NCC Pediatrics Continuity Clinic Curriculum: **Pharyngitis**

Goals & Objectives:

- To recognize the common etiologies of pharyngitis in children and their associated clinical presentations
- To understand the indications for diagnostic testing for Group A strep pharyngitis
- To learn the appropriate treatment for Group A strep pharyngitis
- To recognize the suppurative and non-suppurative complications of Group A strep pharyngitis

Pre-Meeting Preparation:

Please read the following:

- "A Clinical Approach to Tonsillitis, Tonsillar Hypertrophy, and Peritonsillar and Retopharyngeal Abscesses," (*PIR 2017*)
- "Group A Streptococcus Infections" (*PIR, 2024*)
- Modified Centor Score (excerpt from *JAMA 2004*) and MD Calc Centor Tool

Conference Agenda:

- Review Pharyngitis Quiz
- Complete Pharyngitis Cases

Extra-Credit Readings:

- "Clinical Practical Guidelines for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America" *(no updates since 2012)*
- "Empirical Validation of Guidelines for the Management of Pharyngitis in Children and Adults" *(JAMA, 2004)*
- "Acute Rheumatic Fever and Rheumatic Heart Disease" (*Nature, 2016*)
- "Some of the People, Some of the Time: Susceptibility to Acute Rheumatic Fever" *(Circulation, 2009)*
- "Diagnostic Methods, Clinical Guidelines, and Antibiotic Treatment for Group A Streptococcal Pharyngitis: A Narrative Review" *(frontiers in Cellular and Infection Microbiology, 2020)*
- "Antibiotic Treatment, Mechanisms for Failure, and Adjunctive Therapies for Infections by Group A Streptococcus"*(frontiers in Cellular and Infection Microbiology, 2020)*
- "A Longitudinal Study of Group A Streptococcal Colonization and Pharyngitis in US Children" *(PIDJ, Dec 2023)*
- "The global burden of sore throat and group A *Streptococcus* pharyngitis: A systematic review and meta-analysis" *(Lancet, June 2022)*
- "Evaluating the Diagnostic Paradigm for Group A and Non–Group A Streptococcal Pharyngitis in the College Student Population" *(Open Forum Infectious Diseases, 2021)*
- "The *Streptococcus pyogenes* vaccine landscape" *(Nature Portfolio Journals, 2023)*
- CDC Website: Group A Streptococcal (GAS)Disease

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A Clinical Approach to Tonsillitis, Tonsillar Hypertrophy, and Peritonsillar and Retropharyngeal Abscesses

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Practice Gap

Despite established guidelines for group A *Streptococcus* pharyngitis diagnosis and treatment, pediatricians are overtreating and mistreating sore throat in children. (1) This results in unnecessary antibiotic use and contributes to antimicrobial resistance, increased health care costs, and risk for adverse drug reactions. In addition, controversy exists among pediatricians regarding the indications for tonsillectomy and adenoidectomy in children.

Objectives

After completing this article, readers should be able to:

1. Describe the clinical presentation, differential diagnosis, diagnostic evaluation, and management of tonsillitis/pharyngitis in pediatric patients.
2. Describe the clinical presentation, diagnostic evaluation, and management of peritonsillar abscess in pediatric patients.
3. Describe the clinical presentation, diagnostic evaluation, and management of retropharyngeal abscess in pediatric patients.
4. Describe the indications for tonsillectomy and adenoidectomy in pediatric patients and associated complications.

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ABBREVIATIONS

ALPS	Autoimmune lymphoproliferative syndrome
ARF	Acute rheumatic fever
CMV	Cytomegalovirus
CT	Computed tomography
EBV	Epstein-Barr virus
GAS	Group A *Streptococcus*
HIV	Human immunodeficiency virus
NSAIDs	Nonsteroidal anti-inflammatory drugs
OSA	Obstructive sleep apnea
PFAPA	Periodic fever, apthous stomatitis, pharyngitis, and adenitis
PSGN	Poststreptococcal glomerulonephritis
PTA	Peritonsillar abscess
RADT	Rapid antigen detection test
SDB	Sleep-disordered breathing
T&A	Tonsillectomy and adenoidectomy

TONSILLITIS, PHARYNGITIS

Epidemiology

Sore throat is a common complaint in children and adolescents. Most cases of pharyngitis are viral and self-limited. Group A *Streptococcus* (GAS) pharyngitis is the only commonly occurring infectious pharyngitis in which antimicrobial treatment is indicated. Treatment of GAS decreases the risk of acute rheumatic fever (ARF), suppurative complications and transmission of disease, and provides symptomatic relief. GAS pharyngitis accounts for 20%-30% of office visits for sore throats in children. (2) Infection typically occurs in school-age children and

adolescents, and is uncommon in children younger than 3 years. GAS pharyngitis occurs most commonly in the winter and early spring months and is spread through contact with oral and respiratory secretions of other humans. The relative predominance of the common viral causes varies by season with predominantly cold viruses (eg, rhinovirus, coronavirus, respiratory syncytial virus, parainfluenza) in the winter and enteroviruses in the warmer months.

Clinical Presentation

The signs and symptoms of pharyngitis due to GAS and other pharyngitides overlap and there is no universally agreed upon algorithm to guide clinicians' decision to forgo GAS testing. However, the history and physical examination should directly focus on differentiating between viral etiologies and GAS to guide the need for GAS testing. Fever, throat pain, and pharyngeal and/or tonsillar exudates are nonspecific findings. Concomitant cough, rhinorrhea, hoarseness, diarrhea, and/or the presence of oropharyngeal vesicles are highly suggestive of a viral etiology. Although nonspecific in isolation, the presence of scarletiniform rash, palatal petechiae, pharyngeal exudate, vomiting, and tender cervical nodes in combination increase the likelihood of GAS to greater than 50%. (3) Stridor, neck stiffness, or head tilt, limitation of neck movement, drooling, respiratory distress, or a toxic appearance are concerning for more serious diseases such as epiglottitis, retropharyngeal abscess, or Lemierre syndrome. Click on the following link, http://pedsinreview.aappublications.org/content/38/2/81.figures-only, for a video demonstration of the oropharyngeal examination technique.

Differential Diagnosis

Recognized viral etiologies of acute pharyngitis include adenovirus, rhinovirus, Epstein-Barr virus (EBV), parainfluenza, influenza, coxsackie, measles, and herpes simplex virus. *Mycoplasma pneumonia* is a common bacterial cause of pharyngitis. Pharyngitis can be a predominant symptom of acute retroviral syndrome secondary to infection with human immunodeficiency virus (HIV). Sexually active adolescents may also present with an acute pharyngitis caused by infection with *Neisseria gonorrhea*. Mononucleosis, commonly caused by EBV or cytomegalovirus (CMV) infection, often presents with an exudative pharyngitis, tender cervical lymphadenopathy, and constitutional symptoms. Immunocompromised patients are susceptible to opportunistic infections such as pharyngeal candidiasis (thrush) caused by *Candida albicans* infection. *Corynebacterium diphtheria* and *Haemophilus influenzae* b are uncommon causes of acute pharyngitis in developed countries but are possible in recent immigrants and unvaccinated children. A person infected with *Francisella tularensis* from ingestion of undercooked wild game meat may complain of pharyngitis. Traumatic or chemical pharyngitis can result from foreign body or caustic ingestion, respectively. Table 1 lists the full differential diagnosis and Table 2 infectious pathogens involved.

Diagnosis

Pharyngitis is a clinical diagnosis; additional testing should be focused on identifying children with the treatable causes of pharyngitis, atypical symptoms, and prolonged illness. Children and adolescents with signs and symptoms of acute pharyngitis in the absence of overt viral symptoms should be tested for GAS pharyngitis either with throat culture or rapid antigen detection test (RADT). Throat culture is the gold standard and most cost-effective test, with a sensitivity of 90% to 95%. The RADT has a specificity of 95% but variable sensitivity (ie, false-negative results occur).(2) A negative RADT should therefore be followed by throat culture for confirmatory testing. The sensitivity of throat culture and RADT are dependent on proper specimen collection that requires vigorous swabbing of both tonsils

TABLE 1. **Differential Diagnosis of Tonsillitis/ Pharyngitis**

Infectious	Viral Bacterial Fungal Peritonsillar abscess Lemierre syndrome Epiglottitis Tracheitis Croup Lateral/retropharyngeal abscess Uvulitis
Allergic/inflammatory	Kawasaki disease PFAPA Stevens-Johnson syndrome Behçet syndrome Angioedema Anaphylaxis
Environmental exposure	Foreign body ingestion Chemical exposure Irritative pharyngitis
Referred pain	Psychogenic pharyngitis Referred from dental abscess, otitis media, cervical adenitis
Oncologic	Lymphangioma, hemangioma of the airway

PFAPA=periodic fever, apthous stomatitis, pharyngitis, and adenitis.

TABLE 2. **Infectious Pathogens That Cause Tonsillitis/Pharyngitis**

Viral	Epstein-Barr virus, cytomegalovirus, adenovirus, enterovirus (coxsackie A and B), herpes simplex virus, HIV, influenza, RSV, parainfluenza, rhinovirus, coronavirus
Bacterial	Group A *Streptococcus*, *Mycoplasma pneumonia*, *Corynebacterium diphtheria*, *Neisseria gonorrhea*, *Arcanobacterium haemolyticum*, other Streptococci (group G and C), *Haemophilus influenza* type b, *Francisella tularenis*, *Fusobacterium necrophorum*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Yersinia enterolitica*, *Coxiella burnetii*
Fungal	*Candida* species

HIV=human immunodeficiency virus; RSV=respiratory syncytial virus.

and posterior pharynx without touching the tongue or buccal mucosa. Serologic tests are not routinely used in the diagnosis of acute GAS pharyngitis because antibody response does not occur until 2 to 3 weeks after initial infection. In general, testing for GAS in children younger than 3 years and in asymptomatic family or classroom contacts is not recommended.

The judicious and targeted use of the RADT is warranted. The ease of use and availability of the RADT in children with complaints of sore throat can lead to overuse in children with viral pharyngitis. This can, in turn, lead to the identification and unnecessary treatment of GAS carriers who are exposed to unnecessary courses of antibiotics. Standing orders for ancillary personnel to perform a RADT in every child with a chief complaint of sore throat before a clinical evaluation to assess for a viral etiology should be avoided.

