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Review Article

The treatment of streptococcal tonsillitis/ pharyngitis in young children

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Abstract   Pharyngitis is common in children, accounting for nearly 12 million visits annually in the United States. Streptococcus pyogenes or group A streptococcus (GAS) is the most common bacterial cause of pharyngitis for which antibiotics are indicated. Antibiotic treatment of streptococcal pharyngitis virtually eliminates the presence of bacteria from the pharynx and thus removes the risk of subsequent rheumatic fever. GAS is spread from person to person via respiratory droplets with a short incubation period of 2~5 days. GAS pharyngitis peaks in the late winter and early spring months when children are predominately indoors for school and sports. Colonization is also higher in winter months, and while up to 20% of school age children are colonized with GAS in their throat during this time, colonization has not been shown to contribute to the spread of disease. In low- and middle-income countries and other situations in which crowding is common (e.g., schools), outbreaks of pharyngitis are common. GAS pharyngitis can occur at all ages and it is most common in school-aged children with a peak at 7~8 years of age. Pharyngitis caused by GAS is rare in children <3 years of age and becomes much less common in late adolescence through adulthood.
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Microbiology/epidemiology

Pharyngitis is common in children, accounting for nearly 12 million visits annually in the United States.[1] *Streptococcus pyogenes* or group A streptococcus (GAS) is the most common bacterial cause of pharyngitis for which antibiotics are indicated. There are more than 240 known M protein types encoded by the *emm* gene and conferring a specific *emm* type. Specific *emm* types have long been associated with

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sequelae such as rheumatic fever (e.g. type 1) and acute glomerulonephritis (e.g., type 12).[2–4] Antibiotic treatment of streptococcal pharyngitis virtually eliminates the presence of bacteria from the pharynx and thus removes the risk of subsequent rheumatic fever.

GAS is spread from person to person via respiratory droplets with a short incubation period of 2~5 days. GAS pharyngitis peaks in the late winter and early spring months when children are predominately indoors for school and sports. Colonization is also higher in winter months, and while up to 20% of school age children are colonized with GAS in their throat during this time, colonization has not been shown to contribute to the spread of disease.[5–7] In low- and middle-income countries and other situations in which crowding is common (e.g., schools), outbreaks of pharyngitis are common.[8] GAS pharyngitis can occur at all ages and it is most common in school-aged children with a peak at 7~8 years of age. Pharyngitis caused by GAS is rare in children <3 years of age and becomes much less common in late adolescence through adulthood.[9,10]

Clinical presentation

The classic presentation of GAS pharyngitis includes sudden onset of fever and sore throat with inflammation of the tonsils noted on exam in the absence of viral respiratory features.[9] Tender anterior cervical lymphadenopathy is often present. Palatal petechiae, strawberry tongue, red swollen uvula, or scarlatiniform rash may also be present. However, overlap with other clinical diagnoses exists (e.g., viral pharyngitis and Kawasaki Disease) and none of these are pathognomonic for GAS pharyngitis. Other clinical features include headache, myalgias, vomiting, and abdominal pain. Separating out children who may be colonized with GAS in their pharynx from those with GAS pharyngitis can be difficult. It is recommended that streptococcal testing be avoided in children with clinical features of a viral infection such as cough, rhinorrhea, congestion, hoarse voice, diarrhea, conjunctivitis, coryza, or oral ulcers.[9,11] Recent data from Shapiro and colleagues supports this recommendation. They found that children with viral features, especially rhinorrhea, were less likely to have a positive streptococcal antigen test. Additionally, the likelihood of a positive antigen test result declined as the number of viral features increased.[11]

Typical clinical presentations of GAS tonsillitis are rare in children <3 years of age. In young children, GAS infection generally has more of a subacute presentation with low grade fever, fussiness, anorexia, congestion, mucopurulent rhinorrhea, and anterior lymphadenopathy.[12,13]

Peritonsillar abscess
Peritonsillar abscess (PTA) is a collection of purulence between the tonsillar capsule and the pharyngeal constrictor muscle. PTA presents similarly to streptococcal pharyngitis, although additional clinical symptoms of dysphagia, odynophagia, drooling, muffled voice, and trismus may be present. On exam, an apparent bulging tonsil may be seen causing deviation of the uvula away from the abscess.[14] Younger children may be less likely to present with sore throat and may have noted neck swelling and tenderness on exam.[15]

