



Clinical Pearls

- Pharyngitis is usually self-limiting (4-5d; up to ≤10d); **most cases do NOT require antibiotics as they are viral infections** (80-90% in adults, >70% in children).
- Scoring systems e.g. **modified Centor score**, **FeverPAIN** can help identify low risk patients who do not require diagnostic testing or antibiotics.
- For confirmed Group A Streptococcus (**GAS**) **pharyngitis, penicillin x10d (started within 9 days of symptom onset) is 1st line**. There is no documented GAS resistance to penicillin. Consider stewardship strategies e.g. delayed antibiotic pending throat swab results.
- Advise on treatments for **symptomatic relief**: e.g. NSAIDs, acetaminophen, lozenges, topical anesthetics, warm liquids, saltwater gargle.
- Patients should **see their prescriber if**: ① symptoms worsen, ② symptoms take longer than 4 to 5 days to resolve, &/or ③ unilateral neck swelling, shortness of breath or severe dysphagia develops (r/o abscess).

Overview

- Etiology: **viral 80-90% of adults (>70% of children)**; therefore, the majority do **NOT** require antibiotics; minority bacterial Group A Streptococcus (GAS); rarely other bacteria (e.g. Chlamydia, *F. necrophorum*) or fungal. GAS pharyngitis most common in kids 5-11 years and in winter/spring.^{CPS}
- Scoring systems e.g. **modified Centor score** (94% sensitivity; 54% specificity) can help with clinical assessment. **Exception**: modified Centor score may not accurately predict risk during epidemics or in groups at high-risk for acute rheumatic fever / complications e.g. remote Indigenous communities, history of acute rheumatic fever, valvular heart disease, immunosuppression. Use clinical judgment & consider testing (RADT/throat swab) more broadly.
- Diagnostics (**POCT: RADT, NAAT, throat swab**) ± antibiotics **not** recommended if: ① Modified Centor ≤1 (Table 1). ② **symptoms of viral infection** e.g. rhinorrhea, cough, oral ulcers, hoarseness.^{IDSA*12 (strong, high)} ③ **<3 years**, unless risk factors present e.g. sibling with GAS, outbreak.^{IDSA*12 (strong, moderate), CPS} ④ asymptomatic household contacts of patient with GAS pharyngitis.^{IDSA*12 (strong, moderate)}
- Positive POCT confirms diagnosis (specificity 95-99%).^{Craig*20} Varying practise if negative POCT: (throat swab ↑sensitivity) - **negative RADT** → throat swab suggested in **kids** (e.g. 5-15 years^{IDSA}), Mums, Sanfords & ARF high-risk groups.^{CPS} - **negative NAAT** → throat swab not required^{medSask} (NAAT ↑sensitivity vs RADT). Negative RADT acceptable in adults.
- GAS pharyngitis is often self-limiting; however, antibiotics recommended to ↓ complications, including:**
 - Suppurative complications** e.g. peritonsillar abscess (quinsy), sinusitis, otitis media, lymphadenitis, mastoiditis.
 - Non-suppurative complications** e.g. acute rheumatic fever, rare in Canada (0.3 cases per 100,000 children/year)^{Templeton*07} but higher in resource-poor settings (e.g. lower socioeconomic status, household crowding, limited access to health). Antibiotic ↓ acute rheumatic fever (RR ~70%, ARR 1%), but studies outdated & not reflective of current Canadian incidence.^{Spinks*21}

Table 1. Modified Centor (or McIsaac) Score

Criteria		Points
Temp >38°C (>100.5 °F) oral temp		1
Absence of cough		1
Swollen, tender anterior cervical nodes		1
Tonsillar swelling or exudate		1
Age 3 years to 14 years		1
Age 15 to 44 years		0
Age ≥45 years		-1
Score	Risk of GAS	Suggested Management
-1 to 0	1 - 2.5%	Symptomatic tx. No POCT, throat swab, or antibiotic*
1	5 - 10%	
2	11 - 17%	POCT or throat swab. If GAS positive ⇒ antibiotic. <i>Using a cutoff of 3 is recommended by some to ↓ false positives.^{Expert}</i>
3	28 - 35%	
4+	51 - 53%	

