پنی سیلین عضلانی درمان شوند.

الگوریتم تشخیصی و درمانی گلو درد



جدول یک: رژیمهای آنتی بیوتیکی توصیه شده برای گلو درد استرپتکوکی "گروه آ"

آنتی بیوتیک	راه تجویز و دوزاژ	مدت درمان یا مقدار
افراد بدون سابقه حساسیت به پنی سیلین		
پنی سیلین "وی"	خوراکی، - کودکان (وزن کمتر از ۲۷ ک.گ.): ۲۵۰ م.گ. دو یا سه بار روزانه - نوجوانان و بزرگسالان (وزن ۲۷ ک.گ. و بیشتر): ۲۵۰ م.گ. چهار با در روز یا ۵۰۰ م.گ. دو بار در روز	۱۰ روز
آموکسی سیلین	خوراکی، ۵۰ م.گ./ ک.گ. یکبار در روز (حداکثر ۱۰۰۰ م.گ. در روز) جایگزین: ۲۵ م.گ./ ک.گ. (حداکثر ۵۰۰ م.گ./دوز) دو بار در روز	۱۰ روز
پنی سیلین بنزاتین "جی"	داخل عضلانی، وزن کمتر از ۲۷ ک.گ.: ۶۰۰۰۰۰ واحد وزن ۱۷ ک.گ.یا بیشتر: ۱۲۰۰۰۰۰ واحد	یک دوز
افراد با سابقه حساسیت به پنی سیلین		
سفالکسین *	خوراکی، ۲۰ م.گ./ ک.گ.در هر دوز دو بار در روز (حداکثر ۵۰۰ م.گ. در هر دوز)	۱۰ روز
کلیندامایسین	خوراکی، ۱۷ م.گ./ ک.گ. در هر دوز سه بار در روز (حداکثر ۳۰۰ م.گ./ دوز)	۱۰ روز
آزیترومایسین **	خوراکی، ۱۲ میلیگرم به ازا هر کیلوگرم یک بار در روز (حداکثر ۵۰۰ م.گ.)	۵ روز
کلاریترومایسین **	خوراکی،۱۷/۵ م.گ./ ک.گ.در هر دوز دو بار در روز (حداکثر ۲۵۰ م.گ. در هر دوز)	۱۰ روز

کلمات مخفف: ک.گ. = کیلوگرم، م.گ.= میلیگرم

*** در افرادی که سابقه واکنش پرحساسیتی نوع یک (سریع) دارند، نبایستی استفاده شود.**

**** مقاومت استرپتوکوک گروه آ به این داروها به خوبی شناخته شده است و به میزان متفاوتی از مناطق مختلف گزارش شده است.**

1.2 Summary and algorithm for management of sore throat

Objectives.

• Minimize the risk of developing acute rheumatic fever (ARF) and suppurative complications.

• Utilize clinical findings to determine probability of group A strep (GAS) pharyngitis.

• Reduce indiscriminate use of antibiotics, minimizing adverse effects & bacterial drug resistance.

Key points

General principals.

• Viral pathogens cause most cases of pharyngitis: around 90% in adults and 70% in children.

• The primary reason to identify and treat GAS pharyngitis is to decrease the risk of acute rheumatic fever (ARF).

• Early treatment of GAS can decrease the time a patient is symptomatic by 1-2 days from a typical 3-7 days and can decrease the period of contagiousness.

Diagnosis.

• Algorithms of clinical factors improve diagnosis by identifying patients with an exceedingly low risk of GAS infection.

• Patients with manifestations highly suggestive of a viral infection such as sneezing, rhinorrhea, hoarseness, cough, diarrhea, scleral conjunctival inflammation, or discrete ulcerative lesions inn posterior pharynx are unlikely to have GAS infection and generally should NOT be treated or tested for GAS infection (Group 1 in algorithm).

• In patients with sore throat, signs/symptoms of fever, tender anterior cervical lymphadenopathy, red pharynx with tonsillar swelling and exudate, and no cough indicate a higher probability of GAS pharyngitis for both adults and children. Patients, 3- 15 years old, could treat as SGA

pharyngitis without performing laboratory test (Group 2 in algorithm). RADT is recommended in patient older than 15 years old, but if there are obstacles for laboratory confirmation such as lack of accessibility, cost and lack of follow-up, antibiotics for SGA pharyngitis could be started. Developing GAS pharyngitis and acute rheumatic fever in infants and children under three years old is rare, so treatment for GAS pharyngitis is not indicated.

- Patients who never have clinical findings suggestive of viral pharyngitis (group 1) and also never have the typical findings of streptococcal pharyngitis (group 2) need laboratory confirmation of SGA pharyngitis by rapid antigen detection test (RADT) and throat culture according to algorithm (group 3).
- In a patient who is categorized in group 3, if there are obstacles for laboratory confirmation such as lack of accessibility, cost and lack of follow-up, antibiotics for SGA pharyngitis may be started if the patient is 3 years old or older. If patient is less than 3 years old, antibiotic for SGA pharyngitis should not be prescribed and the patient only need supportive care and follow-up because streptococcal sore throat is usually rare in this age group.

Treatment.

- Penicillin V is the drug of choice in patients who can swallow pills and had a good compliance to complete the antibiotic course.
- If using suspension, penicillin V or amoxicillin can be prescribed. Amoxicillin is better tolerated than penicillin V due to the salty/bitter taste.
- Amoxicillin as a single daily dose (1 gram/day for adults and 50 mg/kg/day for children with body weight < 30 kg) for 10 days is as effective as penicillin V or amoxicillin given multiple times per day for 10 days.

- A single dose of intramuscular penicillin G benzathine avoids the problem of adherence, but is painful.
- If allergic to penicillin, a 10-day course of a first generation cephalosporin (cephalexin) is indicated if no history of a type I hypersensitivity to penicillin.
- If allergic to penicillin, oral clindamycin is an acceptable alternative, if one is unable to use a first generation cephalosporin or if the history of a type I hypersensitivity to penicillin is present.
- An oral macrolide (erythromycin or clarithromycin) or azalide (azithromycin) is acceptable alternative for clindamycin (resistant rates range 5-40%).
- Antibiotics must be started within 9 days after onset of acute illness and continued for 10 days (5 days for azithromycin, 12 mg/kg/day) to eradicate GAS from the upper respiratory tract and prevent ARF.
- Failure to treatment (after 48 hours) may indicate alternative causes such as viral pharyngitis, development of suppurative complications such as peritonsillar abscess, inappropriate antibiotic therapy (e.g. cotrimoxazole), inadequate dose or duration of previous therapy, non-compliance and co-pathogenicity by beta-lactamase producing organisms and warrant reassessment.
- Children with a recurrence of GAS pharyngitis shortly after completing a course of an oral antimicrobial agent can be retreated with the same agent, given an alternative oral drug, or given an intramuscular injection of penicillin G benzathine (expert opinions differ).

