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Clinical Guideline

Practice Recommendation for the Management of Acute Pharyngitis

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Abstract Acute pharyngitis is commonly seen in children, and the majority of cases are caused by viral infection. Group A streptococcus (GAS) is the only common bacterial cause for which antibiotic therapy is definitely indicated. With the weak differentiating power of clinical features between GAS and non-streptococcal causes, clinicians are encouraged to perform either throat culture or rapid antigen detection test for GAS confirmation before initiating antibiotic therapy if doubt exists. Based on latest literature and approved by The Working Group on The Development of Clinical Practice Guidelines of the Hong Kong College of Paediatricians, this practice recommendation is intended for use by paediatricians and primary care physicians for their evidence-based management of acute pharyngitis in children.

Key words Children; Management; Pharyngitis

Introduction

Acute pharyngitis is one of the most frequent illnesses for which paediatricians and primary care physicians are consulted. Being the most common bacterial cause of acute pharyngitis, group A streptococcus (GAS) is responsible for a relatively small percentage (20-30%) of sore throat visits in children aged 5 to 15 years.[1] A local study at an accident and emergency department in Hong Kong showed a 38.6% detection rate of GAS pharyngitis in children presented with sorethroat.[2] Accurate diagnosis of GAS pharyngitis followed by appropriate antibiotic therapy is important for the prevention of non-suppurative complications (e.g. acute rheumatic fever) and suppurative complications (e.g. peritonsillar abscess, and mastoiditis); the improvement of clinical symptoms; and the reduction in transmission of GAS to household members, classmates, and other close contacts of the patient.[3] Except very rare infections by certain organisms such as Neisseria gonorrhoeae and Corynebacterium diphtheria, antibiotic therapy is of no proven benefit as treatment for acute pharyngitis caused by other bacterial pathogens other than GAS. Moreover, the clinical features of GAS pharyngitis and non-streptococcal pharyngitis overlap so broadly that diagnosis based solely on clinical grounds is often inaccurate.[4,5] As a result, inappropriate administration of antibiotics to large numbers of patients with non-streptococcal pharyngitis are not uncommonly seen.[6-8] In addition to unnecessary exposure of patients to the adverse effects and costs of antibiotics, inappropriate prescription of antibiotics has been an important attributing factor to the emergence of antimicrobial resistance among common bacterial pathogens.[8,9]

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Methodology

A panel of 6 multidisciplinary experts in the management of streptococcal pharyngitis in children was convened in 2010. The panel consisted of paediatric infectious disease specialist, paediatric respirology specialist, and general paediatricians in both public hospitals and private sector. The group convened face-to-face meetings in which an outline of the guideline and the process of development of the guideline were discussed. This was followed by a series of telecommunications in which a list of clinical questions to be addressed in the guideline was generated, discussed, and prioritised. We identified up-to-date valid systematic reviews from the MEDLINE database, PubMed, and the Cochrane Library. Unless specified otherwise, the search period was 1980-2014 and was restricted to the English-language literature. Articles were also retrieved by searches for clinical diagnosis, laboratory diagnosis, symptoms and signs, and microbiology. The panel members contributed reference lists in these areas. Primary key search terms included as follows pharyngitis, streptococcus, throat culture, rapid streptococcal tests, and pharyngeal carriers. All members of the Panel participated in the preparation and review of the draft guideline. Feedback was obtained from external peer reviews. The guideline was reviewed and approved by the Paediatric Practice Guidelines Committee of the Hong Kong College of Paediatricians prior to dissemination.

I. Diagnosis of Group A Streptococcal Pharyngitis

Indications for GAS Testing

Acute pharyngitis is most commonly caused by viruses (Table 1).[1] Among all other bacterial pathogens causing acute pharyngitis, GAS is the only common bacterial cause for which antibiotic therapy is definitely indicated. In order to appropriately prescribe antibiotic therapy, it is important for clinicians to rule out the possibility of GAS pharyngitis. Although acute GAS pharyngitis has certain characteristic clinical and epidemiological features (Table 2), there is