Additional testing may be useful to diagnose non-GAS infectious tonsillopharyngitis. The need for additional testing should be individualized based on clinical signs and symptoms. With respect to EBV infection, in many cases, a clinical diagnosis can be made. However, in cases of diagnostic uncertainty and when an explanation is desired for persistent symptoms, a definitive diagnosis may be sought. There are several approaches, but no consensus exists regarding a diagnostic algorithm for EBV infection. The usefulness of the available tests varies with the duration of illness and age of the patient. In children older than 4 years who have symptoms for 2 weeks, a positive heterophile antibody test in conjunction with an absolute increase in the number of atypical lymphocytes is often considered diagnostic. The EBV viral capsid antigen immunoglobulin M test may be used in younger patients. If *Neisseria gonorrhea* is suspected, nucleic acid amplification testing or culture on special media (Thayer-Martin or Martin-Lewis medium) is necessary for diagnosis. Specimens should be obtained using swabs with plastic or wire shafts and rayon, polyester textile fabric, or calcium alginate tips because wood shafts and cotton tips may be toxic to the organism. (4) If acute retroviral syndrome is suspected, the combination HIV antibody/antigen test should be performed because it is the most sensitive immunoassay for HIV. Serologic testing is used to diagnose tularemia and should be ordered in patients with exposure history.

Treatment

Early antibiotic therapy for GAS pharyngitis (up to 9 days after illness onset) has been shown to prevent ARF, decrease symptom duration and severity, and reduce suppurative complications. (2) Whether antibiotic therapy reduces the risk of poststreptococcal glomerulonephritis (PSGN) is uncertain. Oral penicillin V is the treatment of choice for GAS pharyngitis given its proven efficacy, narrow spectrum, safety, and low cost. Oral amoxicillin may be used as a more palatable alternative that is equally effective. A single dose of intramuscular penicillin G benzathine can be used for patients who cannot tolerate a 10-day course of oral therapy, in patients with a history of poor compliance to oral therapy, and in those at increased risk for ARF. First-generation cephalosporins are an acceptable alternative for patients who report a penicillin allergy but do not have a history of anaphylaxis. Macrolides or clindamycin are acceptable alternatives in patients with a history of anaphylactic reactions to penicillin or with an unclear allergy history. Sulfonamide antibiotics, tetracyclines, and fluoroquinolones should not be used for treatment of GAS infections. Improvement is expected by 3 to 4 days after antibiotic initiation. Children are no longer considered contagious after 24 hours of treatment and may return to school. Table 3 provides specific antibiotic dosing information. (5)

Treatment of viral pharyngitis is symptomatic. Systemic analgesics are the mainstay of treatment and may be used for moderate to severe throat pain (nonsteroidal anti-inflammatory drugs [NSAIDs], acetaminophen). Although glucocorticoids may reduce pain from sore throat, there is limited high-quality evidence for this indication and, therefore, their use is not recommended in children at this time. Topical therapies include oral rinses, sprays, and lozenges. Oral rinses containing salt water have not been systematically studied. Rinses containing topical anesthetics (eg, lidocaine) and topical NSAIDs (eg, benzydamine hydrochloride) have been studied systematically, mainly in patients with postoperative

TABLE 3. **Antibiotic Treatment of GAS Tonsillitis/Pharyngitis**

ANTIBIOTIC	DOSE	ROUTE	DURATION
Penicillin V	400,000 U (250 mg) 2-3 times per day for children <27 kg 800,000 U (500 mg) 2-3 times per day for children >27 kg	Oral	10 days
Penicillin G benzathine	600,000 U (375 mg) for children <27 kg 1,200,000 U (750 mg) for children >27 kg	Intramuscular	1 time dose
Amoxicillin	50 mg/kg daily (max 1,000-1,200 mg)	Oral	10 days
First-generation cephalosporins	Cephalexin 20 mg/kg/dose twice a day (max 500 mg/dose)	Oral	10 days
Clindamycin	20 mg/kg/day in 3 divided doses (max 1.8 g/day)	Oral	10 days
Macrolides	Azithromycin 12 mg/kg/day max 500 mg daily Clarithromycin 7.5 mg/kg/dose BID max 250 mg/dose	Oral	5 days azithromycin 10 days clarithromycin

BID=twice a day; GAS=group A Streptococcus.

throat pain or throat pain because of chemotherapy-induced mucositis. The current evidence base is insufficient to draw conclusions. Sprays and medicated lozenges containing local anesthetics (benzocaine, phenol) are no more effective than candy at relieving throat pain and are not recommended because of the risk for methemoglobinemia and allergic reactions.

Group A *Streptococcus* Carriers

Asymptomatic patients with cultures that remain positive after a full course of treatment are likely carriers. Carrier status may be as high as 25% of asymptomatic children in high prevalence areas. (2) Carriers are not at increased risk for ARF or suppurative complications. Carriage of GAS can persist for many months but the risk of transmission from a carrier to another person is low. (2) A "test of cure" for GAS and repeated antimicrobial courses are, therefore, not indicated. Although it is possible that the child with frequent sore throats and positive cultures for GAS has recurrent GAS infections, it is more likely the child is a GAS carrier with recurrent viral illnesses. Compliance with oral therapy should be assessed, and the decision to treat should be made based on clinical findings and epidemiologic factors (patient age, season, history of contact with a person with GAS infection, family history of ARF or PSGN). Because it is not possible to differentiate a carrier state from an active GAS infection in real time, treatment is often chosen. The best strategy to avert this is to avoid overtesting and retesting. Exceptions to this rule are a personal or family history of ARF, community outbreaks of ARF or PSGN, GAS pharyngitis outbreaks in "closed" communities such as a daycare center, and "ping-pong" episodes of GAS pharyngitis among family members. (2) Children in these exceptional circumstances should be retested and re-treated despite suspicion for carrier status. GAS carriage is difficult to eradicate with conventional antimicrobials. Oral clindamycin at a dose of 30 mg/kg per day divided into 3 doses (maximum 900 mg/day) for 10 days is the recommended treatment for GAS carriers. (2)

PERITONSILLAR ABSCESS

Epidemiology

Peritonsillar cellulitis and abscess are among the most common deep space neck infections in children and adolescents. Peritonsillar abscess (PTA) is defined as a suppurative infection of the tissue between the palatine tonsil capsule and the pharyngeal muscles. The term peritonsillar cellulitis is used when tissue inflammation is present without a discrete pus collection. According to one US study, the incidence of PTA was 9.4 per 100,000 children younger than 20 years in 2009. (6) Its incidence peaks in adolescence with an average age of 13.6 years. (6) Most PTAs are polymicrobial, with *Streptococcus* and *Fusobacterium* species being the most common etiologic agents.

Clinical Presentation

Patients with PTAs most commonly present with sore throat and fever. Other symptoms include dysphagia, odynophagia, voice change, drooling, and trismus (due to spasm of the internal pterygoid muscle). Physical examination signs include uvular deviation toward the contralateral side,

ipsilateral tonsillar bulging, the presence of a tender neck mass, and cervical and/or submandibular lymphadenopathy. Patients may appear anxious or irritable and be unable to take anything by mouth. Younger children are less likely to complain of sore throat and are more likely to present with a neck mass. (7) Clinicians should suspect PTA in patients with symptoms of pharyngitis who have a prolonged or progressive course. Untreated PTA can lead to serious complications such as airway obstruction, aspiration pneumonia, carotid artery pseudoaneurysm or rupture with resulting sepsis and hemorrhage, and septic thrombophlebitis of the internal jugular vein (Lemierre syndrome). The differential diagnosis is similar to that for tonsillopharyngitis (Table 1).

Diagnosis

Diagnosis of a PTA is largely made on clinical suspicion, and laboratory evaluation is usually unnecessary. Similarly, imaging studies are generally not required. If the diagnosis is in question, intraoral ultrasonography was recently found to be an effective tool to determine the presence or absence of a fluid collection. Although contrast-enhanced computed tomography (CT) of the neck is also effective in determining the presence of a PTA, its use should be avoided if possible because of the close proximity of radiation-sensitive tissues such as the thyroid gland. Clinicians are encouraged to consult the American College of Radiology Appropriateness Criteria before considering CT for this indication. (8) According to the criteria, any recommended imaging studies for children who present with neck masses must take into consideration the risk of sedation and radiation dose. CT of the neck with contrast has a relative radiation level of 0.3 to 3 millisievert compared to zero radiation risk with ultrasonography. However, CT of the neck with contrast may be appropriate if there is concern for malignancy or a deep neck abscess that may require surgical drainage.

Treatment

Because PTA is a disease process found more commonly in adolescents, drainage while awake is considered the treatment of choice. This can often be performed under local anesthesia in the emergency department or in the office of a pediatric otolaryngologist. For younger or uncooperative patients, general anesthesia may be required. Controversy exists regarding needle aspiration versus incision and drainage. With the patient in an upright sitting position, topical or infiltrative anesthesia is applied and an 18-gauge needle is used to localize and aspirate the abscess pocket, usually in the soft palate superior to the superior tonsillar pole. If an incision is to be made, it is created at the area of maximal bulging in a lateral to medial fashion. A clamp can then be used to open the abscess pocket and drain additional purulent material. An experienced clinician, usually an otolaryngologist, should perform these procedures. Cultures of any recovered material should be performed. Patients can usually be discharged after the procedure with oral antibiotic therapy for 7 to 10 days. Penicillins, cephalosporins, or clindamycin are good empirical options while awaiting culture results. Indications for admission include the need for intravenous hydration due to poor oral intake, pain management, no reliable outpatient follow-up, and management of complications after drainage such as severe bleeding or respiratory distress secondary to aspiration of abscess contents into the patient's airway. In the past, quinsy tonsillectomy (tonsillectomy in the presence of a PTA) was used as a drainage treatment; however, this has largely been abandoned as a first-line treatment.

RETROPHARYNGEAL ABSCESS

Epidemiology

A retropharyngeal abscess is a suppurative deep neck infection that occurs in the potential space extending from the base of the skull to the posterior mediastinum between the posterior pharyngeal wall and prevertebral fascia. The retropharyngeal space houses a chain of lymph nodes that drains the nasopharynx, adenoids, eustachian tubes, middle ears, and posterior paranasal sinuses. The pathogenesis of retropharyngeal abscess is thought to frequently follow an upper respiratory tract infection with resulting suppuration of the retropharyngeal lymph nodes and abscess formation. The abscess may also form secondary to trauma from an ingested foreign body or instrumentation in the posterior oropharynx. According to one US study, the incidence of retropharyngeal abscess has increased from 2.98 to 4.10 per 100,000 children younger than 20 years from 2003 to 2012. (9) Incidence is highest among children younger than 5 years and in boys. (9) The microbiology of retropharyngeal abscesses is often polymicrobial. Streptococcal, staphylococcal species, and respiratory anaerobes are the most common organisms isolated.