Algorithm for management of sore throat

Sore throat → **Pharyngitis** → **If an emergency situation, recognized by signs & symptoms of respiratory distress, is present, refer the patient to ER; but if no, categorize patient in one of following three groups:**

Group 1

Strong clinical evidence of viral infections

A
Two out of ٥ following symptoms:
- Cough
- Sneezing
- Rhinorrhea
- Hoarseness
- Diarrhea

B
- Presence of conjunctivitis

(Suggestive of pharyngoconjunctival fever caused by adenovirus)

C
- Presence of vesicle and ulcer in posterior of pharynx

(Suggestive of herpangina caused by coxsackievirus)

Supportive care and following- up as non-GASP

Group 2

Strong clinical evidence of Group A streptococcal pharyngitis (GASP)

The presence of **all** following findings:
- The absence of viral symptoms
- Moderate to high grade fever (≥ 39◦C)
- Exudative pharyngitis
- Tender cervical lymphadenopathy

- In **3-15 years old**, treat as GASP
- In **>15 years old**, if laboratory test is unavailable, treat as GASP ; if RADT or throat culture is available, perform it and If positive, treat as GASP.
- **Under 3 years old**, supportive care and following- up as non-GASP

Group 3

No strong clinical evidence of viral infection or GASP

Patients who never have clinical findings of group 1 and also never have the typical findings of group 2

If l**aboratory test is available**: perform RDAT, If positive, treat as GASP; If negative, perform throat culture and if positive treat patient as GASP.

- If **laboratory test is unavailable**: the patient is 3 years old or over, treat as GASP; under 3 years old, supportive care and following- up as non-GASP

Table 1. Antibiotic Regimens Recommended for Group A Streptococcal Pharyngitis

Drug	Route, Dose or Dosage	Duration or Quantity	Levels of evidence scale
For individuals without penicillin allergy			
Penicillin V	oral children (<27 kg) : 250 mg twice daily or 3 times daily; adolescents and adults (≥27 kg): 250 mg 4 times daily or 500 mg twice daily	10 d	**I**
Amoxicillin	oral 50 mg/kg once daily (max = 1000 mg); alternate: 25 mg/kg (max = 500 mg) twice daily	10 d	**I**
Benzathine penicillin G	intramuscular <27 kg: 600 000 U; ≥27 kg: 1 200 000 U	1 dose	**I**
For individuals with penicillin allergy			
Cephalexin*	oral 20 mg/kg/dose twice daily (max = 500 mg/dose)	10 d	**I**
Clindamycin	oral 7 mg/kg/dose 3 times daily (max = 300 mg/dose)	10 d	**II-1**
Azithromycin**	oral 12 mg/kg once daily (max = 500 mg)	5 d	**II-1**
Clarithromycin**	oral 7.5 mg/kg/dose twice daily (max = 250 mg/dose)	10 d	**II-1**

Abbreviation: Max, maximum; d, day.

* Avoid in individuals with immediate type hypersensitivity to penicillin.

** Resistance of GAS to these agents is well-known and varies geographically and temporally.

* Adapted from Stanford T. S. et al. (1)

2. INTRODUCTION

2.1 Epidemiology

The epidemiology of sore throats in Iran with respect to its prevalence, age specific incidence, aetiology and complications has not been well studied and documented. Although the prevalence of tonsillopharyngitis was not documented in Iran, undoubtedly URTI is the most common reason for seeking treatment in general practice and hospital outpatient departments. (1-3) Epidemiological data from Western countries on sore throat in general and specifically GABHS infections, both community and hospital-based, are more readily available. However, there is considerable variation in the prevalence of GABHS sore throats from one country to another. (4-9) Overall, only a relatively small percentage of patients with acute pharyngitis (20%–30% of children and a smaller percentage of adults, about 5-10% of cases) have GAS pharyngitis (Table1). (9-11) With the exception of very rare infections by certain other bacterial pharyngeal pathogens (eg, *Corynebacterium diphtheria* and *Neisseria gonorrhoeae*), antimicrobial therapy is of no proven benefit as treatment for acute pharyngitis due to organisms other than GAS. (1) Therefore, for a patient with acute pharyngitis, the clinical decision that usually needs to be made is whether or not the pharyngitis is attributable to GAS. Inappropriate antimicrobial use for upper respiratory tract infections, including acute pharyngitis, has been a major contributor to the development of antimicrobial resistance among common pathogens. (12)

The economic impact of pharyngitis locally is not known due to paucity of studies, although this has been studied in some Western countries. In the adult population, about 6.7 million visits annually to a medical practitioner were for sore throat. (13) Estimated economic costs of pediatric streptococcal pharyngitis in the United States range from $224 million to $539 million per year, including indirect

costs related to parental work losses. (14) Consequently, treating pharyngitis in both children and adults has significant economic and health impact.

Table 2. Microbial Causes of Sore Throat*

Pathogen		Estimated %
Viral		
	Rhinovirus	20
	Coronavirus	>5
	Adenovirus	5
	Herpes virus	4
	Parainfluenza virus	2
	Influenza virus	2
	Coxsackie A	<1
	Epstein-Barr virus	<1
	Cytomegalovirus	<1
	HIV	<1
Bacterial		
	Streptococcus , Group A	15-30
	Streptococcus , Group C	5
	Neisseria gonorrhoea	<1
	Corynebacterium diptheriae	<1
	Arcanobacterium haemolyticus	<1
	Chlamydia pneumoniae	Unknown
	Mycoplasma pneumoniae	<1

* Adapted from Gwaltney JM et al. (15)

3. INFECTIOUS ETIOLOGY

The etiologic agents of sore throat are listed in Table 1. (15) Viral pathogens are more frequent causes of infective sore throat compared to bacterial pathogens. GABHS is the most common bacterial cause of acute pharyngitis, accounting for approximately 15-30% of cases in children and is also the only common form of pharyngitis for which antibiotic therapy is indicated. (9, 16) GABHS causes only 5%–15% of cases of acute pharyngitis in adults. (9, 11, 17-21) A recent study in Hong Kong revealed a rate of only 2.65%in those > 14 years of age (22).

