

Pharmacotherapy 2

Upper Respiratory Tract Infections

Oct 2022– Jan 2023

Dr Enaam M. Al Momany

Faculty of Pharmaceutical Sciences

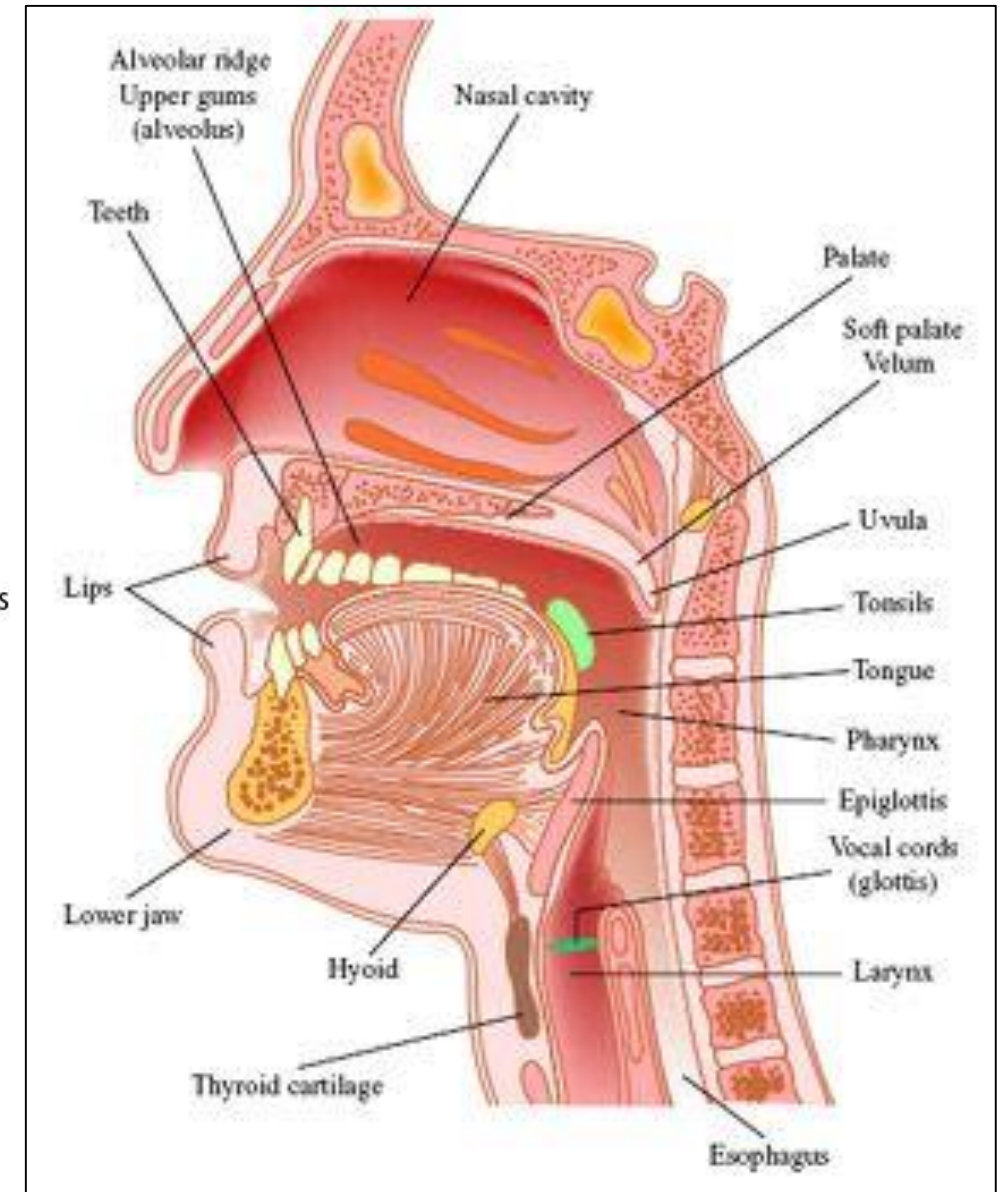
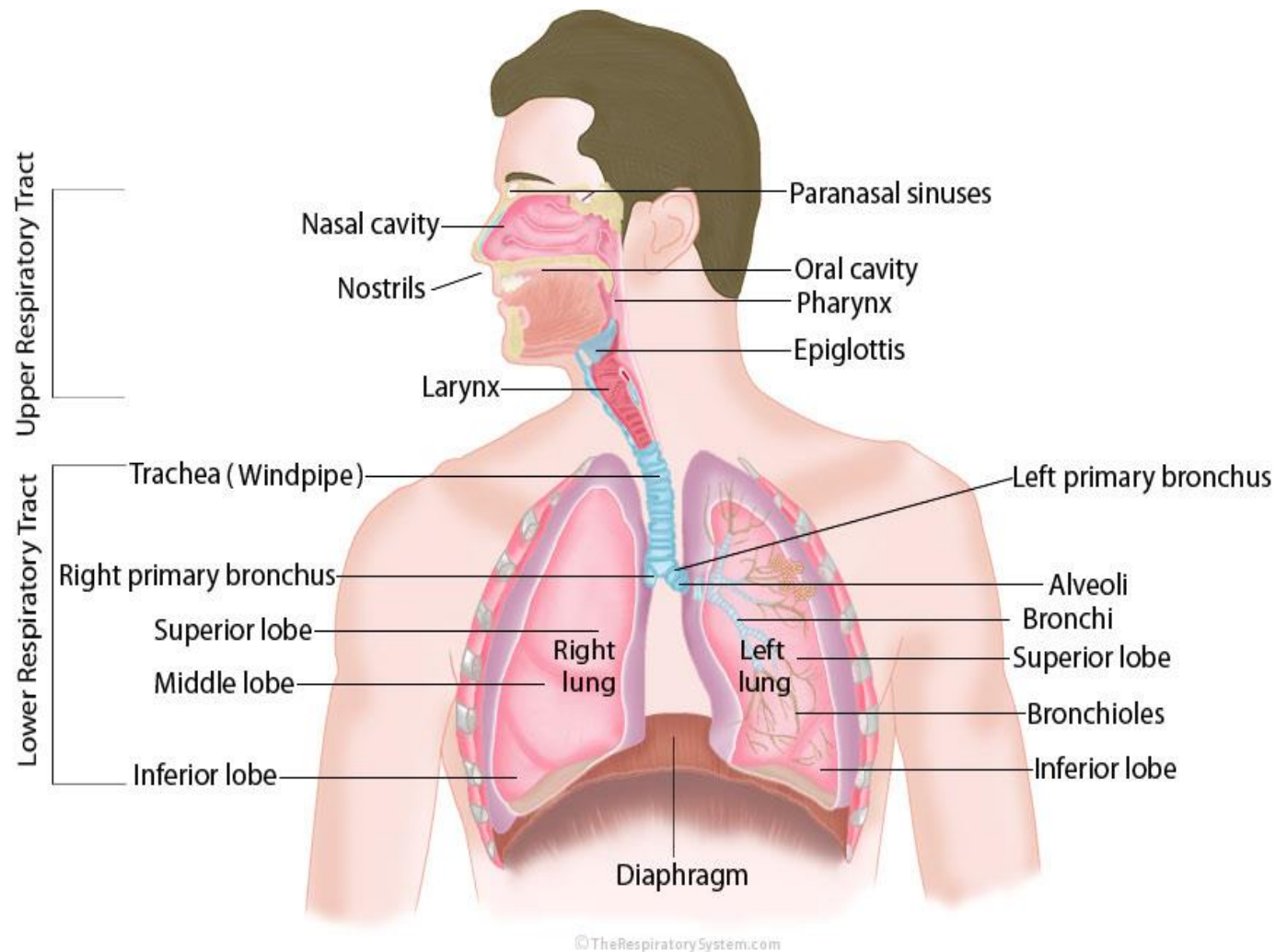
Department of Clinical Pharmacy and Pharmacy Practice



