

Treatment and prevention of streptococcal pharyngitis in adults and children

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INTRODUCTION

Group A *Streptococcus* (GAS), or *Streptococcus pyogenes*, is the leading bacterial cause of tonsillopharyngitis in adults and children worldwide. GAS is one of the few causes of tonsillopharyngitis or pharyngitis for which antibiotic treatment is recommended.

The treatment and prevention of group A streptococcal tonsillopharyngitis is reviewed here. The clinical features and diagnostic evaluation of patients with tonsillopharyngitis are discussed separately. (See "[Group A streptococcal tonsillopharyngitis in children and adolescents: Clinical features and diagnosis](#)" and "[Evaluation of acute pharyngitis in adults](#)".)

DEFINITIONS

Group A *Streptococcus* (GAS) can cause symptomatic infection or can colonize the oropharynx.

- Active infection refers to symptomatic infection caused by GAS.
- Persistent infection refers to symptomatic infection caused by GAS that does not resolve after appropriate antibiotic treatment. This is synonymous with treatment failure.

- Recurrent infection refers to a new symptomatic infection with GAS that occurs after appropriate antibiotic treatment. Recurrent infection can be caused by the same GAS serotype that caused the initial infection or by a different serotype. Recurrent infections most often occur among members of the same household or in other settings such as schools or daycare centers where close contact facilitates GAS transmission [1].
- Chronic carriage refers to asymptomatic colonization or the persistent presence of GAS in the oropharynx in the absence of symptoms or host immune response. The prevalence of chronic carriage has not been comprehensively studied, but reported rates are about 4 to 5 percent in healthy adults [2] and range from about 2 to 20 percent in children [2-9]. Carriage can persist for months to years [8,10].

Distinguishing among these states is important. In general, only patients with symptomatic GAS infection require treatment. Exceptions include patients with a history of acute rheumatic fever, and chronic GAS carriers during outbreaks of acute rheumatic fever and/or poststreptococcal glomerulonephritis, or when GAS infections are recurring in households or other close-contact settings.

GOALS OF TREATMENT

The goal of antibiotic therapy for streptococcal pharyngitis is multifold and includes:

- Reducing symptom severity and duration
- Prevention of acute complications, such as otitis media, peritonsillar abscesses, or other invasive infections
- Prevention of delayed complications or immune sequelae, particularly acute rheumatic fever
- Prevention of spread to others

Symptom reduction — Antibiotic treatment has been shown to reduce symptom severity and hasten the rate of recovery in patients with streptococcal pharyngitis [11,12]. However, even without antibiotic therapy, symptoms typically resolve in about three to five days for most patients [13], making the prevention of complications a key goal of care.

Prevention of complications — Complications of streptococcal pharyngitis can result from extension of infection beyond the oropharynx, termed suppurative complications, or as immune phenomena, termed nonsuppurative complications. Suppurative complications of GAS pharyngitis include otitis media, peritonsillar cellulitis or abscess, sinusitis, meningitis, bacteremia, and necrotizing fasciitis. Nonsuppurative complications of GAS pharyngitis include

acute rheumatic fever, poststreptococcal glomerulonephritis, and reactive arthritis. The spectrum of complications associated with streptococcal pharyngitis is discussed in detail separately. (See "[Complications of streptococcal tonsillopharyngitis](#)".)

Suppurative complications — Rates of otitis media and peritonsillar abscesses are each reduced with antibiotic use. In a large meta-analysis of randomized trials comparing antibiotics to placebo in adults and children with streptococcal pharyngitis, antibiotics reduced the incidence of acute otitis media within 14 days (0.47 versus 2.0 percent; risk ratio [RR] 0.30, 95% CI 0.15-0.58) and peritonsillar abscess at two months (0.24 versus 2.3 percent; RR 0.15, 95% CI 0.05-0.47) [11]. Reduction in the rates of acute sinusitis were also observed but did not reach statistical significance. The effect on less common but severe suppurative complications including bacteremia and necrotizing fasciitis has not been studied, though it is reasonable to surmise that antibiotics would have a protective effect.

Non-suppurative complications

Acute rheumatic fever — The prevention of acute rheumatic fever is one of the main indications for antibiotic treatment of streptococcal pharyngitis. Acute rheumatic fever and rheumatic heart disease are important causes of cardiovascular death worldwide [14,15]. In a meta-analysis of 14 randomized trials comparing penicillin with placebo in over 8000 adults and children with sore throat, penicillin decreased the risk of rheumatic fever by about two-thirds [11]. The absolute risk reduction is likely highest in children aged 5 to 15 residing in developing nations, where incidence of rheumatic fever peaks [15,16]. Additional detail on acute rheumatic fever is provided separately. (See "[Acute rheumatic fever: Epidemiology and pathogenesis](#)" and "[Acute rheumatic fever: Clinical manifestations and diagnosis](#)" and "[Acute rheumatic fever: Treatment and prevention](#)".)

Other non-suppurative complications — Data on the benefits of antibiotics in preventing other non-suppurative complications are limited. Antibiotics probably prevent poststreptococcal glomerulonephritis based on a meta-analysis of 10 randomized trials comparing antibiotics with placebo in adults and children with sore throat, though there were too few cases in these trials to conclude this with certainty [11]. The effect of antibiotics on other non-suppurative complications such as poststreptococcal arthritis and pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS) is not well studied. Additional details on these complications are provided separately. (See "[Poststreptococcal glomerulonephritis](#)" and "[Complications of streptococcal tonsillopharyngitis](#)".)

Prevention of transmission — GAS can spread among close contacts, leading to clusters of cases and recurrent infections in households or other close-contact settings. The rate of GAS

transmission from an infectious case to close contacts is estimated to be between 5 and 50 percent [17-19]. Although no studies have directly evaluated the effect of antibiotic treatment on transmission, antibiotic use appears to eliminate GAS from the oropharynx in about 80 to 90 percent of cases after 24 hours of therapy [20,21]. When untreated, historic epidemiologic data suggest approximately 50 percent of patients with streptococcal pharyngitis will continue to harbor GAS in the oropharynx three to four weeks after symptom onset [13,22].

WHOM TO TREAT

We recommend antibiotic treatment for any patient with symptomatic pharyngitis or tonsillopharyngitis who has a positive microbiologic test (ie, nucleic acid amplification test [NAAT], rapid antigen test, or culture) for group A *Streptococcus* (GAS) ([algorithm 1](#)). (See "[Evaluation of acute pharyngitis in adults](#)", section on '[Evaluation](#)' and "[Group A streptococcal tonsillopharyngitis in children and adolescents: Clinical features and diagnosis](#)".)

Empiric treatment is generally not recommended, as the clinical features of GAS pharyngitis and nonstreptococcal pharyngitis broadly overlap ([figure 1](#)) [23,24]. Short delays in therapy (eg, while awaiting culture results) have not been associated with increased rates of complications such as acute rheumatic fever [22]. However, whether such delays effect rates of other complications (eg, development of peritonsillar abscess) is not known. If clinical suspicion for GAS pharyngitis is high and testing results cannot be obtained rapidly, it is reasonable to start antibiotic treatment while test results are pending [25]. If testing does not confirm the diagnosis, antibiotics should be discontinued.

Antibiotic treatment is not recommended for asymptomatic chronic GAS carriers or for GAS carriers who have superimposed viral infections [23,24,26]. (See '[Chronic GAS carriers](#)' below.)

TREATMENT OF INITIAL EPISODES

Antibiotic treatment is the mainstay of care.

Supportive care measures such as nonsteroidal anti-inflammatory drugs (NSAIDs) or [acetaminophen](#) may be administered to relieve fever and pain.

Antibiotic treatment — The antibiotic treatment recommendations presented below are largely consistent with recommendations from the Infectious Diseases Society of America, the American Heart Association, and the American Academy of Pediatrics ([algorithm 2](#)) [23,26-28]. Guidelines from other regions vary [29-31].

Penicillin — Penicillin is the treatment of choice for group A *Streptococcus* (GAS) pharyngitis due to its efficacy, safety, narrow spectrum, and low cost. Resistance to penicillin among clinical GAS isolates has not been documented. Penicillin is the only antibiotic that has been studied and shown to reduce rates of acute rheumatic fever [11]. Dosing and duration of therapy are outlined in the tables ([table 1](#) and [table 2](#)).

- For most adult patients, we use oral [penicillin V](#) 500 mg two to three times daily for 10 days. Oral [amoxicillin](#) is also a reasonable option.
- For most children, we use either oral [penicillin V](#) or [amoxicillin](#). Amoxicillin is often preferred for young children because the taste of the amoxicillin suspension is more palatable than that of penicillin. Amoxicillin can also be given once daily. In several randomized trials, standard-dose and once-daily dosing of amoxicillin appeared to have equivalent efficacy as oral penicillin [32-36].
- For patients with a history of acute rheumatic fever who are not receiving antibiotic prophylaxis, we select among oral [penicillin V](#), oral [amoxicillin](#), or a single dose of intramuscular (IM) [penicillin G benzathine](#). Because adherence is critical for patients with a history of acute rheumatic fever, we base our choice on patient values and preferences. While IM benzathine penicillin can be given as a single dose, the drug is expensive in some regions, frequently unavailable, and causes injection site pain. In contrast, oral options are readily available but carry the risk of incomplete adherence. (See "[Acute rheumatic fever: Treatment and prevention](#)".)

The duration of therapy for oral penicillin or [amoxicillin](#) is 10 days. Although symptoms typically improve within the first few days of treatment [13,37,38], treating for 10 days appears to enhance the rate of GAS eradication from the oropharynx when compared with 5 or 7 days [3,23,39-41]. One randomized trial directly compared a 5-day course of [penicillin V](#) 800 mg four times daily with a 10-day course of penicillin V dosed at 1000 mg three times daily in 433 patients (age ≥ 6) with microbiologically confirmed streptococcal pharyngitis [42]. Clinical cure rates were similar between groups (89.6 versus 93.8 percent; difference -4.2, 95% CI -9.9 to 1.5); however, wide confidence intervals suggest that treatment differences may become apparent with a larger sample size. In addition, bacterial eradication rates were lower in the 5-day treatment group (80.4 versus 90.7 percent). Complication rates were also similar between groups but their overall frequency was low (1 percent). Because complications, particularly immune sequelae, are likely related to the presence of GAS in oropharynx and can be severe, treating with a 10-day course seems prudent.

IM penicillin appears to be more effective than oral penicillin at eradication of GAS from the oropharynx [43] and has been most well studied for the prevention of acute rheumatic fever [11]. However, as noted above, IM penicillin is expensive in some regions and not always available. Thus, for patients with a history of acute rheumatic fever (who are high risk for cardiac complications compared with those without this history), we discuss the risk and benefits of its use on an individual basis.

Alternatives to penicillin — Cephalosporins, [clindamycin](#), and macrolides are alternatives for patients who are allergic to penicillin or who cannot otherwise tolerate penicillin. Dosing and duration of therapy are outlined in the tables ([table 1](#) and [table 2](#)).

Selection of an agent depends on the type of allergy, local antibiotic resistance rates, and patient values and preferences ([table 3](#) and [algorithm 2](#)).

The approach to antibiotic selection for patients with penicillin allergy varies among experts:

- For patients with mild, non-IgE-mediated reactions to penicillin (eg, maculopapular rash beginning days into therapy), the author and editors of this topic generally select a first-generation cephalosporin such as [cephalexin](#) because of its narrow spectrum and the low likelihood of cross-reactivity.

For patients with mild, possibly IgE-mediated reactions (eg, urticaria or angioedema but **not** anaphylaxis), they use a second- or third-generation cephalosporin with a side chain that is dissimilar to penicillin, such as [cefuroxime](#), [cefdinir](#), or [cefpodoxime](#).

When using an oral cephalosporin, we generally treat for 10 days. A five-day treatment course with [cefdinir](#) or [cefpodoxime](#) is also acceptable. These shorter treatment courses are US Food and Drug Administration approved and, in randomized trials, had similar clinical and microbiologic efficacy as 10-day courses of oral penicillin [44-47].

- For patients with a history of severe angioedema and/or anaphylaxis or with serious delayed reactions or for patients who cannot take cephalosporins, we generally use a macrolide, such as [azithromycin](#). A major advantage of azithromycin is that it can be given for a three- or five-day course due to its extended half-life [48].