4. CLINICAL MANIFESTATIONS OF SORE THROAT

Acute GAS pharyngitis has certain characteristic epidemiological and clinical features (22, 23) (Table 4). In both children and adults, the usual incubation period for streptococcal pharyngitis is 2-5 days (24). The disorder is usually rare in children < 3 years (9), and is primarily a disease of children 5–15 years of age, and, in temperate climates, it usually occurs in the winter and early spring (1). Symptoms and signs of GABHS pharyngitis are fairly similar in children and adults. Symptoms include sudden onset of sore throat, pain on swallowing, fever, headache, abdominal pain, nausea and vomiting. Signs include tonsillopharyngeal erythema, tonsillopharyngeal exudate, soft palate petechiae; beefy-red swollen uvula, swollen and tender anterior cervical lymph nodes and rash. (9) Not all patients have the full-blown syndrome and many cases are milder and do not have exudates.

The clinical picture in adults is characterized by an abrupt onset of the following (1, 2):

• Sore throat associated with difficulty in swallowing

•Age 5–15 years

• Fever moderate (≥ 39°C)

• Headache

• Nausea, vomiting, abdominal pain (35-50% of cases)

• Tonsillopharyngeal inflammation

• Patchy tonsillopharyngeal exudates

• Palatal petechiae

• Anterior cervical adenitis (tender nodes)

• Winter and early spring presentation

• History of exposure to strep pharyngitis

• Scarlatiniform rash

Rhinorrhea, cough, hoarseness, conjunctivitis, anterior stomatitis, discrete intra-oral ulcerative lesion and diarrhea are typically not seen in streptococcal infection, being more often seen in infections of viral aetiology (9, 25). Unfortunately, the clinical manifestations of GAS and non-GAS pharyngitis overlap quite a bit, so accurate diagnosis on the basis of clinical grounds alone is usually impossible. (3,10) Efforts have been made to incorporate the clinical and epidemiological features of acute pharyngitis into scoring systems that attempt to predict the probability that a particular illness is caused by GAS pharyngitis. (26-31) A scoring system has been devised by McIsaac to increase the clinical diagnostic accuracy , based on age and four clinical symptoms ,i.e. tonsillar swelling / exudates, swollen anterior cervical nodes, fever > 38◦C & lack of a cough. (26, 27, 32, 33) In emergency department practice, a 4-factor algorithm predicted a positive result of

GAS throat culture with an accuracy of 32%–56%, depending on the number of required clinical features present. (28) However, presence of certain clinical features such as rhinorrhea, hoarseness, cough ,conjunctivitis ,diarrhea and oropharyngeal ulceration may suggest a likely viral etiology. (9, 25, 34)

As mentioned above, exudative pharyngitis is rare in children <3 years old and GABHS infection is often associated with fever, mucopurulent rhinitis, excoriated nares, and diffuse adenopathy. (35) In addition, the reports of acute rheumatic fever in children <3 years of age are very rare (32, 36–40).

5. DIAGNOSIS AND LABORATORY INVESTIGATIONS

As the precise clinical diagnosis of GABHS pharyngitis is difficult, it is recommended that the clinician's decision to perform a laboratory test for a patient with suspected GABHS pharyngitis be based on the McIssac scoring system (Evidence level II-2). (31) This system attempts to predict the probability that the pharyngitis is caused by GABHS. Hence, testing need not be performed for patients with acute pharyngitis whose clinical and epidemiological features do not suggest GABHS infection (group 1 in algorithm). Unless diagnosis of group A streptococcal pharyngitis can be confidently excluded, bacteriologic studies should be performed guided by this scoring system (Evidence level II-2). Selective use of the suggested diagnostic test for group A streptococci will result in an increase in both the proportion of positive test results and the percentage of patients with positive test who are truly infected than are merely carriers (Evidence level II-2). Methods for the diagnosis of group A streptococcal pharyngitis are based on recommendations from the Public Health Laboratory Service Standard Operating Procedure on Investigation of Throat Swabs and the guideline on diagnosis of GAS pharyngitis by the Infectious Diseases Society of America. (41, 42)

5.1. Laboratory diagnosis

Culture of throat swab for the presence of GABHS remains the gold standard for the confirmation of the clinical diagnosis of acute streptococcal pharyngitis (Evidence level II-2). (1-3) A single throat swab collected, transported and cultured under recommended conditions has a sensitivity of 90%-95% in detecting the presence of group A streptococcus in the pharynx. Variations in the collection, transport and culture methods can affect the accuracy of the culture results. (1-2)

Measurement of anti-streptococcal antibody titers is not useful in the diagnosis of acute pharyngitis because antibody titers of the 2 most commonly used tests, antistreptolysin O (ASO) and anti-DNase B, may not reach maximum levels until 3–8 weeks after acute GAS pharyngeal infection and may remain elevated for months even without active GAS infection .(43, 44) However, such testing is often useful for diagnosis of the nonsuppurative sequelae of GAS pharyngitis, such as acute rheumatic fever and acute glomerulonephritis . (45) Therefore, anti-streptococcal antibody titers are not recommended in the routine diagnosis of acute pharyngitis as they reflect past but not current events (Evidence level I-A). (1-2)

5.2. Rapid Antigen Detection Tests (RADT)

With the availability of RADT, group A streptococci can be identified directly from throat swabs. The former has an advantage of speed in providing results (within minutes) as compared to the gold standard culture method (48 hours). Rapid identification and treatment of patients with GAS pharyngitis can reduce the risk of spread, allowing the patient to return to school or work sooner, and can reduce the acute associated morbidity. (46, 47) Other advantages of this diagnostic test, besides being a point of care test, in view of its turn around time would help reduced the risk of spread of this infection, allow patients to return to work or school earlier, reduce acute morbidity as

well as increase the number of patients appropriately treated for streptococcal pharyngitis. (48) RADTs currently available are highly specific (approximately 95%) when compared with blood agar plate cultures. (49-51) With the availability of RADT locally, this test allows therapeutic decisions to be made with greater degree of confidence during the patient's initial encounter with the clinician. Techniques of RADT include optical immunoassay and EIA. (25, 52) Unfortunately, the sensitivity of most of these tests is 70%–90%, compared with throat culture. (47, 53) Because the sensitivities of the various RADTs are <90% in most studied populations of children and adolescents (49-51) and because the proportion of acute pharyngitis due to GAS in children and adolescents is sufficiently high (20%–30%), a negative RADT should be accompanied by a follow-up or back-up throat culture in children and adolescents, while this is not necessary in adults under usual circumstances, as noted above. (Evidence level II-2). (1-3)