Clinical Presentation

Presentation of retropharyngeal abscess is variable and no particular constellation of symptoms and signs is diagnostic. Patients commonly present with complaints of fever, neck pain, and dysphagia. Other symptoms include sore throat, odynophagia, decreased oral intake, drooling,

dyspnea, and even chest pain if there is mediastinal extension. Common physical examination signs include cervical lymphadenopathy, limited neck movement or meningismus, torticollis, and the presence of a palpable neck mass. Tonsillar displacement, dysphonia, trismus, and stridor may also be appreciated. Patients may appear ill and anxious, and exhibit posturing. Care must be taken when examining these children because the stress of the oropharynx examination can result in partial or complete airway obstruction. There is also a risk of abscess rupture. For ill-appearing patients with signs of partial upper airway obstruction such as stridor or stertor, performing the oropharynx examination in the operating room where an emergent surgical airway can be established, if necessary, is recommended. Untreated retropharyngeal abscess can lead to serious infectious and obstructive complications similar to those described for PTA. Additional complications include atlantoaxial dislocation and mediastinitis because of the proximity of the retropharyngeal space to these critical structures. The differential diagnosis includes causes of sore throat and airway obstruction as outlined in Table 1. In patients presenting with neck pain or stiffness, the differential diagnosis should also include meningitis, cervical spine arthritis, spinal trauma, dystonic reaction, tuberculous abscess of the spine, and various toxin-mediated diseases (tetanus, black widow spider bite, scorpion bite).

Diagnosis

If the diagnosis is apparent from history and physical examination findings, laboratory studies may not be necessary. In cases of diagnostic uncertainty, a complete blood cell count may be helpful to identify signs of inflammation (leukocytosis, thrombocytosis). A throat culture for GAS and a peripheral blood culture, if positive, can help guide antibiotic therapy. Other tests to consider, especially in patients with unusual presentations, include EBV, CMV and toxoplasmosis titers, purified protein derivative placement, erythrocyte sedimentation rate, and C-reactive protein.

Imaging should be reserved for cases in which the diagnosis is in question, if operative management is required or no improvement is seen after 48 to 72 hours of intravenous antibiotic therapy. Lateral neck radiography is often the first imaging modality pursued and may reveal thickening of the prevertebral soft tissues (Fig 1). At the level of the second cervical vertebrae, thickening greater than 7 mm is considered abnormal, or greater than 14 mm at the level of the sixth cervical vertebrae. Unfortunately, lateral neck radiography has a high false-positive rate secondary to variations in positioning, swallowing, and respiration. In addition, plain radiography cannot differentiate between phlegmon and frank abscess formation. A chest radiograph should be obtained if mediastinitis is suspected. Contrast-enhanced neck CT is the imaging modality of choice to differentiate abscess from phlegmon and for operative planning (Figs 2 and 3). However, judicious use of CT is recommended given the harmful effects of radiation exposure in children. For example, one should limit CT to children who have failed conservative treatment and require operative management. Ultrasonography is generally not helpful unless an associated neck mass is identified.

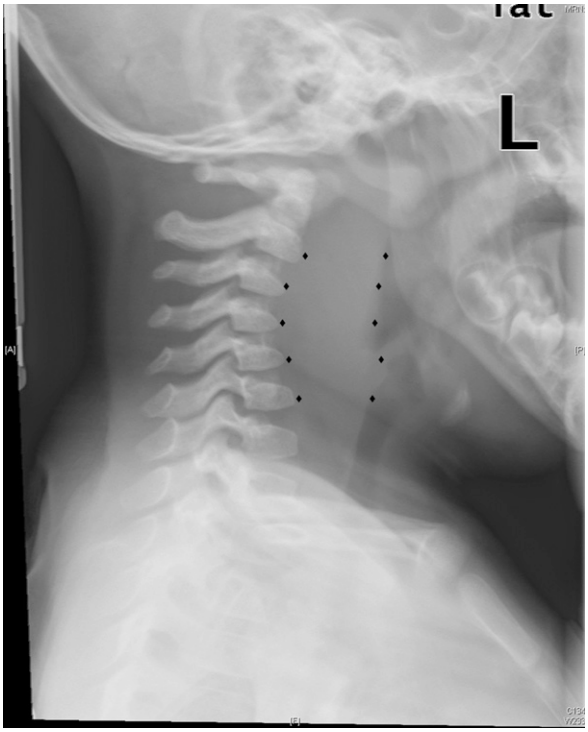


Figure 1. Lateral neck radiograph showing widening of the prevertebral soft tissue suggestive of retropharyngeal abscess.

Treatment

When considering management of retropharyngeal abscesses, the first consideration is the airway. Supplemental humidified oxygen, nasal trumpet, or positive pressure ventilation may be sufficient for moderate airway obstruction, but intubation or tracheotomy is rarely necessary. Although this topic continues to be debated, deep neck space infections are commonly treated initially with 24 to 48 hours of broad-spectrum parenteral antibiotics (eg, clindamycin, cephalosporins, β-lactamase penicillins), because approximately 60% of infections may resolve with medical management alone. For patients who fail to improve or progress despite antimicrobial therapy, surgical treatment should be considered. Generally a transoral approach is used to drain the abscess via an incision in the posterior pharyngeal

wall. For abscesses with cervical extension lateral to the great vessels, inferior to the hyoid bone or into other neck spaces, a transcervical approach is generally applied. Purulent fluid is sent for culture and a biopsy may be taken if another process is suspected. CT-guided drainage by interventional radiology can also be considered for abscesses in difficult to access locations. Recurrent abscesses should be considered for patients who fail to improve or whose symptoms return after a short period of improvement.

TONSILLAR AND ADENOIDAL HYPERTROPHY

Indications for Tonsillectomy and Adenoidectomy

Tonsillectomy and adenoidectomy (T&A) is the second most common surgery performed in the United States. (10) The 2 main indications for tonsillectomy are sleep-disordered breathing (SDB) and severe recurrent throat infections.

Severe throat infection, as defined by the Paradise criteria (11) is a documented sore throat plus 1 of the following: temperature greater than 38.3°C, cervical lymphadenopathy (tender nodes or >2 cm in diameter), tonsillar exudate, positive GAS RADT or culture. Recurrent infection is defined as more than 7 documented episodes of severe throat infections in 1 year, more than 5 episodes per year for 2 consecutive years, or more than 3 episodes per year for 3 consecutive years. Patients who do not meet these strict criteria should be evaluated for the presence of modifying factors that may make them candidates for T&A (eg, family or personal history of ARF, history of PTA, Lemierre syndrome, periodic fever, apthous stomatitis, pharyngitis, and adenitis [PFAPA], and multiple antibiotic allergies).

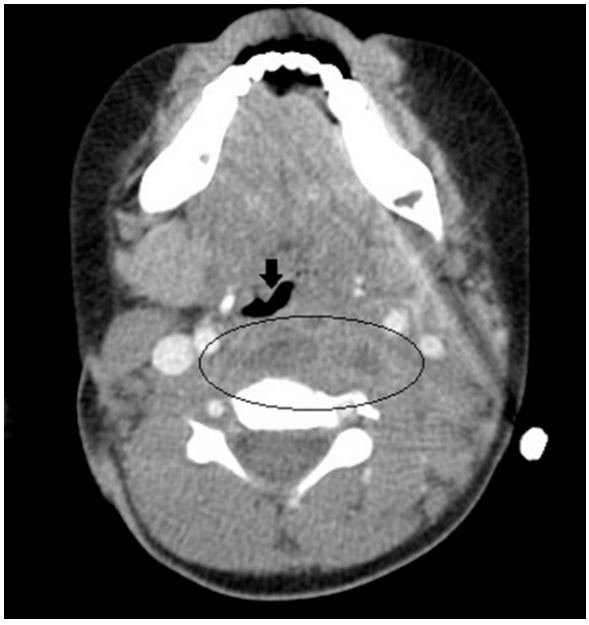


Figure 2. Contrast axial computed tomographic image showing heterogenous material with areas of hypodensity (circled) representing phlegmon with developing retropharyngeal abscess. The airway is displaced anteriorly (arrow) secondary to the retropharyngeal process.

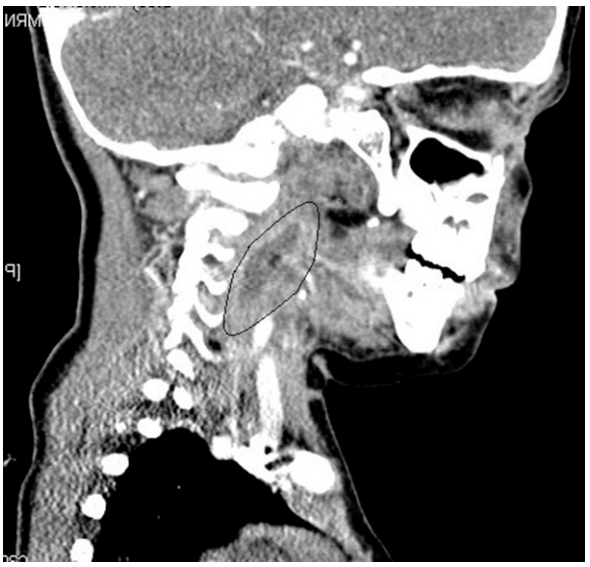


Figure 3. Contrast sagittal computed tomographic image demonstrating a retropharyngeal abscess (circled).