A key consideration when using a macrolide is potential drug resistance. Macrolide resistance rates are growing and vary with geography [49-54]. Generally, higher macrolide resistance rates have been observed in Asia and Europe when compared with the United States. Clinicians should take into account local resistance patterns or consult local antibiograms when prescribing macrolides, if possible.

- For patients with known or suspected macrolide-resistant GAS who cannot tolerate cephalosporins, we treat with a 10-day course of [clindamycin](#).

The above approach is generally consistent with recommendations from both the American Academy of Pediatrics and the Infectious Diseases Society of America [23,28].

Other experts, including UpToDate allergy specialists, prefer to perform a test-dose procedure before prescribing cephalosporins to patients with penicillin allergies ([algorithm 3](#)). Because this is generally not feasible in the outpatient clinic, a more conservative approach to treatment is an option for patients with mild, non-IgE-mediated reactions or IgE-mediated reactions:

- For patients with mild, non-IgE-mediated reactions, a third-generation cephalosporin, such as [cefepodoxime](#) or [cefdinir](#), is selected.
- For patients with any possible IgE-mediated reactions (including anaphylaxis), an alternative to cephalosporins such as a macrolide or [clindamycin](#) is selected.

The approach to the management of patients with penicillin allergy is reviewed separately. (See "[Choice of antibiotics in penicillin-allergic hospitalized patients](#)".)

No clinically relevant differences in symptom resolution were detected in a meta-analysis of 19 randomized trials comparing cephalosporins, macrolides, or [clindamycin](#) with either penicillin or [amoxicillin](#) in over 5000 adults or children with GAS [55]. While the incidence of clinical relapse was lower when comparing treatment with cephalosporins versus penicillins (26 versus 46 per 1000 patients; odds ratio 0.55, 95% CI 0.30-0.99), broad use of cephalosporins may promote antimicrobial resistance and are generally more costly than penicillins. No trial has evaluated the use of alternatives to penicillin for the prevention of acute rheumatic fever; thus, penicillin remains the treatment of choice when feasible.

Tetracyclines, sulfonamides, and fluoroquinolones should not be used for treatment of streptococcal pharyngitis due to the high prevalence of resistance [49-54], potential for clinical failure, and/or high side-effect profile [56].

Adjunctive treatment — We offer supportive care (rest, adequate fluid intake, avoidance of respiratory irritants, soft diet) to all patients and systemic agents such as NSAIDs or [acetaminophen](#) for patients who desire medication for fever or pain control. We avoid using systemic glucocorticoids for symptom relief because antibiotics and systemic analgesics are generally effective, and the addition of systemic glucocorticoids increases the likelihood of adverse events.

Symptomatic treatment for sore throat is discussed in detail separately. (See "Acute pharyngitis in children and adolescents: Symptomatic treatment" and "[Symptomatic treatment of acute pharyngitis in adults](#)".)

RESPONSE TO THERAPY

Resolution of symptoms — Fever and constitutional symptoms typically resolve within one to three days of starting treatment [13,57-61]. Follow-up visits are not needed for most patients.

Most patients can return to work or school after completing one full day of treatment, provided they are afebrile and otherwise well. This recommendation is based on a small cohort study in children that showed that about 80 percent of patients with culture-proven group A streptococcal (GAS) pharyngitis clear the organism from the oropharynx within 24 hours of starting therapy [20]. A second cohort study evaluating 111 children with pharyngitis and a positive rapid antigen detection test (RADT) showed that 91 percent of patients treated with [amoxicillin](#) by 5:00 PM on the day of therapy had negative follow-up RADTs the following morning [21].

Indications for test of cure — For patients who are asymptomatic at the end of a course of antibiotic therapy, a test of cure is typically not needed [62]. We generally perform a test of cure (culture or RADT) in the following patients, who are at risk for complications, recurrent infection, or spreading infection to others:

- Patients with a history of acute rheumatic fever
- Patients who acquired infection during an outbreak of acute rheumatic fever or poststreptococcal glomerulonephritis
- Patients who acquired infection during a cluster of cases in their household or other close-contact setting

For patients who test positive in these circumstances, we repeat a full 10-day course of therapy. We usually select an antibiotic that has greater beta-lactamase stability than the one used for the initial treatment course. As examples, if penicillin was used for initial treatment, we use either [amoxicillin-clavulanate](#) or a first-generation cephalosporin; if a first-generation cephalosporin was used, we select a later-generation cephalosporin. The rationale for this strategy is based on clinical data that suggest relapse rates may be lower with cephalosporin use, as well as scientific observations that antibiotics with greater beta-lactamase activity may be more effective in eradicating GAS from the oropharynx. (See '[Antibiotic treatment](#)' above.)

We do not treat patients who are asymptomatic following an appropriate course of therapy who test positive but lacked an appropriate indication for a test of cure. The patients are likely chronic carriers. (See '[Definitions](#)' above.)

Persistent or recurrent symptoms

Evaluation — For patients who have persistent or recurrent symptoms consistent with GAS pharyngitis after completing a course of antibiotic therapy, we generally repeat testing for GAS. Because chronic GAS carriage can occur after antibiotic therapy [2-9], we generally avoid testing in patients whose symptoms are highly consistent with viral pharyngitis (eg, sore throat accompanied by cough, conjunctivitis, or rhinorrhea) or other etiology. For patients with persistent or recurrent symptoms consistent with GAS pharyngitis, a positive test result should raise suspicion for any of the following:

- Nonadherence with the prescribed antimicrobial regimen
- Recurrent infection, which refers to new infection with the initial infecting strain or a new strain
- Persistent infection, also termed treatment failure
- Infection with a different pathogen superimposed on chronic GAS carriage
- Presence of a suppurative complication, such as a peritonsillar abscess

Distinguishing among these states is typically based on epidemiologic and clinical history, which can be challenging as symptoms overlap and GAS testing can be positive in all.

Suspicion for recurrent infection should be raised when clusters of GAS infections are occurring within the patient's household, school, workplace, or other close-contact setting. Symptoms associated with recurrent infection with the same serotype may be milder than with the initial infection [63]. Persistent infection is rare but most often occurs in children, particularly those under age 5 [64]. Initial antibiotic choice may also influence the likelihood of recurrent or persistent infection. Selection of an antibiotic to which there is potential GAS resistance, such as a macrolide or [clindamycin](#), increases the likelihood of treatment failure. Additionally, some studies suggest that cephalosporins may be more effective than penicillin for preventing relapse [65].

The presence of persistent or recurrent symptoms should also raise suspicion for an alternate initial diagnosis or new infection with a different pathogen in a chronic GAS carrier. For patients with repeated episodes of pharyngitis, culturing for GAS when patients are between episodes

may help distinguish chronic carriage from active infection. A positive culture in an asymptomatic patients suggests that the patient is a carrier and that symptoms are due to an alternate cause ([table 4](#) and [table 5](#)). Additional details on the evaluation of acute pharyngitis are discussed separately. (See "[Evaluation of acute pharyngitis in adults](#)" and "[Group A streptococcal tonsillopharyngitis in children and adolescents: Clinical features and diagnosis](#)".)

A persistent, severe sore throat accompanied by fever, trismus, or a muffled voice suggests a local complication such as peritonsillar cellulitis or abscess. These diagnoses are discussed separately. (See "[Complications of streptococcal tonsillopharyngitis](#)" and "[Peritonsillar cellulitis and abscess](#)".)

Antibiotic treatment — We generally repeat a 10-day course of antibiotic treatment for patients with persistent or recurrent streptococcal pharyngitis. The selection of an antibiotic varies based on patient history ([table 1](#)).

- For patients who were nonadherent to the initial antibiotic regimen, we typically treat with intramuscular penicillin. Injections of [penicillin G benzathine](#) provide bactericidal levels against GAS for 21 to 28 days. For those who are allergic or who cannot otherwise tolerate penicillin, we individualize antibiotic selection based on the patient's preferences and reasons for nonadherence.
- For patients with persistent infection or an initial recurrence, we usually select an antibiotic that has greater beta-lactamase stability than the one used for the initial treatment course. As examples, if penicillin was used for initial treatment, we use either [amoxicillin-clavulanate](#) or a first-generation cephalosporin; if a first-generation cephalosporin was used, we select a later-generation cephalosporin ([table 6](#)).

The approach is based on a meta-analyses of four randomized trials evaluating over 1300 adults and children with GAS pharyngitis that showed decreased clinical relapse rates when comparing cephalosporins with penicillins (25 versus 46 percent; odds ratio 0.55, 95% CI 0.30-0.99) [66]. Additional studies suggest that bacteriologic cure rates may be higher for cephalosporins compared with penicillin [67-70]. Scientific observations also support the selection of antibiotics with beta-lactamase stability when treating persistent or recurrent GAS infection [71-73]. Some bacteria that colonize the oropharynx, such as *Staphylococcus aureus*, *Haemophilus influenza*, and *Moraxella catarrhalis*, produce beta-lactamases that inactivate penicillin, leading to decreased activity of penicillin against GAS [74-76]. Penicillin also decreases the quantity of alpha-streptococci in the oropharynx, which naturally protect against GAS infection [77-79]. Cumulatively, these effects may inadvertently promote the survival and persistence of GAS in

the oropharynx. By contrast, antibiotics with beta-lactamase activity may have a more balanced effect on the oropharyngeal flora, resulting in greater likelihood of GAS eradication.

A small number of patients experience multiple recurrences, which may be related to the infecting GAS strain [80-82], host immune response [58,83], or other factors that are not yet well characterized.

- For patients with multiple recurrences of GAS pharyngitis, we attempt treatment with an antibiotic from a class that has not been used previously, such as [clindamycin](#).
- For patients with frequent, mild to moderate recurrent infections, delaying the start of antibiotic therapy by two to three days is an alternate approach. This approach is derived from observational data that suggest delaying therapy may allow the development of immunity against the infecting strain, resulting in higher eradication rates [58,64,83] without increasing the risk of acute rheumatic fever [84,85]. We generally avoid this approach in patients with severe symptoms or when GAS is actively circulating in the community, as it prolongs symptom duration and may increase the risk of suppurative complications and/or transmission of GAS to others.
- For patients with frequent, severe episodes of GAS pharyngitis that recur despite appropriate antibiotic treatment, we consider tonsillectomy. (See '[Tonsillectomy](#)' below.)

It is not necessary to perform follow-up testing for persistent or recurrent infection unless the patient becomes symptomatic after antibiotic treatment or special circumstances as outlined above are present. (See '[Indications for test of cure](#)' above.)

When recurrent infections are thought to be due to ongoing GAS circulation among household members, we consider testing all household members and treating those who test positive. When recurrent infections are thought to be due to ongoing GAS circulation in other close-contact settings such as daycare centers or workplaces, we determine the best management approach on a case-by-case basis.

Tonsillectomy — Tonsillectomy is rarely indicated for patients with recurrent GAS pharyngitis. We determine the need for tonsillectomy in each individual case based on the patient age, the frequency and severity of infections, history of antibiotic use, and patient values and preferences.

Detailed indications for tonsillectomy in adults and children with recurrent pharyngitis and supporting evidence are discussed separately. (See "[Tonsillectomy and/or adenoidectomy in](#)

children: Indications and contraindications", section on 'Recurrent throat infection' and "Tonsillectomy in adults: Indications", section on 'Recurrent and chronic pharyngotonsillitis'.)

PREVENTION

General prevention

Hand hygiene — Hand hygiene is a key measure for preventing spread to others, especially after coughing or sneezing and before preparing foods or eating, and we remind all patients of its importance.

Postexposure prophylaxis — Testing and treatment of asymptomatic persons who have been exposed to a patient with group A *Streptococcus* (GAS) pharyngitis are not routinely recommended [23], except for patients with a history of acute rheumatic fever, during outbreaks of acute rheumatic fever and/or poststreptococcal glomerulonephritis, or when GAS infections are recurring in households or other close-contact settings.

Special populations

Patients with a history of acute rheumatic fever — Patients with a history of acute rheumatic fever are at high risk for recurrent rheumatic fever and the development of chronic valvular heart disease with any subsequent GAS infection. We educate these patients on the risk of recurrence and its complications and recommend long-term antibiotic prophylaxis. Antibiotic selection and duration of therapy vary based on patient characteristics and medication availability ([table 7](#) and [table 8](#)).

Details on acute rheumatic fever, rheumatic heart disease, and their prevention are discussed separately. (See "[Acute rheumatic fever: Clinical manifestations and diagnosis](#)" and "[Acute rheumatic fever: Treatment and prevention](#)" and "[Clinical manifestations and diagnosis of rheumatic heart disease](#)" and "[Management and prevention of rheumatic heart disease](#)".)