*See exceptions in Overview section

An Approach to Treatment


- Most cases do **NOT** require antibiotics due to viral etiology. Advise on symptomatic management (see Table 2).
- Strategies**: watchful waiting (e.g. 4-5d), delayed ABX (await throat swab results), empiric ABX (stop if throat swab negative).
- Use validated clinical decision tool (see Table 1) to determine risk of GAS infection. If **≥2, POCT or throat swab**. Patients with a **positive throat swab should receive an antibiotic** (Table 3) to decrease risk of complications.
- The turn-around-time for throat swab results can take a few days. Antibiotics **started within 9 days of symptom onset and given for 10 days** in confirmed GAS will help prevent rheumatic fever (see )^{Casey*05, BMJ*19}

Table 2. Symptom Management

see [RxFiles OTC Products Chart](#) page 227 for more details

ANALGESICS	NSAIDs e.g. Ibuprofen ADVIL , g ▼ OTC Peds: 5-10 mg/kg po q6-8hr PRN (susp X ▼) (max 40mg/kg/day) Adults: 400mg q6-8hr PRN (\$7/50 tabs g) (max 2.4-3.2g/day)	- Reduce fever. - Ibuprofen decreased associated pain more than acetaminophen and placebo. ^{Gehanno*03} - Alternative: Naproxen , g prescription, susp & tab; on SPDP, ▼ ALEVE , g ▼ OTC : ≥12 years (\$12/100 tab g) -Peds, >2yrs: 5-7mg/kg/dose q8-12hr (max 1g/day) -Adults: 220-500mg BID (max=1-1.5g/day)
	Acetaminophen TYLENOL , g X ▼ OTC Peds: 10-15mg/kg po q4-6hr PRN (max 75 mg/kg/day) Adults: 1g q4-6hr PRN (max 4g/d) (\$8/120 tabs g)	
LOCAL AGENTS	Benzocaine CEPACOL , CHLORASEPTIC X ⊗ OTC 10mg lozenge q2hr PRN (\$6/18 lozenges) Phenol CHLORASEPTIC X ⊗ OTC 5 sprays q2hr PRN (\$15/177 mL)	- Alleviates throat pain if used frequently. ^{Chrubasik*12} - Avoid in peds: choking & methemoglobinemia risks. - Alternative: hard candy e.g. HALLS , honey (>1 year)
RINSES	Warm liquids e.g. tea, warm saltwater gargle (recipe: ¼ to ½ tsp salt per 240mL warm water) Benzzydamine , PHARIXIA , g X ⊗ ≥6 years 15mL gargle/rinse q1.5-3hr PRN (\$38/250mL)	- Little evidence, but anecdotally provide relief from associated pain/discomfort. - Rinses: gargle and expectorate, do not swallow liquid.

Systemic corticosteroids (dexamethasone 10mg adults or 0.6mg/kg pediatrics oral x 1 dose) **not recommended for symptom management**; ^{NICE*18, IDSA*12 (weak, moderate)} however, **opinions vary**. Shared decision making may be used to consider corticosteroids in select, severe cases.^{BMJ*17 (weak), eCPS}

- Oral/IM corticosteroids x1-2 doses have been shown to decrease pain vs placebo (**NNT=5**) but have **no effect on clinical course or days missed from school/work**. No difference in adverse events (but poor reporting).
- Caution**: there is concern that corticosteroids may mask possible underlying complications in children.^{Cochrane*20 (9 RCTs, n=1319), Chiappini*17}

Management of Chronic GAS Carriage and Recurrent GAS Pharyngitis: antibiotics **not** routinely recommended for chronic GAS carriers (unlikely to transmit infection, low risk for complications).^{CPS}

For high-risk patients, eradication therapy (e.g. amoxicillin-clavulanate, clindamycin) may be considered.

Abbreviations: CPS=Canadian Pediatric Society NAAT=nucleic acid amplification test POCT=point of care test RADT=rapid antigen detecting test

Table 3. GAS Drug Regimens

see [RxFiles Oral & IV Antibiotics Chart](#) page 85 for available products, price, etc.