T&A is now being performed much more commonly for obstructive rather than infectious indications. (12) It should be considered for patients with SDB who also have comorbid conditions (eg, growth restriction, poor school performance, nocturnal enuresis, behavioral problems). (12) The role of polysomnography before T&A is controversial. According to the American Academy of Otolaryngology and Head and Neck Surgery, polysomnography is not necessary before T&A in otherwise healthy children with SDB but may be helpful in certain situations: in children predisposed to obstructive sleep apnea (OSA) and, therefore, at risk for perioperative respiratory complications (eg, children with trisomy 21, morbid obesity, neuromuscular disorders, or craniofacial abnormalities). (12)(13) The American Academy of Pediatrics recommends screening of otherwise healthy children and adolescents for snoring and signs/symptoms of SDB at routine health maintenance visits. They also recommend polysomnography or referral to a specialist such as a pediatric otolaryngologist for those who have positive screening results. (14) Polysomnography, although not necessary before T&A for SDB, is helpful to quantify the severity of OSA and the risk for postoperative complications. The current literature generally supports T&A as an acceptable treatment for

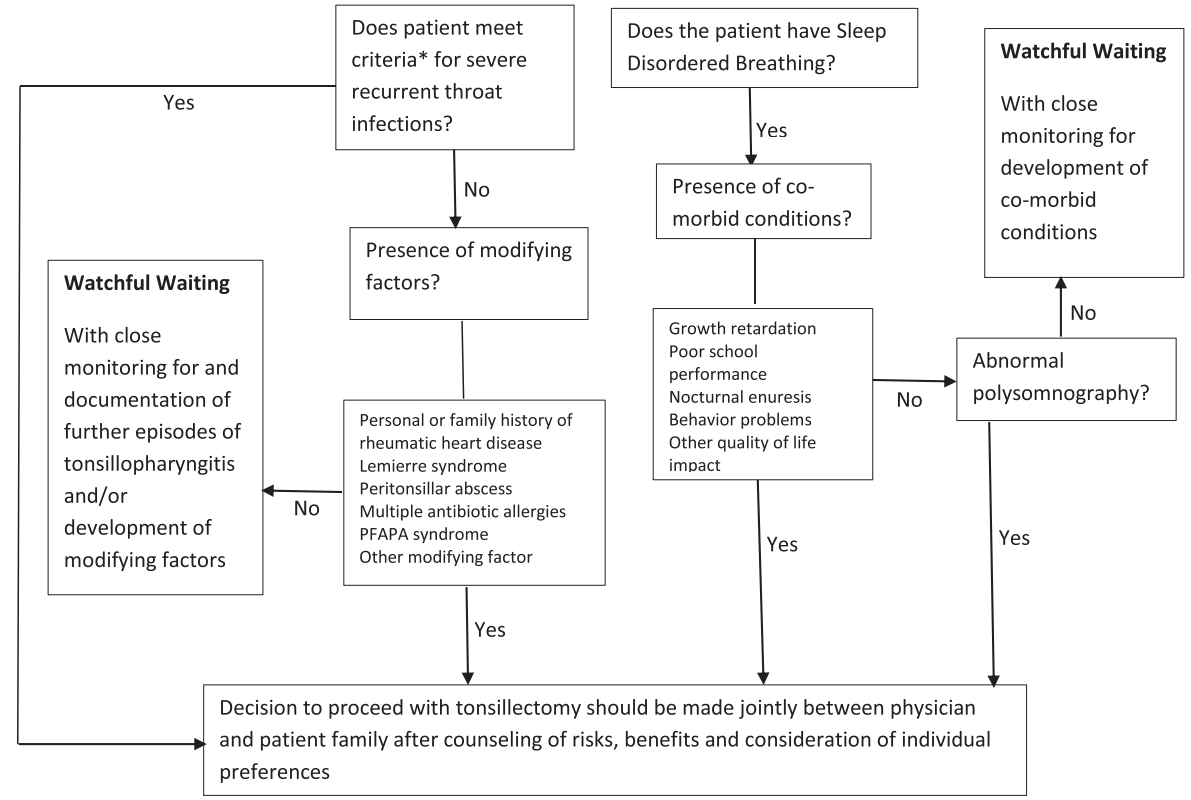
SDB/OSA. Studies have reported polysomnography normalization and improvement in parent- and patient-reported quality of life measures after T&A. However, OSA resolution is less likely in children with obesity, those of African American race, and those who have severe OSA at baseline. (13)

The decision to proceed with T&A should, therefore, be made jointly between the physician and patient family after counseling about risks, benefits, and consideration of individual preferences. (12) Shared decision-making tools such as option grids (15) are helpful to empower patients with the information necessary for them to take an active part in the decision-making process. Watchful waiting with close monitoring for and documentation of further episodes of tonsillopharyngitis, development of modifying factors, and/or development of comorbid conditions associated with SDB are recommended for patients who do not meet the aforementioned criteria. Figure 4 shows our recommended clinical decision pathway.

The main indication for adenoidectomy alone is severe nasal obstruction. Symptoms of severe nasal obstruction include mouth breathing, hyponasal speech, and impaired olfaction. Symptoms must present for more than 1 year and must persist despite conservative treatment such as a trial of antimicrobial therapy and nasal corticosteroids to exclude infectious and allergic causes of adenoidal hypertrophy. Relative indications for adenoidectomy include refractory chronic sinusitis, recurrent acute otitis media, and chronic otitis media with effusion in children who failed tympanostomy tube placement.

Complications

The overall frequency of postoperative complications after T&A is around 19%. (16) Postoperative bleeding occurs in



Modified Paradise Criteria*

1. Frequency of Episodes: > 7 episodes in 1 year, > 5 episodes per year for 2 years, >3 episodes per year for 3 years
2. Episode Criteria: Sore throat and 1 of the following: T>38.3, Cervical lymphadenopathy (tender or > 2cm), tonsillar exudate, positive GAS

Figure 4. Decision tree for tonsillectomy.
GAS=group A *Streptococcus*, PFAPA=periodic fever, apthous stomatitis, pharyngitis, and adenitis.

TABLE 4. **Conditions Associated with Tonsillar and Adenoidal Hypertrophy**

Infection
Allergy
Chronic inflammation
Malignancy- lymphoma or squamous cell carcinoma of the tonsil
Autoimmune lymphoproliferative syndrome
Lysosomal storage diseases and mucopolysaccharidoses
Idiopathic

approximately 5% of T&As. (16) Bleeding is characterized as primary if it occurs within the first 24 hours after surgery and secondary if it is more than 24 hours after surgery. Secondary hemorrhage is thought to be due to premature separation of eschar from the tonsillar bed and occurs most frequently on postoperative day 5 to 6. The bleeding usually stops spontaneously but sometimes requires repeat surgical intervention. Preoperative assessment of personal or family history of bleeding dyscrasias and postoperative anticipatory guidance regarding this potential complication are therefore essential.

Respiratory complications occur in approximately 9.4% of T&As. (16) These may be minor such as increased postoperative snoring or mouth breathing but may also be more serious. Perioperative desaturations, apneas or respiratory failure requiring supplemental oxygen, continuous positive airway pressure, oral or nasal airway insertion or reintubation, and assisted ventilation have been reported. Children with OSA are 5 times more likely to have perioperative respiratory complications than those undergoing T&A for other indications. (16)

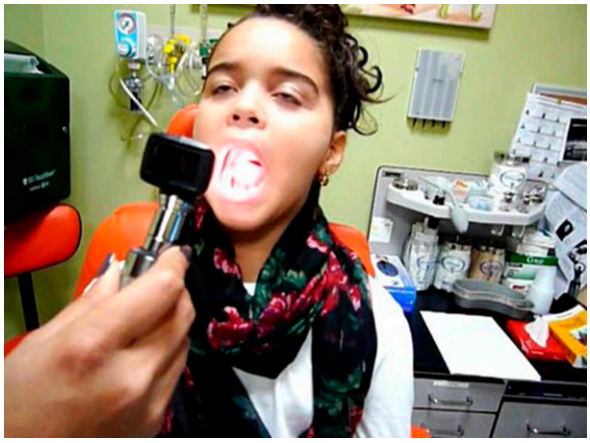
Velopharyngeal insufficiency, characterized by hypernasal speech, nasal air emission, and nasal liquid regurgitation, may also occur after T&A. Patients with cleft palate, submucous clefts, bifid uvula, neuromuscular disorders, and 22Q11 syndrome are particularly at risk for this complication. When it occurs postoperatively, velopharyngeal insufficiency is most often temporary. Nasopharyngeal stenosis may also occur after adenoidectomy. This presents with hyponasal speech and difficulty breathing through the nose.

Other complications of T&A include anesthesia-related bronchospasm/laryngospasm, electrocautery burn injuries, and temporomandibular joint dysfunction from the mouth gag used during the procedure. Postoperative pain, nausea, vomiting, and dehydration are also common. Acetaminophen with or without ibuprofen is recommended for postoperative pain control with sparing use of opioids due to increased risk for respiratory complications with this class of medication. (12) As with any surgical procedure, there is also a risk of infection. However, the American Academy of Otolaryngology–Head and Neck Surgery recommends against routine perioperative antimicrobial prophylaxis. (12) Studies have documented weight gain as a potential complication after T&A due to the decreased work of breathing postoperatively. It is therefore important to counsel all patients planning to undergo T&A about healthy nutrition and physical activity. Other rare complications of T&A include Grisel syndrome, a nontraumatic subluxation of the atlantoaxial joint that presents as severe neck pain and torticollis. Children with trisomy 21 are more predisposed to this complication. The risk of mortality with T&A is 1 in 16,000 to 35,000. (16)

In general, one should consider postoperative hospitalization in children who are younger than 3 years, children with severe OSA at baseline, and those with significant preoperative comorbid conditions that put them at increased risk for postoperative respiratory complications (eg, obesity, cardiac disease, neuromuscular disorders, prematurity, and craniofacial abnormalities). (13)

Conditions Associated with Tonsillar/Adenoidal Hypertrophy

In addition to acute or chronic infection, other processes can lead to tonsillar and adenoidal hypertrophy. In the case of unilateral tonsillar enlargement, it is important to evaluate for potential neoplastic processes such as lymphoma or human papillomavirus–associated squamous cell carcinoma of the tonsil. Although very rare,



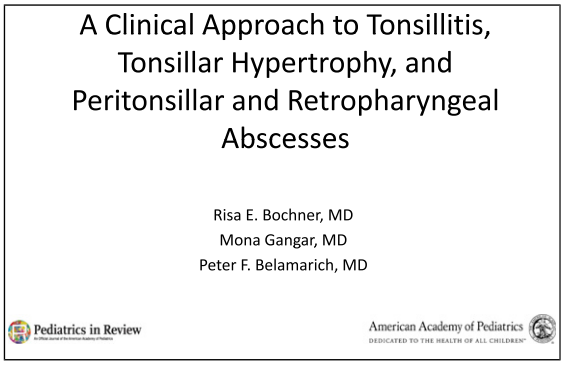
Video. Click here to view the video. Video shows the oropharyngeal examination technique.

autoimmune lymphoproliferative syndrome is also possible. In addition, some lysosomal storage diseases such as the mucopolysaccharidoses are associated with tonsillar and adenoidal hypertrophy (Table 4).