Chronic GAS carriers — Antibiotic treatment is not routinely recommended for chronic carriers [23]. Carriers are unlikely to transmit group A *Streptococcus* (GAS) to others [62,86,87] and are at very low risk for developing suppurative complications or acute rheumatic fever [10]. However, we do consider treating carriers during outbreaks of acute rheumatic fever and/or poststreptococcal glomerulonephritis or when GAS infections are recurring in households or other close-contact settings.

Oral options for treatment of chronic carriage include [clindamycin](#), [amoxicillin-clavulanate](#), and penicillin plus [rifampin](#); the duration of treatment is usually 10 days [23]. When used with either

oral or parenteral penicillin, rifampin is typically given only during the last four days of therapy.

Prevention of foodborne illness — Streptococcal contamination of food has been implicated in foodborne outbreaks of pharyngitis [88-92], and foodborne transmission of GAS pharyngitis by asymptomatic food service workers with nasopharyngeal carriage has been reported [91,93,94]. Factors that can reduce foodborne transmission of GAS pharyngitis include thorough cooking, complete reheating, and use of gloves while handling food [88,95].

Vaccination — No vaccine against GAS is available for clinical use. However, research on GAS vaccine development is ongoing [96-100]. An important area of uncertainty is whether vaccine-induced antibodies may cross-react with host tissue to produce nonsuppurative sequelae in the absence of clinical infection.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "[Society guideline links: Streptococcal tonsillopharyngitis](#)".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "[Patient education: Strep throat in adults \(The Basics\)](#)" and "[Patient education: Strep throat in children \(The Basics\)](#)" and "[Patient education: Scarlet fever \(The Basics\)](#)")

- Beyond the Basics topics (see "[Patient education: Sore throat in children \(Beyond the Basics\)](#)" and "[Patient education: Sore throat in adults \(Beyond the Basics\)](#)")
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SUMMARY AND RECOMMENDATIONS

- **Importance of treatment** – Group A *Streptococcus* (GAS), or *Streptococcus pyogenes*, is the leading bacterial cause of tonsillopharyngitis in adults and children worldwide. GAS is one of the few causes of tonsillopharyngitis or pharyngitis for which antibiotic treatment is recommended. (See '[Introduction](#)' above.)

The goals of antibiotic therapy for GAS pharyngitis include symptom relief, preventing complications, and preventing transmission to others. (See '[Goals of treatment](#)' above.)

- **Treatment recommendations**

- **Whom to treat** – We recommend antibiotic treatment for any patient with symptomatic pharyngitis or tonsillopharyngitis who has a positive microbiologic test (ie, nucleic acid amplification test [NAAT], rapid antigen test, or culture) for GAS (**Grade 1A**). We generally do not treat patients who do not have microbiologic confirmation of infection or who are chronic carriers. (See '[Whom to treat](#)' above.)
- **Preferred treatment for adults** – For most adults, we treat with oral [penicillin V](#) 500 mg two to three times daily for a total of 10 days. Penicillin is the treatment of choice for GAS pharyngitis due to its efficacy, safety, narrow spectrum, and low cost ([table 1](#) and [algorithm 2](#)). (See '[Antibiotic treatment](#)' above.)
- **Preferred treatment for children** – For most children, we use either oral [penicillin V](#) or [amoxicillin](#). For young children, amoxicillin is often preferred because the taste of the amoxicillin suspension is more palatable than that of penicillin ([table 2](#) and [algorithm 2](#)). (See '[Antibiotic treatment](#)' above.)
- **Treatment for patients with a history of acute rheumatic fever** – For patients with a history of acute rheumatic fever who are not receiving antibiotic prophylaxis, we select among oral [penicillin V](#), oral [amoxicillin](#), or a single dose of intramuscular [penicillin G benzathine](#). The choice is based on drug availability, cost, likelihood of adherence with oral therapy, and patient values and preferences ([table 1](#) and [table 2](#) and [algorithm 2](#)). (See '[Antibiotic treatment](#)' above.)
- **Alternatives for patients who cannot tolerate penicillin** – For patients who are allergic to or who cannot tolerate penicillin, alternatives include cephalosporins,

clindamycin, and macrolides. Selection among these agents is based on the nature of the drug allergy or intolerance and local antibiotic resistance rates ([table 3](#) and [table 1](#) and [table 2](#) and [algorithm 2](#)). (See '[Alternatives to penicillin](#)' above.)

- **Symptom resolution and return to work** – Fever and sore throat typically resolve within one to three days. Most patients can return to work, school, or daycare after 12 to 24 hours of antibiotic therapy, provided they are afebrile and otherwise well. (See '[Resolution of symptoms](#)' above.)

A test of cure is usually not needed for patients who are asymptomatic at the end of a course of antibiotic therapy, except for those with a history of acute rheumatic fever or in other special circumstances. (See '[Indications for test of cure](#)' above.)

- **Management of persistent symptoms after a course of antibiotics** – For patients who have persistent or recurrent symptoms after completing a course of antibiotic therapy, we repeat microbiologic testing when symptoms are compatible with GAS infection. Because chronic GAS carriage can occur after antibiotic therapy, we generally avoid testing in patients who have symptoms that are more compatible with viral pharyngitis or other etiology. (See '[Persistent or recurrent symptoms](#)' above.)

For patients with microbiologically proven recurrent or persistent GAS pharyngitis, we repeat a 10-day course of antibiotic therapy (**Grade 2C**) and generally select an antibiotic that has greater beta-lactamase stability than the one used initially. Tonsillectomy is rarely indicated for such patients. (See '[Antibiotic treatment](#)' above and '[Tonsillectomy](#)' above.)

- **Prophylaxis for patients with a history of acute rheumatic fever** – Antibiotic prophylaxis is used for patients with a history of acute rheumatic fever because these patients are at high risk for recurrence and for the development of chronic valvular heart disease. Antibiotic prophylaxis is not recommended for chronic carriers, except in special circumstances. (See '[Prevention](#)' above.)

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REFERENCES

1. Efstratiou A, Lamagni T. Epidemiology of Streptococcus pyogenes. In: *Streptococcus pyogenes: Basic Biology to Clinical Manifestations*, Ferretti JJ, Stevens DL, Fischetti VA (Eds), University of Oklahoma Health Sciences Center, Oklahoma City 2016.

2. Gunnarsson RK, Holm SE, Söderström M. The prevalence of beta-haemolytic streptococci in throat specimens from healthy children and adults. Implications for the clinical value of throat cultures. *Scand J Prim Health Care* 1997; 15:149.
3. Schwartz RH, Wientzen RL Jr, Pedreira F, et al. Penicillin V for group A streptococcal pharyngotonsillitis. A randomized trial of seven vs ten days' therapy. *JAMA* 1981; 246:1790.
4. Pontin IP, Sanchez DC, Di Francesco R. Asymptomatic Group A Streptococcus carriage in children with recurrent tonsillitis and tonsillar hypertrophy. *Int J Pediatr Otorhinolaryngol* 2016; 86:57.
5. Abdissa A, Asrat D, Kronvall G, et al. Throat carriage rate and antimicrobial susceptibility pattern of group A Streptococci (GAS) in healthy Ethiopian school children. *Ethiop Med J* 2011; 49:125.
6. Nayiga I, Okello E, Lwabi P, Ndeezi G. Prevalence of group a streptococcus pharyngeal carriage and clinical manifestations in school children aged 5-15 yrs in Wakiso District, Uganda. *BMC Infect Dis* 2017; 17:248.
7. Marshall HS, Richmond P, Nissen M, et al. Group A Streptococcal Carriage and Seroepidemiology in Children up to 10 Years of Age in Australia. *Pediatr Infect Dis J* 2015; 34:831.
8. Martin JM, Green M, Barbadora KA, Wald ER. Group A streptococci among school-aged children: clinical characteristics and the carrier state. *Pediatrics* 2004; 114:1212.
9. Shaikh N, Leonard E, Martin JM. Prevalence of streptococcal pharyngitis and streptococcal carriage in children: a meta-analysis. *Pediatrics* 2010; 126:e557.
10. Kaplan EL. The group A streptococcal upper respiratory tract carrier state: an enigma. *J Pediatr* 1980; 97:337.
11. Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. *Cochrane Database Syst Rev* 2013; :CD000023.
12. Little P, Hobbs FD, Moore M, et al. Clinical score and rapid antigen detection test to guide antibiotic use for sore throats: randomised controlled trial of PRISM (primary care streptococcal management). *BMJ* 2013; 347:f5806.
13. BRINK WR, RAMMELKAMP CH Jr, DENNY FW, WANNAMAKER LW. Effect in penicillin and aureomycin on the natural course of streptococcal tonsillitis and pharyngitis. *Am J Med* 1951; 10:300.
14. Roth GA, Huffman MD, Moran AE, et al. Global and regional patterns in cardiovascular mortality from 1990 to 2013. *Circulation* 2015; 132:1667.

15. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. *Lancet Infect Dis* 2005; 5:685.
16. Beaudoin A, Edison L, Introcaso CE, et al. Acute rheumatic fever and rheumatic heart disease among children--American Samoa, 2011-2012. *MMWR Morb Mortal Wkly Rep* 2015; 64:555.
17. Brundage JF, Gunzenhauser JD, Longfield JN, et al. Epidemiology and control of acute respiratory diseases with emphasis on group A beta-hemolytic streptococcus: a decade of U.S. Army experience. *Pediatrics* 1996; 97:964.
18. BREESE BB, DISNEY FA. Factors influencing the spread of beta hemolytic streptococcal infections within the family group. *Pediatrics* 1956; 17:834.
19. Lamagni TL, Oliver I, Stuart JM. Global assessment of invasive group a streptococcus infection risk in household contacts. *Clin Infect Dis* 2015; 60:166.
20. Snellman LW, Stang HJ, Stang JM, et al. Duration of positive throat cultures for group A streptococci after initiation of antibiotic therapy. *Pediatrics* 1993; 91:1166.
21. Schwartz RH, Kim D, Martin M, Pichichero ME. A Reappraisal of the Minimum Duration of Antibiotic Treatment Before Approval of Return to School for Children With Streptococcal Pharyngitis. *Pediatr Infect Dis J* 2015; 34:1302.
22. WANNAMAKER LW, RAMMELKAMP CH Jr, DENNY FW, et al. Prophylaxis of acute rheumatic fever by treatment of the preceding streptococcal infection with various amounts of depot penicillin. *Am J Med* 1951; 10:673.
23. Shulman ST, Bisno AL, Clegg HW, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2012; 55:1279.
24. Harris AM, Hicks LA, Qaseem A, High Value Care Task Force of the American College of Physicians and for the Centers for Disease Control and Prevention. Appropriate Antibiotic Use for Acute Respiratory Tract Infection in Adults: Advice for High-Value Care From the American College of Physicians and the Centers for Disease Control and Prevention. *Ann Intern Med* 2016; 164:425.
25. Tanz RR, Gewitz MH, Kaplan EL, Shulman ST. Stay the Course: Targeted Evaluation, Accurate Diagnosis, and Treatment of Streptococcal Pharyngitis Prevent Acute Rheumatic Fever. *J Pediatr* 2020; 216:208.
26. Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of rheumatic fever and diagnosis and treatment of acute Streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the

Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Academy of Pediatrics. *Circulation* 2009; 119:1541.

27. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Thorac Cardiovasc Surg* 2014; 148:e1.
28. American Academy of Pediatrics. Group A Streptococcus. In: Red Book: 2015 Report of the Committee of Infectious Diseases, 30th, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics, Elk Grove Village, IL 2018. p.732.
29. ESCMID Sore Throat Guideline Group, Pelucchi C, Grigoryan L, et al. Guideline for the management of acute sore throat. *Clin Microbiol Infect* 2012; 18 Suppl 1:1.
30. The Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (2nd edition) https://www.rhdaustralia.org.au/sites/default/files/resources/guideline_0_0.pdf (Accessed on October 27, 2017).
31. New Zealand Guidelines for Rheumatic Fever. Group A Streptococcal Sore Throat Management Guideline: 2014 Update <http://assets.heartfoundation.org.nz/shop/heart-healthcare/non-stock-resources/gas-sore-throat-rheumatic-fever-guideline.pdf> (Accessed on October 27, 2017).
32. Gopichand I, Williams GD, Medendorp SV, et al. Randomized, single-blinded comparative study of the efficacy of amoxicillin (40 mg/kg/day) versus standard-dose penicillin V in the treatment of group A streptococcal pharyngitis in children. *Clin Pediatr (Phila)* 1998; 37:341.
33. Curtin-Wirt C, Casey JR, Murray PC, et al. Efficacy of penicillin vs. amoxicillin in children with group A beta hemolytic streptococcal tonsillopharyngitis. *Clin Pediatr (Phila)* 2003; 42:219.
34. Lennon DR, Farrell E, Martin DR, Stewart JM. Once-daily amoxicillin versus twice-daily penicillin V in group A beta-haemolytic streptococcal pharyngitis. *Arch Dis Child* 2008; 93:474.
35. Feder HM Jr, Gerber MA, Randolph MF, et al. Once-daily therapy for streptococcal pharyngitis with amoxicillin. *Pediatrics* 1999; 103:47.
36. Clegg HW, Ryan AG, Dallas SD, et al. Treatment of streptococcal pharyngitis with once-daily compared with twice-daily amoxicillin: a noninferiority trial. *Pediatr Infect Dis J* 2006; 25:761.
37. Kaplan EL, Gooch III WM, Notario GF, Craft JC. Macrolide therapy of group A streptococcal pharyngitis: 10 days of macrolide therapy (clarithromycin) is more effective in streptococcal

- eradication than 5 days (azithromycin). Clin Infect Dis 2001; 32:1798.
38. Altamimi S, Khalil A, Khalaiwi KA, et al. Short-term late-generation antibiotics versus longer term penicillin for acute streptococcal pharyngitis in children. Cochrane Database Syst Rev 2012; :CD004872.
39. WANNAMAKER LW, DENNY FW, PERRY WD, et al. The effect of penicillin prophylaxis on streptococcal disease rates and the carrier state. N Engl J Med 1953; 249:1.
40. Gerber MA, Randolph MF, Chanatry J, et al. Five vs ten days of penicillin V therapy for streptococcal pharyngitis. Am J Dis Child 1987; 141:224.
41. Falagas ME, Vouloumanou EK, Matthaiou DK, et al. Effectiveness and safety of short-course vs long-course antibiotic therapy for group a beta hemolytic streptococcal tonsillopharyngitis: a meta-analysis of randomized trials. Mayo Clin Proc 2008; 83:880.
42. Skoog Ståhlgren G, Tyrstrup M, Edlund C, et al. Penicillin V four times daily for five days versus three times daily for 10 days in patients with pharyngotonsillitis caused by group A streptococci: randomised controlled, open label, non-inferiority study. BMJ 2019; 367:I5337.
43. BREESE BB, DISNEY FA. Penicillin in the treatment of streptococcal infections; a comparison of effectiveness of five different oral and one parenteral form. N Engl J Med 1958; 259:57.
44. Tack KJ, Henry DC, Gooch WM, et al. Five-day cefdinir treatment for streptococcal pharyngitis. Cefdinir Pharyngitis Study Group. Antimicrob Agents Chemother 1998; 42:1073.
45. Pichichero ME, Gooch WM 3rd. Comparison of cefdinir and penicillin V in the treatment of pediatric streptococcal tonsillopharyngitis. Pediatr Infect Dis J 2000; 19:S171.
46. Pichichero ME, Gooch WM, Rodriguez W, et al. Effective short-course treatment of acute group A beta-hemolytic streptococcal tonsillopharyngitis. Ten days of penicillin V vs 5 days or 10 days of cefpodoxime therapy in children. Arch Pediatr Adolesc Med 1994; 148:1053.
47. Tack KJ, Hedrick JA, Rothstein E, et al. A study of 5-day cefdinir treatment for streptococcal pharyngitis in children. Cefdinir Pediatric Pharyngitis Study Group. Arch Pediatr Adolesc Med 1997; 151:45.
48. Casey JR, Pichichero ME. Higher dosages of azithromycin are more effective in treatment of group A streptococcal tonsillopharyngitis. Clin Infect Dis 2005; 40:1748.
49. Richter SS, Heilmann KP, Beekmann SE, et al. Macrolide-resistant *Streptococcus pyogenes* in the United States, 2002-2003. Clin Infect Dis 2005; 41:599.
50. Lin JN, Chang LL, Lai CH, et al. High prevalence of fluoroquinolone-nonsusceptible *Streptococcus pyogenes* emm12 in Taiwan. Diagn Microbiol Infect Dis 2015; 83:187.

51. Petrelli D, Di Luca MC, Prenna M, et al. Characterization of levofloxacin non-susceptible clinical *Streptococcus pyogenes* isolated in the central part of Italy. *Eur J Clin Microbiol Infect Dis* 2014; 33:241.
52. Van Heirstraeten L, Leten G, Lammens C, et al. Increase in fluoroquinolone non-susceptibility among clinical *Streptococcus pyogenes* in Belgium during 2007-10. *J Antimicrob Chemother* 2012; 67:2602.
53. Palmieri C, Vecchi M, Littauer P, et al. Clonal spread of macrolide- and tetracycline-resistant [erm(A) tet(O)] emm77 *Streptococcus pyogenes* isolates in Italy and Norway. *Antimicrob Agents Chemother* 2006; 50:4229.
54. Michos AG, Bakoula CG, Braoudaki M, et al. Macrolide resistance in *Streptococcus pyogenes*: prevalence, resistance determinants, and emm types. *Diagn Microbiol Infect Dis* 2009; 64:295.
55. van Driel ML, De Sutter AI, Thorning S, Christiaens T. Different antibiotic treatments for group A streptococcal pharyngitis. *Cochrane Database Syst Rev* 2021; 3:CD004406.
56. US Food and Drug Administration. FDA Drug Safety Communication; May 12, 2016 <https://www.fda.gov/Drugs/DrugSafety/ucm511530.htm> (Accessed on September 11, 2017).
57. Randolph MF, Gerber MA, DeMeo KK, Wright L. Effect of antibiotic therapy on the clinical course of streptococcal pharyngitis. *J Pediatr* 1985; 106:870.
58. Pichichero ME, Disney FA, Talpey WB, et al. Adverse and beneficial effects of immediate treatment of Group A beta-hemolytic streptococcal pharyngitis with penicillin. *Pediatr Infect Dis J* 1987; 6:635.
59. Krober MS, Bass JW, Michels GN. Streptococcal pharyngitis. Placebo-controlled double-blind evaluation of clinical response to penicillin therapy. *JAMA* 1985; 253:1271.
60. Del Mar CB, Glasziou PP, Spinks AB. Antibiotics for sore throat. *Cochrane Database Syst Rev* 2000; :CD000023.
61. Gilbert GG, Pruitt BE. School health education in the United States. *Hygie* 1984; 3:10.
62. Kaplan EL, Gastanaduy AS, Huwe BB. The role of the carrier in treatment failures after antibiotic for group A streptococci in the upper respiratory tract. *J Lab Clin Med* 1981; 98:326.
63. Woodin KA, Lee LH, Pichichero ME. Milder symptoms occur in recurrent episodes of streptococcal infection. *Am J Dis Child* 1991; 145:389.
64. Pichichero ME, Hoeger W, Marsocci SM, et al. Variables influencing penicillin treatment outcome in streptococcal tonsillopharyngitis. *Arch Pediatr Adolesc Med* 1999; 153:565.

65. Cohen JF, Bertille N, Cohen R, Chalumeau M. Rapid antigen detection test for group A streptococcus in children with pharyngitis. *Cochrane Database Syst Rev* 2016; 7:CD010502.
66. van Driel ML, De Sutter AI, Habraken H, et al. Different antibiotic treatments for group A streptococcal pharyngitis. *Cochrane Database Syst Rev* 2016; 9:CD004406.
67. Yildirim I, Ceyhan M, Gür D, Kaymakoğlu I. Comparison of the effect of benzathine penicillin G, clarithromycin, cefprozil and amoxicillin/clavulanate on the bacteriological response and throat flora in group A beta hemolytic streptococcal tonsillopharyngitis. *Turk J Pediatr* 2008; 50:120.
68. Brook I, Gober AE. Failure to eradicate streptococci and beta-lactamase producing bacteria. *Acta Paediatr* 2008; 97:193.
69. Casey JR, Pichichero ME. Symptomatic relapse of group A beta-hemolytic streptococcal tonsillopharyngitis in children. *Clin Pediatr (Phila)* 2007; 46:307.
70. Brook I, Gober AE. Recovery of interfering and beta-lactamase-producing bacteria from group A beta-haemolytic streptococci carriers and non-carriers. *J Med Microbiol* 2006; 55:1741.
71. Gaffney RJ, Freeman DJ, Walsh MA, Cafferkey MT. Differences in tonsil core bacteriology in adults and children: a prospective study of 262 patients. *Respir Med* 1991; 85:383.
72. Lund B, Edlund C, Rynnel-Dagöö B, et al. Ecological effects on the oro- and nasopharyngeal microflora in children after treatment of acute otitis media with cefuroxime axetil or amoxycillin-clavulanate as suspensions. *Clin Microbiol Infect* 2001; 7:230.
73. Lafontaine ER, Wall D, Vanlerberg SL, et al. *Moraxella catarrhalis* coaggregates with *Streptococcus pyogenes* and modulates interactions of *S. pyogenes* with human epithelial cells. *Infect Immun* 2004; 72:6689.
74. Gaffney RJ, Cafferkey MT. Bacteriology of normal and diseased tonsils assessed by fine-needle aspiration: *Haemophilus influenzae* and the pathogenesis of recurrent acute tonsillitis. *Clin Otolaryngol Allied Sci* 1998; 23:181.
75. Brook I, Yocom P, Foote PA Jr. Changes in the core tonsillar bacteriology of recurrent tonsillitis: 1977-1993. *Clin Infect Dis* 1995; 21:171.
76. Brook I. Overcoming penicillin failures in the treatment of Group A streptococcal pharyngo-tonsillitis. *Int J Pediatr Otorhinolaryngol* 2007; 71:1501.
77. Falck G, Grahn-Håkansson E, Holm SE, et al. Tolerance and efficacy of interfering alpha-streptococci in recurrence of streptococcal pharyngotonsillitis: a placebo-controlled study. *Acta Otolaryngol* 1999; 119:944.