Topic Outline

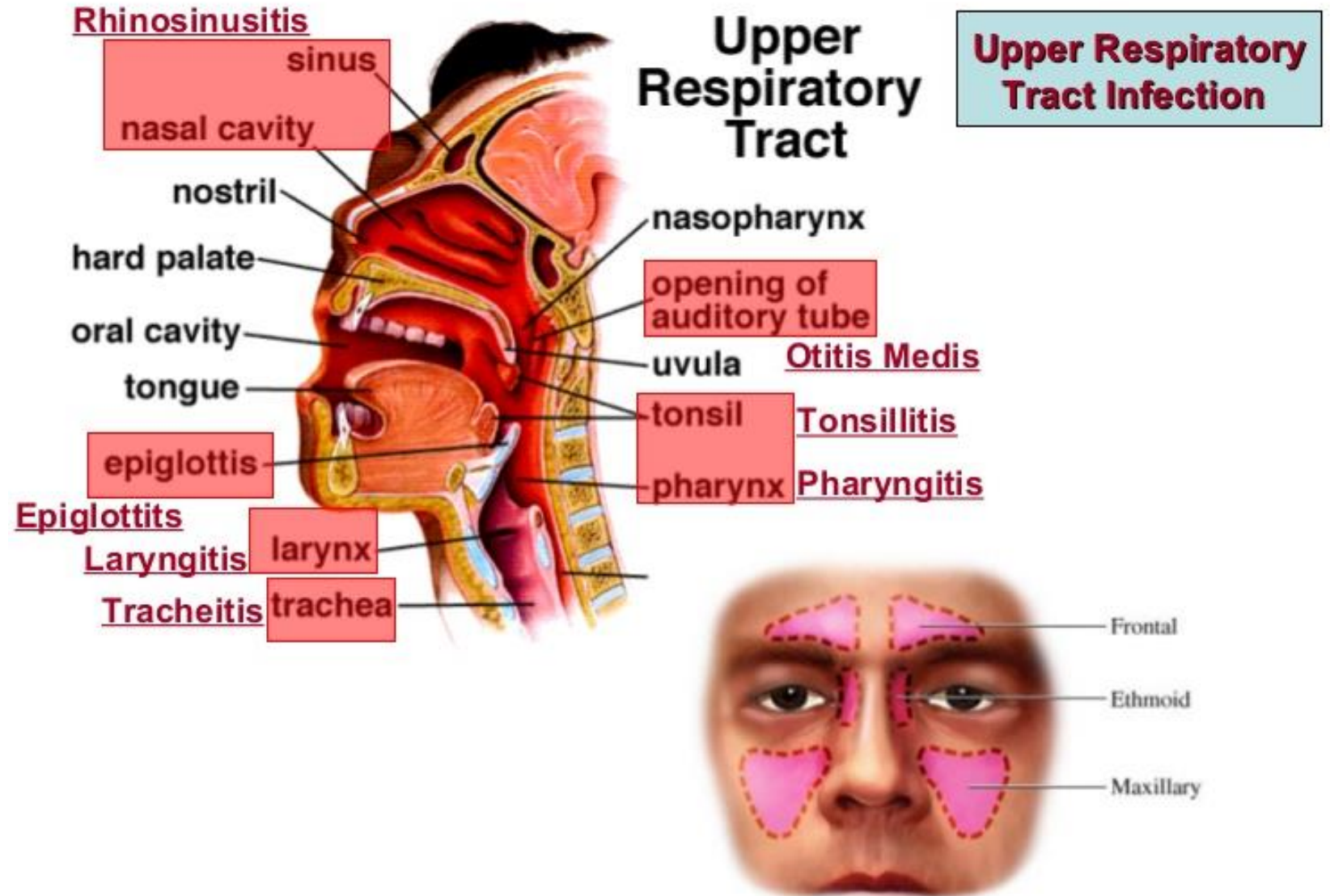
- Pharyngitis (general principles, diagnosis, treatment)
- Rhinosinusitis (general principles, diagnosis, treatment)
- Otitis Media (general principles, diagnosis, treatment)
- Influenza Virus Infection (general principles, diagnosis, treatment, complications)

Upper and Lower Respiratory Tract



Upper Respiratory Tract Infections (URIs)

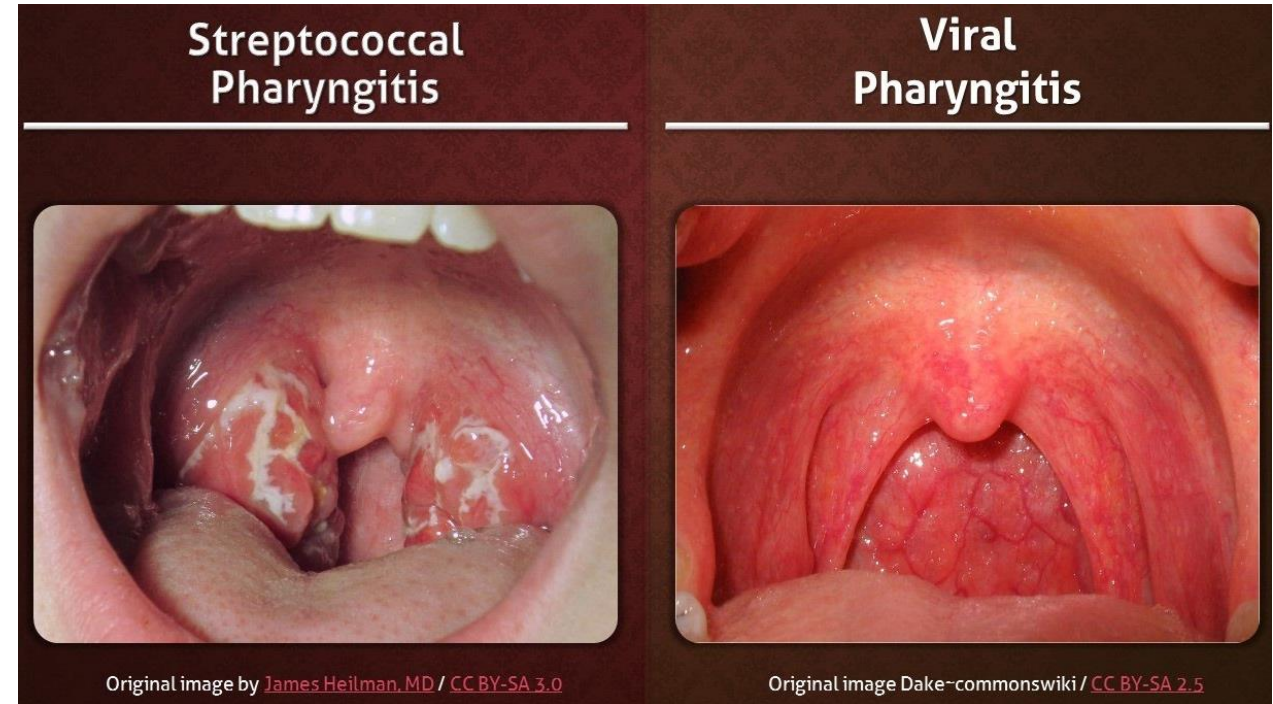
- ✓ Pharyngitis, rhinosinusitis, and otitis media are the 3 most common URIs.
- ✓ Because URIs are so common, antibiotics used to treat them serve as catalysts for the emergence and spread of antibiotic resistance, thereby making wise antibiotic use critically important.