FIRST LINE		
No antibiotic	Mostly viral. Antibiotics only in confirmed bacterial pharyngitis. ^{Choosing Wisely} See Table 2.	
Penicillin V PEN-VK , g	Peds: ≤27 kg: 300mg po BID or TID x10 days <i>No commercially available suspension</i> >27kg or Adults: 300mg TID or 600mg BID x10 days	- 1st line due to narrow spectrum, efficacy, safety & low cost. - No documented resistance to GAS . - Admin: preferred when given on an empty stomach ↑absorption.
Amoxicillin AMOXIL , g ☺	Peds: 40-50mg/kg/day ÷ BID x10 days (max 1g/day), or 50mg/kg/day daily x10 days (max 1g/day) ^{CPS} Adults: 500mg BID x10 days	- Compared to penicillin: ① broader spectrum ↑selective pressure, ② as effective, ③ liquid more palatable for peds ④ if mononucleosis, may cause skin rash.
PENICILLIN ALLERGY: NON-SEVERE (e.g. delayed >72h rash) see Beta-lactam Allergy page 90, SHA Firstline .		
Consider oral penicillin or amoxicillin direct challenge/de-labeling and patient education.		
Cephalexin KEFLEX , g	Peds: 25-50mg/kg/day ÷ BID or QID x10 days (max 1g/day) Adults: 250mg QID x10 days, or 500mg BID x10 days	- 1 st generation (cephalexin, cefadroxil) preferred over 2 nd gen (cefuroxime, cefprozil) due to narrower spectrum. - Alternatives: Cefuroxime CEFTIN , g Peds: 20mg/kg/day cc ÷ BID x10 days (max 500mg/day) Adults: 250mg BID cc x10 days Cefprozil CEFZIL , g Peds: 15mg/kg/day ÷ BID x10 days (max 500mg/day) Adults: 250mg BID x10 days
Cefadroxil DURICEF , g	Peds: 30mg/kg daily or ÷ BID x10 days (max 1g/day) <i>No commercially available suspension</i> Adults: 500mg BID x10 days, or 1000mg daily x10 days	
PENICILLIN ALLERGY: SEVERE (e.g. anaphylaxis, angioedema) see Beta-lactam Allergy page 90, SHA Firstline .		
Only use in confirmed GAS & serious reaction to penicillin, due to ↑resistance ^{SK*23 ~7% to 18%} & AE e.g. <i>C. difficile</i> .		
Clindamycin DALACIN C , g	Peds: 20-30mg/kg/day ÷ TID x10 days (max 900mg/day) Adults: 300mg TID x10 days	Macrolide considerations: - Clarithromycin x10 days superior to azithromycin x5 days for bacterial eradication (NNT=9) in adults, but equivalent for clinical cure. ^{Kaplan*01} - Azithromycin : no head-to-head trials of 3d vs 5d; both provide same total dose over course of tx (i.e. 60mg/kg; 1.5g). There is some uncertainty whether 3-5d of azithromycin is sufficient to ↓ARF risk. 101
Clarithromycin BIAXIN , g	Peds: 15mg/kg/day ÷ BID x10d (max 500mg/day) Adults: 250mg BID x10 days	
Azithromycin ZITHROMAX , g	Peds: 12mg/kg/day daily x5 days, or Adults: 500mg Day 1, 250mg x Days 2-5, or 500mg daily x3 days	

Evolving controversy: antibiotic needed in uncomplicated GAS pharyngitis as self-limiting & ↓complication rate?^{Ebel*24l}

Pharyngitis: Management Considerations

Abbreviations: ☺=tastes good **ABX**=antibiotics **ARF**=acute rheumatic fever **ARR**=absolute risk reduction **CPS**=Canadian Pediatric Society **GAS**=Group A Streptococcus **GI**=gastrointestinal **IDSA**=Infectious Diseases Society of America **NAAT**=nucleic acid amplification test **NSAID**=non-steroidal anti-inflammatory drug **NNT**=number needed to treat **OR**=odds ratio **PRN**=as needed **RADT**=rapid antigen detecting test **RCT**=randomized controlled trial **RR**=relative risk **Rx**=prescription/prescribe **SOB**=shortness of breath **tx**=therapy

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Modified Centor score: sensitivity 94% (95% CI 92-97%), specificity 54% (95% CI 49-59%). Lower specificity leans towards false positives & over-treatment.

Duration of Antibiotic Therapy:

- Confirmed bacterial pharyngitis should be treated with **10 days of antibiotics**. Exception: if azithromycin is used in penicillin allergic patients; other options available.
- Patients will likely have clinical improvement within the first few days of therapy (symptoms usually self-limiting resolving in 4-5 days), but 10 days of therapy is recommended for preventing acute rheumatic fever. However, some uncertainty exists regarding optimal duration in populations with a low burden of acute rheumatic fever.
 - meta-analysis comparing 5 vs 10 days of penicillin (2 RCTs, n=309) concluded short courses were inferior in achieving bacterial cure, OR 0.29 (CI 95% 0.13-0.63).^{Casey'05}
 - RCT (n=433) found 5d of penicillin non-inferior to 10d in achieving clinical cure.^{BMJ'19}

Treatment Evidence Summary Cochrane'21

Penicillin vs Cephalosporins vs Macrolides: penicillin remains the antibiotic of choice.

