

Antibiotic management of acute pharyngitis in primary care

The Advisory Group on Antibiotic Stewardship Programme in Primary Care

ABSTRACT

The Centre for Health Protection of the Department of Health has convened the Advisory Group on Antibiotic Stewardship Programme in Primary Care (the Advisory Group) to formulate guidance notes and strategies for optimising judicious use of antibiotics and enhancing the Antibiotic Stewardship Programme in Primary Care. Acute pharyngitis is one of the most common conditions among out-patients in primary care in Hong Kong. Practical recommendations on the diagnosis and antibiotic treatment of acute streptococcal pharyngitis are made by the Advisory Group based on the best

available clinical evidence, local prevalence of pathogens and associated antibiotic susceptibility profiles, and common local practice.

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The Advisory Group on Antibiotic Stewardship Programme in Primary Care

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Introduction

The Government of the Hong Kong Special Administrative Region attaches great importance to the threat of antimicrobial resistance. Under the authority of the Food and Health Bureau, and with collaborative efforts from stakeholders, the Hong Kong Strategy and Action Plan on Antimicrobial Resistance (2017–2022) was established in July 2017. Recommendations in six key areas and 19 objectives were included in this Action Plan, aiming to slow the emergence of antimicrobial resistance and prevent its spread.

In connection with this Action Plan, the Centre for Health Protection of the Department of Health convened the Advisory Group on Antibiotic Stewardship Programme in Primary Care (the Advisory Group) comprising key stakeholders in the public and private sectors, academia, and major professional societies. Its objective is to formulate guidance notes and strategies for optimising the judicious use of antibiotics and enhancing the Antibiotic Stewardship Programme in Primary Care (<https://www.chp.gov.hk/en/features/49811.html>). Guidance notes on antibiotic treatments for common infections seen by primary care doctors have been developed based on the best available clinical evidence, local prevalence of pathogens and associated antibiotic susceptibility profiles, and local practice. Clinical evidence has mainly referred to international practices, the latest guidelines from international organisations, and systematic review articles. In addition, simple information sheets for out-patients are prepared to raise awareness and enable them to use antibiotics appropriately. Primary care doctors play an important role in

antimicrobial resistance containment measures by not only practising rational antibiotic prescriptions but also educating and engaging out-patients about the safe use of antibiotics during clinical encounters.

Acute pharyngitis is the acute inflammation of the oropharynx. It is characterised by sore throat and pharyngeal erythema. It is one of the most common conditions among out-patients in primary care in Hong Kong.^{1,2}

Acute pharyngitis is usually a benign, self-limiting illness with an average length of illness of 1 week. It is often caused by respiratory viruses (eg, rhinovirus, coronavirus, adenovirus, influenza virus, parainfluenza virus, respiratory syncytial virus and metapneumovirus). The other viruses of concern are enterovirus, herpes simplex virus, Epstein-Barr virus, cytomegalovirus, and human immunodeficiency virus (HIV). Viral pharyngitis is a condition for which antibiotics are not necessary. Out-patients with a sore throat and associated symptoms and signs, including conjunctivitis, coryza, cough, discrete ulcerative stomatitis, hoarseness, diarrhoea, and viral exanthema, are most likely to have a viral illness, such as common cold, influenza, herpangina, and oral herpes.

Beta-haemolytic streptococci, particularly group A *Streptococcus* (GAS), are the most common bacterial pathogens of acute pharyngitis. Group A *Streptococcus* is estimated to be responsible for approximately 10% of cases of acute pharyngitis in adults and 15% to 30% of those in children.³ A local study at an accident and emergency department in Hong Kong showed that for those presenting with a sore throat and without symptoms of common cold or influenza, the prevalence rates of GAS pharyngitis

were 2.65% in adults and adolescents aged >14 years and 38.6% in children aged 3 to 14 years; none of the children aged <3 years had GAS pharyngitis.⁴ Group A *Streptococcus* pharyngitis can lead to suppurative (eg, quinsy, otitis media, and other invasive infections) and non-suppurative (eg, acute rheumatic fever, poststreptococcal glomerulonephritis) complications. However, acute rheumatic fever has not been described as a complication of either group C *Streptococcus* or group G *Streptococcus* pharyngitis. Streptococcal pharyngitis is the most common form of acute pharyngitis, in which antibiotic treatment is indicated.