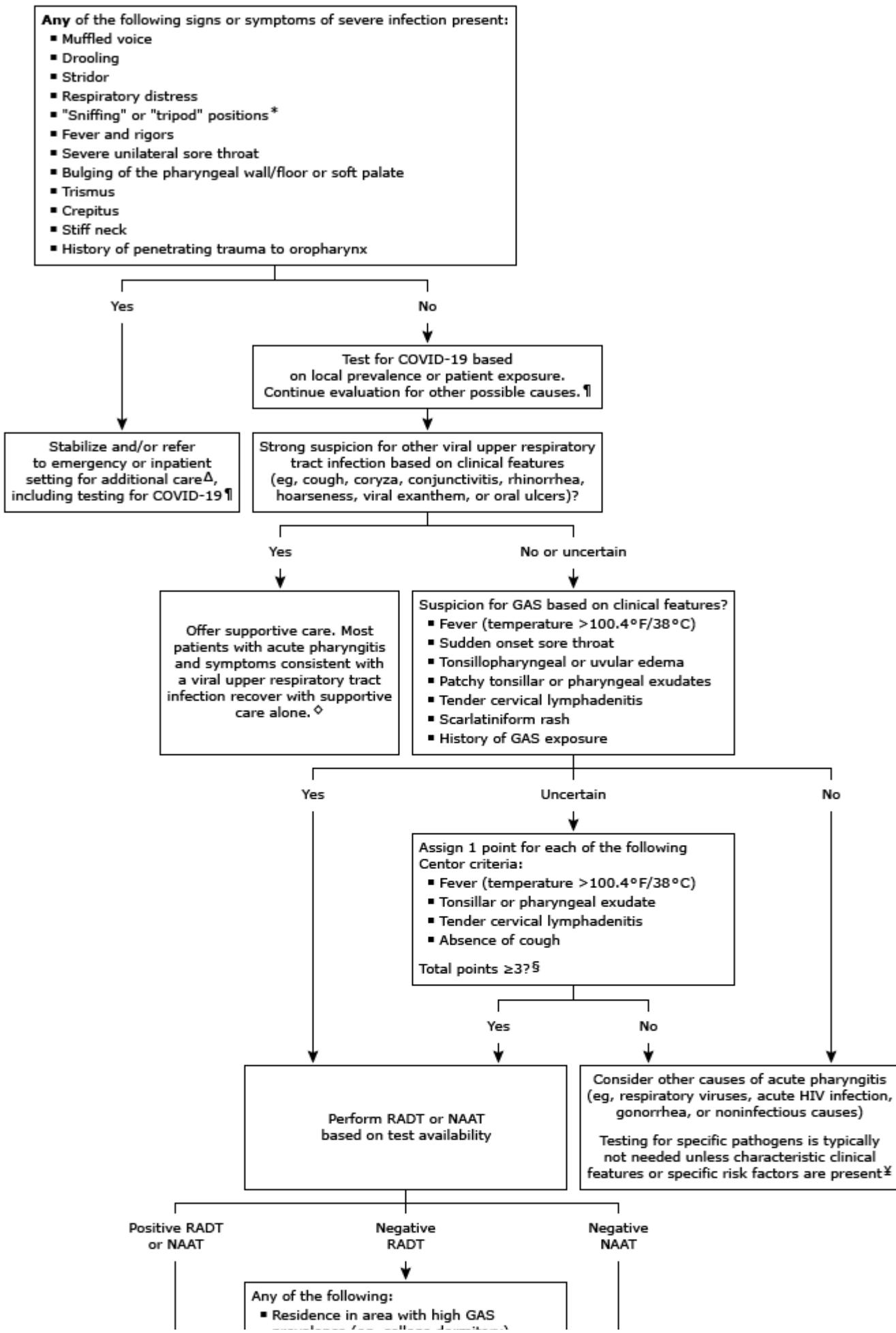
78. Roos K, Holm SE, Grahn-Håkansson E, Lagergren L. Recolonization with selected alpha-streptococci for prophylaxis of recurrent streptococcal pharyngotonsillitis--a randomized placebo-controlled multicentre study. *Scand J Infect Dis* 1996; 28:459.
79. Roos K, Holm SE, Grahn E, Lind L. Alpha-streptococci as supplementary treatment of recurrent streptococcal tonsillitis: a randomized placebo-controlled study. *Scand J Infect Dis* 1993; 25:31.
80. Wozniak A, Scioscia N, Geoffroy E, et al. Importance of adhesins in the recurrence of pharyngeal infections caused by *Streptococcus pyogenes*. *J Med Microbiol* 2017; 66:517.
81. Ogawa T, Terao Y, Okuni H, et al. Biofilm formation or internalization into epithelial cells enable *Streptococcus pyogenes* to evade antibiotic eradication in patients with pharyngitis. *Microp Pathog* 2011; 51:58.
82. Podbielski A, Beckert S, Schattke R, et al. Epidemiology and virulence gene expression of intracellular group A streptococci in tonsils of recurrently infected adults. *Int J Med Microbiol* 2003; 293:179.
83. el-Daher NT, Hijazi SS, Rawashdeh NM, et al. Immediate vs. delayed treatment of group A beta-hemolytic streptococcal pharyngitis with penicillin V. *Pediatr Infect Dis J* 1991; 10:126.
84. CATANZARO FJ, STETSON CA, MORRIS AJ, et al. The role of the streptococcus in the pathogenesis of rheumatic fever. *Am J Med* 1954; 17:749.
85. BROCK LL, SIEGEL AC. Studies on the prevention of rheumatic fever; the effect of time of initiation of treatment of streptococcal infections on the immune response of the host. *J Clin Invest* 1953; 32:630.
86. Davies HD, McGeer A, Schwartz B, et al. Invasive group A streptococcal infections in Ontario, Canada. Ontario Group A Streptococcal Study Group. *N Engl J Med* 1996; 335:547.
87. KRAUSE RM, RAMMELKAMP CH Jr, DENNY FW Jr, WANNAMAKER LW. Studies of the carrier state following infection with group A streptococci. 1. Effect of climate. *J Clin Invest* 1962; 41:568.
88. Kemble SK, Westbrook A, Lynfield R, et al. Foodborne outbreak of group a streptococcus pharyngitis associated with a high school dance team banquet--Minnesota, 2012. *Clin Infect Dis* 2013; 57:648.
89. Levy M, Johnson CG, Kraa E. Tonsillopharyngitis caused by foodborne group A streptococcus: a prison-based outbreak. *Clin Infect Dis* 2003; 36:175.
90. Katzenell U, Shemer J, Bar-Dayan Y. Streptococcal contamination of food: an unusual cause of epidemic pharyngitis. *Epidemiol Infect* 2001; 127:179.

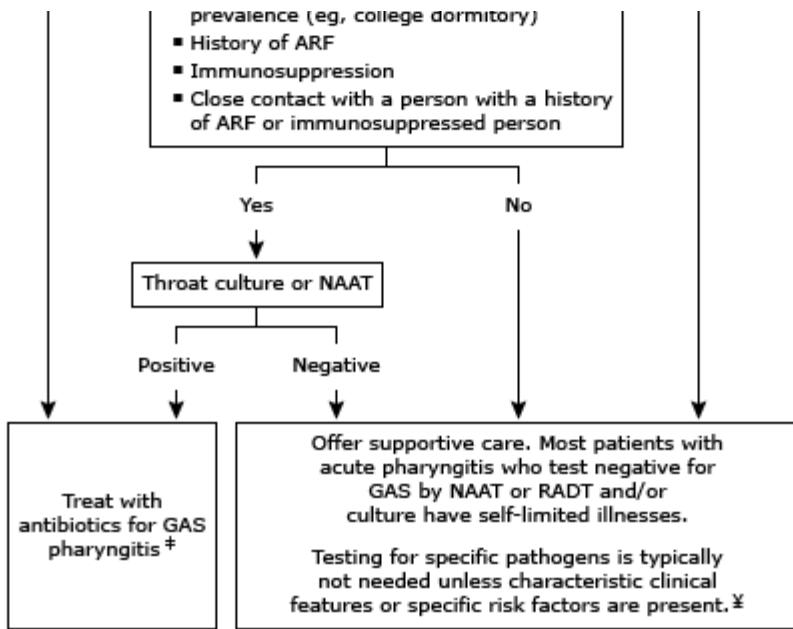
91. Decker MD, Lavelly GB, Hutcheson RH Jr, Schaffner W. Food-borne streptococcal pharyngitis in a hospital pediatrics clinic. *JAMA* 1985; 253:679.
92. Todd EC, Greig JD, Michaels BS, et al. Outbreaks where food workers have been implicated in the spread of foodborne disease. Part 11. Use of antiseptics and sanitizers in community settings and issues of hand hygiene compliance in health care and food industries. *J Food Prot* 2010; 73:2306.
93. Sarvghad MR, Naderi HR, Naderi-Nassab M, et al. An outbreak of food-borne group A Streptococcus (GAS) tonsillopharyngitis among residents of a dormitory. *Scand J Infect Dis* 2005; 37:647.
94. McCormick JB, Hayes P, Feldman R. Epidemic streptococcal sore throat following a community picnic. *JAMA* 1976; 236:1039.
95. Kaplan EL. Editorial commentary: The epidemiology of group a streptococci: a need to understand the significance of the fertile fields. *Clin Infect Dis* 2012; 55:488.
96. Nordström T, Pandey M, Calcutt A, et al. Enhancing Vaccine Efficacy by Engineering a Complex Synthetic Peptide To Become a Super Immunogen. *J Immunol* 2017; 199:2794.
97. Burlet E, HogenEsch H, Dunham A, Morefield G. Evaluation of the Potency, Neutralizing Antibody Response, and Stability of a Recombinant Fusion Protein Vaccine for Streptococcus pyogenes. *AAPS J* 2017; 19:875.
98. Williamson DA, Smeesters PR, Steer AC, et al. Comparative M-protein analysis of Streptococcus pyogenes from pharyngitis and skin infections in New Zealand: Implications for vaccine development. *BMC Infect Dis* 2016; 16:561.
99. Good MF, Pandey M, Batzloff MR, Tyrrell GJ. Strategic development of the conserved region of the M protein and other candidates as vaccines to prevent infection with group A streptococci. *Expert Rev Vaccines* 2015; 14:1459.
100. Lewnard JA, King LM, Fleming-Dutra KE, et al. Incidence of Pharyngitis, Sinusitis, Acute Otitis Media, and Outpatient Antibiotic Prescribing Preventable by Vaccination Against Group A Streptococcus in the United States. *Clin Infect Dis* 2021; 73:e47.

Topic 8049 Version 94.0

GRAPHICS

Evaluation of acute pharyngitis in adults





All adults presenting with acute pharyngitis should have a thorough history and physical, including assessment for risk factors for acute HIV infection and sexually transmitted infections.

ARF: acute rheumatic fever; COVID-19: coronavirus disease 2019; GAS: group A *Streptococcus*; HIV: human immunodeficiency virus; NAAT: nucleic acid amplification test; RADT: rapid antigen detection test.

* A sitting position with the trunk leaning forward, neck hyperextended, and chin thrust forward in an effort to maximize the diameter of the obstructed airway.

¶ Refer to UpToDate content on COVID-19 for additional detail on clinical features, testing, and infection control.

Δ Refer to UpToDate topics on evaluation of pharyngitis in adults, evaluation of the adult with dyspnea, and deep neck space infections.

◊ Refer to UpToDate content on symptomatic treatment of pharyngitis in adults.

§ Some practitioners test patients with Centor scores ≥2.

¥ Refer to UpToDate topic on evaluation of pharyngitis in adults.

‡ Refer to UpToDate content on treatment and prevention of streptococcal pharyngitis.

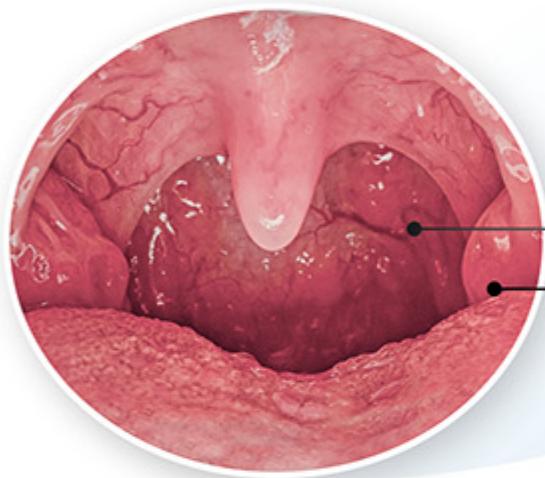
Distinguishing viral pharyngitis from streptococcal pharyngitis in adults



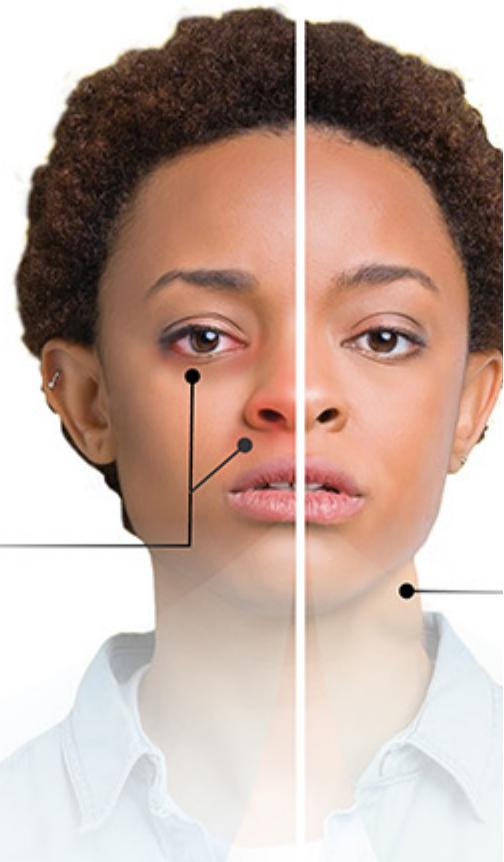
UpToDate®

Viral Pharyngitis vs. Streptococcal Pharyngitis - in Adults -

Viral Pharyngitis



Coryza
(nasal and lacrimal edema and congestion)



Pharyngeal erythema
Tonsillar edema

Features Suggestive of Viral Pharyngitis	Feature
■ Subacute onset of sore throat	■ Acute
■ Associated upper respiratory infection symptoms (cough, congestion, conjunctivitis, hoarse voice)	■ Absent
■ Pharyngeal erythema and tonsillar edema	■ Pharyngeal
■ Low-grade or absent fever	■ Fever
Other Findings (variably present)	■ Tonsillar
■ Pharyngeal/tonsillar exudates	■ Known
■ Oral ulcers	■ Palatal
■ Viral exanthem	■ Scarlet
	■ “Strawberry”