- There is no clinically relevant difference in symptom resolution between antibiotics.
- Penicillin has the most evidence for preventing complications; has a narrow spectrum; is efficacious, safe, inexpensive; & there is no documented resistance to GAS.

Clinical Q&A

What is the risk of acute rheumatic fever?

- In Canada, the current prevalence of acute rheumatic fever is 0.1 to 2 cases per 100,000.
 - Risk is higher in resource-poor settings (e.g. lower socioeconomic status, household crowding, limited access to health care).
 - Higher incidence in some remote, Canadian Indigenous communities has been documented (i.e. Northern Ontario 8.33/100,000).
 - The risk may also be higher in immigrants from endemic areas, e.g. Philippines, China.
- It is difficult to estimate the risk of acute rheumatic fever due to untreated pharyngitis:
 - acute rheumatic fever is not a reportable disease in Canada
 - the majority of studies comparing antibiotics versus placebo were conducted prior to the 1960s (higher rate of acute rheumatic fever, and in young males from the US Armed Forces)
 - bacterial versus viral etiology was often not confirmed
 - newer studies have either no documented cases or did not assess this outcome
- In an effort to balance unnecessary antibiotic use with preventing rheumatic fever:
 - use the modified Centor score to identify patients who require a throat swab/RADT
 - wait to prescribe antibiotics until the results of the throat swab are available
 - starting antibiotics within 9 days of symptom onset prevents acute rheumatic fever
 - if antibiotics are started empirically, discontinue if throat swab is negative
 - children are at a greater risk of complications (e.g. otitis media, peritonsillar abscess, rheumatic fever); may initiate antibiotics sooner
- A full 10 day course of penicillin is recommended for confirmed GAS pharyngitis.

Pharyngitis caused by *Chlamydia trachomatis*

- It is rare that Chlamydia trachomatis causes pharyngitis, but rates appear to be ↑. However, the clinical significance of pharyngeal chlamydial infections remains unclear with most infections being asymptomatic.
- A systematic review has estimated the prevalence of pharyngeal chlamydia to be 1.7% among MSM, 1.7% among women, and 1.6% among men who have sex with women.
- Risk factors include: age 15 -24 years, sexually active, engagement in oral sex.
- In Saskatchewan, *Chlamydia trachomatis* screening requires a different lab requisition.
- Treatment: doxycycline 100mg po BID x 7days, or azithromycin 1g x 1 dose.

Pharyngitis caused by *Fusobacterium necrophorum*

- F. necrophorum* may be involved in pharyngotonsillitis especially in adolescent and young adults (incidence peaks at 15-25 years of age) & it may be the second most common bacterial cause of pharyngotonsillitis after GAS.
- F. necrophorum* can lead to the potentially life threatening, invasive disease Lemierre's syndrome.

- Adolescents and young adults with pharyngotonsillitis who develop bacteremic symptoms or unilateral neck swelling should be treated empirically with penicillins or cephalosporins rather than macrolides (resistance to macrolides is common).

Management of Recurrent Pharyngitis

- Potential causes: recurrent pharyngitis due to inadequate eradication, new infection, viral infection in an asymptomatic carrier ~20% of the population are GAS carriers.
- Controversial as to whether or not asymptomatic carriers **with recurrent pharyngitis** need to be identified.
 - Identification may help avoid antibiotics in those with recurrent **viral** pharyngitis.
 - Avoid identifying asymptomatic carriers **without recurrent pharyngitis**. These individuals only need to be identified or treated if there is a family history of rheumatic fever, an outbreak of rheumatic fever, an outbreak of pharyngitis in a closed community, or repeat transmission within families. Perform swab during an asymptomatic period of patient and household members to determine carrier status. Use same dosage for treatment.
- Consider age, season, signs/symptoms to rule out viral etiology (see modified Centor score).

Acetaminophen	101
Acute Rheumatic Fever	101
ADVIL	101
Amoxicillin	101
AMOXIL	101
Antibiotic	101
Azithromycin	101
Benzocaine	101
Benzydamine	101
Beta-Lactam	101
BIAXIN	101
Cefprozil	101
CEFTIN	101
Cefuroxime	101
CEFZIL	101
Centor Score	101
CEPACOL	101
Cephalexin	101
Cephalosporin	101
CHLORASEPTIC	101
Clarithromycin	101
Clindamycin	101
DALACIN	101
Ibuprofen	101
KEFLEX	101
Macrolide	101
Penicillin	101
PEN-VK	101
PHARIXIA	101
Pharyngitis	101
Phenol	101
TYLENOL	101
ZITHROMAX	101
Cefadroxil	101
DURICEF	101

References – Pharyngitis - RxFiles.ca

Guidelines:

2021 Laura Sauve, A. Michael Forrester, Karina A Top; Canadian Paediatric Society (CPS), Infectious Diseases and Immunization Committee. Group A streptococcal (GAS) pharyngitis: A practical guide to diagnosis and treatment Paediatr Child Health 2021 26(5): 319.