Pharyngitis

General Principles:

- ✓ An acute infection of oropharynx or nasopharynx.
- ✓ Viruses [rhinovirus (20%), coronavirus (5%), adenovirus (5%), HSV (4%), influenza virus (2%), parainfluenza virus (2%), Epstein–Barr virus (1%)] are the most common cause of pharyngitis.
- ✓ GABHS (group A β -hemolytic Streptococcus) pharyngitis: primary bacterial cause, 5– 15% of cases in adults, 15-30% in children
- ✓ **Children** 5 to 15 years of age are **most susceptible** (At increased risk: parents of school-age children and those who work with children)



Diagnosis:

✓ Clinical Presentation:

- Fever, cervical lymphadenopathy, tonsillar exudates & throat pain → most common clinical manifestations
- Distinguishing bacterial from viral pharyngitis on clinical grounds alone is difficult → microbiologic testing is recommended for symptomatic patients unless they have symptoms suggestive of viral etiology or are younger than 3 years of age.

CLINICAL PRESENTATION

Group A Streptococcal Pharyngitis

General

- A sore throat of sudden onset that is mostly self-limited
- Fever and constitutional symptoms resolving in about 3 to 5 days
- Clinical signs and symptoms are similar for viral causes and nonstreptococcal bacterial causes

Signs and Symptoms of GABHS Pharyngitis

- Sore throat
- Pain on swallowing
- Fever
- Headache, nausea, vomiting, and abdominal pain (especially in children)

- Erythema/inflammation of the tonsils and pharynx with or without patchy exudates
- Enlarged, tender lymph nodes
- Red swollen uvula, petechiae on the soft palate, and a scarlatiniform rash

Signs Suggestive of Viral Origin for Pharyngitis

- Conjunctivitis
- Coryza
- Cough

Laboratory Tests

- Throat swab and culture
- Rapid antigen-detection test (RADT)

Data from Reference 19.

Reference 19: 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;55:1279–1282.

✓ Diagnostic Testing

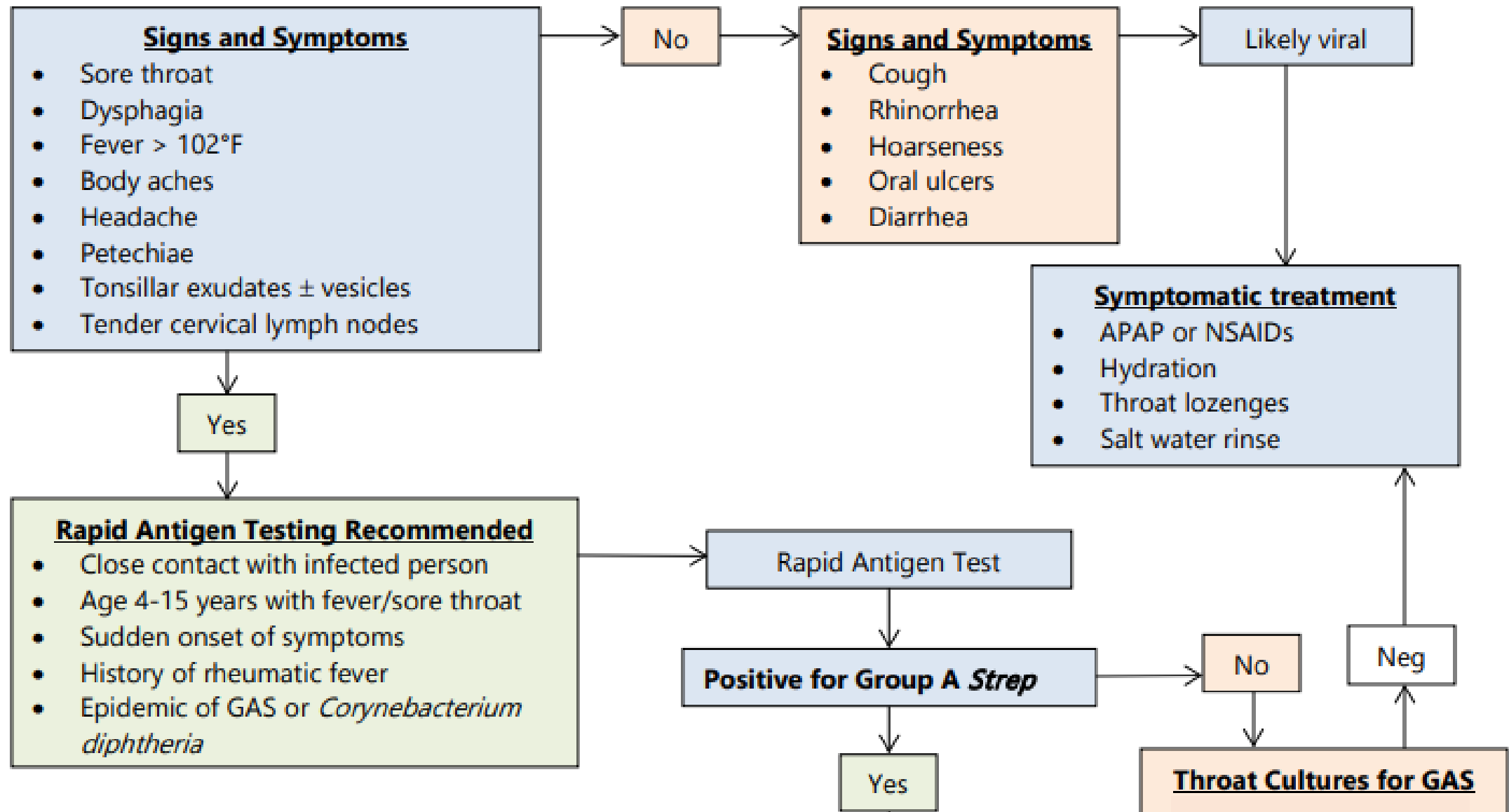
- Reserved for:
 - symptomatic patients with exposure to a case of strep. pharyngitis
 - those with signs of significant infection (fever, tonsillar exudates, & cervical adenopathy)
 - whose symptoms persist despite symptomatic therapy
 - patients with a history of rheumatic fever
- Rapid antigen detection testing (RADT) is useful for diagnosing GABHS (> 90% sensitivity and specificity). A negative test does not reliably exclude GAS, making throat culture necessary if clinical suspicion is high.
- Delaying therapy while awaiting culture results does not affect the risk of complications (but symptomatic benefit is postponed, contagion remains), and patients must be educated as to the value of waiting, given the low false-negative rate of RADT.

