

PEARLS for the MANAGEMENT of PHARYNGITIS

- Pharyngitis is typically self-limiting (often 4-5d; up to ≤10d), and the majority of cases do **NOT** require antibiotics as they are viral infections (80-90% in adults, >70% in children).
- 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. Consider stewardship strategies such as delayed antibiotics while awaiting throat swab results.
- 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 e.g. **modified Centor**, FeverPAIN 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 years 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. RADT is useful for ruling in a diagnosis when results are positive. Back-up throat cultures recommended to confirm a negative RADT in some children & may be used in others.

- Diagnostic testing e.g. RADT, culture is **not** recommended if:
 - A modified Centor score of ≤1
 - symptoms of a viral infection rhinorrhea, cough, oral ulcers, hoarseness IDSA'12 (strong, high)
 - <3yrs, unless other risk factors e.g. outbreak, sibling with GAS infection IDSA'12 (strong, moderate), CPS
 - asymptomatic contact of patient with GAS pharyngitis IDSA'12 (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.
- Possible strategies: watchful waiting, delayed ABX, empiric ABX (stop if throat swab negative).

MOST COMMON BACTERIAL PATHOGEN

- Group A Streptococcus (GAS)

EMPIRIC DRUG REGIMENS OF CHOICE & SUSCEPTIBILITY CONCERNS

FIRST LINE		
No antibiotic	- Majority of cases are viral. - Only use antibiotics in confirmed bacterial pharyngitis. Choosing Wisely IDSA'15	- 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, efficacy, safety & low cost. No documented resistance to GAS. - No suspension available CDN.
Amoxicillin AMOXIL, g ☺	Peds: 40-50mg/kg/day ÷ BID x10 days (maximum 1000mg/day) or 50mg/kg/day daily x10 days (max 1g/d) ^{CPS} 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.
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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. *C. diff*.

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 ÷ 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 (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}

SYMPTOM MANAGEMENT		
SYSTEMIC ANALGESICS	e.g. Ibuprofen ADVIL, g Peds: 5-10 mg/kg po q6-8hr PRN (maximum 40mg/kg/day) Adults: 400mg q6-8hr PRN	- Ibuprofen ↓ associated pain more than acetaminophen & placebo. - Reduces fever.
	Acetaminophen TYLENOL, g Peds: 10-15mg/kg po q4-6hr PRN (maximum 75 mg/kg/day) Adults: 1000mg q4-6hr PRN max=4g/d	- Less effective than NSAIDs for ↓ associated pain but more effective than placebo. - Reduces fever.
MEDICATED LOZENGES	Benzocaine CEPACOL ES, CHLORASEPTIC 10mg lozenge q2hr PRN	- Alleviates throat pain if used frequently. - Avoid in children due to: choking & methemoglobinemia concerns.
MEDICATED SPRAYS	Phenol CHLORASEPTIC 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 Benzylamine TANTUM, PHARIXIA, g 15mL gargle or rinse q1.5-3hr PRN X ♂ 	- Little evidence, but anecdotally provide relief from associated pain.

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

- A Cochrane review of 9 RCTs (including 950 adults & 369 children) found po or IM corticosteroids, in addition to antibiotics and analgesics, ↑ pain relief at 24 hours (**NNT~5** ~38% vs ~16%, high certainty evidence) and at 48 hours. AEs were not different, but most did not study multiple corticosteroid doses were not studied & would likely lead to greater harms e.g. ↑glucose.^{de Cassan'2020}
- Some may consider ↓ in duration of pain is not clinically significant, and NSAIDs/acetaminophen have less adverse events. Shared decision-making is required.

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.
 - The incidence in some remote, Canadian Indigenous 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:
 - 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 CPS=Canadian Pediatric Society GAS=Group A Streptococcus GI=gastrointestinal IDSA=Infectious Diseases Society of America NSAID=non-steroidal anti-inflammatory drug NNT=number needed

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RR=relative risk

Acknowledgements: Originally written by Lynette Kosar 2016. Ongoing updated by Marlys LeBras.

This topic was part of a larger Antibiotics & Common Infections Academic Detailing Topic. RxFiles is very pleased to acknowledge those who contributed to Part 1 topic development & review. Overall ABX topic/project guidance: Lynette Kosar Pharmacist, RxFiles Loren Regier Pharmacist, RxFiles Tessa Laubscher Family Physician, Saskatoon Yvonne Shevchuk UoF, College of Pharmacy Pam Komonoski RN(NP) UoF Student Health Linda Sulz Pharmacist, RQHR Justin Kosar Pharmacist, SHR Stewardship Casey Phillips Pharmacist, RQHR Stewardship Content development – ABX Part 1: Lynette Kosar Pharmacist, RxFiles Topic Lead Alex Crawley Pharmacist, RxFiles Andrew Plishka Pharmacy Resident, SHR Rachel Martin Pharmacy Resident, SHR Loren Regier Pharmacist, RxFiles Co-Lead Topic input and review: Anne Nguyen Pharmacist, BC Brent Jensen Pharmacist, RxFiles Jessica Minion RQHR Microbiology Jill Blaser-Farrukh Family physician, Saskatoon Joe Blondeau SHR Microbiology John Alport Family Physician, Regina Jonathan Hey Family Physician, Saskatoon Marlys LeBras Pharmacist, RxFiles Nora McKee Family Physician, Saskatoon Reid McGonigle Family Physician, Northern SK Roger Bristol Emergency Med, SHR Shaqil Peermohamed MD, SHR Infectious Disease Tom Smith-Windsor Family Physician, Prince Albert The RxFiles academic detailing team (Zack Dumont, Vaughn Johnson, Tanya Nystrom, Lisa Rutherford, Brenda Schuster, Pam Karlson)

Disclosures: No conflicts of interest are reported.

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