KEY CONCEPTS

There is no single clinical feature that distinguishes viral pharyngitis from streptococcal pharyngitis. The combination of the following findings is highly suggestive of streptococcal pharyngitis:

- Acute onset pharyngitis with tonsillar exudates
- Fever
- Cervical lymphadenopathy
- Absence of other upper respiratory infection symptoms (eg, cough)

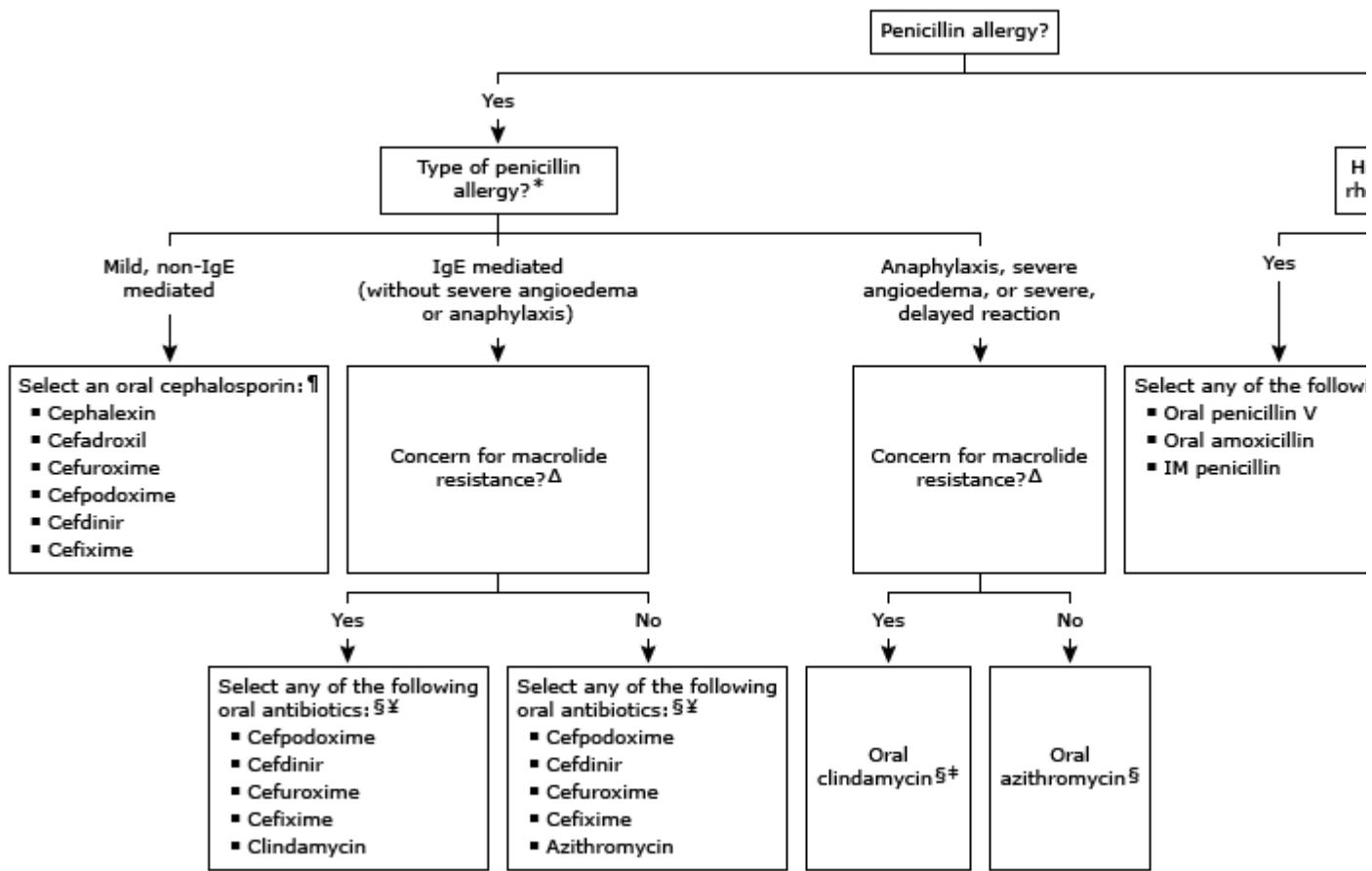
Distinguishing viral pharyngitis from group A *Streptococcus* (GAS) pharyngitis can be challenging. Although symptomatic care alone is appropriate for patients with pharyngitis, patients with confirmed streptococcal pharyngitis require antibiotic treatment.

Confirmatory testing for GAS (with a rapid antigen detection test [RADT], throat culture, or rapid molecular test) is not recommended for all patients with suspected streptococcal pharyngitis. When there is uncertainty, however, confirmatory testing can help determine whether testing for GAS is warranted.

Streptococcal pharyngitis image reproduced with permission from Dr. P. Marazzi/Science Photo Library.

Graphic 139794 Version 3.0

Treatment of streptococcal pharyngitis in children and adults



IgE: immunoglobulin E; IM: intramuscular.

* Examples of mild, non-IgE-mediated reactions include maculopapular rashes. Examples of IgE-mediated reactions include hives, wheezing, angioedema, and anaphylaxis. Examples of severe, delayed reactions include Steven-Johnson syndrome, toxic epidermal necrolysis, acute interstitial nephritis, drug-induced hepatitis, and serum sickness.

¶ Approach to selecting among cephalosporins varies among experts. Some prefer to use a first-generation cephalosporin (eg, cephalexin) because of its narrow spectrum and low likelihood of cross reactivity. Others select a third-generation cephalosporin with a side chain that is dissimilar to penicillin (eg, cefpodoxime, cefdinir), although these agents have a broader spectrum.

Δ Macrolide resistance varies considerably by region, with higher rates observed in Asia and Europe when compared with the United States. Knowledge of local resistance patterns should guide antibiotic selection.

◊ Selection among these agents should be based on drug availability and patient preference. For patients with a history of acute rheumatic fever and penicillin allergy, antibiotic selection should be individualized.

§ Many patients with IgE-mediated reactions can tolerate cephalosporins. These patients should be referred for allergy consultation following treatment for streptococcal pharyngitis.

¥ Approach to selecting among these agents varies among experts. Some prefer cephalosporins due their high efficacy and low risk of cross-reactivity, while others favor selecting a non-cephalosporin alternative to avoid any possibility of cross-reactivity.

‡ Rates of resistance to clindamycin are high and can be higher than rates of resistance to macrolides. Therefore, when beta-lactams and macrolides cannot be used, knowledge of local resistance rates should guide antibiotic selection or culture with susceptibility testing should be obtained.

Graphic 115985 Version 13.0

Treatment of pharyngitis due to group A *Streptococcus* in adults

Antibiotic class	Drug	Dosing in adults*	Advantages	Disadvantages
Penicillins (preferred)	Penicillin V	<ul style="list-style-type: none"> ▪ 500 mg orally two to three times daily for 10 days 	<ul style="list-style-type: none"> ▪ Narrow spectrum ▪ No documented resistance ▪ Low cost 	<ul style="list-style-type: none"> ▪ Three-times-daily dosing; however, twice-daily regimen appears to be as effective as thrice daily^[1]
	Amoxicillin [¶]	<ul style="list-style-type: none"> ▪ 500 mg orally twice daily for 10 days ▪ 1000 mg (immediate release) once daily for 10 days 		
	Penicillin G benzathine* (Bicillin L-A)	<ul style="list-style-type: none"> ▪ 1.2 million units IM as a single dose 	<ul style="list-style-type: none"> ▪ Can be given as a single dose ▪ Ensured adherence ▪ Only drug studied for prevention of acute rheumatic fever 	<ul style="list-style-type: none"> ▪ Variable availability ▪ High cost ▪ Injection site pain
Cephalosporins (potential alternatives for mild reactions to penicillin ^Δ)	Cephalexin* (first generation)	<ul style="list-style-type: none"> ▪ 500 mg orally twice daily for 10 days 	<ul style="list-style-type: none"> ▪ High efficacy rate ▪ Narrower spectrum than later-generation cephalosporins 	<ul style="list-style-type: none"> ▪ Broader spectrum than penicillin ▪ Greater potential to induce antibiotic resistance
	Cefadroxil* (first generation)	<ul style="list-style-type: none"> ▪ 1 g orally daily for 10 days 	<ul style="list-style-type: none"> ▪ Once daily ▪ High efficacy rate ▪ Narrower spectrum than 	<ul style="list-style-type: none"> ▪ Broader spectrum than penicillin ▪ Greater potential to

			later-generation cephalosporins	induce antibiotic resistance
Cefuroxime* (second generation)	■ 250 mg orally twice daily for 10 days	■ High efficacy rate ■ Narrower spectrum than later-generation cephalosporins	■ Broader spectrum than penicillin and first-generation cephalosporins ■ Greater potential to induce antibiotic resistance	
Cefpodoxime* (third generation)	■ 100 mg orally twice daily for 5 to 10 days	■ High efficacy rate ■ FDA approved for 5-day course	■ Broader spectrum than penicillin and earlier-generation cephalosporins ■ Greater potential to induce antibiotic resistance	
Cefdinir* (third generation)	■ 300 mg orally twice daily for 5 to 10 days or 600 mg orally once daily for 10 days	■ Once-daily option ■ High efficacy rate ■ FDA approved for 5-day course	■ Broader spectrum than penicillin and earlier-generation cephalosporins ■ Greater potential to induce antibiotic resistance	
Macrolides (alternatives for patients with anaphylaxis or other IgE-mediated reactions or severe	Azithromycin	■ 12 mg/kg/day (maximum 500 mg/dose) 5 days [◊]	■ Once daily	■ Growing rates of resistance ■ Associated with QTc prolongation and, rarely, life-threatening cardiovascular

delayed reactions to penicillin ^Δ)				events including TdP; assess risk (eg, history of long QT interval, interacting medications, electrolyte abnormalities)
	Clarithromycin*	<ul style="list-style-type: none"> ▪ 250 mg orally twice daily for 10 days 		<ul style="list-style-type: none"> ▪ Growing rates of resistance ▪ Greater gastrointestinal side effects than azithromycin ▪ Causes CYP3A4 drug interactions ▪ QTc prolongation: Refer to azithromycin
Lincosamides (alternative when macrolide resistance is a concern and penicillins and cephalosporins cannot be used)	Clindamycin [§]	<ul style="list-style-type: none"> ▪ 300 mg orally three times daily for 10 days 		<ul style="list-style-type: none"> ▪ Growing rates of resistance ▪ High side-effect profile (ie, gastrointestinal)

FDA: US Food and Drug Administration; IM: intramuscularly; TdP: torsades de pointes.

* Dose alteration may be needed for renal insufficiency.

¶ Once-daily immediate-release amoxicillin appears to be non-inferior to penicillin V or amoxicillin administered in multiple daily doses, primarily based on studies in children and adolescents.

Δ Approach to patients with penicillin allergy varies among experts and allergy severity; refer to the UpToDate text for additional detail.

◊ A 3-day course is approved and widely prescribed in Europe and other regions.

§ Rates of resistance to clindamycin are high and can be higher than rates of resistance to macrolides. Therefore, when beta-lactams and macrolides cannot be used, knowledge of local resistance rates should guide antibiotic selection or culture with susceptibility testing should be obtained.

Reference:

1. Lan AJ, Colford JM, Colford JM Jr. *The impact of dosing frequency on the efficacy of 10-day penicillin or amoxicillin therapy for streptococcal tonsillopharyngitis: A meta-analysis.* Pediatrics 2000; 105:E19.

Data from:

1. Shulman ST, Bisno AL, Clegg HW, et al. *Clinical practice guideline for the diagnosis and management of Group A Streptococcal pharyngitis: 2012 Update by the Infectious Diseases Society of America.* Clin Infect Dis 2012; 55:e86.
2. Gerber MA, Baltimore RS, Eaton CB, et al. *Prevention of rheumatic fever and diagnosis and treatment of acute streptococcal pharyngitis: A scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research: Endorsed by the American Academy of Pediatrics.* Circulation 2009; 119:1541.