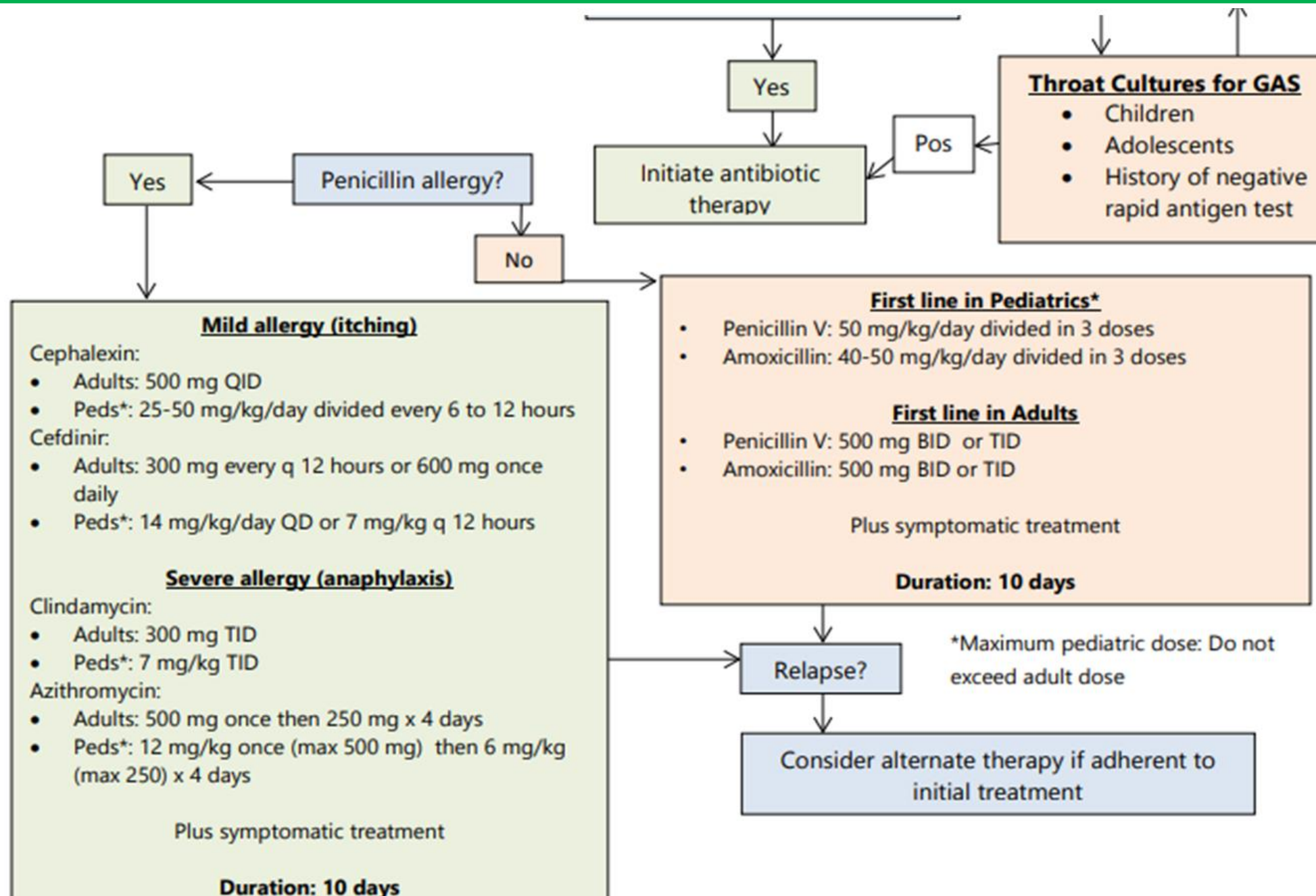
Treatment:

- ✓ Most cases of pharyngitis are self-limited and do not require antimicrobial therapy.
- ✓ Empirical therapy is not recommended; however, if used while results are pending, it is important to discontinue empirical antibiotics once laboratory results come back as negative.
- ✓ Treatment for GABHS is indicated with a positive culture or RADT, or if the diagnosis is strongly suspected, pending culture results.
- ✓ Treatment options include penicillin V 500 mg PO every 12h for 10 days, clindamycin 300 mg PO every 8h for 10 days, azithromycin 500 mg PO on day 1 followed by 250 mg every day on days 2– 5, or benzathine penicillin G 1.2 million units IM as a one-time dose.
- ✓ Effective antibiotic therapy reduces the infectious period to about 24 hours.

- ✓ The duration of therapy for GABHS pharyngitis is 10 days, except for benzathine penicillin and azithromycin, to maximize bacterial eradication.
- ✓ Supportive care should be offered to all patients with acute pharyngitis (antipyretic medications, analgesics, and nonprescription lozenges and sprays containing menthol and topical anesthetics for temporary relief of pain).
- ✓ GABHS carriers (33% of household contacts of acute case) do not need antimicrobial therapy due to low risk of spreading GABHS pharyngitis or developing complications.