2019 Sanfords

2018 NICE Sore throat (acute): antimicrobial prescribing (published January 2018). Available at: <https://www.nice.org.uk/guidance/ng84>

Aertgeerts B, Agoritsas T, Siemieniuk RAC, et al. Corticosteroids for sore throat: a clinical practice guideline. BMJ. 2017 Sep 20;358:j4090.

2023 Bugs & Drugs

2019 Anti-infective Guidelines for Community-acquired Infections. Anti-infective Review Panel.

Shulman ST, Bisno AL, Clegg HW, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis. 2012 Nov 15;55(10):1279-82.

General:

Centor RM. Expand the pharyngitis paradigm for adolescents and young adults. Ann Intern Med. 2009 Dec 1;151(11):812-5.

Cohen JF, Cohen R, Levy C, et al. Selective testing strategies for diagnosing group A streptococcal infection in children with pharyngitis: a systematic review and prospective multicentre external validation study. CMAJ. 2015 Jan 6;187(1):23-32.

Cohen JF, Pauchard JY, Hjelm N, et al. Efficacy and safety of rapid tests to guide antibiotic prescriptions for sore throat. Cochrane Database Syst Rev. 2020;6(6):CD012431

Craig R, Nickonchuk T, Korownyk C. Point-of-care testing for group A streptococcal pharyngitis. Canadian Family Physician. 2020 Jan 1;66(1):41.

Dooling KL, Shapiro DJ, Van Beneden C, et al. Overprescribing and inappropriate antibiotic selection for children with pharyngitis in the United States, 1997-2010. JAMA Pediatr. 2014 Nov;168(11):1073-4.

Ebell MH. Diagnosis of streptococcal pharyngitis. Am Fam Physician. 2014 Jun 15;89(12):976-7.

eCPS. William Ciccotelli. Group A Streptococcal Pharyngitis.

Fine AM, Nizet V, Mandl KD. Large-scale validation of the Centor and Mclsaac scores to predict group A streptococcal pharyngitis. Arch Intern Med. 2012 Jun 11;172(11):847-52.

Hamilton JL, McCrea Li L. Streptococcal Pharyngitis: Rapid Evidence Review. Am Fam Physician. 2024 Apr;109(4):343-349.

Hocking JS, Geisler WM, Kong FYS. Update on the Epidemiology, Screening, and Management of Chlamydia trachomatis Infection. Infectious Disease Clinics of North America. 2023. 37(2): 267-288.

Holm K, Bank S, Nilsen H, et al. The role of *Fusobacterium necrophorum* in pharyngotonsillitis - A review. Anaerobe. 2016; 42: 89-97.

Kalra MG, Higgins KE, Perez ED. Common Questions About Streptococcal Pharyngitis. Am Fam Physician. 2016 Jul 1;94(1):24-31. Diagnosis of Streptococcal Pharyngitis MARK H. EBELL, MD, MS, University of Georgia, Athens, Georgia.

Kocielek LK, Shulman ST. In the clinic. Pharyngitis. Ann Intern Med. 2012 Sep 4;157(5):ITC3-1- ITC3-16.

Morgan M, Shaw S, Ali T, Hodges Y. Group A beta-haemolytic streptococcal infection in children. BMJ. 2024 Apr 2;385:e077561.

Norton LE, Lee BR, Harte L, et al. Improving Guideline-Based Streptococcal Pharyngitis Testing: A Quality Improvement Initiative. Pediatrics. 2018 Jun 20.

Rayborn CH, Jackson CD, Summers NA. What Is Strep Throat? JAMA. 2024 May 2. doi: 10.1001/jama.2024.3326.

Science M, Bitnun A, Mclsaac W. Identifying and treating group A streptococcal pharyngitis in children. CMAJ. 2015 Jan 6;187(1):13-4.