Diagnosis of acute streptococcal pharyngitis

There are different recommendations on the diagnostic strategy of acute streptococcal pharyngitis. Ideally, to obtain a definitive diagnosis, out-patients with symptoms and signs suggestive of a bacterial cause (eg, sudden onset of fever, anterior cervical lymphadenopathy, tonsillopharyngeal exudates) should be tested for GAS with a rapid antigen detection test (RADT) and/or throat culture.⁵⁻⁸ A negative RADT should be backed up by a throat culture in children and adolescents, but not in adults. Practically and clinically, different various clinical scoring criteria have been developed to estimate the likelihood of acute streptococcal pharyngitis, and we recommend that practitioners make clinical decisions about laboratory testing and/or antibiotic prescribing.⁹⁻¹¹ The FeverPAIN score was developed in the primary care setting in the United Kingdom in 2013.¹² The Centor criteria were developed in the emergency department setting in the United States in 1981; the modified Centor criteria add age to the original Centor criteria.^{13,14} The FeverPAIN score criteria are Fever (during the previous 24 hours), Purulence (pus on tonsils), Attend rapidly (within 3 days after onset of symptoms), severely Inflamed tonsils, and No cough or coryza; each of the criteria is worth 1 point (maximum score of 5). A score of 0 or 1 is associated with a 13% to 18% likelihood of isolating *Streptococcus*. A score of 2 or 3 is associated with a 34% to 40% likelihood of isolating *Streptococcus*. A score of 4 or 5 is associated with a 62% to 65% likelihood of isolating *Streptococcus*. In contrast, the modified Centor criteria are age 3 to 14 years, history of fever (over 38°C), absence of cough, exudate or swelling on tonsils, and tender/swollen anterior cervical lymph nodes; each of the criteria is worth 1 point (maximum score of 5); note that 0 points are assigned for age 15 to 44 years, whereas -1 point is given for age ≥45 years. A score of -1, 0 or 1 is associated with a 1% to 10% likelihood of isolating *Streptococcus*. A score of 2 or 3 is associated with an 11% to 35% likelihood of isolating *Streptococcus*. A score of 4 or 5 is associated with a 51% to 53%

急性咽喉炎在基層醫療的抗生素治療

基層醫療抗生素導向計劃諮詢小組

衛生署衛生防護中心已召開基層醫療抗生素導向計劃諮詢小組，以製訂優化合理使用抗生素及提升基層醫療抗生素導向計劃執行的指引和策略。急性咽喉炎是香港基層醫療門診患者中最常見的病症之一。諮詢小組根據現有最佳的臨床證據、本地病原體流行情況和相關的藥敏測試結果以及本地常見做法，對急性鏈球菌性咽喉炎的診斷和抗生素治療提出實用建議。

likelihood of isolating *Streptococcus*. There is currently uncertainty about which clinical scoring tool is more effective.

Based on the clinical experience that RADT is not commonly available, and throat culture is time consuming, requiring a 2- to 3-day turnaround time, the Advisory Group agreed that using clinical scoring criteria is preferential to not using any laboratory tests or clinical scoring criteria, and the modified Centor criteria are more widely and easily used (Table 1).

Antibiotic treatment of acute streptococcal pharyngitis

Although the symptoms of acute streptococcal pharyngitis resolve without antibiotic treatment, there are arguments that justify antibiotic treatment for acute symptom relief, prevention of suppurative and non-suppurative complications, and reduction of communicability. A recent systematic review on antibiotics for sore throat found that the clinical benefits were modest and required treatment of many with antibiotics for one to benefit (the number of people with sore throat who must be treated to resolve the symptoms of one by day 3 was about 3.7 for those with positive throat swabs for *Streptococcus*; 6.5 for those with a negative swab, and 14.4 for those in whom no swab had been taken).¹⁵ Antibiotic treatment may shorten the duration of sore throat by 1 to 2 days. Antibiotics may prevent complications of GAS infection, including acute rheumatic fever or suppurative complications.¹⁵ Out-patients are considered no longer contagious after 24 hours of antibiotic treatment. However, little evidence supports the prevention of poststreptococcal glomerulonephritis by antibiotic treatment.¹⁵

Although scarlet fever occurs throughout the year, there has been a seasonal pattern in Hong Kong, with higher activity observed from May to June and from November to March in the past few years.¹⁶ Scarlet fever is a bacterial infection caused by GAS, and it classically presents with fever, sore throat, red and swollen tongue (known as strawberry tongue),

TABLE 1. Modified Centor score

Criteria						Score
Age range (Group A Streptococcus pharyngitis is rare under 3), years						
3-14						+1
15-44						0
≥45						-1
Fever (temperature >38°C/100.4°F)						
No						0
Yes						+1
Cough						
Present						0
Absent						+1
Exudate or swelling on tonsils						
No						0
Yes						+1
Tender/swollen anterior cervical lymph nodes						
No						0
Yes						+1
Total score	-1 or 0	1	2	3	4 or 5	
Likelihood of acute streptococcal pharyngitis (%)	1-2.5	5-10	11-17	28-35	51-53	

and erythematous rash with a sandpaper texture. It is mainly a clinical diagnosis and can be treated by appropriate antibiotics effectively.