Graphic 64596 Version 47.0

Treatment of pharyngitis due to group A *Streptococcus* in children and adolescents

Antibiotic class	Drug	Dosing in children and adolescents*	Advantages	Disadvantages
Penicillins (preferred)	Penicillin V	<ul style="list-style-type: none"> ▪ If ≤ 27 kg: 250 mg 2 to 3 times daily for 10 days ▪ If >27 kg: 500 mg 2 to 3 times daily for 10 days 	<ul style="list-style-type: none"> ▪ Narrow spectrum ▪ No documented resistance ▪ Low cost 	<ul style="list-style-type: none"> ▪ Thrice-daily dosing; however, twice-daily regimen appears to be as effective as thrice daily^[1]
	Amoxicillin*	<ul style="list-style-type: none"> ▪ 50 mg/kg per day orally (maximum 1000 mg per day) for 10 days ▪ May be administered once daily or in 2 equally divided doses 	<ul style="list-style-type: none"> ▪ Taste of suspension more palatable than penicillin, often preferred for children 	
	Penicillin G benzathine (Bicillin L-A)	<ul style="list-style-type: none"> ▪ If ≤ 27 kg: Penicillin G benzathine (Bicillin L-A) 600,000 units IM as a single dose^[1] ▪ If >27 kg: Penicillin G benzathine (Bicillin L-A) 1.2 million units IM as a single dose 	<ul style="list-style-type: none"> ▪ Can be given as a single dose ▪ Ensured adherence ▪ Only drug studied for prevention of acute rheumatic fever 	<ul style="list-style-type: none"> ▪ Variable availability ▪ High cost ▪ Injection site pain
Cephalosporins (potential alternatives for	Cephalexin* (first generation)	<ul style="list-style-type: none"> ▪ 40 mg/kg/day divided twice daily for 10 days 	<ul style="list-style-type: none"> ▪ High efficacy rate ▪ Narrower spectrum than penicillin 	<ul style="list-style-type: none"> ▪ Broader spectrum than penicillin

mild reactions to penicillin ^A)		(maximum 500 mg/dose)	later-generation cephalosporins	<ul style="list-style-type: none"> ▪ Greater potential to induce antibiotic resistance
	Cefuroxime* (second generation)	<ul style="list-style-type: none"> ▪ 10 mg/kg/dose orally twice daily for 10 days (maximum 250 mg/dose) 	<ul style="list-style-type: none"> ▪ High efficacy rate ▪ Narrower spectrum than later-generation cephalosporins 	<ul style="list-style-type: none"> ▪ Broader spectrum than penicillin and first-generation cephalosporins ▪ Greater potential to induce antibiotic resistance
	Cefpodoxime* (third generation)	<ul style="list-style-type: none"> ▪ 5 mg/kg/dose orally every 12 hours (maximum 100 mg/dose) for 5 to 10 days 	<ul style="list-style-type: none"> ▪ High efficacy rate ▪ FDA approved for 5-day course 	<ul style="list-style-type: none"> ▪ Broader spectrum than penicillin and earlier-generation cephalosporins ▪ Greater potential to induce antibiotic resistance
	Cefdinir* (third generation)	<ul style="list-style-type: none"> ▪ 7 mg/kg/dose orally every 12 hours for 5 to 10 days or 14 mg/kg/dose every 24 hours for 10 days (maximum 600 mg/day) 	<ul style="list-style-type: none"> ▪ High efficacy rate ▪ FDA approved for 5-day course when dosed twice daily 	<ul style="list-style-type: none"> ▪ Broader spectrum than penicillin and earlier-generation cephalosporins ▪ Greater potential to induce antibiotic resistance
Macrolides (alternatives for patients with anaphylaxis or other IgE-mediated	Azithromycin	<ul style="list-style-type: none"> ▪ 12 mg/kg/day (maximum 500 mg/dose) for 5 days 	<ul style="list-style-type: none"> ▪ Can be given as a 5-day course due to extended half-life 	<ul style="list-style-type: none"> ▪ Growing rates of resistance ▪ Associated with QTc prolongation and, rarely, life-

reactions or severe delayed reactions to penicillin ^Δ)				threatening cardiovascular events including TdP; assess risk (eg, history of long QT interval, interacting medications, electrolyte abnormalities)
	Clarithromycin*	<ul style="list-style-type: none"> ■ 7.5 mg/kg/dose (maximum 250 mg per dose) orally twice daily for 10 days 		<ul style="list-style-type: none"> ■ Growing rates of resistance ■ Greater gastrointestinal side effects than azithromycin ■ Causes CYP3A4 drug interactions ■ QTc interval prolongation: Refer to azithromycin
Lincosamides (alternative when macrolide resistance is a concern and penicillins and cephalosporins cannot be used)	Clindamycin	<ul style="list-style-type: none"> ■ 7 mg/kg/dose (maximum 300 mg per dose) orally 3 times daily for 10 days 		<ul style="list-style-type: none"> ■ Growing rates of resistance ■ High side effect profile (ie, gastrointestinal)

IM: intramuscularly; FDA: US Food and Drug Administration; TdP: torsades de pointes.

* Dose alteration may be needed for renal insufficiency.

¶ In children weighing ≤27 kg, the combination IM formulation of 900,000 units benzathine penicillin G with 300,000 units procaine penicillin G (Bicillin C-R 900/300) is a less painful alternative. Efficacy in larger children and adults has not been established.

Δ Approach to patients with penicillin allergy varies among experts and allergy severity; refer to UpToDate text for additional details.

Reference:

1. Lan AJ, Colford JM, Colford JM Jr; *The impact of dosing frequency on the efficacy of 10-day penicillin or amoxicillin therapy for streptococcal tonsillopharyngitis: A meta-analysis*. Pediatrics; 2000 Feb; 105:E19.

Data from:

1. Shulman ST, Bisno AL, Clegg HW, et al. *Clinical practice guideline for the diagnosis and management of Group A Streptococcal pharyngitis: 2012 Update by the Infectious Diseases Society of America*. Clin Infect Dis 2012; 55:e86.
2. Gerber MA, Baltimore RS, Eaton CB, et al. *Prevention of rheumatic fever and diagnosis and treatment of acute streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Academy of Pediatrics*. Circulation 2009; 119:1541.
3. American Academy of Pediatrics. *Group A Streptococcal Infections*. In: *Red Book: 2021-2024 Report of the Committee on Infectious Diseases*, 32nd ed, Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH (Eds), American Academy of Pediatrics 2015. p.694.

Graphic 115983 Version 10.0

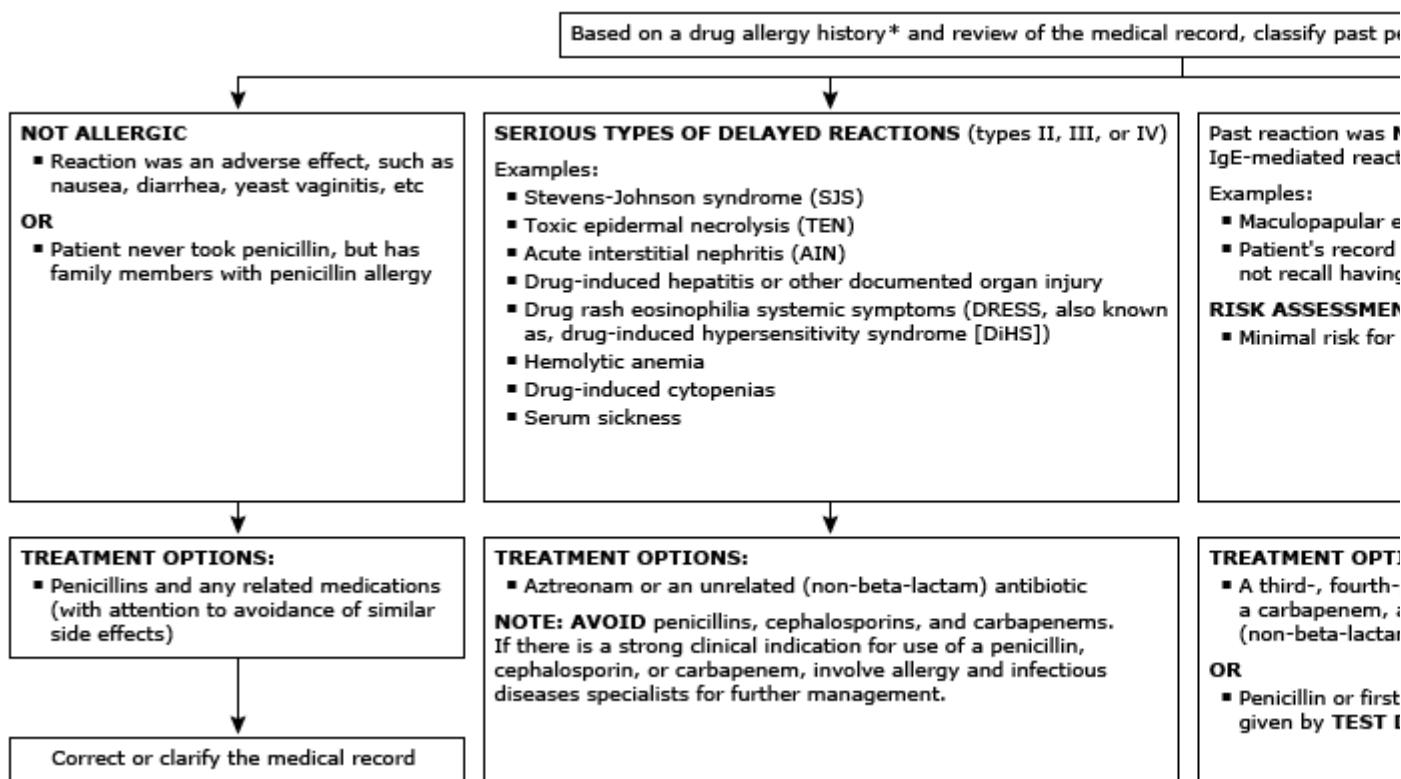
Type of drug reactions

Type of reaction	Common features
Non-allergic reaction	<ul style="list-style-type: none">▪ Adverse effects (eg, diarrhea, vomiting, yeast vaginitis)▪ Family history of penicillin allergy but no personal history
Mild non-IgE-mediated reaction	<ul style="list-style-type: none">▪ Maculopapular rash (with or without itching)▪ Medical record lists penicillin allergy but patient unaware of reaction
IgE-mediated reaction	<ul style="list-style-type: none">▪ Anaphylaxis▪ Angioedema▪ Wheezing▪ Laryngeal edema▪ Hypotension▪ Hives/urticaria
Serious delayed reactions	<ul style="list-style-type: none">▪ Toxic epidermal necrolysis (TEN)▪ Stevens-Johnson syndrome (SJS)▪ Drug reaction with eosinophilia and systemic symptoms/drug-induced hypersensitivity syndrome (DRESS/DiHS)▪ Other exfoliating dermatoses/erythroderma▪ Serum sickness-like reactions▪ Drug-induced cytopenias▪ Drug-induced renal, hepatic, or other specific organ damage

IgE: immunoglobulin E.

Graphic 117212 Version 2.0

Approach to the patient with a past penicillin reaction who requires antibiotics



This algorithm is intended for use in conjunction with the UpToDate content on choice of antibiotics in penicillin-allergic hospitalized patients. It is oriented toward hospitalized patients but also applies to outpatients if test dose procedures can be performed in an appropriately monitored setting with the staff and equipment needed to manage allergic reactions, including anaphylaxis.

IgE: immunoglobulin E.

* Ask the following:

1. What exactly were the symptoms?
 - Raised, red, itchy spots with each lesion lasting less than 24 hours (hives/urticaria)?
 - Swelling of the mouth, eyes, lips, or tongue (angioedema)?
 - Blisters or ulcers involving the lips, mouth, eyes, urethra, vagina, or peeling skin (seen in SJS, TEN, other severe type IV reactions)?
 - Respiratory or hemodynamic changes (anaphylaxis)?
 - Joint pains (seen in serum sickness)?
 - Did the reaction involve organs like the kidneys, lungs, or liver (seen in DRESS, other severe type IV reactions)?
2. What was the timing of the reaction after taking penicillin: Minutes, hours, or days later? Was it after the first dose or after multiple doses?
3. How long ago did the reaction happen? (After 10 years of avoidance, only 20% of patients with IgE-mediated penicillin allergy will still be allergic).
4. How was the reaction treated? Was there a need for urgent care or was adrenaline/epinephrine administered?

5. Has the patient tolerated similar medications, such as ampicillin, amoxicillin, or cephalexin since the penicillin reaction?

¶ Isolated mild hives, without other symptoms of an IgE-mediated reaction, can often occur in the setting of an infection. Patients with this history, especially if it occurred in childhood or >10 years ago, may also be considered to be at minimal risk for a recurrent serious reaction.