Summary

- On the basis of strong research evidence (level A), children older than 3 years with sore throat in the absence of viral symptoms should be tested for group A *Streptococcus* (GAS) pharyngitis.
- On the basis of strong research evidence (level A), oral or intramuscular penicillin and amoxicillin are first-line treatments for GAS pharyngitis.
- On the basis of research evidence (level B), first-generation cephalosporins, macrolides, or clindamycin are acceptable alternatives for penicillin-allergic patients.
- On the basis of research evidence (level B), asymptomatic carriers of GAS should not be treated with antibiotic therapy.
- On the basis of limited evidence (level C), diagnosis of peritonsillar abscesses can usually be made based on clinical suspicion and laboratory testing/imaging are often unnecessary.
- On the basis of research evidence (level C), imaging for retropharyngeal abscess should be reserved only when the diagnosis is in question, when operative management is required, or when there is lack of improvement after 48 to 72 hours of intravenous antibiotic therapy.
- On the basis of expert opinion (level D), decision to proceed with tonsillectomy and adenoidectomy (T&A) should be made jointly between the physician and patient family after counseling them about the risks, benefits, and consideration of individual preferences. Cases that do not meet the criteria for T&A (severe recurrent throat infections, moderate throat infection with modifying factors, sleep-disordered breathing with comorbid conditions and/or abnormal polysomnography) should be managed by watchful waiting.

To view the teaching slides that accompany this article, visit http://pedsinreview.aappublications.org/content/38/2/81.supplemental.



References for this article are at http://pedsinreview.aappublications.org/content/38/2/81.

Parent Resources from the AAP at HealthyChildren.org

- Tonsillitis: https://www.healthychildren.org/English/health-issues/conditions/ear-nose-throat/Pages/Tonsillitis.aspx
- The Difference between a Sore Throat, Strep & Tonsillitis: https://www.healthychildren.org/English/health-issues/conditions/ear-nose-throat/Pages/The-Difference-Between-a-Sore-Throat-Strep-and-Tonsillitis.aspx

For a comprehensive library of AAP parent handouts, please go to the *Pediatric Patient Education* site at http://patiented.aap.org.

Group A *Streptococcus* Infections

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EDUCATION GAPS

Clinicians should know: 1) throat swabs for rapid antigen detection tests and/or cultures are not recommended for children younger than 3 years unless the patient has a close infected contact; 2) treatment regimens exist for eradication of the carrier state and should be trialed before tonsillectomy; and 3) Clindamycin is important in the treatment of invasive group A *Streptococcus* infection for toxin mediation but should not be used alone due to possible resistance. Clindamycin can be used alone when sensitivities are known or to eliminate the group A *Streptococcus* pharyngeal carrier state.

OBJECTIVES *After completing this article, readers should be able to:*

1. Plan the appropriate diagnostic evaluation for a patient suspected of having group A *Streptococcus* (GAS) infection or postinfectious complications.
2. Recognize the features of invasive GAS infections.
3. Plan appropriate management for patients with different manifestations of GAS infection.

ABSTRACT

Group A *Streptococcus* causes a variety of clinical manifestations, including pharyngitis and skin and soft tissue infections as well as more invasive disease. There are also multiple nonsuppurative complications of group A *Streptococcus* infection, including acute rheumatic fever and poststreptococcal glomerulonephritis. Pediatricians should be able to diagnose and treat the various presentations of the infection.

AUTHOR DISCLOSURE: Dr Bhavsar has disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

ABBREVIATIONS

ANF	acute necrotizing fasciitis
ARF	acute rheumatic fever
GAS	group A *Streptococcus*
PSGN	poststreptococcal glomerulonephritis
STSS	streptococcal toxic shock syndrome

EPIDEMIOLOGY

Streptococcus pyogenes, also known as group A *Streptococcus* (GAS), is a gram-positive coccus that grows in chains. GAS exhibit β-hemolysis when grown on blood agar plates. Transmission of GAS infections occur by respiratory droplets from persons with pharyngeal infection or by direct contact from those with skin manifestations. In those with invasive GAS infections, the bacteria spread to deep tissues and the

bloodstream. GAS pharyngitis and invasive infections most commonly occur in the winter months. Impetigo most commonly occurs in the summer months. (1) GAS is responsible for a variety of clinical manifestations, from less severe infections such as pharyngitis, impetigo, cellulitis, and erysipelas to more severe invasive diseases such as septicemia, streptococcal toxic shock syndrome (STSS), and acute necrotizing fasciitis (ANF). GAS is also linked to multiple nonsuppurative complications, including acute rheumatic fever (ARF) and poststreptococcal glomerulonephritis (PSGN). (1)(2) The virulence and ranges of infections are due to specific characteristics that the bacterium possesses, including the M protein, which inhibits opsonization and phagocytosis and facilitates tissue invasion and the hyaluronic acid capsule, which protects GAS from phagocytosis. For invasive GAS infections, streptococcal toxins called superantigens play an important role stimulating massive cytokine release, responsible for the rapid and overwhelming progression of disease. (3)

In 2020 and 2021 during the COVID-19 pandemic, invasive GAS infection rates in children 2 through 17 years of age were the lowest on record since 1997. There were also low numbers of less severe infections in all age groups. This decrease is likely attributable to school and work closures, social distancing, and masking. The Centers for Disease Control and Prevention (CDC) is currently investigating an increase in invasive GAS infections during the fall of 2022 and winter of 2023, with rates higher than prepandemic years, and occurring during the same time as increases in respiratory viruses. (4)

CLINICAL ASPECTS

Noninvasive GAS Infections

Streptococcal Pharyngitis. The most common GAS infection is acute pharyngitis. It is most common in school-age children, peaking at age 7 to 8 years, but can occur at all ages. It is uncommon in children younger than 3 years. For school-age children and adolescents, clinical signs and symptoms include fever, sore throat, vomiting, abdominal pain, tender anterior cervical adenopathy, and pharyngeal and tonsillar exudate (Fig 1). Younger children may present with rhinitis, fever, irritability, and generalized lymphadenopathy. Purulent complications of pharyngitis include suppurative cervical adenitis and retropharyngeal and peritonsillar abscesses. Acute bacterial sinusitis and acute otitis media can rarely occur. Scarlet fever occurs most commonly with pharyngitis, instead of other GAS manifestations. The rash of scarlet fever involves sandpaper-like tiny papules with a predilection for the neck and shoulder. (2)(5)

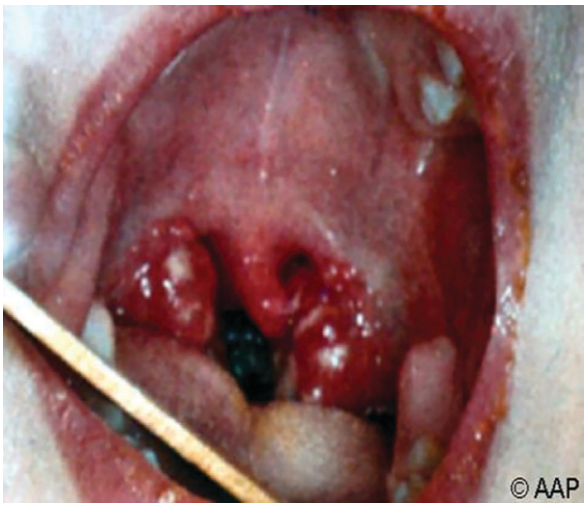

Figure 1. Erythematous tonsils with exudate in a child with group A streptococcal pharyngitis.

Children with signs and symptoms of acute GAS pharyngitis should be tested. Children with pharyngitis with other associated viral symptoms (conjunctivitis, rhinitis, coryza, rash, and cough) should not be tested or treated. Testing is also not generally recommended for children who are younger than 3 years because they are unlikely to manifest ARF. However, physicians may choose to test those younger than 3 years if risk factors exist, for example, the child has a relative with GAS. Several rapid antigen detection tests for GAS pharyngitis are available. The specificity of these tests is high, but sensitivity is generally 80% to 85%. Negative rapid antigen results require a confirmatory throat culture. Children with GAS in the pharynx without clinical symptoms are considered to be GAS carriers. Carriers are typically not infectious. Treatment is not recommended in patients with positive throat cultures without clinical symptoms of streptococcal pharyngitis. Throat cultures should not be obtained in asymptomatic patients. (2)(5)

Impetigo. Impetigo is a superficial skin infection most commonly affecting children 2 to 5 years of age but can occur at any age. Lesions typically occur at the site of breaks in the skin (eg, insect bites, traumatic wounds, varicella lesions). Nonbullous impetigo typically manifests as erythematous papules, which later evolve to vesicles that rupture to form characteristic "honey-colored" exudate and thick crust (Fig 2). Bullous lesions are most commonly caused by *Staphylococcus aureus,* whereas nonbullous impetigo may result from either GAS or *S aureus.* In the 1950s through the 1970s, the most common cause of impetigo was GAS, but now, *S aureus* is more common,

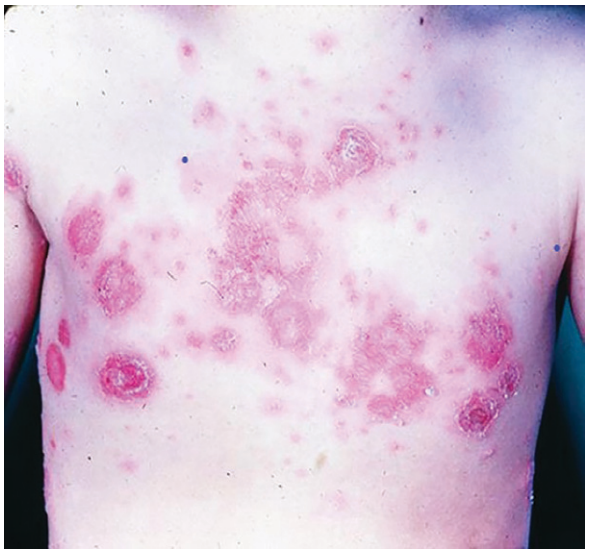

Figure 2. Group A streptococcal impetigo.

accounting for more than 80% of impetigo infections. Culture of the lesions can determine the responsible organism. (2)(5)

Erysipelas and Cellulitis. Erysipelas is an infection of the deeper dermis, whereas cellulitis is an infection of the dermis and subcutaneous tissue. Erysipelas classically presents as raised, painful skin erythematous lesions with distinct borders, most commonly on the face or extremities (Fig 3). Lymphatic involvement is frequently seen with ascending lymphangitis (erythematous streaking). In contrast, cellulitis typically presents as erythema and edema that is not sharply demarcated but can have associated pain and warmth. These infections are primarily caused by GAS; however, the presence of purulent lesions or abscesses should raise a clinician's suspicion for *S aureus*. (2)(6)

Invasive GAS Infections

In invasive infections, GAS is isolated from a normally sterile site, including blood, joint fluid, or cerebrospinal fluid.