Table 1 Microbial aetiology of acute pharyngitis

	Organisms	Clinical syndrome(s)
Bacteria	Group A streptococcus	Pharyngotonsillitis, scarlet fever
	Group C & G streptococcus	Pharyngotonsillitis
	Arcanobacterium haemolyticum	Scarlatiniform rash, pharyngitis
	Neisseria gonorrhoeae	Tonsillopharyngitis
	Corynebacterium diphtheria	Diphtheria
	Mixed anaerobes	Vincent's angina
	Fusobacterium necrophorum	Lemierre's syndrome, peritonsillar abscess
	Francisella tularensis	Tularemia (oropharyngeal)
	Yersinia pestis	Plague
	Yersinia enterocolitica	Enterocolitis, pharyngitis
	Mycoplasma pneumoniae	Pneumonitis, bronchitis
	Chlamydophila pneumoniae	Bronchitis, pneumonia
	Chlamydophila psittaci	Psittacosis
Viral	Adenovirus	Pharyngoconjunctival fever
	Herpes simplex virus 1 & 2	Gingivostomatitis
	Coxsackievirus	Herpangina
	Rhinovirus	Common cold
	Coronavirus	Common cold
	Influenza A & B	Influenza
	Parainfluenza	Cold, croup
	EBV	Infectious mononucleosis
	Cytomegalovirus	CMV mononucleosis
	HIV	Primary acute HIV Infection

Abbreviations: CMV, cytomegalovirus; EBV, Epstein-Barr virus; HIV, human immunodeficiency virus.

often broad overlap between the symptoms and signs of GAS and non-streptococcal pharyngitis.[1,4] Various scoring systems, such as the modified Centor or McIsaac scores, have been used to predict the probability of GAS pharyngitis based on clinical features.[10-13] However, these scoring systems generally have a relatively lower positive predictive values, with only about 35-50% confirmed GAS pharyngitis even in patients with all typical clinical features in a particular scoring system.[11,14] The use of clinical signs and symptoms is not for diagnosis, but to select those necessary for GAS laboratory testing. On the other hand, studies have shown that the prevalence of GAS pharyngitis is significantly lower for children under 3 years of age (10-14%), compared to school-age children (37%).[15,16] A local study at an accident and emergency department in Hong Kong reported that none of the children aged <3 years had GAS pharyngitis in their study cohort.[2] Furthermore, studies have reported only a very rare occurrence of acute rheumatic fever complicating acute pharyngitis in children aged below 3 years.[17-23]

An additional consideration for GAS testing would lie on history of household contacts. A high rate of secondary streptococcal infections as high as 25% from symptomatic index case among household contacts has been reported in previous studies.[3,24] During an outbreak, up to one-third of persons in a semi-closed community could become infected and develop symptomatic pharyngitis.[25-27] Therefore, it is recommend for symptomatic children in day care or institution setting to have GAS testing. However, routine testing or treatment of asymptomatic household contacts of patients with GAS pharyngitis is not generally indicated.

In summary, acute onset of sore throat in children with signs and symptoms suggestive of bacterial cause (Table 2), age greater than 3 years or with known GAS contact is recommended to have GAS laboratory testing, such as throat culture or rapid antigen detection test (RADT) (Figure 1).[1,23] Otherwise, no further investigation or treatment is indicated.

Laboratory Tests

a) Throat Culture

Culture of a throat swab offers a sensitivity of 90-95%, and is the gold standard for the confirmation of GAS pharyngitis.[1,28,29] Specimens for throat swab should be collected from the surface of the tonsils and the posterior pharyngeal wall.[29-32] A culture should be incubated at 35-37°C for 18-24 hours before reading of the result.[33] One should note that prior antibiotic treatment shortly before the collection of the throat swab may result in false-negative results. The turnaround time of throat culture is around 2-3 days.

b) Rapid Antigen Detection Tests

A major disadvantage of throat cultures is the long turnaround time (around 2-3 days for positive growth). Rapid antigen detection tests (RADTs) directly from throat swabs have been developed with a shorter turnaround time.[30,34,35] With a specificity of around 95%, one can be reasonably certain about the diagnosis of GAS with a positive RADT result, and subsequent antibiotic therapy can be commenced without a follow-up throat culture.[34-36] The sensitivity of RADTs is 70%-90%. Hence, a negative RADT warrants a follow-up throat culture before GAS can be confidently excluded.[34,35] However, RADT is not routinely available in Hospital Authority hospitals.

c) Anti-streptococcal Antibody Titers

Measurement of anti-streptococcal antibody titers, such as antistreptolysin O (ASO) and anti-DNase B, can help the diagnosis of the nonsuppurative sequelae of GAS pharyngitis, such as acute rheumatic fever and acute glomerulonephritis.[37] However, antibody titers may not reach maximum levels until 3-8 weeks after acute GAS infection and may remain elevated for months even without active GAS infection.[14,38] Therefore, such testing is not recommended in the diagnosis of acute GAS pharyngitis.