Δ This algorithm is intended for use in conjunction with additional UpToDate content. For a description of how to safely perform a TEST DOSE PROCEDURE, refer to the UpToDate topic on choice of antibiotics in penicillin-allergic hospitalized patients.

◊ Consult allergist to perform skin testing. If skin testing is not possible, patient may still be able to receive penicillins or first- or second-generation cephalosporins using a desensitization (also known as tolerance induction) procedure. Refer to the UpToDate topic on rapid drug desensitization for immediate hypersensitivity reactions.

Original figure modified for this publication. Blumenthal KG, Shenoy ES, Varughese CA, et al. Impact of a clinical guideline for prescribing antibiotics to inpatients reporting penicillin or cephalosporin allergy. Ann Allergy Asthma Immunol 2015; 115:294. Illustration used with the permission of Elsevier Inc. All rights reserved.

Graphic 112936 Version 5.0

Causes of acute pharyngitis

	Estimated frequency, percent	Examples
Common bacterial pathogens	15	Group A streptococci Group C streptococci Group G streptococci
Less common bacterial pathogens	<5	<i>Chlamydophila pneumoniae</i> (TWAR) <i>Mycoplasma pneumoniae</i> <i>Arcanobacterium haemolyticum</i> <i>Corynebactrium diphtheriae</i> <i>Fusobacterium necrophorum</i> <i>Neisseria gonorrhoeae</i> <i>Treponema pallidum</i> <i>Francisella tularensis</i>
Viruses	50	Rhinovirus Adenovirus Influenza A and B Parainfluenza Coxsackievirus Coronavirus Echo virus Herpes simplex virus Epstein Barr virus Human immunodeficiency virus Cytomegalovirus Respiratory syncytial virus Metapneumovirus
No pathogen isolated	30	

Infectious causes of acute pharyngitis in children and adolescents

	Clinical syndrome	Clinical clues
Bacteria (requires antimicrobial therapy)		
<i>Streptococcus</i> , group A (most common cause requiring antimicrobial therapy)	Tonsillopharyngitis and scarlet fever	Acute onset, fever, headache, abdominal pain, tonsillopharyngeal erythema and exudate, tender anterior cervical lymph nodes
<i>Streptococcus</i> , groups C and G	Tonsillopharyngitis and scarlatiniform rash	
<i>Neisseria gonorrhoeae</i>	Pharyngitis	Oral-genital contact in sexually active adolescents
<i>Fusobacterium necrophorum</i>	Jugular vein suppurative thrombophlebitis (Lemierre syndrome)	Primarily affects adolescents and young adults, high fever ($>39^{\circ}\text{C}$ [102.2°F]), rigors respiratory symptoms, unilateral neck swelling or pain
<i>Arcanobacterium haemolyticum</i>	Pharyngitis and scarlatiniform rash	More common in adolescents, rash occurs in approximately one-half
<i>Corynebacterium diphtheriae</i>	Diphtheria	Tightly adherent membrane in nose and throat, history of travel (particularly to former Soviet Union, Africa, or Asia), lack of immunizations
Tularemia	Ulcerative-exudative pharyngitis	Ingestion of poorly cooked wild animal meat or contaminated water
Atypical bacteria (may require specific therapy or infection control measures)		
<i>Mycoplasma pneumoniae</i>	Pneumonia, bronchitis, and pharyngitis	Adolescents and adults
Viruses that infect the pharynx directly		
Epstein-Barr virus (EBV)	Infectious mononucleosis	Fever, severe pharyngitis, frequent exudates, anterior and posterior cervical lymphadenopathy, prominent constitutional symptoms
Cytomegalovirus (CMV)	Infectious mononucleosis	Fever, mild or no pharyngitis, anterior and posterior cervical lymphadenopathy, prominent constitutional symptoms

Human immunodeficiency virus (HIV)	Primary HIV infection	Mononucleosis-like syndrome with fever, weight loss, diffuse adenopathy, rash, splenomegaly, lymphopenia
Herpes simplex virus types 1 and 2	Pharyngitis	Exudative or nonexudative tonsillopharyngitis in sexually active adolescents, ulcerative lip lesion in 10 to 40 percent of cases
Influenza A and B viruses	Influenza	Fever, cough, pharyngitis, headache, myalgia, seasonal epidemics
Enteroviruses (Coxsackie A)	Herpangina and hand-foot-and-mouth disease	Vesicles in posterior pharynx may be accompanied by lesions on hands and feet
Adenovirus	Pharyngoconjunctival fever and acute respiratory disease	Conjunctivitis, tonsillopharyngeal erythema and exudates
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)*	Pharyngitis COVID-19 MIS-C	Clinical features are variable; may include fever, persistent cough, shortness of breath, gastrointestinal symptoms, cutaneous findings, epidemiologic link to individuals with SARS-CoV-2 infection

Viruses that cause nasopharyngitis (generally do not require specific therapy or infection control measures)

Rhinovirus	Common cold	Nasal symptoms predominate
Coronaviruses, including SARS-CoV-2*	Common cold	Nasal symptoms predominate
Respiratory syncytial virus	Bronchiolitis, common cold	Nasal symptoms predominate, seasonal epidemics
Parainfluenza	Common cold, croup	Stridor, hoarseness, prominent nasal symptoms

This table is meant for use with UpToDate content on acute pharyngitis in children. Refer to UpToDate content for additional information (eg, indications for testing, management).

COVID-19: coronavirus disease 2019; MIS-C: multisystem inflammatory syndrome in children.

* SARS-CoV-2 requires strict infection control measures in health care settings and the community.

Classification of parenteral and oral cephalosporins

First generation	Second generation	Second generation/ Cephamycins*	Third generation	Fourth generation	Adv. gene a comb ag
Parenteral cephalosporins					
<ul style="list-style-type: none"> ■ Cefazolin (Ancef, Kefzol) ■ Cephalothin (Keflin, Seffin)¶ ■ Cephapirin (Cefadyl)¶ ■ Cephadrine (Velosef)¶ 	<ul style="list-style-type: none"> ■ Cefamandole (Mandol)¶ ■ Cefonicid (Monocid)¶ ■ Cefuroxime (Kefurox, Zinacef) 	<ul style="list-style-type: none"> ■ Cefmetazole (Zefazone)¶ ■ Cefotetan (Cefotan) ■ Cefoxitin (Mefoxin) 	<ul style="list-style-type: none"> ■ Cefoperazone (Cefobid)¶ ■ Cefotaxime (Claforan) ■ Ceftazidime (Fortaz)Δ ■ Ceftizoxime (Cefizox)¶ ■ Ceftriaxone (Rocephin) ■ Moxalactam¶ 	<ul style="list-style-type: none"> ■ Cefepime (Maxipime) ■ Cefpirome (Cefrom)¶ 	<ul style="list-style-type: none"> ■ Ceftazidime (Teflafid) ■ Cefclidine (Fetrozole) ■ Ceftazidime (Zeftazidime) ■ Ceftazidime (Zerbactam) ■ Ceftazidime (Avibactam/Zaviceftab) ■ Cefotaxime (Cefotazone)
Oral cephalosporins					
<ul style="list-style-type: none"> ■ Cefadroxil (Duricef, Ultracef) ■ Cephalexin (Keflex, Biocef, Keftab) ■ Cephadrine (Velosef)¶ 	<ul style="list-style-type: none"> ■ Cefaclor (Ceclor) ■ Cefprozil (Cefzil) ■ Cefuroxime-axetil (Ceftin) ■ Loracarbef (Lorabid)¶ 		<ul style="list-style-type: none"> ■ Cefdinir (Omnicef) ■ Cefditoren (Spectracef)¶ ■ Cefixime (Suprax) ■ Cefpodoxime-proxetil (Vantin) ■ Ceftibuten (Cedax)¶ 		

* Cephamycins have a chemical structure that is distinct from that of cephalosporins but functionally similar, and they are often classified as cephalosporins.

¶ Not marketed in the United States.

Δ Unlike most other third generation cephalosporins, ceftazidime has expected activity against *Pseudomonas* species; however, it has relatively poor activity against gram-positive organisms.

Original table modified for this publication. Craig WA, Andes DR. Cephalosporins. In: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Bennett JE, Dolin R, Blaser MJ (Eds), 8th ed, Elsevier, Philadelphia 2015. Table used with the permission of Elsevier Inc. All rights reserved.

Graphic 115428 Version 4.0

Secondary prophylaxis for rheumatic fever - Duration of therapy

Category	Duration after last attack
Rheumatic fever with carditis and residual heart disease (persistent valvular disease*)	10 years or until 40 years of age (whichever is longer) Sometimes lifelong prophylaxis (refer to UpToDate topics on treatment and prevention of acute rheumatic fever and management and prevention of rheumatic heart disease)
Rheumatic fever with carditis but no residual heart disease (no valvular disease*)	10 years or until 21 years of age (whichever is longer)
Rheumatic fever without carditis	5 years or until 21 years of age (whichever is longer)

* Clinical or echocardiographic evidence.

Modified with permission from: Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of Rheumatic Fever and Diagnosis and Treatment of Acute Streptococcal Pharyngitis: A Scientific Statement From the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research. Circulation 2009; 119(11):1541-51. Copyright © 2009 Lippincott Williams & Wilkins.

Graphic 55223 Version 11.0

Choice of antibiotic agent for treatment and prophylaxis of acute rheumatic fever

Scenario	Antibiotic choice(s)
Preferred treatment in endemic areas where IM penicillin is available at low cost	<ul style="list-style-type: none"> ▪ IM penicillin G benzathine given every 28 days
Alternative treatment in nonendemic areas where IM penicillin is unavailable or prohibitively expensive	<ul style="list-style-type: none"> ▪ Oral penicillin V
Confirmed penicillin allergy*	<ul style="list-style-type: none"> ▪ Preferred – Oral azithromycin ▪ Alternative – Oral sulfadiazine
Severe symptomatic RHD¶	<ul style="list-style-type: none"> ▪ Preferred – Oral penicillin V ▪ Alternatives – Oral azithromycin or oral sulfadiazine
Bleeding problems following IM injection that cannot be addressed	<ul style="list-style-type: none"> ▪ Preferred – Oral penicillin V ▪ Alternatives – Oral azithromycin or oral sulfadiazine
Other barriers to using the preferred treatment that cannot be resolvedΔ	<ul style="list-style-type: none"> ▪ Oral penicillin V
Patients at low risk of recurrence◊	<ul style="list-style-type: none"> ▪ Oral penicillin V
Breakthrough infection while on prophylaxis	<ul style="list-style-type: none"> ▪ For treatment of acute infection – Oral clindamycin§ ▪ For ongoing prophylaxis – IM penicillin G benzathine given every 21 days

This table summarizes our suggested approach to selecting an antibiotic agent for treatment and prophylaxis of ARF. Patients who have had ARF who subsequently develop GAS infections are at high risk for a recurrent ARF attack, which increases the risk of developing more severe RHD. GAS infection need not be symptomatic to trigger a recurrent attack of ARF. Thus, the most effective method to limit progression of RHD is prevention of recurrent GAS infections. IM penicillin G benzathine is the preferred agent for treatment and prophylaxis of ARF in most cases. However, in select circumstances, an alternative agent may be appropriate, as summarized above. For additional details, refer to UpToDate topics on ARF and RHD.

ARF: acute rheumatic fever; EF: ejection fraction; GAS: Group A *Streptococcus*; IM: intramuscular; NYHA: New York Heart Association; RHD: rheumatic heart disease.

* Penicillin allergy should be verified by history and confirmed with testing by an allergy specialist if available before choosing an alternative to penicillin G benzathine.

¶ This includes patients with severe symptomatic valvular disease, NYHA class III or IV heart failure symptoms, and/or ventricular dysfunction (ie, EF <50%). Oral therapy is preferred for these patients because they can experience vasovagal reactions with IM injections, and this may increase the risk of sudden death.

Δ Additional barriers include patient concerns (eg, extreme needle phobia) that persist despite appropriate counseling and reassurance.

◊ Patients at low risk of recurrence include those who have reached young adulthood and have remained free of ARF attacks for several years.

§ Rates of resistance to clindamycin are high and can be higher than rates of resistance to macrolides. Therefore, when beta-lactams and macrolides cannot be used, knowledge of local resistance rates should guide antibiotic selection or culture with susceptibility testing should be obtained.

Graphic 138985 Version 2.0