Suppurative and non-suppurative sequelae
Children with a missed diagnosis of GAS tonsillitis are at increased risk of developing suppurative complications such as otitis media, sinusitis, and peritonsillar abscess (PTA), and treatment has been shown to mitigate this risk in systematic reviews.[16] However, the magnitude of the risk of non-treatment appears to be small. Data from Little and colleagues found that the number of GAS tonsillitis cases needed to treat (NNT) to prevent one otitis media or sinusitis complication was 193 for those prescribed antibiotics at the time of the initial visit and was 174 in those who received a delayed antibiotic prescription.[17] PTA is a less frequent sequelae of GAS tonsillitis than otitis media and sinusitis with an annual incidence of 9.4 per 100 000 children under 20 years of age. It is most common in adolescents with a peak age of 13 years.[18] Similar to otitis media and sinusitis, newer observational data suggests that immediate antibiotics are not better than either delayed or no antibiotics in preventing PTA, indicating that early evidence of peritonsillar abscess may be present at the initial clinical presentation.[17,19] The risk of adverse events from antibiotic exposure has been found to be much higher than the risk of otitis media, sinusitis, and PTA following a missed GAS pharyngitis. A recent Cochrane review found that the risk of vomiting, diarrhea, or rash was higher for children treated with antibiotics than those who were not treated with a relative risk of 1.38 (95%CI 1.19 to 1.59) and the NNT to cause a harmful outcome was 14.[20]

Acute rheumatic fever (ARF) occurs primarily in untreated school-aged children aged 5~14 years with antecedent history of untreated tonsillitis.[21] There are rare cases of ARF in young children aged 2~3 years in high-risk populations.[22] The Jones criteria for diagnosis of ARF was revised in 2015 to better discern those at low-risk from those at moderate- or high-risk of ARF.[21] This revision maintains major and minor criteria, but these differ for low-risk and moderate-to-high-risk populations. The changes to the diagnostic criteria were an important update as ARF is rare in industrialized nations and is no longer a reportable disease to the Centers for Disease Control and Prevention (CDC).[21,23,24] However, ARF and rheumatic heart disease continue to be a major cause of morbidity in low- and middle-income countries and in certain populations, emphasizing the importance of timely diagnosis and treatment of GAS tonsillitis in these groups to improve population health.[25–27]

Diagnosis

Accurately diagnosing GAS pharyngitis is important to reduce sequelae of untreated infection and to limit transmission. Since the majority of pediatric sore throats are caused by viruses, accurate diagnosis of the etiology of pharyngitis also prevents unnecessary antibiotic use. Clinical signs and symptoms, even when combined into prediction rules, are not reliable to diagnose GAS pharyngitis in children.[28] Testing by rapid antigen detection test (RADT) is recommended by the Infectious Diseases Society of America (IDSA) to definitely diagnose GAS pharyngitis.[9] The sensitivity of RADTs, which is affected by specimen quality, is generally reported to be 70%~90% when compared to blood

agar plate culture.[29–31] The IDSA and the American Heart Association recommend back up culture for children with negative RADTs, while the European guideline states throat culture is not necessary after a negative RADT in children or adults with acute sore throat.[9,32,33] False positive RADT results can occur in children recently treated for GAS pharyngitis or when the test incubation period exceeds manufacturer recommendations.[34,35]

Nucleic acid amplification tests (NAATs) offer greater sensitivity than RADTs and provide a result in a shorter turnaround time than culture. Some institutions have replaced RADT-reflex culture algorithms with NAAT alone.[36] However, NAATs, RADTs, and throat culture do not distinguish between GAS infection and colonization. Appropriate patient selection for testing is necessary to avoid misdiagnosis and unnecessary antibiotic exposure. Testing for GAS pharyngitis is typically not indicated for children <3 years old, or for patients of any age with epidemiological and clinical features that suggest a viral etiology of pharyngitis.[9] Testing asymptomatic contacts of patients with GAS pharyngitis is not routinely recommended unless the contacts are at increased risk of developing sequelae from GAS infection, such as patients with a history of ARF.[9] Post-treatment testing is only recommended in special circumstances, such as patients at high risk of ARF or patients with recurrence of symptoms highly suggestive of GAS pharyngitis.

Treatment

Antibiotic therapy (Table 1) is indicated for patients with signs and symptoms of pharyngitis and laboratory confirmation of GAS as the causative pathogen. GAS resistance to penicillin has not been documented to date. Given its narrow spectrum, low cost, and efficacy in preventing ARF, penicillin is the drug of choice for treatment of GAS pharyngitis. Amoxicillin is a more palatable suspension than penicillin V and is equally effective when used as a single daily dose (50 mg/kg, max 1000 mg) for 10 days. Penicillin G benzathine can be given as an intramuscular (IM) injection in a single dose if medication adherence is uncertain; however, the injection can be painful. For patients with non-anaphylactic allergy to penicillin, a first-generation cephalosporin, such as cephalexin, is appropriate therapy. Clindamycin or a macrolide (e.g. azithromycin) can be used for treatment in patients with anaphylactic, or Type 1 hypersensitivity, to penicillin.