Shapiro DJ, Barak-Corren Y, Neuman MI, et al. Identifying Patients at Lowest Risk for Streptococcal Pharyngitis: A National Validation Study. J Pediatr. 2020 Feb 14. doi: 10.1016/j.jpeds.2020.01.030

Sykes EA, Wu V, Beyea MM, et al. Pharyngitis: Approach to diagnosis and treatment. Can Fam Physician. 2020 Apr;66(4):251-257.

Ronny K. Gunnarsson, Mark Ebell, Robert Centor, Paul Little, Theo Verheij, Morten Lindbæk & Pär-Daniel Sundvall (2023) Best management of patients with an acute sore throat – a critical analysis of current evidence and a consensus of experts from different countries and traditions, Infectious Diseases, 55:6, 384-395, DOI:10.1080/23744235.2023.2191714.

Antibiotics:

Casey JR, Pichichero ME. Metaanalysis of short course antibiotic treatment for group a streptococcal tonsillopharyngitis. Pediatr Infect Dis J. 2005 Oct;24(10):909-17.

Casey JR, Pichichero ME. Higher dosages of azithromycin are more effective in treatment of group A streptococcal tonsillopharyngitis. Clin Infect Dis. 2005 Jun 15;40(12):1748-55.

Clegg HW, Ryan AG, Dallas SD, Kaplan EL, Johnson DR, Norton HJ, Roddey OF, Martin ES, Swetenburg RL, Koonce EW, Felkner MM, Giftos PM. Treatment of streptococcal pharyngitis with once-daily compared with twice-daily amoxicillin: a noninferiority trial. Pediatr Infect Dis J. 2006 Sep;25(9):761-7.

Ebell MH, Barry HC. Management of Sore Throat: Time to Update. Am Fam Physician. 2024 Apr;109(4):301-302.

Feder HM Jr, Gerber MA, Randolph MF, Stelmach PS, Kaplan EL. Once-daily therapy for streptococcal pharyngitis with amoxicillin. *Pediatrics*. 1999 Jan;103(1):47-51.

Gerber MA, Randolph MF, Chanatry J, Wright LL, De Meo K, Kaplan EL. Five vs ten days of penicillin V therapy for streptococcal pharyngitis. *Am J Dis Child*. 1987 Feb;141(2):224-7

Gualtieri R, Verolet C, Mardegan C, et al. Amoxicillin vs. placebo to reduce symptoms in children with group A streptococcal pharyngitis: a randomized, multicenter, double-blind, non-inferiority trial. *Eur J Pediatr*. 2024 Aug 31. doi: 10.1007/s00431-024-05705-1.

Gunnarsson RK, Ebell M, Centor R, et al. Best management of patients with an acute sore throat - a critical analysis of current evidence and a consensus of experts from different countries and traditions. *Infect Dis (Lond)*. 2023;55(6):384-395.

Hedin K, Thorning S, van Driel ML. Different antibiotic treatments for group A streptococcal pharyngitis. *Cochrane Database Syst Rev*. 2023 Nov 15;11(11):CD004406. We are uncertain if there are clinically relevant differences in symptom resolution when comparing cephalosporins and macrolides with penicillin in the treatment of GABHS tonsillopharyngitis. Low-certainty evidence in children suggests that carbacephem may be more effective than penicillin for symptom resolution. There is insufficient evidence to draw conclusions regarding the other comparisons in this review. Data on complications were too scarce to draw conclusions. Antibiotics have a limited effect in the treatment of GABHS pharyngitis and the results do not demonstrate that other antibiotics are more effective than penicillin. In the context of antimicrobial stewardship, penicillin can be used if treatment with an antibiotic is indicated. All studies were conducted in high-income countries with a low risk of streptococcal complications, so there is a need for trials in low-income countries and disadvantaged populations, where the risk of complications remains high.

Lennon DR, Farrell E, Martin DR, Stewart JM. Once-daily amoxicillin versus twice-daily penicillin V in group A beta-haemolytic streptococcal pharyngitis. *Arch Dis Child*. 2008 Jun;93(6):474-8.

Logan LK, McAuley JB, Shulman ST. Macrolide treatment failure in streptococcal pharyngitis resulting in acute rheumatic fever. *Pediatrics*. 2012 Mar;129(3):e798-802. doi: 10.1542/peds.2011-1198. Epub 2012 Feb 6. Review. PubMed PMID: 22311996.

Kaplan EL, Gooch III WM, 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 Jun 15;32(12):1798-802.

Pluddemann A, Heneghan C. Short course penicillin for treating patients with pharyngotonsillitis. *BMJ Evid Based Med*. 2021 Jun;26(3):137-138.

