Acute Pharyngitis: Management Considerations [1 Bugs & Drugs'23, 2 MUMS'24, 3 Sanford'24, CPS'21, NICE'18, BMJ'17, IDSA'12, CPS'21]

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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**: ❶ symptoms worsen, ❷ symptoms take longer than 4 to 5 days to resolve, &/or ❸ 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.
- Diagnostic tests (RADT, throat swab) and/or antibiotics **not** recommended if: ❶ Modified Centor score ≤1 (Table 1). ❷ symptoms of viral infection e.g. rhinorrhea, cough, oral ulcers, hoarseness.[IDSA'12 (strong, high)] ❸ <3 years, unless risk factors present e.g. sibling with GAS, outbreak.[IDSA'12 (strong, moderate), CPS] ❹ asymptomatic household contacts of patient with GAS pharyngitis.[IDSA'12 (strong, moderate)]
- Positive RADT confirms diagnosis (high specificity, 88-99%). Throat swabs suggested in kids (e.g. 5-15 years[IDSA]) & high-risk groups with negative RADT (throat swabs have ↑sensitivity). Negative RADT acceptable in adults (low GAS incidence).
- 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'13]

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 RADT, swab, or antibiotic needed.*
1	5 - 10%	
2	11 - 17%	RADT or throat swab. **If GAS positive ⇨ antibiotic.** *Using a cutoff of 3 is recommended by some to ↓false positives.*[Expert]
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, RADT 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 215 for more details

ANALGESICS	**NSAIDs** e.g. **Ibuprofen** ADVIL, g ▼ OTC Peds: 5-10 mg/kg po q6-8hr PRN (susp ✗ ▼) (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 ✗ ▼ 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 ✗ ⊗ OTC 10mg lozenge q2hr PRN ($6/18 lozenges)	- Alleviates throat pain if used frequently.[Chrubasik'12] - Avoid in peds: choking & methemoglobinemia risks. - Alternative: hard candy e.g. HALLS, honey (>1 year)
	Phenol CHLORASEPTIC ✗ ⊗ OTC 5 sprays q2hr PRN ($15/177 mL)	- No evidence, but anecdotally may provide relief from associated pain.
RINSES	**Warm liquids** e.g. tea, warm saltwater gargle (recipe: ¼ to ½ tsp salt per 240mL warm water)	- Little evidence, but anecdotally provide relief from associated pain/discomfort.
	Benzydamine, PHARIXIA, g ✗ ⊗ 15mL gargle/rinse q1.5-3hr PRN ($38/250mL)	

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 cases.[BMJ'17 (weak), AFP'23]

- 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.

Table 3. Empiric Drug Regimens

see RxFiles Oral & IV Antibiotics Chart page 81 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 *No commercially available suspension* >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] (BID & once daily dosing frequency are specific to GAS pharyngitis indication) Adults: 500mg BID x10 days	- Compared to penicillin: ❶ broader spectrum ↑selective pressure, ❷ as effective, ❸ liquid more palatable for peds ❹ if mononucleosis, may cause skin rash.
PENICILLIN ALLERGY: NON-SEVERE (e.g. delayed >72h rash) see Beta-lactam Allergy page 86, 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	- 1st generation (cephalexin, cefadroxil) preferred over 2nd 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) *No commercially available suspension* Adults: 500mg BID x10 days, **or** 1000mg daily x10 days	
PENICILLIN ALLERGY: SEVERE (e.g. anaphylaxis, angioedema) see Beta-lactam Allergy page 86, SHA Firstline.		
Only use in confirmed GAS & serious reaction to penicillin, due to ↑resistance [SK'23 ~7% to 18%] & AE e.g. *C. difficile*.		
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.
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** 20mg/kg/day daily x3 days (max 500mg/day) Adults: 500mg Day 1, 250mg x Days 2-5, **or** 500mg daily x3 days	

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 **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	100
Acute Rheumatic Fever	100
ADVIL	100
Amoxicillin	100
AMOXIL	100
Antibiotic	100
Azithromycin	100
Benzocaine	100
Benzydamine	100
Beta-Lactam	100
BIAXIN	100
Cefprozil	100
CEFTIN	100
Cefuroxime	100
CEFZIL	100
Centor Score	100
CEPACOL	100
Cephalexin	100
Cephalosporin	100
CHLORASEPTIC	100
Clarithromycin	100
Clindamycin	100
DALACIN	100
Ibuprofen	100
KEFLEX	100
Macrolide	100
Penicillin	100
PEN-VK	100
PHARIXIA	100
Pharyngitis	**100**
Phenol	100
TYLENOL	100
ZITHROMAX	100
Cefadroxil	100
DURICEF	100

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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%

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