After considering the benefits and risks (eg, allergies and side-effects) of antibiotic treatment, the Advisory Group agreed that antibiotic treatment is indicated for out-patients presenting with a sore throat and a modified Centor score of 4 or 5 and for out-patients with positive laboratory results or certain special reasons (eg, clinical scarlet fever, household contact with scarlet fever, or known rheumatic heart disease) [Table 2].

Oral penicillin V or amoxicillin are the recommended antibiotics of choice for out-patients who are not allergic to these agents. Resistance of GAS to penicillins and other beta-lactams has not been reported.¹⁷ First-generation cephalosporins (eg, oral cephalexin) are the first-line agents for out-patients with penicillin allergies who are not anaphylactically allergic. Other cephalosporins (eg, oral cefaclor, cefuroxime) are alternatives, but they are not favoured as the first-line agents because of their broad spectrum of activity. Resistance of GAS to macrolides (eg, oral azithromycin, clarithromycin, erythromycin) is known to be common in Hong Kong. Erythromycin-resistant isolates of GAS are regarded as resistant to clarithromycin and azithromycin as well.¹⁷ According to data from the Microbiology Division of the Public Health Laboratory Services Branch of the Centre for Health

Protection, which undertakes bacterial isolation and antibiotic susceptibility testing in public and private out-patient settings in Hong Kong, the erythromycin resistance rates of beta-haemolytic streptococci (in which GAS contributed to majority of them) in throat swab specimens has risen to 59.1% in the last few years.¹⁸ Studies have shown that the erythromycin resistance rates of GAS isolates were 4% in the United States, 3.2% in France, 32.8% in Spain, and 65% in Taiwan.¹⁹⁻²² Respiratory fluoroquinolones (eg, oral levofloxacin) are active against GAS, but they have an unnecessarily broad spectrum of activity and are not recommended for routine treatment of acute streptococcal pharyngitis.⁶ Excessive use of respiratory fluoroquinolones may lead to delay in the diagnosis of tuberculosis and increased fluoroquinolone resistance among *Mycobacterium tuberculosis* in Hong Kong.²³ Trimethoprim-sulfamethoxazole should not be used because it does not eradicate GAS from out-patients with acute pharyngitis.⁶

After considering the basic principle that narrow-spectrum antibiotics should be used as the first-line agents to treat an infection that is not life-threatening, the Advisory Group agreed that oral penicillin V, amoxicillin or cephalexin are the first-line agents to treat acute streptococcal pharyngitis (Table 2). Treatment with oral macrolides or respiratory fluoroquinolones requires sound justifications, including documented history of beta-

TABLE 2. Recommended antibiotic treatment of acute streptococcal pharyngitis*

Drug (route)	Dosage and frequency, adult (usual)	Dosage and frequency, children (usual)	Duration (usual)	Remarks
First line				
Penicillin V (oral)	500 mg 2 to 4 times daily	If ≤27 kg: 250 mg 2 to 3 times daily If >27 kg: 500 mg 2 to 4 times daily	5-7 days†	
Amoxicillin (oral)	1000 mg once daily or 500 mg 2 to 3 times daily	50 mg/kg (maximum = 1000 mg) once daily or 25 mg/kg (maximum = 500 mg) 2 to 3 times daily	5-7 days†	
Cephalexin (oral)	500 mg 2 to 4 times daily	20 mg/kg (maximum = 500 mg) 2 to 4 times daily	5-7 days†	• Cephalosporins should be avoided in individuals with immediate (anaphylactic) type hypersensitivity to penicillin
Second line				
Clarithromycin (oral)	250 mg twice daily	7.5 mg/kg (maximum = 250 mg) twice daily	5 days†	• For individuals with penicillin allergy • Erythromycin-resistant isolates are regarded as resistant to clarithromycin and azithromycin as well
Azithromycin (oral)	500 mg once daily	12 mg/kg (maximum = 500 mg) once daily	3 days†	• For individuals with penicillin allergy • Erythromycin-resistant isolates are regarded as resistant to clarithromycin and azithromycin as well

* Primary care doctors should tailor antibiotic treatment to their clinical judgement. Definitive therapy should be based on microbiological and antibiotic susceptibility results, if available

† For out-patients presenting with a sore throat and a modified Centor score of 4 or 5, a short course of oral antibiotic treatment is recommended. However, for out-patients with positive laboratory results for group A *Streptococcus* or certain special reasons (eg, clinical scarlet fever; household contact with scarlet fever; or known rheumatic heart disease), a 10-day course of oral penicillin V, amoxicillin, cephalexin or clarithromycin, or a 5-day course of oral azithromycin is recommended to achieve maximal eradication of group A *Streptococcus* from the pharynx for primary prevention of acute rheumatic fever

lactam allergy or intolerance, positive throat culture results, and associated antibiotic susceptibility profiles.