Sauve L, Forrester AM, Top KA. Group A streptococcal pharyngitis: A practical guide to diagnosis and treatment. *Paediatr Child Health*. 2021 Jul 28;26(5):319-320

Shvartzman P, Tabenkin H, Rosentzwaig A, Dolginov F. Treatment of streptococcal pharyngitis with amoxycillin once a day. *BMJ*. 1993 May 1;306(6886):1170-2

Skoog Ståhlgrén G, Tyrstrup M, Edlund C, et al. Penicillin V four times daily for five days versus three times daily for 10 days in patients with pharyngotonsillitis caused by group A streptococci: randomised controlled, open label, non-inferiority study. *BMJ*. 2019 Oct 4;367:l5337.

van Driel ML, De Sutter AI, Habraken H, et al. Different antibiotic treatments for group A streptococcal pharyngitis. *Cochrane Database Syst Rev*. 2016 Sep 11;9(9):CD004406

van Driel ML, De Sutter AIM, Keber N, et al. Different antibiotic treatments for group A streptococcal pharyngitis. *Cochrane Database of Systematic Reviews* 2016, Issue 9. Art. No.: CD004406. DOI: 10.1002/14651858.CD004406.pub3.

Venuta A, Laudizi L, Beverelli A, Bettelli F, Milioli S, Garetti E. Azithromycin compared with clarithromycin for the treatment of streptococcal pharyngitis in children. *J Int Med Res*. 1998 Jun-Jul;26(3):152-8.

Rheumatic Fever:

Baker MG, Gurney J, Moreland NJ, et al. Risk factors for acute rheumatic fever: A case-control study. *Lancet Reg Health West Pac*. 2022; 26: 100508.

Brusselen DV, Vleighe E, Schelstraete P et al. Streptococcal pharyngitis in children: to treat or not to treat? *Eur J Pediatr* 2014;173:1275–1283

Carapetis JR, Steer A, Mulholland E, et al. The global burden of group A streptococcal diseases. *Lancet Infect Dis* 2005;5:685-94.

Catanzaro FJ, Stetson CA, Morris AJ, Chamovitz R, et al. The role of the streptococcus in the pathogenesis of rheumatic fever. *Am J Med*. 1954 Dec;17(6):749-56. PubMed PMID: 13207156.

Denny FW, Wannamaker LW, Brink WR, Rammelkamp CH Jr, et al. Landmark article May 13, 1950: Prevention of rheumatic fever. Treatment of the preceding streptococci infection. By Floyd W. Denny, Lewis W. Wannamaker, William R. Brink, Charles H. Rammelkamp Jr. and Edward A. Custer. *JAMA*. 1985 Jul 26;254(4):534-7

Gagnall EM, Ho MG, McCormick IA. A 39-year-old man with recurrent rheumatic fever. *CMAJ* 2015;187:50-54.

Gerber MA, Baltimore RS, Eaton CB, Gewitz M, et al. Prevention of rheumatic fever and diagnosis and treatment of acute Streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Academy of Pediatrics. *Circulation*. 2009 Mar 24;119(11):1541-51.

Gordon J, Kirlew M, Schreiber Y, et al. Acute rheumatic fever in First Nations communities in northwestern Ontario. *Can Fam Physician*. 2015 Oct; 61(10): 881–886.

Herath VCK, Carapetis J. Sore throat: is it such a big deal anymore? *Journal of Infection* 2015;71: S101-S105.

Madden S, Kelly L. Update on acute rheumatic fever: It still exists in remote communities. *Can Fam Physician* 2009;55:475-8.

Robertson KA, Volmink JA, Mayosi BM. Antibiotics for the primary prevention of acute rheumatic fever: a meta-analysis. *BMC Cardiovascular Disorders* 2005;5:11.

Schams SC, Goldman RD. Steroids as adjuvant treatment of sore throat in acute bacterial pharyngitis. *Can Fam Physician*. 2012 Jan;58(1):52-4.

Science M, Bitnun A, McIsaac W. Identifying and treating group A streptococcal pharyngitis in children. *CMAJ* 2015;187:13-4.

Spinks A, Glasziou PP, Del Mar CB. Antibiotics for treatment of sore throat in children and adults. *Cochrane Database Syst Rev*. 2021 Dec 9;12(12):CD000023.

Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. *Cochrane Database of Systematic Reviews* 2013, Issue 11. Art. No.: CD000023.