5.3 Recommendations for diagnosis

Diagnosis of acute GAS pharyngitis should be suspected on clinical and epidemiological grounds, and then supported by laboratory test. Either a positive throat culture or RADT provides adequate confirmation of GAS in the pharynx, but a negative RADT result should be confirmed with a throat culture, especially in children, whenever possible. (Evidence level II-2). (1-3)

Algorithms of clinical factors improve diagnosis by identifying patients with an exceedingly low risk of GAS infection.(2, 3) Patients with manifestations highly suggestive of a viral infection such as sneezing, rhinorrhea, hoarseness, cough, diarrhea, scleral conjunctival inflammation, or discrete ulcerative lesions in posterior pharynx are unlikely to have GAS infection and generally should not be treated or tested for GAS infection (Group 1 in algorithm). (1-3)

In patients with sore throat, signs/symptoms of fever, tender anterior cervical lymphadenopathy, red pharynx with tonsillar swelling and exudate, and no cough indicate a higher probability of GAS pharyngitis for both adults and children. (1-3) We recommend that patients with 15 years old or lesser could treat as SGA pharyngitis without performing laboratory test (Group 2 in algorithm) (Evidence level III). RADT is recommended in patient older than 15 years old, but if there are obstacles for laboratory confirmation such as lack of accessibility, cost and lack of follow-up, we recommend that antibiotics for SGA pharyngitis could be started for decreasing the risk of acute rheumatic fever (Evidence level III).

Patients who never have clinical findings suggestive of viral pharyngitis (group 1 in algorithm) and also never have the typical findings of streptococcal pharyngitis (group 2 in algorithm) need laboratory confirmation of SGA pharyngitis by rapid antigen detection test (RADT) and throat culture according to algorithm (group 3). (1-3) In a patient who is categorized in group 3, if there are obstacles for laboratory confirmation such as lack of accessibility, cost and lack of follow-up, we recommend that antibiotics for SGA pharyngitis may be started if the patient is 3 years old or older (Evidence level III). Also, we recommend whether patient is less than 3 years old, antibiotic for SGA pharyngitis should not be prescribed and the patient only need supportive care and follow-up because streptococcal sore throat is usually rare in this age group (Evidence level III).

6. COMPLICATIONS

Complications of GABHS pharyngitis include both suppurative and nonsuppurative. Suppurative complications are peritonsillar abscess (PTA) and retropharyngeal abscess (RPA). Peritonsillar abscess is the most common complication of acute tonsillitis. (54) 15-36% of patients with PTA had prior history of oropharyngeal infections. (55-57) PTA occur as a direct communication and

progression of acute exudative tonsillitis and the incidence is mainly in adolescent. (58, 59) Nonsuppurative complications include acute rheumatic fever, acute post streptococcal glomerulonephritis and reactive arthritis. (60)The most important nonsuppurative complication is acute rheumatic fever which occurs approximately 3 weeks after streptococcal pharyngitis and its major clinical manifestations are arthritis, carditis, chorea, erythema marginatum and subcutaneous nodules. (60) The risk of acute rheumatic fever complicating untreated streptococcal pharyngitis is 1% and at least one third of episodes of acute rheumatic fever result from sub clinical streptococcal infections. (34, 61) However, a delay of therapy up to 9 days is acceptable without compromising the beneficial effects of antibiotics on the prevention of rheumatic fever.(25, 34) Reports of acute rheumatic fever in children <3 years of age are very rare (32, 36–40). Acute post streptococcal glomerulonephritis also usually occurs 3 weeks after throat or skin infection by Group A streptococci of specific nephritogenic serotypes. Although the general underlying mechanisms may be similar, they differ in their pathogenesis, clinical manifestations, epidemiology and potential morbidity.

7. MANAGEMENT

Management of sore throat include 1) symptomatic treatment, 2) antibiotic therapy for GAS pharyngitis and, if clinically indicated, 3) surgical treatment, including tonsillectomy which is not discussed in this CPG.

7.1 Symptomatic treatment

Symptomatic treatment is an integral part in the management of children and adults with sore throat. It can be broadly divided into following categories (1, 2):

1. General Measures (Evidence level III). (9, 62)

(a) Maintain adequate fluid intake.

(b) Warm water gargle

2. Simple Analgesics / Antipyretic, Non-Steroidal Anti-inflammatory Agents (NSAIDs) (63, 64)

Acetaminophen is an effective and safe analgesic and antipyretic for treatment of moderate to severe symptoms or control of high fever associated with GAS pharyngitis. Multiple studies, including randomized, double-blind, and placebo-controlled studies, support the benefits of NSAIDs such as ibuprofen in reducing fever and pain relative to placebo among both children and adults with pharyngitis. No significant adverse events were noted. In other randomized, doubleblind, and placebo-controlled studies, significantly greater pain relief with use of acetaminophen compared with placebo has been documented among both children and adults, although improvement in symptoms was not always equivalent to that obtained through use of ibuprofen. (65-68) [Evidence level I] Although aspirin has also been shown to reduce pain in adults with upper respiratory tract infection, the use of aspirin for pain relief of pharyngitis in children is prohibited because of the risk of Reye syndrome. (1, 2)

3. Throat Lozenges / Gargles

Throat lozenges and gargles are frequently used by the patient even before they see a general practitioner. They are helpful as adjunctive therapy especially in those with significant throat pain or discomfort (Evidence level I & II-2). Topical agents for pharyngitis in both children and adults have recently been reviewed . (69-74) Lozenges may be effective but represent a choking hazard for

young children. (68) A remedy commonly used in patients old enough to gargle, warm salt water rinses, has not been studied in detail.

4. Others

Adjunctive therapy with a corticosteroid such as dexamethasone is not recommended due to the efficacy of antimicrobials, the self-limited nature of GAS pharyngitis, the efficacy of systemic and some topical analgesics in decreasing the acute symptoms of GAS pharyngitis, and the potential of adverse effects of systemic steroids and the minimal decrease in pain duration (approximately 5 hours). (75, 76) (Evidence level II -2).