For children who experience a recurrence of laboratory confirmed GAS pharyngitis shortly after completion of antibiotic therapy, the same agent or an alternative agent such as a narrow spectrum cephalosporin, amoxicillin-clavulanate, or a macrolide may be used. Laboratory confirmation of GAS isolate susceptibility should be considered when non-beta lactam agents are used since high resistance rates are reported in some geographic areas.[37–40] Sulfonamides,

Table 1 Antibiotic options for treatment of GAS pharyngitis.

Initial and recurrent episodes	Dose and duration	Considerations
PenicillinV (oral)	If ≤ 27 kg: 250 mg per dose, two to three times daily for 10 days If > 27 kg: 500 mg per dose, two to three times daily for 10 days	Preferred therapy
Amoxicillin	50 mg/kg once daily for 10 days; max dose 1000 mg	Preferred therapy
Penicillin G benzathine (IM)	If < 27 kg: 600,000 U (375 mg) as single dose If ≥ 27 kg: 1.2 million U (750 mg) intramuscular as single dose	Preferred therapy in situations of poor medication adherence
Cephalexin	40 mg/(kg·d) divided twice daily for 10 days; max dose 500 mg	Alternative therapy for children with non-anaphylactic penicillin allergy
Clindamycin	20 mg/(kg·d) divided three times daily for 10 days; max dose 300 mg	Alternative therapy for children with anaphylactic penicillin allergy. Consider testing to confirm susceptibility.
Azithromycin	12 mg/kg once on day 1 followed by 6 mg/kg once daily on days 2~5; max dose 500 mg	Alternative therapy for children with anaphylactic penicillin allergy. Consider testing to confirm susceptibility.
Chronic pharyngeal carriage	Dose and duration	Considerations
Clindamycin	20~30 mg/(kg·d) divided three times daily for 10 days	Consider testing to confirm susceptibility.
Penicillin V and rifampin	Penicillin V: 50 mg/(kg·d) divided four times daily for 10 days; max 2000 mg/day rifampin: 20 mg/(kg·d) once daily for last 4 days of treatment; max 600 mg/day	—
Amoxicillin/clavulanate	Amoxicillin : 40 mg/(kg·d) divided three times daily; max 2000 mg amoxicillin/day	—

IM: Intramuscular injection.

tetracyclines, and fluoroquinolones should not be used for treatment of GAS pharyngitis.

Repeated positive tests for GAS pharyngitis may represent chronic pharyngeal carriage of GAS in the setting of viral pharyngitis or pharyngitis from another cause. Antibiotic therapy to eradicate GAS pharyngeal carriage is not routinely indicated since carriers are at low, if any, risk of developing complications and carriers are unlikely to transmit infection.[7,9] Eradication of GAS pharyngeal carriage may be indicated in the following special circumstances:(1) outbreaks of GAS pharyngitis in closed or semi-closed communities; (2) community outbreaks of invasive GAS disease or community outbreaks of GAS complications such as ARF; (3) family or personal history of ARF; (4) multiple episodes of GAS pharyngitis within a household for several weeks despite appropriate antibiotic therapy.[9,12] Penicillin or amoxicillin may not be as effective in eradicating GAS pharyngeal carriage as other antibiotic agents (Table 1).[9] Reacquisition can occur after eradication is achieved and pharyngeal carriage can persist for months to years.[41]

Tonsillectomy solely for the purposes of decreasing the frequency of GAS pharyngitis episodes is not routinely recommended. If the frequency of pharyngitis episodes is at least 7 episodes in one year, 5 episodes per year for 2 years, or 3 episodes per year for 2 years then tonsillectomy should be considered. Tonsillectomy can also be considered for recurrent pharyngitis if additional factors are present such as history of peritonsillar abscess or multiple antibiotic allergies.[42]

Conclusions

Tonsillitis is a common complaint prompting medical attention and GAS as the cause of tonsillitis is a common concern among patients and parents. Most cases of tonsillitis are viral in origin and patients who meet criteria for testing should be determined by after obtaining a careful history, reviewing seasonal epidemiology, and considering physical exam findings. This approach aids in reducing unnecessary testing and subsequent antibiotic exposure and reduces patient and societal healthcare costs.

Declaration of competing interest

None.

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