

PEARLS for the MANAGEMENT of PHARYNGITIS

- The majority of pharyngitis cases do **NOT** require antibiotics as they are viral infections (80-90% in adults, >70% in children).
- Pharyngitis is typically self-limiting (often 3-7 days; up to ≤10 days).
- A validated clinical decision rule e.g. modified Centor score can help identify low risk patients who do not require diagnostic testing (see below) or antibiotics.
- For confirmed Group A Streptococcus (GAS) pharyngitis, penicillin for 10 days is the drug of choice. There is no documented GAS resistance to penicillin.
- Advise on treatments that will provide **symptomatic relief**: NSAIDs, acetaminophen, medicated throat lozenges, topical anesthetics, warm liquids.
- Patients should see their prescriber if: 1) symptoms worsen, 2) symptoms take longer than 3 to 5 days to resolve, &/or 3) unilateral neck swelling develops.

PRE-TREATMENT CONSIDERATIONS

- Inappropriate antibiotic use is driving resistance & leading to a crisis. Please examine your own prescribing practices.
- A validated clinical decision rule, like the modified Centor score, can be used to help identify low risk patients who do not require diagnostic testing or antibiotics.

Modified Centor (or McIsaac) Score		
Criteria		Points
Temperature > 38°C (>100.5 °F) oral temperature used in Centor score (adults)		1
Absence of cough		1
Swollen, tender anterior cervical nodes		1
Tonsillar swelling or exudate		1
Age 3 to 14 years		1
Age 15 to 44 years		0
Age ≥ 45 years		-1
Score	Risk of Streptococcal Infection	Suggested Management
-1 to 0	1 to 2.5%	- Symptomatic treatment - No RADT, culture or antibiotic needed
1	5 to 10%	
2	11 to 17%	- RADT or throat swab for culture. - If positive for GAS ⇒ antibiotic.
3	28 to 35%	
≥4	51 to 53%	

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

Back-up throat cultures are recommended for negative lateral flow RADT in children.

- Diagnostic testing is **not** recommended if:
 - A modified Centor score of ≤1
 - symptoms of a viral infection rhinorrhea, cough, oral ulcers, hoarseness IDSA 2012 (strong, high)
 - <3yrs, unless other risk factors e.g. sibling with GAS infection IDSA 2012 (strong, moderate)
 - asymptomatic contact of patient with GAS pharyngitis IDSA 2012 (strong, moderate)
- **Exceptions:** the modified Centor score may not accurately predict risk of GAS during epidemics or in high risk populations, e.g. individuals with a history of rheumatic fever, valvular heart disease, or immunosuppression. Use clinical judgment & consider testing (RADT/throat swab) more broadly.

SHOULD ANTIBIOTICS BE USED TO TREAT PHARYNGITIS?

- 80-90% of adults (>70% of children) do NOT require antibiotics as infection likely viral.
- Patients with a positive throat swab should receive an antibiotic to ↓ the risk of complications. See modified Centor score on left column, & antibiotic table below.
- The turn-around-time for throat swab results can take a few days. However, antibiotics started **within 9 days of symptom onset** in confirmed GAS will prevent rheumatic fever.
- If antibiotics are started empirically, ensure agent is discontinued if throat swab negative.

MOST COMMON BACTERIAL PATHOGEN

- Group A Streptococcus (GAS) (outpatient Group C and G strep do not require antibiotics)