Streptococcal Toxic Shock Syndrome. STSS is defined as GAS infection accompanied by sudden onset of shock and organ failure. Patients often begin with influenzalike symptoms such as fever, chills, myalgias, nausea, and vomiting and then rapidly progress to sepsis with signs and symptoms concerning for multiorgan failure within 24 to 48 hours (Table 1). (2)

Type II ANF. ANF is a rare infection involving rapidly progressing deep tissue infection. Type I ANF is a polymicrobial infection, whereas type II is caused by GAS alone or in combination with another bacterium. It is a rare

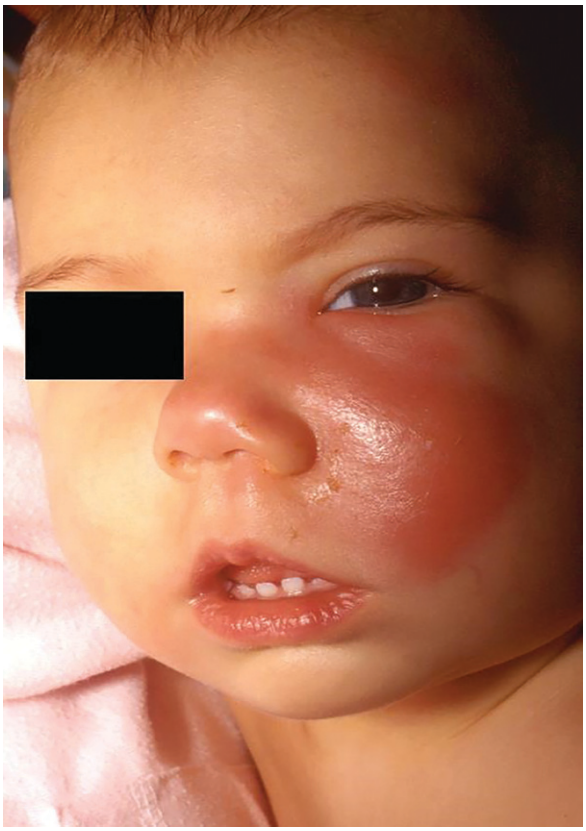

Figure 3. Facial erysipelas in a 1-year-old.

infection that usually occurs after trauma or surgery. Type II ANF can also occur as a superinfection complication of varicella infection. Type II ANF most commonly affects the extremities, particularly the legs. Clinical findings of necrotizing fasciitis include profound pain, swelling, and erythema in the affected area. Typically, the pain experienced by the patient is out of proportion to the signs of the local skin infection. Within 24 to 48 hours, skin necrosis may occur, indicating that small vessels have thrombosed in the dermal papilla. Decreased sensation due to destruction of superficial nerves, bullae with hemorrhagic fluid, and crepitus can be palpated. Prompt surgical exploration and obtaining cultures is recommended if there is clinical suspicion. If there is low suspicion for necrotizing fasciitis, imaging studies such as computed tomography or magnetic resonance imaging can aid in the diagnosis by detecting subcutaneous and fascial edema or tissue gas (which is a classic finding in ANF). (6)

NONSUPPURATIVE COMPLICATIONS

Acute Rheumatic Fever

ARF is a nonsuppurative sequela after untreated GAS pharyngitis, and in endemic areas, it is the leading cardiovascular

Table 1. Streptococcal Toxic Shock Syndrome: Clinical Case Definition[a]

I. Isolation of group A *Streptococcus (Streptococcus pyogenes)*
A. From a normally sterile site (eg, blood or cerebrospinal, peritoneal, joint, pleural, or pericardial fluid)
B. From a nonsterile site (eg, throat, sputum, vagina, open surgical wound, or superficial skin lesion)
II. Clinical signs of severity
A. Hypotension: systolic pressure ≤90 mm Hg in adults or lower than the fifth percentile for age in children <16 y
and
B. ≥2 of the following signs of multiorgan involvement:
• Renal impairment: creatinine concentration ≥2 mg/dL (≥177 μmol/L) for adults or ≥2 times the upper limit of normal for age[b]
• Coagulopathy: platelet count ≤100×10^3/μL (≤100×10^9/L) and/or disseminated intravascular coagulation defined by prolonged clotting times, low fibrinogen level, and the presence of fibrin degradation products
• Hepatic involvement: elevated alanine aminotransferase, aspartate aminotransferase, or total bilirubin concentrations ≥2 times the upper limit of normal for age[b]
• Acute respiratory distress syndrome defined by acute onset of diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure or by evidence of diffuse capillary leak
• A generalized erythematous macular rash that may desquamate
• Soft tissue necrosis, including necrotizing fasciitis, myositis, or gangrene

[a]An illness fulfilling criteria IA, IIA, and IIB can be defined as a confirmed case. An illness fulfilling criteria IB, IIA, and IIB can be defined as a probable case if no other cause for the illness is identified. Manifestations need not be detected within the first 48 hours of illness or hospitalization.
[b]In patients with preexisting renal or hepatic disease, concentrations 2-fold or greater over patient's baseline.
Adapted with permission from The Working Group on Severe Streptococcal Infections. Defining the group A streptococcal toxic shock syndrome: rationale and consensus definition. *JAMA*. 1993;269(3):390–391.

cause of death in children. Typical onset is 2 to 4 weeks after GAS pharyngitis. Children aged 5 to 14 years have the greatest incidence of ARF. Jones criteria for diagnosis of ARF were established in 1944 and were revised and modified most recently in 2015. The revised Jones criteria distinguish between low-risk and moderate- to high-risk populations (Table 2). Laboratory evidence of antecedent GAS infection must be confirmed in suspected ARF cases because this is part of the diagnostic criteria. Laboratory evidence includes increased or an increasing antistreptolysin O or anti-DNAse B titer or a positive streptococcal rapid antigen test or throat culture. (2)(7)(8)

Poststreptococcal Reactive Arthritis

Reactive arthritis may develop after an episode of acute GAS pharyngitis without other clinical or laboratory findings to fulfill the Jones criteria for the diagnosis of ARF. This syndrome is referred to as poststreptococcal reactive arthritis. In contrast to patients with ARF, patients with poststreptococcal reactive arthritis do not respond dramatically to nonsteroidal anti-inflammatory agents. Careful observation is recommended for 1 to 2 years for the development of carditis because a small proportion of patients with poststreptococcal reactive arthritis have been reported

Table 2. Modified Jones Criteria 2015

1. All patients require evidence of antecedent GAS infection for diagnosis of ARF (except in case of chorea, where evidence of antecedent GAS infection is not required).
2. To confirm an initial diagnosis of ARF, need 2 major OR 1 major and 2 minor criteria.
3. To confirm recurrent ARF diagnosis, need 2 major OR 1 major and 2 minor OR 3 minor criteria.
4. Criteria for diagnosis depend on whether the patient is from a low-risk or a moderate-/high-risk population. Moderate- and high-risk populations include countries where ARF remains endemic (Africa, Asia-Pacific, indigenous population of Australia). The United States, Canada, and Europe are examples of low-risk areas.
5. Major and minor criteria are listed below, by risk categorization; differences for moderate-/high-risk populations are **bolded**.

Low-risk population	Moderate- and high-risk population
Major criteria	Major criteria
• Carditis (clinical or subclinical)	• Carditis (clinical or subclinical)
• Arthritis (polyarthritis only)	• Arthritis (polyarthritis **or monoarthritis, or polyarthralgia**)
• Chorea	• Chorea
• Subcutaneous nodules	• Subcutaneous nodules
• Erythema marginatum	• Erythema marginatum
Minor criteria	Minor criteria
• Polyarthralgia	• **Monoarthralgia**
• Fever (≥101.3°F [≥38.5°C])	• **Fever (≥100.4°F [≥38°C])**
• ESR ≥60 mm/hr and/or CRP ≥3 mg/dL (≥30 mg/L)	• **ESR ≥30 mm/hr** and/or CRP ≥3 mg/dL (≥30 mg/L)
• Prolonged PR interval (in the absence of carditis)	• Prolonged PR interval (in the absence of carditis)

ARF=acute rheumatic fever; CRP=C-reactive protein; ESR=erythrocyte sedimentation rate; GAS=group A streptococcal.
Modified with permission from Gewitz MH, Baltimore RS, Tani LY, et al. Revision of the Jones criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. *Circulation*. 2015;131(20):1806–1818.

to develop late valvular disease. Secondary prophylaxis during the observation period is recommended by some experts, and if carditis develops, the patient is considered to have ARF. (2)

Poststreptococcal Glomerulonephritis

PSGN is a nonsuppurative complication occurring during or after GAS infection. It most commonly occurs after GAS impetigo infections. Typical onset is 2 to 4 weeks after infection in the skin and 7 to 10 days after streptococcal pharyngitis. Presenting signs and symptoms include hematuria, proteinuria, hypertension, and edema. PSGN usually manifests as acute nephritic syndrome but can cause nephrotic syndrome, and rarely, rapidly progressive glomerulonephritis and renal failure. Laboratory findings may be significant for evidence of past GAS infection with elevated antistreptolysin O or anti-DNAse B antibody titers and a low complement C3 level. (2)

Pediatric Autoimmune Neuropsychiatric Disorder Associated with GAS or Pediatric Acute-Onset Neuropsychiatric Syndrome

An association between GAS infection and sudden onset of tic disorders and obsessive-compulsive behaviors has been proposed based on a small number of studies, and this proposal remains a controversial diagnosis. The diagnosis of pediatric autoimmune neuropsychiatric disorder associated with GAS must be preceded by a documented GAS infection with elevated antistreptolysin O or anti-DNAse B antibody titers. Symptoms typically occur within days to weeks after infection. GAS testing by culture or antigen testing is not recommended in the absence of acute clinical symptoms of pharyngitis for these patients. Currently there is also insufficient evidence to support treatment or prophylaxis with antibiotics, immunoglobulin, and plasmapheresis. Management entails psychiatric treatments focusing on tics, obsessive-compulsive behaviors, and other neurologic and behavioral manifestations. (2)

MANAGEMENT

Streptococcal Pharyngitis

To prevent ARF, treatment for patients with streptococcal pharyngitis must be initiated within 9 days of symptom onset. (7)(8) Treating the infection does not prevent PSGN but will help prevent nephritogenic strains from being spread to close contacts. The preferred oral antibiotic regimen is oral penicillin V or amoxicillin for a 10-day course. Intramuscular benzathine penicillin G is also an option in patients who may have difficulty taking oral medications. In penicillin-allergic patients, an oral first-generation cephalosporin is recommended for a 10-day course. Other options include clarithromycin or clindamycin for 10-day courses or azithromycin for 5 days, but there are evolving increasing resistance patterns of GAS to antibiotics other than penicillin, in particular clindamycin and macrolides. (2)(5) See Table 3 for suggested antibiotic dosing for streptococcal infections.