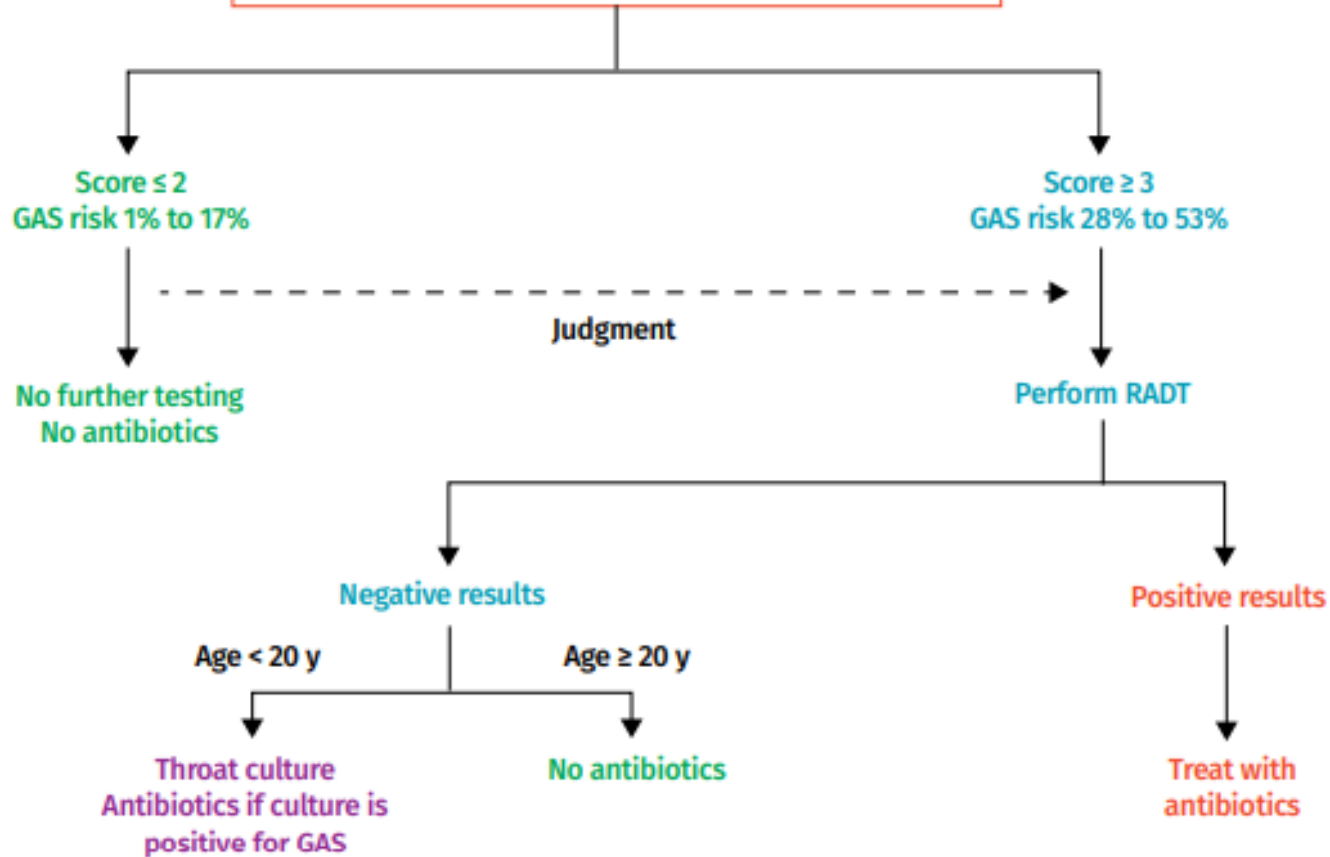
Acute Pharyngitis for Adult and Pediatric Patients Algorithm





(2018) Outpatient Acute Pharyngitis for Adults and Pediatric Patients Algorithm. Retrieved from 2020 Virginia Department of Health website.
<https://www.vdh.virginia.gov/haiar/vhag/>

MODIFIED CENTOR CRITERIA: "STREP"		POINTS
Sans cough (absence)		1
Tender, swollen anterior cervical lymph nodes		1
Right age		
• 5-14 y*		1
• 15-44 y		0
• ≥ 45 y		-1
Exudates (tonsillar)		1
Pyrexia (temperature > 38°C)		1



Modified Centor scoring system:

Used to calculate the risk of streptococcal pharyngitis and to decide whether RADT and antimicrobial therapy should be initiated in patients presenting with sore throat. Clinicians should consider performing RADT for those with scores of 2 if they are pediatric patients, if they are at risk of complications (immunocompromised or frail), or if they appear clinically unwell.

Ref.: Sykes EA, Wu V, Beyea MM, Simpson MTW, Beyea JA. Pharyngitis: Approach to diagnosis and treatment. *Can Fam Physician*. 2020 Apr;66(4):251-257. PMID: 32273409; PMCID: PMC7145142.

TABLE 126-4 Antibiotics and Doses for Group A β -Hemolytic Streptococcal Pharyngitis

Antibiotic	Brand Name	Dose	Duration	Rating
Preferred Antibiotics				
Penicillin V	Pen-V ^a	Children: 250 mg twice daily or three times daily orally. Adult: 250 mg four times daily or 500 mg twice daily orally	10 days	IB
Penicillin G benzathine	Bicillin L-A ^a	<27 kg: 0.6 million units; 27 kg or greater: 1.2 million units intramuscularly	One dose	IB
Amoxicillin ^a	Amoxil ^a	50 mg/kg once daily (maximum 1,000 mg); 25 mg/kg (maximum 500 mg) twice daily	10 days	IB
Penicillin Allergy				
Cephalexin	Keflex ^a	20 mg/kg/dose orally twice daily (maximum 500 mg/dose)	10 days	IB
Cefadroxil	Duricef ^a	30 mg/kg orally once daily (maximum 1 g)	10 days	IB
Clindamycin	Cleocin ^a	7 mg/kg/dose orally thrice daily (maximum 300 mg/dose)	10 days	IlaB
Azithromycin ^b	Zithromax ^a	12 mg/kg orally once daily (maximum 500 mg) for one day, then 6 mg/kg orally once daily (maximum 250 mg) for four days	5 days	IlaB
Clarithromycin ^b	Biaxin ^a	15 mg/kg orally per day divided in two doses (maximum 250 mg twice daily)	10 days	IlaB

These guidelines provide a systematic weighting of the strength of the recommendation (Class I, conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective; Class II, conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment; Class IIa, weight of evidence/opinion is in favor of usefulness/efficacy; Class IIb, usefulness/efficacy is less well established by evidence/opinion; Class III, conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful) and quality of evidence (A, data derived from multiple randomized clinical trials or meta-analyses; B, data derived from a single-randomized trial or nonrandomized studies; C, only consensus opinion of experts, case studies, or standard of care).

^aStandard formulation, not extended release.

^bResistance of group A β -hemolytic *Streptococcus* (GABHS) to these agents may vary and local susceptibilities should be considered with these agents.

Data from Reference 19.

TABLE 126-5

Antibiotics and Doses for Eradication of Group A β -Hemolytic Streptococcal Pharyngitis in Chronic Carriers

Antibiotic	Brand Name	Dose
Clindamycin	Cleocin®	20-30 mg/kg/day orally in three divided doses (maximum 300 mg/dose)
Amoxicillin-clavulanate	Augmentin®	40 mg/kg/day orally in three divided doses (maximum 2,000 mg/day of amoxicillin)
Penicillin V and rifampin	Pen-V®, Rifadin®	Penicillin V: 50 mg/kg/day orally in four doses for 10 days (maximum 2,000 mg/day); <i>and</i> rifampin: 20 mg/kg/day orally in one dose for the last 4 days of treatment (maximum 600 mg/day)
Penicillin G benzathine and rifampin	Bicillin L-A®, Rifadin®	Penicillin G benzathine: <27 kg—0.6 million units, 27 kg or greater—1.2 million units intramuscularly; <i>and</i> rifampin: 20 mg/kg/day orally in two doses during last 4 days of treatment with penicillin (maximum 600 mg/day)

Data from Reference 19.