Absolute risk reduction (ARR) calculated in house using numbers from Analysis 4.1

Antibiotic group: 37 cases ARF/5656 participants; Experimental event rate (EER) = 0.0065

Placebo group: 75 cases ARF/4445 participants; Control event rate (CER) = 0.0169

$ARR = CER - EER = 0.0169 - 0.0065 = 0.0104 = 1\%$

Templeton C, Cooper A, Dancey P, Human D, Rahman P. Acute Rheumatic Fever. April 2005 to March 2007 (final report). Canadian Paediatric Surveillance Program. 2007.

<https://cpsp.cps.ca/uploads/publications/Results-2007.pdf> (accessed Mar 4, 2024).

Wannamaker LW, Rammelkamp CH Jr, Denny FW, Brink WR, et al. Prophylaxis of acute rheumatic fever by treatment of the preceding streptococcal infection with various amounts of depot penicillin. *Am J Med.* 1951 Jun;10(6):673-95

Webb RH. Acute rheumatic fever. *BMJ* 2015;351:h3443.

Wodu B, Bloomfield GS. Rheumatic Heart Disease in the Twenty-First Century. *Curr Cardiol Rep* 2016;18:96.

van Driel ML, De Sutter AI, Habraken H, Thorning S, Christiaens T. Different antibiotic treatments for group A streptococcal pharyngitis. *Cochrane Database Syst Rev.* 2016 Sep 11;9:CD004406.

Symptom Management:

Bertin L, Pons G, d'Athis P, Lasfargues G, 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 Nov;119(5):811-4.

Chrubasik S, Beime B, Magora F. Efficacy of a benzocaine lozenge in the treatment of uncomplicated sore throat. *Eur Arch Otorhinolaryngol.* 2012 Feb;269(2):571-7.

Chiappini E, Bortone B, Di Mauro G, et al. Choosing Wisely: TheTop-5 Recommendations from the Italian Panel of the National Guidelines for the Management of Acute Pharyngitis in Children. *Clin Ther.* 2017 Mar; 39(3):646-649.

de Cassan S, Thompson MJ, Perera R, Glasziou PP, Del Mar CB, Heneghan CJ, Hayward G. Corticosteroids as standalone or add-on treatment for sore throat. *Cochrane Database Syst Rev.* 2020 May 1;5(5):CD008268.

Gehanno P, Dreiser RL, Ionescu E, et al. Lowest effective single dose of diclofenac for antipyretic and analgesic effects in acute febrile sore throat. *Clin Drug Investig.* 2003;23(4):263-71.

Hayward GN, Hay AD, Moore MV, et al. Effect of Oral Dexamethasone Without Immediate Antibiotics vs Placebo on Acute Sore Throat in Adults: A Randomized Clinical Trial. *JAMA.* 2017 Apr 18;317(15):1535-1543.

Kagan G, Huddleston L, Wolstencroft P. Two lozenges containing benzocaine assessed in the relief of sore throat. *J Int Med Res.* 1982;10(6):443-6.

Little P, Stuart B, Wingrove Z, et al. Probiotic capsules and xylitol chewing gum to manage symptoms of pharyngitis: a randomized controlled factorial trial. *CMAJ.* 2017 Dec 18;189(50):E1543-E1550.

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 Jan;64(2):194-207.

Pierce CA, Voss B. Efficacy and safety of ibuprofen and acetaminophen in children and adults: a meta-analysis and qualitative review. *Ann Pharmacother.* 2010 Mar;44(3):489-506.

Ruperto N, Carozzino L, Jamone R, Freschi F, et al. A randomized, double-blind, placebo-controlled trial of paracetamol and ketoprofen lysine salt for pain control in children with pharyngotonsillitis cared by family pediatricians. *Ital J Pediatr.* 2011 Sep 29;37:48.

Sadeghirad B, Siemieniuk RA, Brignardello-Petersen R, et al. Corticosteroids for treatment of sore throat: systematic review and meta-analysis of randomised trials. *BMJ* 2017;358:j3887.

Schachtel BP, Fillingim JM, Thoden WR, Lane AC, Baybutt RI. Sore throat pain in the evaluation of mild analgesics. *Clin Pharmacol Ther.* 1988 Dec;44(6):704-11. PubMed PMID: 3197368.

Weckx LL, Ruiz JE, Duperly J, Mendizabal GA, et al. Efficacy of celecoxib in treating symptoms of viral pharyngitis: a double-blind, randomized study of celecoxib versus diclofenac. *J Int Med Res.* 2002 Mar-Apr;30(2):185-94.