For children who are GAS carriers, eradication may be considered in specific situations, such as 1) a community outbreak of PSGN or ARF, 2) patients with a family history of ARF, 3) patients with multiple episodes of documented symptomatic GAS pharyngitis occurring in the family for many weeks despite appropriate antimicrobial therapy, or 4) when a patient is being considered for tonsillectomy due to frequent GAS infections. Antibiotic options for eradication include a 10-day course of clindamycin, penicillin with rifampin, and amoxicillin/clavulanic acid. (2) Based on the Infectious Diseases Society of America guidelines, there is no credible evidence suggesting that family pets serve as reservoirs for GAS, and, therefore, culturing of pets is not recommended. (5)

Skin Manifestations

Impetigo is a self-limited disease, but treatment can shorten the time to resolution and decrease direct spread of the infection to others. For localized lesions, topical treatment such as mupirocin or retapamulin ointment is recommended.

For more extensive impetigo lesions, and for cellulitis and erysipelas, oral antibiotics may be considered. A first-generation cephalosporin, cephalexin, is effective at treating GAS and methicillin-susceptible *S aureus*. If the prevalence of methicillin-resistant *S aureus* is high in the community, clindamycin or trimethoprim/sulfamethoxazole can be prescribed. (2)(6)

Invasive Infections

Treatment of STSS involves initiation of broad-spectrum antibiotics as soon as possible. Once STSS is confirmed, penicillin or ampicillin combined with clindamycin (to inhibit toxin production) should be administered. Clindamycin should not be used alone in life-threatening infections because of potential resistance. In 2017, 22% of invasive GAS case isolates from the CDC Active Bacterial Core surveillance system in the United States were resistant to clindamycin. Surgical debridement of deep tissue infections may be necessary.

Treatment of necrotizing fasciitis involves early and aggressive surgical debridement of necrotic tissue along with

Table 3. Suggested Antibiotic Dosing for Select Group A *Streptococcus* Infections

INFECTION/CONDITION	ANTIBIOTIC (ROUTE)	DOSING	DURATION
Pharyngitis	Penicillin V (oral)	≤27 kg: 250 mg 2–3 times daily >27 kg: 500 mg 2–3 times daily	10 d
	Amoxicillin (oral)	50 mg/kg per day once daily (max: 1,000 mg/dose)	10 d
	Benzathine penicillin G (IM)	≤27 kg: 600,000 units IM as a single dose >27 kg:1.2 million units IM as a single dose	1 dose
	Cephalexin (oral) (preferred for nonanaphylactic allergy to penicillin)	40 mg/kg per day divided 2 times daily (max: 500 mg/dose)	10 d
	Clindamycin (oral) (preferred for anaphylactic or type I hypersensitivity to penicillin)	20 mg/kg per day divided 3 times daily (max: 300 mg/dose)	10 d
	Azithromycin	12 mg/kg per day once daily (max: 500 mg/dose)	5 d
	Clarithromycin	15 mg/kg per day divided 2 times daily (max: 250 mg/dose)	10 d
Decolonization	Clindamycin (oral)	20–30 mg/kg per day divided 3 times daily (max: 300 mg/dose)	10 d
	Penicillin and rifampin (oral)	Penicillin V 50 mg/kg per day divided 4 times daily for 10 d (max: 500 mg/dose) and rifampin 20 mg/kg per day once daily for the last 4 d of treatment (max: 600 mg/dose)	10 d of penicillin and 4 d of rifampin
	Amoxicillin-clavulanic acid (oral)	Amoxicillin 40 mg/kg per day divided 3 times daily (max: 2,000 mg/d)	10 d
	Benzathine penicillin G (IM) and rifampin (oral)	≤27 kg: 600,000 units IM as a single dose >27 kg:1.2 million units IM as a single dose and rifampin 20 mg/kg per day divided 2 times daily (max: 600 mg/d)	1 dose of benzathine penicillin G and 4 d of rifampin
Acute rheumatic fever prophylaxis	Benzathine penicillin G (IM)	≤27 kg: 600,000 units >27 kg:1.2 million units	1 dose every 4 wk
	Penicillin V (oral)	250 mg 2 times daily	
	Sulfadiazine or sulfisoxazole	≤27 kg: 0.5 g once daily >27 kg: 1 g once daily	
Skin infections	Mupirocin (topical)	3 times daily	5 d
	Retapamulin (topical)	2 times daily	5 d
	Cephalexin (oral)	50 mg/kg per day divided 4 times daily (max: 500 mg/dose)	5 d
	Clindamycin (oral)	30–40 mg/kg per day divided 3 times daily (max: 450 mg/dose)	5 d
Empirical therapy for streptococcal toxic shock syndrome and streptococcal acute necrotizing fasciitis	Clindamycin (IV)	40 mg/kg per day divided 3–4 times daily (max: 2,700 mg/d)	
	AND Meropenem (IV) OR	30–60 mg/kg per day divided 3 times daily (max: 1,000 mg/dose)	
	Piperacillin-tazobactam (IV)	≥9 mo of age: 300 mg/kg per day piperacillin component divided 3–4 times daily (max: 16 g/d)	
	AND Vancomycin (if *Staphylococcus aureus* cannot be ruled out)	45–60 mg/kg per day divided 3–4 times daily (max: 4 g/d)	

IM=intramuscular, IV=intravenous, max=maximum.

broad-spectrum parenteral antibiotic therapy. Intravenous immunoglobulin can be considered in severe cases of STSS and necrotizing fasciitis, although efficacy has not been proved. (2)(6)(9)

Nonsuppurative Complications

Treatment for ARF includes the eradication of GAS with a standard pharyngitis regimen and the treatment of acute manifestations such as arthritis or valvulitis-associated heart failure. Patients are also initiated on secondary prophylaxis to prevent subsequent GAS infections. Prophylaxis regimens include intramuscular benzathine penicillin G once monthly or daily oral penicillin. A macrolide is typically used for penicillin-allergic patients. See Table 4 for duration of prophylaxis. (8)

Typical treatment of PSGN is supportive but may also include antihypertensive medications, sodium and fluid restrictions, corticosteroid administration, and in severe cases,

Table 4. Duration of Prophylaxis for People Who Have Had Acute Rheumatic Fever (ARF): Recommendations of the American Heart Association

CATEGORY	DURATION
Rheumatic fever without carditis	5 y since last episode of ARF or until age 21 y, whichever is longer
Rheumatic fever with carditis but without residual heart disease (no valvular disease[a])	10 y since last episode of ARF or until age 21 y, whichever is longer
Rheumatic fever with carditis and residual heart disease (persistent valvular disease[a])	10 y since last episode of ARF or until age 40 y, whichever is longer; consider lifelong prophylaxis for people with severe valvular disease or likelihood of ongoing exposure to group A streptococcal infection

[a]Clinical or echocardiographic evidence.

Modified with permission from Gerber M, Baltimore R, Eaton C, 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, Council on Cardiovascular Disease in the Young, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation*. 2009;119(11):1541–1551.

dialysis. If GAS infection is still present at the time of diagnosis of PSGN, appropriate antibiotics should be prescribed.

PROGNOSIS

Despite aggressive treatment, the mortality rates of STSS and necrotizing fasciitis are quite high, ranging from 30% to 70% for STSS and 11% to 22% for necrotizing fasciitis. Mortality rates are lower in children compared with adults. (9) Complications of shock and organ failure can occur, including tissue necrosis and loss of extremities. The CDC does not recommend routine screening or initiating chemoprophylaxis for household contacts of patients with invasive GAS infection.

Summary

- Group A *Streptococcus* (GAS) is responsible for a variety of clinical manifestations, from less severe infections such as pharyngitis, impetigo, cellulitis, and erysipelas to more severe invasive diseases such as septicemia, streptococcal toxic shock syndrome (STSS), and acute necrotizing fasciitis. GAS is also linked to multiple nonsuppurative complications, including acute rheumatic fever and poststreptococcal glomerulonephritis. (Based on high-quality evidence) (1)(2)
- Children with signs and symptoms of acute GAS pharyngitis should be tested. Testing is not generally recommended for children who are younger than 3 years because they are unlikely to manifest acute rheumatic fever. However, physicians may choose to test those younger than 3 years if risk factors exist, for example, the child has a relative with GAS. (Strong recommendation, high-quality evidence) (2)(5)
- Patients with acute GAS pharyngitis should be treated with an appropriate antibiotic at an appropriate dose for a duration likely to eradicate the organism from the pharynx (usually 10 days). (Strong recommendation, high-quality evidence) (2)(5)
- Treatment is not recommended in patients with positive throat cultures without clinical symptoms of streptococcal pharyngitis. (Strong recommendation, high-quality evidence) (2)(5)
- To prevent acute rheumatic fever, treatment for patients with streptococcal pharyngitis must be initiated within 9 days of symptom onset. Treating the infections does not prevent poststreptococcal glomerulonephritis but will help prevent nephritogenic strains from being spread to close contacts (Strong recommendation, high-quality evidence) (7)(8)
- Treatment of STSS involves initiation of broad-spectrum antibiotics as soon as possible. Once STSS is confirmed, penicillin or ampicillin combined with clindamycin (to inhibit toxin production) should be administered. Clindamycin should not be used alone in life-threatening infections because of potential resistance (Strong recommendation, high-quality evidence) (2)(3)(4)

Take the quiz! Scan this QR code to take the quiz, access the references and teaching slides, and view and save images and tables (available on March 1, 2024).

PIR QUIZ

1. A 9-year-old girl is brought to the clinic in March by her parents with a 1-day history of sore throat and fever (maximum temperature, 101.9°F [38.8°C]). She does not have cough, nasal congestion, conjunctival redness, or eye discharge. There have been multiple school classmates with a sore throat the past 1 to 2 weeks. Five weeks ago, she was diagnosed as having group A *Streptococcus* (GAS) pharyngitis at an urgent care center and was treated with amoxicillin for 10 days. She has no allergies. On physical examination, she is mildly ill-appearing. Her oral temperature is 101.5°F (38.6°C). There is increased pharyngeal erythema with an exudate. She has bilateral anterior cervical lymphadenopathy. Which one of the following is the most appropriate next step in management?