7.2 Antibiotic therapy for GAS pharyngitis

The majority of sore throats is of viral origin and does not need antibiotic therapy. Antibiotics should not be used routinely to secure symptomatic relief in sore throat (Evidence level I). (77) Antimicrobial therapy is of no proven benefit in the treatment of acute pharyngitis due to bacteria other than Group A streptococci. (9) The exceptions are infections caused by *Corynebacterium diptheriae* and *Neisseria gonorrhea*. Over-prescription of antibiotics for sore throat may lead to emergence of antibiotic resistance and exposes the patient to potential adverse effects. (9) Ideally, a throat swab should be taken before starting empiric antibiotics and treatment started only for documented Group A streptococcal infection. However, due to practical constraints such as lack of accessibility and cost of throat cultures and lack of follow-up, antibiotics may be started if streptococcal sore throat is clinically suspected, the patient is toxic-looking and follow-up is not possible (group 2). The objectives of treating Group A streptococcal pharyngitis are to prevent acute

rheumatic fever, prevent suppurative complications, decrease infectivity and shorten the clinical course of the disease. (78)

When selecting an antimicrobial for treatment of GAS pharyngitis, important issues to consider include efficacy, safety, antimicrobial spectrum (narrow vs broad), dosing schedule, compliance with therapy (ie, adherence), and cost. (1-3) A number of antibiotics have been shown to be effective in treating GAS pharyngitis (Table 2). These include penicillin and its congeners (eg, ampicillin and amoxicillin), as well as cephalexin, macrolides, and clindamycin. (1-3) Based on their narrow spectrum of activity, infrequency of adverse reactions, and modest cost, penicillin or amoxicillin is the recommended drug of choice for those non-allergic to these agents (Evidence level I). (25, 34, 79, 80) There has never been a clinical isolate of Group A streptococci documented to be resistant to penicillin so far. If oral therapy is chosen, a full 10-day course of treatment is recommended to ensure maximal rate of eradication of the infection from the pharynx. Penicillin-resistant GAS has never been documented. Amoxicillin is often used in place of penicillin V as oral therapy for young children; the efficacy appears to be equal. This choice is primarily related to acceptance of the taste of the suspension. (1) Shorter treatment eradicates GAS less effectively and clinical recurrence level is more common (Evidence level I). (81, 82)

Antimicrobials for GAS pharyngitis may be given either orally or parenterally. Intramuscular benzathine penicillin G therapy is preferred for patients deemed unlikely to complete a full 10-day course of oral therapy. (1) Also, this route can be very useful in children who present with severe abdominal pain and vomiting along with their GAS pharyngitis. (3) It does, however, produce a significant amount of pain at the injection site that may last a 2–3 days following injection. (3)

Certain antimicrobials are not recommended for treatment of GAS pharyngitis. Tetracyclines should not be used because of the high prevalence of resistant strains. Sulfonamides and trimethoprim-

sulfamethoxazole should not be used because they do not eradicate GAS from patients with acute pharyngitis . (83, 84) Older fluoroquinolones (eg, ciprofloxacin) have limited activity against GAS pharyngitis and should not be used to treat GAS pharyngitis. (84) Newer fluoroquinolones (eg, levofloxacin and moxifloxacin) are active in vitro against GAS, but they are expensive and have an unnecessarily broad spectrum of activity and are therefore not recommended for routine treatment of GAS pharyngitis. (85)

Narrow spectrum cephalosporins (such as cephalexin) for 10 days are now recommended for those who cannot be safely prescribed a penicillin due to penicillin-allergy (for those not anaphylactically sensitive). (1- 3) Some penicillin-allergic persons (up to 10%) are also allergic to cephalosporins, and these agents should not be used in patients with immediate (anaphylactic-type) hypersensitivity to penicillin , (86) Clindamycin or oral macrolide (erythromycin or clarithromycin) or azalide (azithromycin) should be used in these patients (Evidence level II-1). (46, 47, 53, 87) Clindamycin resistance among GAS isolates in the United States is approximately 1%, and this is a reasonable agent for treating penicillin-allergic patients. (88)

Erythromycin is associated with substantially higher rates of gastrointestinal side effects than the other agents. Strains of GAS resistant to these agents have been highly prevalent in some areas of the world and have resulted in treatment failures. (89) In recent years, macrolide resistance rates among pharyngeal isolates in most areas of the United States have been around 5%–8%. (88) One study suggests that 10 days of clarithromycin may be more effective in eradicating GAS pharyngitis than 5 days of azithromycin (at a dose of 12 mg/kg/day, up to a maximum of 500 mg for 5 days). (90)

8. Failure to improve with treatment.

Clinical response of children with Group A streptococcal pharyngitis to appropriate antimicrobial therapy is usually evident within 24-48 hours. This may indicate alternative causes such as viral pharyngitis, development of suppurative complications such as peritonsillar abscess and warrant reassessment. (1-3)

8.1 Local complications.

An exam should be performed to rule out occurrence of a local complication, such as peritonsillar abscess (Quinsy) or retropharyngeal abscess. These complications require immediate consultation with otolaryngology as they may necessitate surgical drainage and pose a serious threat to the patient's airway. (1- 3)

8.2 No local complications.

Persistence of pharyngitis despite adequate therapy suggests several possibilities:

1) Pharyngitis has a nonstrptococcal etiology such as viral infection or a non-infectious etiology such as Kawasaki disease. Patient should be reevaluated and followed up to when the symptoms would resolve. (1, 3)

2) Organism was not killed by the antibiotic treatment. This may be due to inappropriate antibiotic therapy (e.g. cotrimoxazole), inadequate dose or duration of previous therapy, non-compliance and co-pathogenicity by beta-lactamase producing organisms. (25) For patient nonadherent with antibiotic course, the decision may be made to opt for intramuscular benzathine penicillin G in order to ensure adequate treatment. Also, the use of a better tolerated oral antibiotic, the use of a

once-a-day antibiotic, or the use of a short-course antibiotic may improve adherence.Co-pathogenicity with oral bacteria (such as Staph) secreting beta-lactamases is an theory that has yet to be convincingly documented. These organisms passively protect GAS from the actions of penicillin. (3) Therapy with intramuscular benzathine penicillin (Evidence level I), clindamycin (Evidence level II-1), amoxicillin-clavulanate (children: 40 mg amoxicillin/kg/day in 2 doses; adolescence and adults: 500 mg amoxicillin with 125 mg clavulanate BID; max = 2000 mg amoxicillin/d) (Evidence level II-1) and cefuroxime (Evidence level II-1) may be beneficial in these cases. (91-96)