A 10-day course of oral penicillin V, amoxicillin, cephalexin or clarithromycin, or a 5-day course of oral azithromycin is recommended by the Infectious Diseases Society of America, the American College of Physicians, and the American Academy of Pediatrics to achieve maximal eradication of GAS from the pharynx for primary prevention of acute rheumatic fever.⁶⁻⁸ However, a recent systematic review comparing a 3- to 6-day course of oral antibiotics (primarily cephalosporins) with a conventional 10-day course of oral penicillin found similar effectiveness in children, but no conclusions could be drawn on the complication rates of acute rheumatic fever and poststreptococcal glomerulonephritis.²⁴ Furthermore, a 5-day course of antibiotic treatment is sufficient to mitigate the clinical course of group C *Streptococcus* and group G *Streptococcus* pharyngitis, as acute rheumatic fever is not a complication of infections due to these organisms.⁸

Based on the clinical experience that the prevalence of acute rheumatic fever is very low in Hong Kong nowadays, the Advisory Group agreed that a 5- to 7-day course of oral penicillin V,

amoxicillin or cephalexin, or a 5-day course of oral clarithromycin, or a 3-day course of oral azithromycin is sufficient to treat out-patients presenting with a sore throat and a modified Centor score of 4 or 5. However, for out-patients with positive laboratory results for GAS or certain special reasons (eg, clinical scarlet fever; household contact with scarlet fever; or known rheumatic heart disease), a 10-day course of oral penicillin V, amoxicillin, cephalexin or clarithromycin, or a 5-day course of oral azithromycin is recommended to achieve maximal eradication of GAS from the pharynx for primary prevention of acute rheumatic fever (Table 2).

Other issues

Alternative diagnosis should be considered for out-patients who present with unusually severe signs and symptoms, such as difficulty swallowing, drooling, neck tenderness or swelling, or systemic unwellness. They should be evaluated for potentially dangerous infections (eg, peritonsillar abscess, retro-/para-pharyngeal abscess, acute epiglottitis and systemic infections). Out-patients who do not improve within 5 to 7 days or who have worsening symptoms should be evaluated for a previously unsuspected diagnosis (eg, infectious mononucleosis, primary

HIV infection, or gonococcal pharyngitis). Infectious mononucleosis is a clinical syndrome characterised by fever, severe pharyngitis (which lasts longer than GAS pharyngitis), cervical or diffuse lymphadenopathy, and prominent constitutional symptoms. Out-patients who have infectious mononucleosis and are treated with amoxicillin may develop a generalised, erythematous, maculopapular rash, and this should not be regarded as a penicillin allergy. A properly taken sexual history may hint at possibility of sexually transmitted infections like HIV and gonorrhoea.

Management of out-patients with infections should be individualised. Primary care doctors should check, document, and inform out-patients well about antibiotic treatment (eg, indications, side-effects, allergies, contra-indications, potential drug-drug interactions). Out-patients should take antibiotics exactly as prescribed by their doctors. If their symptoms change, persist, or get worse, they should seek medical advice promptly.

Primary care doctors are invited to show their commitment on judicious use of antibiotics by visiting the “I Pledge” website (<https://www.chp.gov.hk/en/static/100755.html>) and signing a certificate on pledging to use antibiotics responsibly. Furthermore, this invitation is open to general public. Primary care doctors can engage their out-patients on “I Pledge” during clinical encounters to facilitate shared decision making on antibiotic prescribing.

Conclusion

Acute pharyngitis is one of the most common conditions among out-patients in primary care in Hong Kong. Practical recommendations on the diagnosis and antibiotic treatment of acute streptococcal pharyngitis are made in consultation with key stakeholders in primary care settings such that the recommendations can be tailored to their needs. The recommendations are under regular review, in consideration of the latest research, together with local prevalence of pathogens and associated antibiotics susceptibility profiles, and common local practice.

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Author contributions

All authors have made substantial contributions to the viewpoints of this study, literature review, and critical revision for important intellectual content. ETK Lam was responsible for literature search and drafting of the manuscript. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As editors of this journal, DVK Chao and MCS Wong were not involved in the peer review process of this article. All other authors have no conflicts of interest to disclose.

Declaration

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