   A. Intramuscular benzathine penicillin.
   B. Oral amoxicillin.
   C. Oral cefdinir.
   D. Pharyngeal swab for GAS rapid antigen assay, and if negative, check culture.
   E. Pharyngeal swab for GAS rapid antigen assay, and if negative, no further testing is recommended.

2. A previously healthy 28-month-old boy is brought to the clinic by his parents in June with fever and mildly decreased appetite for 2 days. He has had nasal congestion and cough and developed nonbloody diarrhea today. Mom states that multiple other children at his daycare center have been ill. No household contacts have been recently ill. At 5 months of age, he had a generalized erythematous rash when taking amoxicillin for an ear infection. His temperature is 100.6°F (38.1°C), and his other vital signs are normal. He is alert and in no distress. Physical examination is remarkable for increased pharyngeal erythema and no ulcerative lesions. The remainder of his physical examination findings are normal. Which one of the following is the most appropriate next step in management?

   A. No further testing or antimicrobial treatment is indicated.
   B. Oral amoxicillin.
   C. Oral cephalexin.
   D. Pharyngeal swab for GAS testing.
   E. Stool for multiplex polymerase chain reaction panel.

3. An 8-year-old boy is brought by his parents to the emergency department with a painful red area of his left calf that started last night and has increased in size. He was thought to have a previous mosquito bite at that site that he scratched to the point of bleeding. He has had tactile fever at home. On physical examination his temperature is 101.1°F (38.4°C) and his other vital signs, including blood pressure, are normal. He answers questions appropriately, and he rates the pain as 6 of 10 when the area is touched. There is a raised 5 × 7-cm area of erythema with sharply demarcated margins of his left calf. There is a linear erythematous streak extending to his knee. There is no discharge or fluctuance, and there are no bullae. Which one of the following is the most likely diagnosis?

   A. Abscess.
   B. Cellulitis.
   C. Erysipelas.
   D. Necrotizing fasciitis.
   E. Pyomyositis.

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4. A 10-year-old girl is brought to the clinic by her parents with a 1-day history of right knee pain. Eight days ago, she complained of a sore throat, and her maximum recorded oral temperature was 100.6°F (38.1°C). A throat swab performed in the office at that time had a positive GAS antigen assay. She has been taking oral penicillin for the past 7 days. She has been afebrile since starting the penicillin. She had mild relief of the joint pain with ibuprofen. She has never traveled outside the United States. On physical examination she is afebrile, and her vital signs are normal. Her pharyngeal examination findings are normal. There is pain with motion of her right knee and mild swelling. There is no redness or warmth of the knee. Cardiac examination has normal heart sounds and no murmur. There is no rash or subcutaneous nodules, and her neurologic examination findings are normal. Her erythrocyte sedimentation rate is 28 mm/hr and c-reactive protein level is 1.6 mg/dL (16 mg/L). Electrocardiography and echocardiography findings are normal. Which one of the following is the most likely diagnosis?

   A. Acute rheumatic fever.
   B. GAS pyogenic arthritis.
   C. Pauciarticular juvenile idiopathic arthritis.
   D. Reactive arthritis.
   E. Systemic-onset juvenile idiopathic arthritis.

5. A 9-year-old girl is seen in the office for a 1-day history of sore throat and temperatures up to 101.1°F (38.4°C). The GAS antigen assay from a throat swab is positive. During the past 14 months she has been diagnosed with 5 episodes of GAS pharyngitis and has been treated with oral amoxicillin each time with clinical improvement. When she was seen 2 weeks ago for a preparticipation sports physical examination, mom asked that she have a throat swab done to see whether she is a carrier and her GAS antigen was positive. Mom had a history of recurrent pharyngitis as a child resulting in a tonsillectomy and asks if her daughter should be referred to an otolaryngologist. Which one of the following is the most appropriate next step in management?

   A. Intravenous ampicillin.
   B. Intravenous azithromycin.
   C. Oral penicillin and oral rifampin.
   D. Referral to otolaryngology for tonsillectomy and adenoidectomy.
   E. Throat swab for culture of all household members and the pet dog.

EXCERPT FROM *Empirical Validation of Guidelines for the Management of Pharyngitis in Children and Adults*

Strategy 5: Modified Centor Score and Culture Management Approach

Perform throat culture on all children and adults having a Centor score of 2 or 3 and treat those having positive culture results. Treat those having a score of 4 or more empirically. (*Clinical outcome of this approach*: 100% sensitivity, 90% specificity for Group A strep. 6.4% of prescriptions written using these criteria were "unnecessary" based on negative throat culture).

MODIFIED CENTOR SCORE	
Criteria	**Points**
Temp >38°C	1
Absence of Cough	1
Swollen, Tender Anterior Cervical Nodes	1
Tonsillar Swelling or Exudate	1
Age *3-14 Years* *15-44 Years* *45 Years or Older*	 1 0 -1

Modified from McIsaac et al. Empirical validation of guidelines for the management of pharyngitis in children and adults. JAMA. 2004. Apr 7;291(13):1587-95.

Pharyngitis Quiz

1. Name 3 non-infectious causes of pharyngitis in children: _____, _____, _____.

2. The most common causes of acute pharyngitis in children are _____.

3. The most common bacterial cause of pharyngitis is _____, causing _____% of acute pharyngitis in children. Peak incidence is between _____ years; infection is rare before _____.

4. One rash manifested by Group A strep infection concentrates along flexor creases (antecubital fossa, axillary, inguinal areas), these are called _____**.**

5. Match the clinical description with the most suspicious etiology:

Adolescent with 2 weeks of sore throat, fatigue, and hepatosplenomegaly.	NEISSERIA GONORRHOEAE
4-year-old girl with vesicles along posterior pharynx, hands, and feet.	ADENOVIRUS
2-year-old boy with pharyngeal erythema and vesicles isolated to lips and buccal mucosa.	EBV (Infectious mononucleosis)
Exudative pharyngitis with conjunctivits after swimming in pool during summer.	ENTEROVIRUS
Teenage girl with exudative pharyngitis following oral-genital sexual contact.	HSV (gingivostomatitis)

6. RADTs for Group A Strep have a high _____ (95-99%) but lower _____ (70-90%). A negative RADT **should/should not** be followed up with a confirmatory throat culture. PCRs for Group A Strep have high _____ and high _____. A confirmatory throat culture is **sometimes/never/always** necessary.

7. The primary goal of treating Group A Strep infections is to prevent _____ (effective within ____ days of symptom onset) as well as suppurative complications such as _____ and _____. Treatment is not effective in preventing _____.

8. The first-line treatment for Group A strep infections is _____, given as 10-day oral course of _____or single IM injection of _____**.** In younger children, oral _____ may be used as a more palatable alternative.

9. **TRUE/FALSE:** Tonsillectomy is recommended for patients with recurrent Group A Strep infections (without other complications).

10. A throat culture you sent on a patient grows out *Group C beta-hemolytic streptococci*. Will you treat with antibiotics?

11. **TRUE/FALSE:** Laboratory testing and radiologic imaging are usually unnecessary in diagnosing peritonsillar and retropharyngeal abscesses.

PHARYNGITIS CASES

Case 1

You log into MHS Genesis and see that your first appointment is Henry Lemierre for "sore throat". Reviewing the chart, you see that Henry is a previously healthy 7-year-old boy with no acute visits in the recent past. Henry has checked in late and is just being brought back by the corpsman to get vitals. While you are waiting you think of the questions you will ask his parents. What would you like to know?

Henry is accompanied by his mother, who states that he was completely fine until he came home from school yesterday looking "wiped out" and said that his head, throat, and stomach hurt. Since then he has thrown up twice and eaten very little but mother has been pushing fluids. Denies any congestion or cough. Has not taken any medications. His vitals show T *103.7* HR *95* BP *95/57* RR *15* SpO2 *100% on room air*. What will you focus on and look for on exam?

On exam, Henry is lying curled up on the table and appears uncomfortable when asked to sit up. His tonsils are symmetrically enlarged with bilateral purulent exudate and palatal petechiae and he has scattered palpable anterior cervical lymph nodes. He has moist mucous membranes with cap refill <2 seconds. Exam is otherwise normal.

What is your suspected diagnosis?

How will you initially confirm your diagnosis?

Rapid strep returns positive. What is your management plan?

Henry's mother remembers that he was diagnosed with an ear infection in the emergency department when he was 15 months old and had an allergic reaction to amoxicillin. He got a rash and might have had mouth swelling, she can't remember. How would you treat him?

Henry lives at home with his parents and 1-year-old younger brother. No one else has symptoms. Ms. Lemierre wants to know if she should bring Henry's brother and father in to have the whole family tested.

Ms. Lemierre wants to know if there is any way you can give the rest of the family a prescription to take to prevent them from getting strep throat?

Case 2

Your next patient, a 5-year-old girl, Noa Dinah Fagia, is also running late. You see that her complaint is "ED f/u strep throat." Looking back in her Genesis record, you see that she has been to the ED or urgent care for cough, congestion, and runny nose 3 times in the past 2 months and diagnosed with strep throat each time. Are you suspicious?

Mr. Fagia carries Noa into the room and she is crying with a runny nose but otherwise well-appearing. Vital signs are normal with no concerning findings on exam (oropharynx clear, non-tender shotty anterior cervical lymphadenopathy). Mr. Fagia states that Noa has been having low-grade fevers for the past 4 days (Tmax 101) with mild sore throat, cough and a lot of congestion and runny nose. She has been fussy but symptoms are gradually improving. Her appetite has decreased but she has maintained normal fluid intake and urine output. They went the ED 3 days ago to get her checked out with her history of strep throat. At that time they performed a urinalysis and urine culture which were negative but rapid strep was positive. She was given a 10-day course of amoxicillin (50mg/kg/d), is on day 3 and tolerating well. She attends daycare and has experienced 2 similar episodes in the past 3 months, both lasting about a week. They went to the ED and urgent care with positive rapid strep both times. What are your thoughts on the history and recommended management recommendations?

Noa returns 1 month later and is asymptomatic. Repeat rapid strep and throat culture are positive, consistent with being a chronic pharyngeal carrier of Group A strep. Mr. Fagia wants to know if Noa needs to take antibiotics to get rid of it, and if she might spread it to others.