3) If throat culture has revealed SGA, organism may be present as a colonizer and does not pose a threat to cause acute rheumatic fever (i.e., a coexisting viral infection is the cause of the acute symptoms). These GAS carriers are defined as individuals with positive throat cultures for GAS without an immunologic response to GAS. Colonization occurs often after a primary GAS pharyngitis and it may persist for many months. Throat culture surveys of asymptomatic children during school outbreaks of pharyngitis have yielded GAS prevalence rates as high as 15-50%. (3) However, in an individual with symptoms compatible with an acute GAS infection, it is not easy to decide whether the GAS isolated from the oropharynx is the cause of symptoms or from GAS carriage. Thus GAS persisting in a symptomatic individual should be retreated. (1, 3)

9. REFERENCES

1. Stanford T. Shulman; Alan L. Bisno; Herbert W. Clegg; Michael A. Gerber; Edward L. Kaplan; Grace Lee; Judith M. Martin; Chris Van Beneden. Clinical practice guideline for the diagnosis and management of group a streptococcal pharyngitis: 2012 update by the infectious diseases society of America. Clinical Infectious Diseases. 2012; 55(10):e86-e102.

2. Kee TK, Tan C, Lee C, Manickam D, Nee KT, Din S, Huat TL. Clinical Practice Guideline: management of sore throat. April 2003. http:// www.acadmed.org.my

3. Terrance P Murphy, R Van Harrison, Annissa J Hammoud, Gary Yen, Kristin C Klein, Grant Greenberg, R Van Harrison. UMHS Clinical Guideline: Pharyngitis. University of Michigan. May, 2013. http://www.med.umich.edu/1info/fhp/practiceguides/pharyngitis/pharyn.pdf

4. Lim TO. Content of general practice. Med J Malaysia 1991; 46: 155-62.

5. Tanz RR, Shulman ST. Streptococcal pharyngitis: the carrier state, definition, and management. Pediatric Annals 1998; 27(5):281-5.

6. Faruq QO, Rashid AK, Ahmed J, Waiz A, Haque KM, Rouf MA, Khan SM, Khan TN. Prevalence of streptococcal sorethroat in the school children of Dhaka. Bangladesh Medical Research Council Bulletin 1995; 21(3):87-94.

7. Amir J, Shechter Y, Eilam N, Varsano I. Group A beta-hemolytic streptococcal pharyngitis in children younger than 5 years. Israel Journal of Medical Sciences 1994; 30(8):619- 22 .

8. Principi N. Marchisio P. Calanchi A. Onorato J. Plebani A. Reali E. Rancilio L. Grasso E. Magni L. Caramia G. Streptococcal pharyngitis in Italian children: epidemiology and treatment with miocamycin. Drugs Under Experimental & Clinical Research 1990; 16(12):639- 47.

9. Van Cauwenberge P. Berdeaux G. Morineau A. Smadja C. Allaire JM. Use of diagnostic clusters to assess the economic consequences of rhinopharyngitis in children in Italy and France during the winter. Rhinitis Survey Group Clinical Therapeutics 1999; 21(2):404-21.

10. Wannamaker LW. Perplexity and precision in the diagnosis of streptococcal pharyngitis. Am J Dis Child 1972 ; 124:352 8.

11. Bisno AL. Acute pharyngitis. N Eng J Med 2001; 344: 205-11.

12. McCaig LF, Besser RE, Hughes JM. Trends in antimicrobial prescribing rates for children and adolescents. JAMA 2002 ; 287: 3096 102.

13. Barlet JG. Management of respiratory tract infections. Baltimore, Maryland: William & Wilkins, 1997: 150-98

14. Pfoh E, Wessels MR, Goldmann D, Lee GM. Burden and economic cost of group A streptococcal pharyngitis. Pediatrics 2008; 121: 229 34

15. Little P, Williamson I. Sorethroat management in general practice. Family Practice 1996 ;13: 317-21.

16. Gwaltney JM, Bisno AL. Pharyngitis. In: Mandel GL,Bennett JE , Dollin R , eds. Mendell , Douglas , and Bennett ‘s Principles and Practice of Infectious Diseases. 5th ed.Vol.1. Philadelphia: Churchill Livingstone, 2000:656-62.

17. Bisno AL. Acute pharyngitis: etiology and diagnosis. Pediatrics 1996; 97: 949–54.

18. Ebell MH, Smith MA, Barry HC, Ives K, Carey M. The rational clinical examination. Does this patient have strep throat? JAMA 2000; 284:2912–8.

19. Komaroff AL, Pass TM, Aronson MD, et al. The prediction of streptococcal pharyngitis in adults. J Gen Intern Med 1986; 1:1–7.

20. Wannamaker LW. Perplexity and precision in the diagnosis of streptococcal pharyngitis. Am J Dis Child 1972; 124:352–8.

21. Cooper RJ, Hoffman JR, Bartlett JG, et al. Principles of appropriate antibiotic use for acute pharyngitis in adults: background. Ann Intern Med 2001; 134:509–17.

22. Efstratiou A. Group A streptococci in the 1990s. J Antimicrob Chemother 2000; 45: 3-12.

23. National Ambulatory Medical Care Survey, US (1989-1999).JAMA 2001; 186: 1181-1186.

24. Wong MCK, et al. GAS infection in patients presenting with sore throat at an A&E dept: a prospective study. HKMJ 2002; 8: 92-98

25. Poses RM, et al. The importance of disease prevalence in transporting clinical prediction rules. Ann Intern Med 1986; 105: 586-589.

26. Breese BB. A simple scorecard for the tentative diagnosis of streptococcal pharyngitis. Am J Dis Child 1977; 131:514–7.

27. 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.

28. 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.

29. Bisno AL,Gerber MA, Gwaltney JM,Kaplan EL,Schwartz RH. Practice guidelines for the diagnosis and management of Group A Streptococcal pharyngitis. Clin Infect Dis 2002; 35:113-25.

30. Wigton RS, et al. Transportability of a decision rule for the diagnosis of streptococcal pharyngitis. Arch Intern Med 1986; 146:81-83.

31. Meland E, at al. Assessment of clinical features predicting streptococcal pharyngitis. Scand J Infect Dis 1993; 25:177-183.

32. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group a streptococcal diseases. Lancet Infect Dis 2005; 5:685–94.

33. Field MJL, Kathleen N. Institute of Medicine Committee to Advise the Public Health Service on Clinical Practice Guidelines. Clinical practice guidelines: directions for a new program. Washington, DC: National Academy Press, 1990 :52–77.