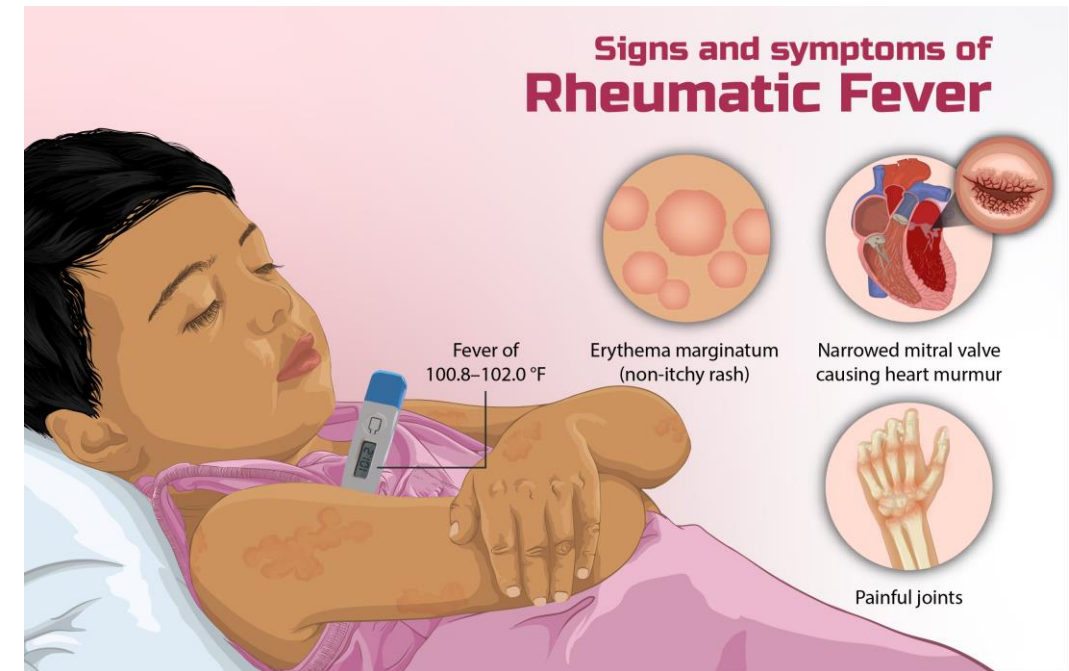
- ✓ Several alternative antibiotics are preferred over penicillin or amoxicillin with GABHS carriers and recurrent pharyngitis.
- ✓ Amoxicillin-clavulanate, clindamycin, penicillin/rifampin combination, and benzathine penicillin G/rifampin combination may be considered for **recurrent episodes** of pharyngitis to maximize bacterial eradication in **potential carriers** and to counter **copathogens** that produce β -lactamases.

✓ Secondary prophylaxis of recurrence of rheumatic fever and/or rheumatic heart disease: patients should receive continuous antibiotic prophylaxis initiated as soon as the patient is diagnosed and the initial infection has been treated

- Intramuscular benzathine penicillin G every 4 weeks
- oral penicillin V or sulfadiazine
- allergic to penicillin and sulfadiazine → a macrolide or azalide

- How rheumatic fever affects the heart:

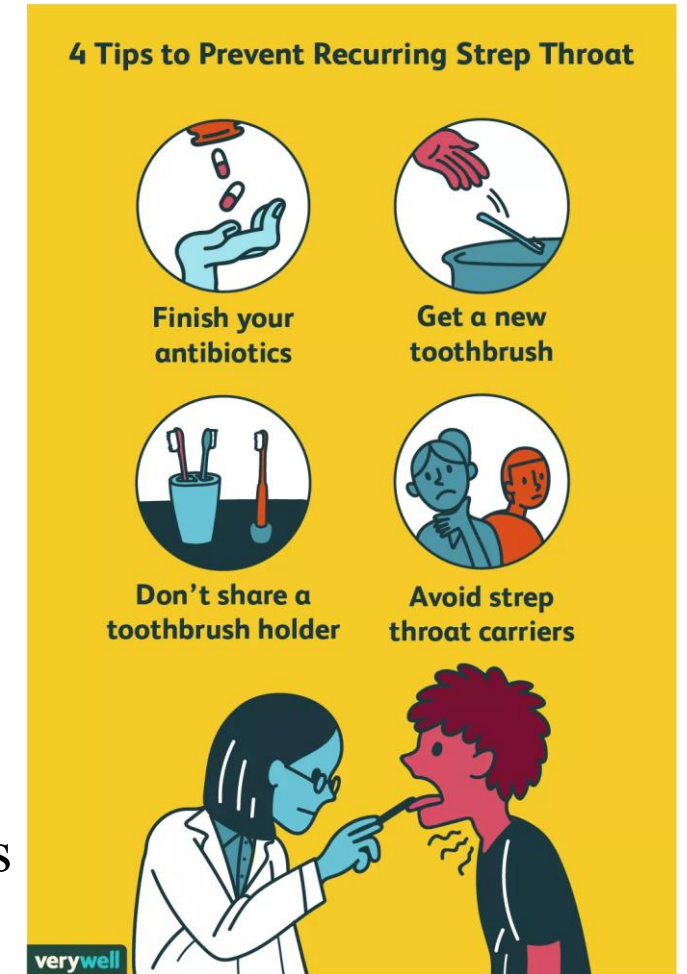
<https://youtu.be/ZB97F-z36Mk>



✓ Patient Education Tips

- Prevention:

- Wash your hands frequently, especially after blowing your nose or after caring for a child with a sore throat.
- If someone in your home has pharyngitis, keep his or her eating utensils and drinking glasses separate from those of other family members. Wash these objects thoroughly in hot, soapy water.
- If a toddler with pharyngitis has been chewing or sucking on toys, wash these objects thoroughly in water and disinfectant soap, then rinse well.
- Promptly dispose of any dirty tissues from runny noses and sneezes, and then wash your hands.
- Do not allow a child who has been diagnosed with strep throat to return to school or day care until he or she has been taking antibiotics for at least 24 hours and symptoms have improved.