Table 2 Epidemiologic and clinical features suggestive of group A streptococcal and viral pharyngitis feature, by suspected aetiologic agent

Grooup A streptococcal	Viral
• Sudden onset of sore throat	• Conjunctivitis
• Age 3-14 years	• Coryza
• Fever	• Cough
• Headache	• Diarrhoea
• Nausea, vomiting, abdominal pain	• Hoarseness
• Tonsillopharyngeal inflammation	• Discrete ulcerative stomatitis
• Patchy tonsillopharyngeal exudates	• Viral exanthema
• Palatal petechiae	
• Anterior cervical adenitis (tender nodes)	
• Winter and early spring presentation	
• History of exposure to GAS pharyngitis	
• Scarlatiniform rash	

II. Treatment for GAS Pharyngitis

Antibiotic Therapy

While early antibiotic therapy hastens clinical recovery and decreases spread of GAS to other children, the predominant rationale for antibiotic treatment of this self-limited illness is to prevent both non-suppurative complications (e.g. acute rheumatic fever), and suppurative complications (e.g. peritonsillar abscess, acute otitis media, and acute sinusitis).[39-42] Table 3 shows the list of recommended antibiotics effective in treating GAS pharyngitis. Penicillin remains the treatment of choice because of its proven efficacy and safety, its narrow spectrum and its low cost.[43-46] Penicillin-resistant GAS has never been documented. Alternative oral therapy with amoxicillin is often used in place of penicillin V for young children with a similar efficacy. Studies have demonstrated that once-daily amoxicillin (50 mg/kg, to a maximum of

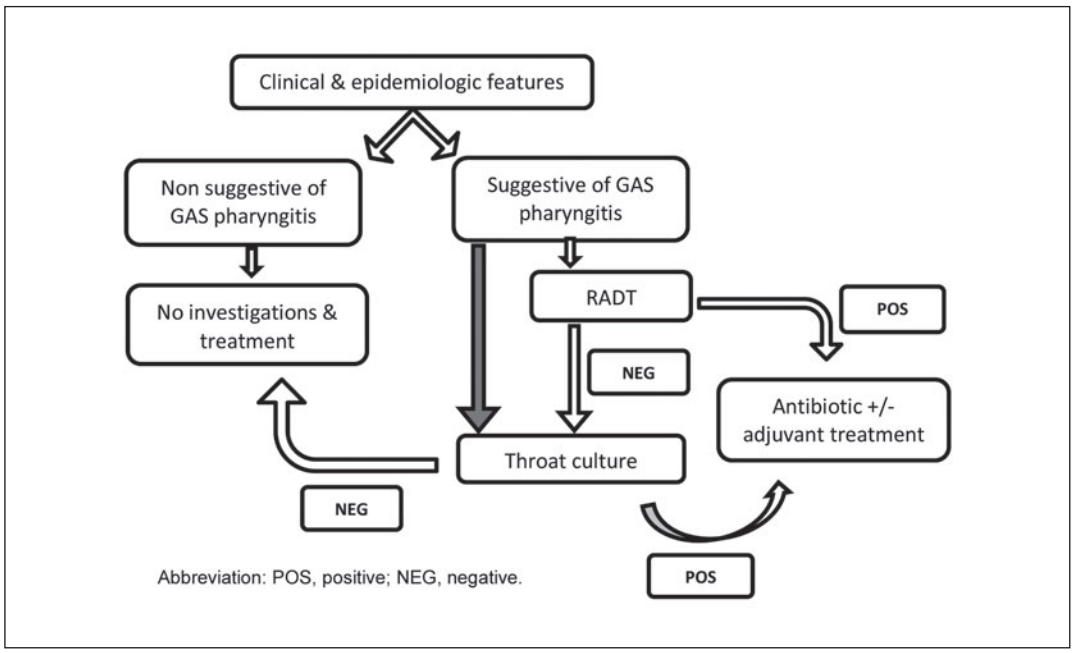

Figure 1 Recommended flow chart for management of acute pharyngitis in children.

Table 3 Antibiotic regimens recommended for group A streptococcal pharyngitis

Patient	Drug, Route	Dosage	Duration/Quantity
For individuals without penicillin allergy	Penicillin V, oral	Children: 250 mg twice daily or 3 times daily Adolescents: 250 mg 4 times daily or 500 mg twice daily	10 days
	Amoxicillin, oral	50 mg/kg once daily (max = 1000 mg) or 25 mg/kg (max = 500 mg) twice daily	10 days
	Benzathine penicillin G, intramuscular	<27 kg: 600,000 U ≥27 kg: 1,200,000 U	1 dose
For individuals with penicillin allergy	Cephalexin*, oral	20 mg/kg/dose twice daily(max = 500 mg/dose)	10 days
	Cefadroxil*, oral	30 mg/kg once daily (max = 1 g)	10 days
	Azithromycin#, oral	12 mg/kg once daily (max = 500 mg)	5 days

Abbreviation: Max, maximum.