34. McIsaac WJ,Goel V,To T,Low DE. The validity of a sore throat score in family practice. CMAJ 2000; 163: 811-5.

35. Boisvert PL, Darrow D, Powers GF, et al. Streptococci in children. Am J Dis Child 1942; 64:516–34.

36. Tani LY, Veasy LG, Minich LL, Shaddy RE. Rheumatic fever in children younger than 5 years: is the presentation different? Pediatrics 2003; 112:1065–8.

37. Gordis L. The virtual disappearance of rheumatic fever in the United States: lessons in the rise and fall of disease. T. Duckett Jones Memorial Lecture. Circulation 1985; 72: 1155–62.

38. Ramanan PV, Premkumar S, Ramnath B. Youngest patient with Sydenham's chorea: a case report. J Indian Med Assoc 2009; 107:246, 53.

39. Vinker S, Zohar E, Hoffman R, Elhayany A. Incidence and clinical manifestations of rheumatic fever: a 6 year community-based survey. Isr Med Assoc J 2010 ; 12:78–81.

40. Paulo LT, Terreri MT, Barbosa CM, Len CA, Hilario MO. [Is rheumatic fever a more severe disease in pre-school children?]. Acta Reumatol Port 2009; 34:66 –70

41. Dajani A,Taubert K,Ferrieri P,Peter G,Shulman S , and the Committee on Rheumatic Fever, Endocarditis,and Kawasaki Disease of the Council on Cardiovascular Disease in the Young,

American Heart Association. Treatment of acute streptococcal pharyngitis and prevention of rheumatic fever: a statement for health professionals. Pediatrics 1995; 96: 758-64.

42. Phls Standard Operating Procedure – Investigation of throat swabs. Reference no: B.SOP 9 Version: 1 Issue date: 29.4.1998 Issued by: Technical services, PHLS HQ Page no. 1 of 8.
43. Kaplan EL, Top FH Jr, Dudding BA, Wannamaker LW. Diagnosis of streptococcal pharyngitis: differentiation of active infection from the carrier state in the symptomatic child. J Infect Dis 1971 ; 23:490–501
44. Johnson DR, Kurlan R, Leckman J, Kaplan EL. The human immune response to streptococcal extracellular antigens: clinical, diagnostic, and potential pathogenetic implications. Clin Infect Dis 2010 ; 50:481–90.
45. Shet A, Kaplan EL. Clinical use and interpretation of group A streptococcal antibody tests: a practical approach for the pediatrician or primary care physician. Pediatr Infect Dis J 2002 ; 21:420–6; quiz 27–30.
46. Bass JW. Antibiotic management of Group A streptococcal pharyngotonsillitis. Pediatr Infect Dis J 1991;10:S43-49.
47. Shapera RM, Hable KA, Matsen JM. Erythromycin therapy twice daily for streptococcal pharyngitis:controlled comparison with erythromycin or penicillin phenoxymethyl four times daily or penicillin G benzathine. JAMA 1973;226:531-5
48. Gerber MA. Diagnosis of pharyngitis : methodology of throat cultures. In: Shulman ST, ed. Pharyngitis: management in an era of declining rheumatic fever. New York: Praeger. 1984:61-72.
49. Gerber MA. Comparison of throat cultures and rapid strep tests for diagnosis of streptococcal pharyngitis. Pediatr Infect Dis J 1989; 8: 820 4.

50. Gerber MA, Shulman ST. Rapid diagnosis of pharyngitis caused bygroup A streptococci. Clin Microbiol Rev

2004; 17: 571 80.

51. Tanz RR, Gerber MA, Kabat W, Rippe J, Seshadri R, Shulman ST. Performance of a rapid antigen-detection test and throat culture in community pediatric of fices: implications for management of pharyngitis. Pediatrics 2009; 123: 437 44.

52. Lieu TA, Fleisher Gr, Schwartz Js. Clinical evaluation of a latex agglutination test for streptococcal pharyngitis: performance and impact on treatment rates. Pediatr Infect Dis J 1988; 7:847-54.

53. Breese BB,Disney FA,Talpey W.et al. Streptococcal infections in children: comparison of the therapeutic effectiveness of erythromycin administered twice daily with penicillin phenoxymethyl and clindamycin administered three times daily. Am J Dis Child 1974;128:457-60.

54. Gerber MA, Tanz RR , Kabat W, Denis E , Bell GL , Kaplan EL et al. Optical immunoassay test for group A beta-hemolytic streptococcal pharyngitis : an office-based , multicenter investigation. JAMA 1997; 277: 899-903.

55. Epperly TD , Wood TC. New trends in management of peritonsillar abscess. Am Fam Physician 1990 ; 42 : 102-12.

56. Holt GR , Tinsley PP. Peritonsillar abscess in chidlren. Laryngoscope 1981; 91: 1226-30.

57. Wolf M , Kronenberg J , Kessler A , Modan M. Peritonsillar abscess in children and its indication for tonsillectomy. Int J Ped Otorhinolaryngol 1988 ; 113-7.

58. Herzon FS. Peritonsillar abscess: incidence , current management practices and a proposal for treatment guidelines. Laryngoscope 1995 ; 105 :1-17.

59. Passy V. Pathogenesis of peritonsillar abscess. Laryngoscope 1994 ; 104 : 184-90.

60. Tsevat J, Kotagal UR. Management of sore throats in children: A cost - effectiveness analysis. Arch Pediatr Adolesc Med 1999;153:681-8.

61. Kirse DJ. Surgical management of retropharyngeal space infections in children. Laryngoscope 2001; 111 : 1413-22.

62. Olivier C. Rheumatic fever- is it still a problem? J Antimicrob Chemother 2000 ; 45: 13-21.

63. Scottish Intercollegiate Guidelines Network. Management of sore throat and indications for tonsillectomy. A national clinical guideline, Jan 1999.

64. Stead W, Aronson MD, Park L. Symptomatic treatment of acute pharyngitis in adults. 2014

65. Schachtel BP, Thoden WR. A placebo-controlled model for assaying systemic analgesics in children. Clin Pharmacol Ther 1993; 53: 593–601.

66. Gehanno P, Dreiser RL, Ionescu E, Gold M, Liu JM. Lowest effective single dose of diclofenac for antipyretic and analgesic effects in acute febrile sore throat. Clin Drug Investig 2003 ; 23:263–71.