EMPIRIC DRUG REGIMENS OF CHOICE & SUSCEPTIBILITY CONCERNS

FIRST LINE		
No antibiotic	- Majority of cases are viral. - Only use antibiotics in confirmed bacterial pharyngitis. <small>Choosing Wisely IDSA'15</small>	- See Symptom Management following page.
Penicillin V PEN-VK, g	Peds: ≤27 kg: 40mg/kg/day ÷ BID or TID x10 days (maximum 750mg/day) >27 kg & Adults: 300mg TID x 10 days, or 600mg BID x 10 days <i>max absorption when given on an empty stomach</i>	- 1 st line due to narrow spectrum of activity, efficacy, safety & low cost. - No documented resistance to GAS.
Amoxicillin AMOXIL, g ☺	Peds: 40-50mg/kg/day ÷ BID x10 days (maximum 1000mg/day) Adults: 500mg BID x 10 days	Compared to penicillin: - broader spectrum than required; as effective - liquid more palatable for peds
PENICILLIN ALLERGY: TYPE IV HYPERSENSITIVITY (e.g. rash)		
Cephalexin KEFLEX, g	Peds: 25-50mg/kg/day ÷ BID or QID x10 days (maximum 1000mg/day) Adults: 250mg QID x 10 days, or 500mg BID x 10 days	- No documented resistance to GAS.
PENICILLIN ALLERGY: TYPE I HYPERSENSITIVITY (i.e. anaphylaxis)		
Do not use the following antibiotics unless confirmed GAS & confirmed type I reaction to penicillin, due to concerns with ↑ resistance to macrolides & adverse events e.g. <i>C. diff.</i>		
Clindamycin DALACIN C, g	Peds: 20mg/kg/day ÷ TID x10 days (maximum 900mg/day) Adults: 300mg TID x 10 days	Macrolide considerations: - Clarithromycin x 10 days was superior to azithromycin x 5 days for bacterial eradication (NNT=9) in adults, but equivalent for clinical cure. - ↑ GI side effects with erythromycin. - Azithromycin 3 vs 5 days: no head-to-head trials. Both regimens provide same total dose over the course of therapy (i.e. 60mg/kg/d; 1.5g).
Clarithromycin BIAXIN, g ☺	Peds: 15mg/kg/day divided BID x10 days (maximum 500mg/day) Adults: 250mg BID x 10 days	
Erythromycin ☺	Peds: 40mg/kg/day ÷ BID or TID x10 days (maximum 2000mg/day) Adults: 250mg QID x 10 days	
Azithromycin ZITHROMAX, g	Peds: 12mg/kg/day daily x5 days, or 20mg/kg/day daily x3 days (max 500mg/d) Adults: 500mg Day 1, 250mg x Days 2-5, or 500mg daily x3 days	

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, but 10 days of therapy is recommended for preventing acute rheumatic fever, & short courses are not as effective for treating the infection.
 - E.g. a 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).

SYMPTOM MANAGEMENT		
SYSTEMIC ANALGESICS	e.g. Ibuprofen <small>ADVIL, g</small> Peds: 5-10 mg/kg po q6-8hr PRN (maximum 40mg/kg/day) Adults: 400mg po q6-8hr PRN	- Ibuprofen ↓ associated pain more than acetaminophen & placebo. - Reduces fever.
	Acetaminophen <small>TYLENOL, g</small> Peds: 10-15mg/kg po q4-6hr PRN (maximum 75 mg/kg/day) Adults: 1000mg po q4-6hr PRN	- Less effective than NSAIDs for ↓ associated pain but more effective than placebo. - Reduces fever.
MEDICATED LOZENGES	Benzocaine <small>CEPACOL ES, CHLORASEPTIC</small> 10mg lozenge q2hr PRN	- Alleviates throat pain if used frequently. - Avoid in children due to: choking & methemoglobinemia concerns.
MEDICATED SPRAYS	Phenol <small>CHLORASEPTIC</small> 5 sprays q2hr PRN	- No evidence, but anecdotally may provide relief from associated pain.
RINSES	<ul style="list-style-type: none"> • Gargling or drinking warm liquids e.g. warm salt water rinse, tea • Benzydamine <small>TANTUM, PHARIXIA, g</small> 15mL gargle or rinse q1.5-3hr PRN ↯ 	- Little evidence, but anecdotally provide relief from associated pain.

Not recommended for symptom management: corticosteroids NICE'18, IDSA'12 (weak, moderate), BMJ'17 (weak), however, opinions vary (e.g., may consider dexamethasone 10mg po x 1 dose).

- A systematic review of 10 RCTs (1426 participants) found a single, low-dose (usually dexamethasone max 10mg) vs standard care ↑ pain relief at 24h & the number of patients' experiencing no pain at 48h (NNT=6, high quality). Pain resolved ~11h (-0.4 to -21.8, low quality) earlier with corticosteroid treatment, but wide variability. AEs were not different, but multiple corticosteroid doses were not studied & would likely lead to greater harms e.g., ↑glucose. Sadeghirad'17
- Some may consider ↓ in duration of pain is not considered clinically significant, and NSAIDs/acetaminophen have less adverse events. Shared decision-making is required.

Treatment Evidence Summary

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.
 - The incidence in some remote, Canadian Aboriginal communities may be higher (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:
 - as 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 ↑.
- 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.

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**.
- Consider age, season, signs/symptoms to rule out viral etiology (see modified Centor score).
- Avoid continuous long-term antibiotic therapy (i.e. repeated courses or prophylaxis).

Abbreviations: ☺=tastes good **GAS**=Group A Streptococcus **GI**=gastrointestinal **IDSA**=Infectious Diseases Society of America **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

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References – Pharyngitis - RxFiles.ca

Guidelines:

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.

2012 Bugs & Drugs

2013 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.

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.

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.

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.

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

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

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.

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

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.

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

van Driel ML, De Sutter AIM, Keber N, Habraken H, Christiaens T. 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:

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.

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 sore throat. *Cochrane Database of Systematic Reviews* 2013, Issue 11. Art. No.: CD000023.

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.

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, Huddlestone 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.

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.