*Avoid in individuals with immediate type hypersensitivity to penicillin.

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

1000 mg) for 10 days is effective for GAS pharyngitis.[47-51] Amoxicillin has the advantage of once-daily dosing, which may enhance adherence, and is relatively inexpensive and palatable. In order to achieve maximal rates of pharyngeal eradication of GAS, most oral antibiotics are recommended for a conventional 10-day course. For most penicillin-allergic individuals (after allergic history being ascertained), an oral narrow-spectrum cephalosporin, such as cephalexin, is recommended. For those who are also allergic to cephalosporins (up to 10%), or immediate anaphylactic-type hypersensitivity to penicillin, cephalosporins should be avoided.[52] Azithromycin for 5 days can be a reasonable alternative.[53] A follow-up appointment can be arranged to watch out for any treatment failure.

Adjunctive Therapy

Multiple studies support the benefits of acetaminophen or NSAIDs such as ibuprofen in reducing fever and pain relative to placebo among children with non-GAS pharyngitis.[54-57] Due to the risk of Reye syndrome, aspirin for pain relief is not recommended.

III. Chronic Pharyngeal Carrier of GAS

Chronic pharyngeal carriers have GAS present in the pharynx for ≥6 months but there is absence of active immunologic response to the organism.[38,58] As many as 20% of asymptomatic schoolchildren may be GAS carriers

Table 4 Treatment regimens for chronic carriers of Group A Streptococci

Drug, Route	Dosage	Duration/Quantity
Clindamycin, oral	20-30 mg/kg/d in 3 doses (max = 300 mg/dose)	10 d
Penicillin and rifampicin, oral	Penicillin V: 50 mg/kg/d in 4 doses x 10 d (max = 2000 mg/d); rifampicin: 20 mg/kg/d in 1 dose x last 4 d of treatment (max = 600 mg/d)	10 d
Amoxicillin-clavulanic acid, oral	40 mg amoxicillin/kg/d in 3 doses (max = 2000 mg amoxicillin/d)	10 d
Benzathine penicillin G (intramuscular) plus rifampicin (oral)	Benzathine penicillin G: 600,000 U for <27 kg and 1,200,000 U for ≥27 kg; rifampicin: 20 mg/kg/d in 2 doses (max = 600 mg/d)	Benzathine penicillin G:1 dose; rifampicin: 4 d

Abbreviation: Max, maximum.

Table 5 Summary of recommendations

Diagnostic testing	• GAS testing is not recommended in children with: – clinical/epidemiological features suggestive of viral aetiology – age <3 years old (unless with other risk factors) – asymptomatic household contacts of patients with GAS pharyngitis • Throat culture or rapid antigen detection test (RADT) should be performed if clinical and epidemiological features strongly suggest GAS. – Positive throat culture or RADTs warrant treatment. – Negative RADTs should be backed up by a throat culture. • Anti-streptococcal antibody titers are not recommended.
Antibiotic treatment	• Penicillin or amoxicillin for 10 days is the recommended for non-allergic patients. • For penicillin-allergic individuals, we recommend: – first generation cephalosporin (if not anaphylactically sensitive) or azithromycin for 5 days
Adjunctive treatment	• Analgesic/antipyretic agent such as acetaminophen or an NSAID should be considered • Aspirin is not recommended.
GAS carriers	• GAS carriers do not ordinarily justify efforts to identify them nor do they generally require antibiotic treatment.

during winter and spring. Chronic pharyngeal GAS carriers may experience episodes of intercurrent viral pharyngitis.[59,60] Repeated positive GAS testing results of such patients often cannot be distinguished from those with recurrent GAS infections. It appears that carriers are unlikely to spread the organism to their close contacts. They are also at very low risk, if any, for developing complications such as acute rheumatic fever.[38,58,61] Chronic pharyngeal GAS carriers are therefore not recommended for further antibiotic therapy. One may consider antibiotic therapy in GAS carriers under special situations, including community outbreak of acute rheumatic fever or post-streptococcal glomerulonephritis, GAS pharyngitis outbreak in a closed or partially closed community, or family/personal history of acute rheumatic fever. To eliminate chronic GAS carriage, several antibiotic schedules are recommended which are more effective than penicillin or amoxicillin (Table 4).

In conclusion, acute pharyngitis is commonly seen in children, and is most commonly caused by viral infection. Among all other bacterial cause of acute pharyngitis, GAS is the only common bacterial cause for which antibiotic therapy is definitely indicated. With the weak differentiating power of clinical features between GAS and non-streptococcal cause, clinicians are encouraged to perform either throat culture or RADT for GAS confirmation before initiating appropriate antibiotic therapy if doubt exists (Table 5).

Declaration of Interest

None.

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