67. Bertin L, Pons G, d' Athis P, et al. Randomized, double-blind, multicenter, controlled trial of ibuprofen versus acetaminophen (paracetamol) and placebo for treatment of symptoms of tonsillitis and pharyngitis in children. J Pediatr 1991; 119:811–4.

68. McNally D, Simpson M, Morris C, Shephard A, Goulder M. Rapid relief of acute sore throat with AMC/DCBA throat lozenges: randomised controlled trial. Int J Clin Pract 2010 ; 64:194–207

69. Thomas M, Del Mar C, Glasziou P. How effective are treatments other than antibiotics for acute sore throat? Br J Gen Pract 2000; 50:817–20

70. Wong A, Sibbald A, Ferrero F, Antipyretic effects of dipyrone versus ibuprofen vs acetaminophen in children: results of a multinational randomized modified double – blind study. ClinPediatr (Phila) 2001: 40 (6) 325 –6.

71. Joseph F. Wethington. Double Blind Study of Benzydamine Hydrochloride: a new treatment for sorethroat. Clinical therapeutics, Vol 7, No.5; 1985.

72. Batista NA. Kyrmie R. Effects of diclofenac resinate drops in combination with an antibiotic in the treatment of infection of the upper airways . Anq Bras Med 1985;59(6) 479 –84

73. Watson N, Mimmo WS, Christian J, et al. Relief of sore throat with the anti-inflammatory throat lozenge flurbiprofen 8.75mg: a randomised, double blind, placebo controlled study of efficacy and safety. Int J. Clin Pract 2000;54(8): 490 –6

74. Benrimoj SI, Langford JH, Christian J, et al. Efficacy & tolerability of the anti-inflammatory throat lozenge flurbiprofen 8.75mg in the treatment of sore throat. Clin Drug Invest 2001;21(3):183-93.

75. Olympia RP, Khine H, Avner JR. Effectiveness of oral dexamethasone in the treatment of moderate to severe pharyngitis in children. Arch Pediatr Adolesc Med 2005; 159:278–82.

76. Bulloch B, Kabani A, Tenenbein M. Oral dexamethasone for the treatment of pain in children with acute pharyngitis: a randomized, double-blind, placebo-controlled trial. Ann Emerg Med 2003; 41:601–8.

77. O'Brien JF, Meade JL, Falk JL. Dexamethasone as adjuvant therapy for severe acute pharyngitis. Ann Emerg Med 1993; 22(2):212-5.

78. Del Mar C. Sore throats and antibiotics (Editorial). Brit Med J 2000; 320:130 - 1.

79. Royal College of Paediatrics and Child Health . Management of acute and recurring sore throat and indications for tonsillectomy; 2000,RCPCH: London.

80. Anon. Diagnosis and treatment of Streptococcal sore throat. Drug and Therapeutics Bulletin 1995; 33: 9-12.

81. Schwartz RH, Wientzen Redreira F, Feroli EJ, Mella GW, Guandolo VL. Penicillin V for group A streptococcal pharyngotonsillitis: a randomised trial of seven vs ten days therapy. *JAMA* 1981; 246: 1790-5.

82. Zwart S, Sachs APE, Ruijs GJHM, Gubbels JW, Hoes AW, de Melker RA. Penicillin for acute sore throat: randomised double blind trial of seven days versus three days treatment or placebo in adults. BMJ. 2000; 15; 320:150-4.

83. Gerber MA. Antibiotic resistance in group A streptococci. Pediatr Clin North Am 1995; 42:539–51.

84. Coonan KM, Kaplan EL. In vitro susceptibility of recent North American group A streptococcal isolates to eleven oral antibiotics. Pediatr Infect Dis J 1994; 13:630–5.

85. Wickman PA, Black JA, Moland ES, Thomson KS. In vitro activities of DX-619 and comparison quinolones against gram-positive cocci. Antimicrob Agents Chemother 2006; 50:2255 –7

86. Pichichero ME. A review of evidence supporting the American Academy of Pediatrics recommendation for prescribing cephalosporin antibiotics for penicillin-allergic patients. Pediatrics 2005;115:1048–57.

87. Hooton TM. A comparison of azithromycin and penicillin V for the treatment of streptococcal pharyngitis. Am J Med 1991 ; 91:23S –6S.

88. Tanz RR, Shulman ST, Shortridge VD, et al. Community-based surveillance in the united states of macrolide-resistant pediatric pharyngeal group A streptococci during 3 respiratory disease seasons. Clin Infect Dis 2004 ; 39:1794–801.

89. Seppala H, Nissinen A, Jarvinen H, et al. Resistance to erythromycin in group A streptococci. N Engl J Med 1992 ; 326:292 –7.

90. Kaplan EL, Gooch IW, Notario GF, Craft JC. Macrolide therapy of group A streptococcal pharyngitis: 10 days of macrolide therapy (clarithromycin) is more effective in streptococcal eradication than 5 days (azithromycin). Clin Infect Dis 2001 ; 32:1798–802.

91. Breese BB, Disney FL, Green JL, et al. The treatment of beta hemolytic streptococcal pharyngitis: comparison of amoxicillin , erythromycin estolate and penicillin V. Clin Pediatr 1977;16:460-3.

92. Sirimanna KS, Madden GJ, Miles SM. The use of long-acting penicillin in the prophylaxis of recurrent tonsillitis. J Otolaryngol 1990 ;19:343-4.

93. Brook I, Hirokawa R. Treatment of patients with a history of recurrent tonsillitis due to group A beta-hemolytic streptococci. A prospective randomized study comparing penicillin , erythromycin, and clindamycin. Clin Pediatr 1985;24:331-6.

94. Orrling A, Stjernquist-Desatnik A, Schalen C. Clindamycin in recurrent group A streptococcal pharyngotonsillitis- an alternative to tonsillectomy? Acta Oto-Laryngologica 1997;117:618-22.

95. Raz R, Hamburger S, Flatau E. Clindamycin in the treatment of an outbreak of streptococcal pharyngitis in a kibbutz due to beta-lactamase producing organisms. J Antimicrob Chemother 1990;2:182-4.

96. Kaplan EL, Johnson DR. Eradication of group A streptococci from the upper respiratory tract by amoxicillin with clavulanate after oral penicillin V treament failure. J Pediatr 1988;113:400-3.


مرکز تحقیقات میکروب شناسی بالینی استاد البرزی
Prof. Alborzi Clinical Microbiology Research Center
P.A.C.M.R.C