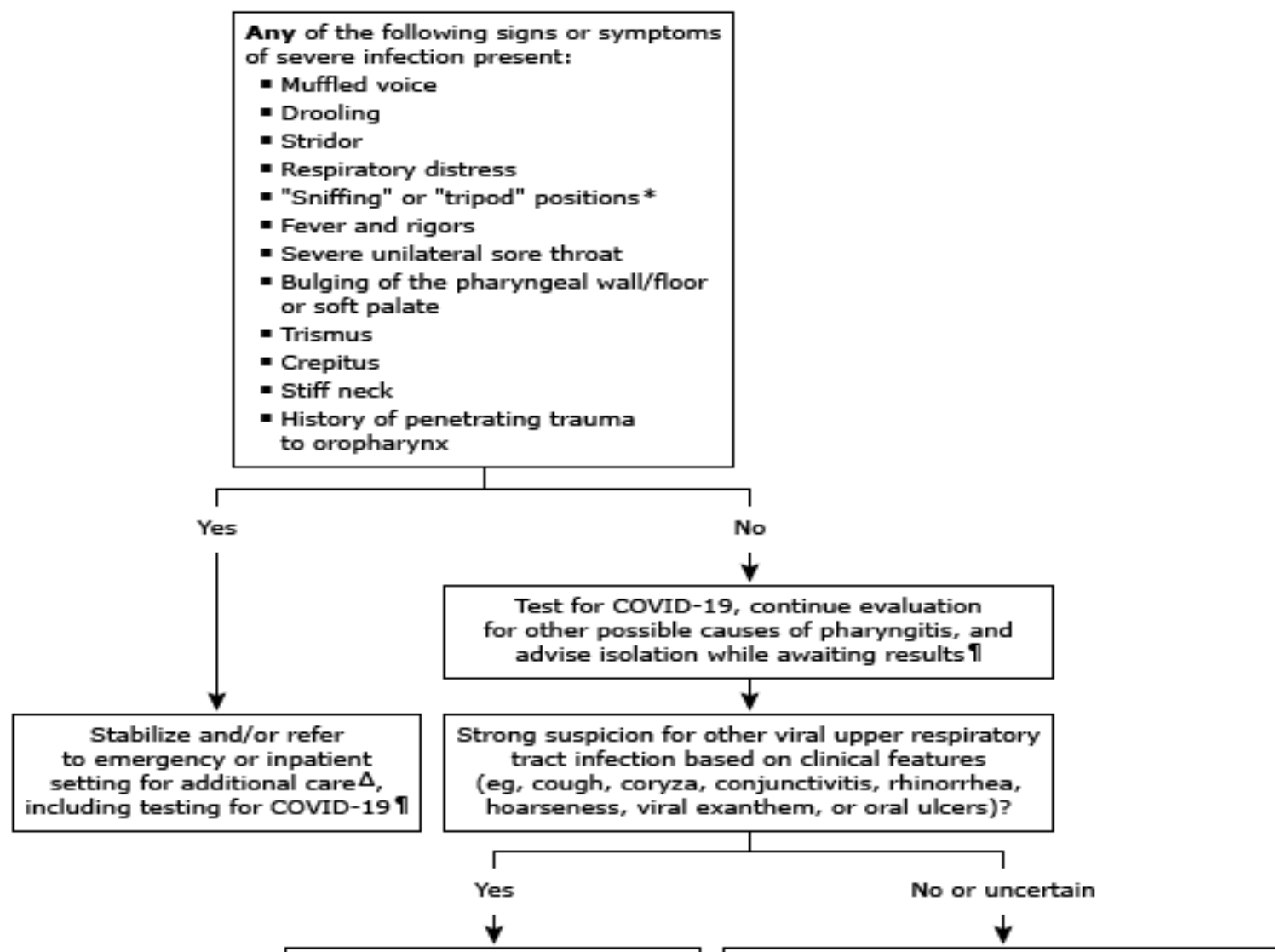
✓ Patient Education Tips

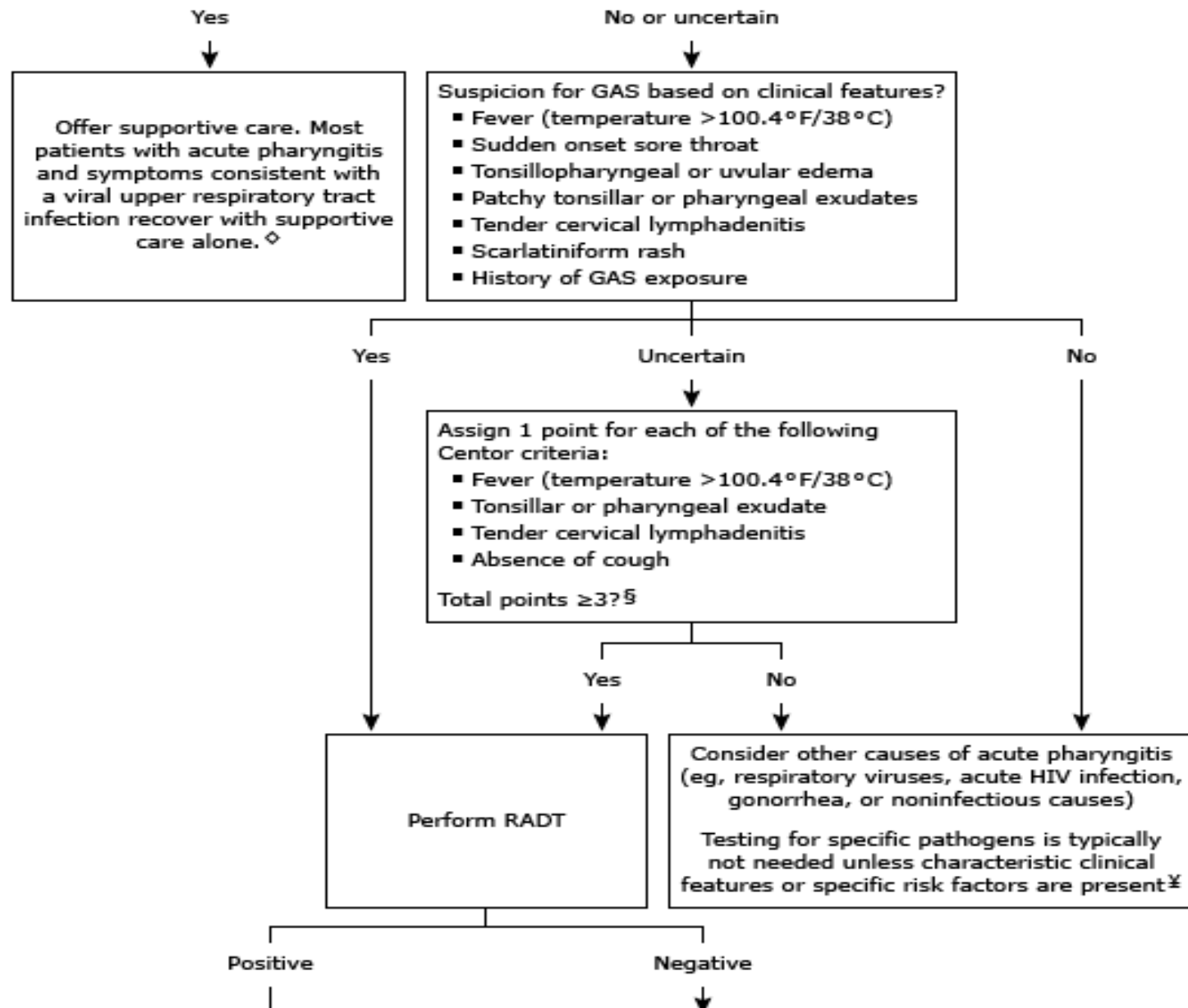
- Treatment:

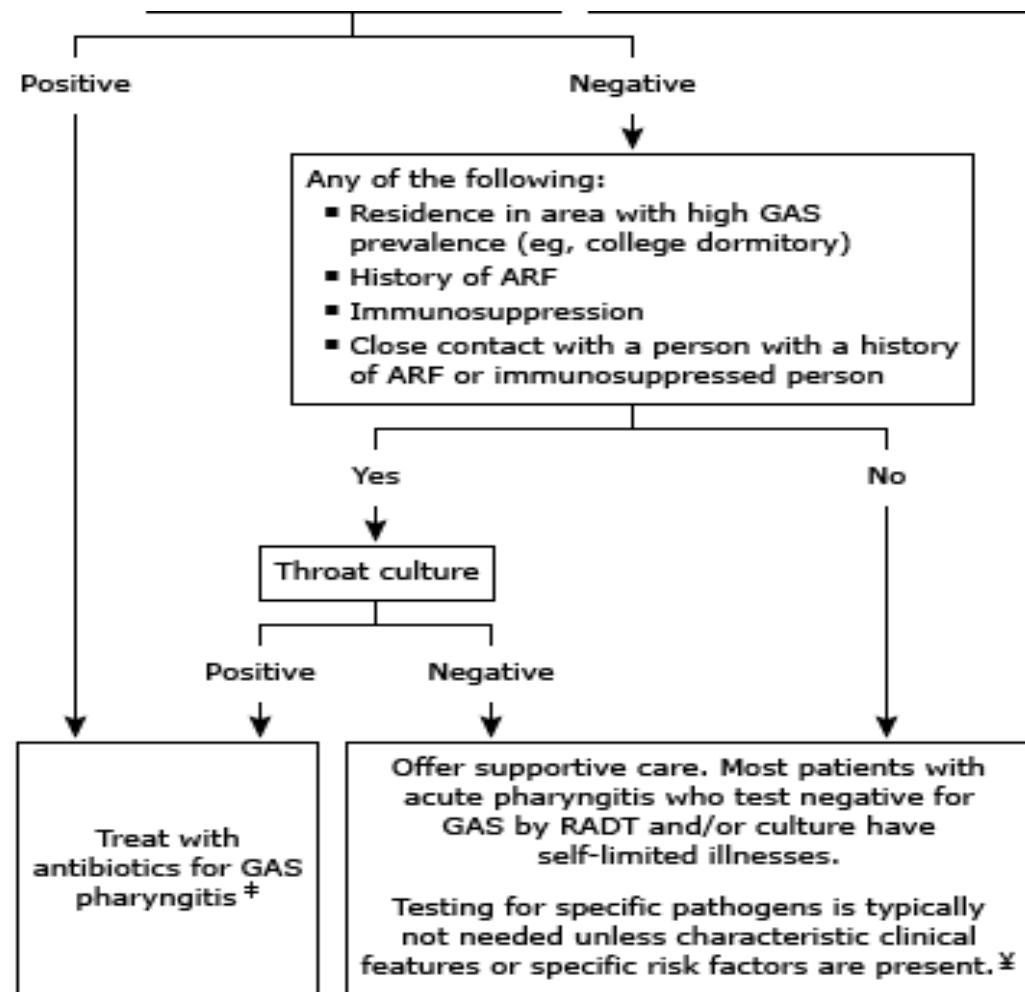
- If you have simple viral pharyngitis, your symptoms should go away gradually over a period of about one week.
- Because antibiotics do not work against viruses, viral pharyngitis usually is treated by treating the symptoms to make you feel more comfortable until your body's immune system defeats the infection. These measures include:
 - Getting plenty of rest (either in or out of bed)
 - Taking ibuprofen, acetaminophen or aspirin (in adults only) to relieve throat pain
 - Drinking plenty of water to prevent dehydration
 - Gargling with warm salty water to ease throat pain
 - Drinking warm liquids (tea or broth) to soothe the throat
 - Using a cool mist vaporizer to relieve throat dryness
 - Using nonprescription throat lozenges or anesthetic throat sprays
- These measures will help to ease your discomfort with any type of throat infection.

- If you have strep throat, you also will take antibiotics to prevent complications.
- Your symptoms should subside within two to three days after you begin taking antibiotics.
- It's important to take all the medication, even after you start to feel better.

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.

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

* 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.

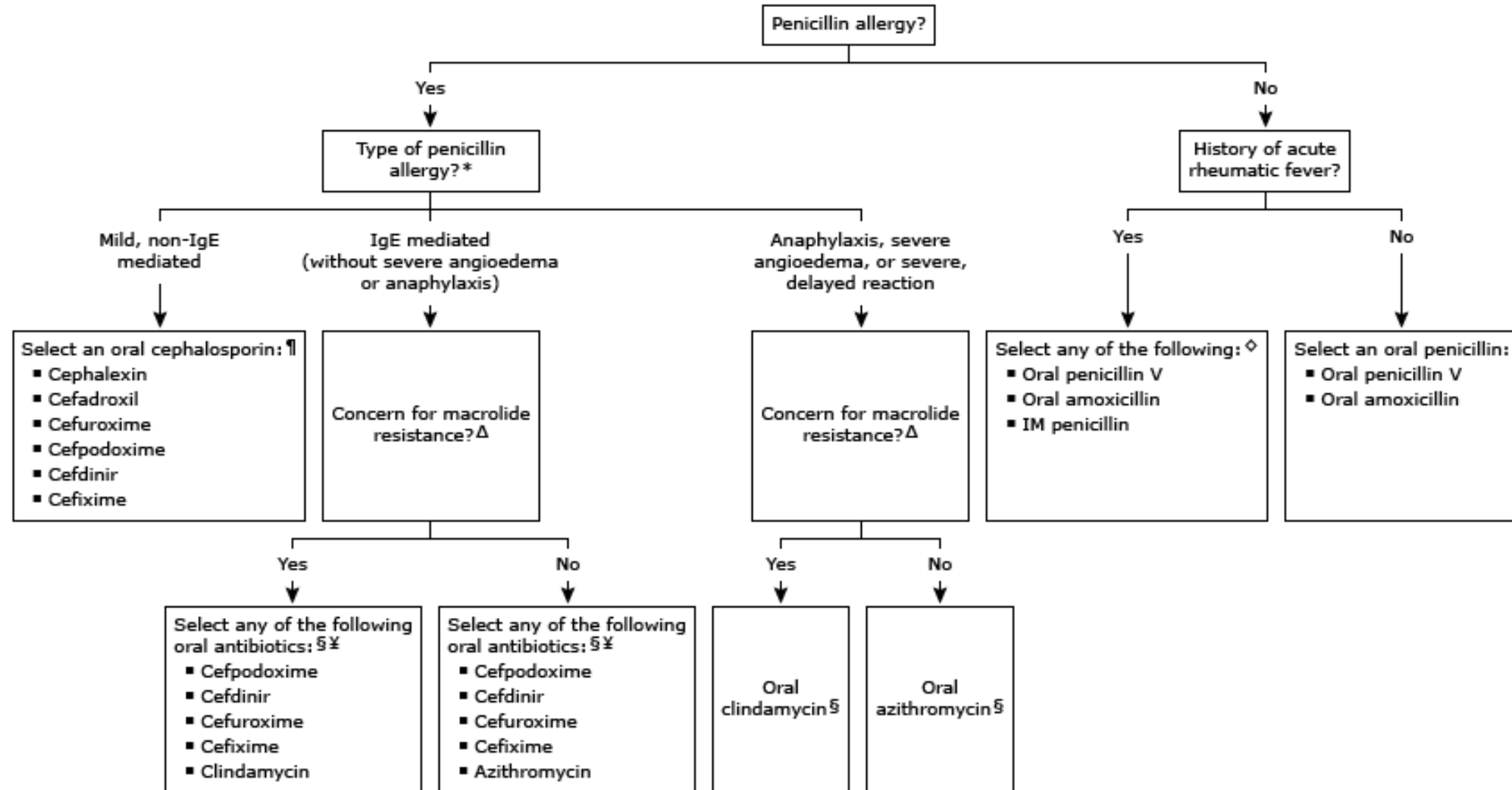
§ Some practitioners test patients with Centor scores ≥ 2 .

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

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

UpToDate®

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.

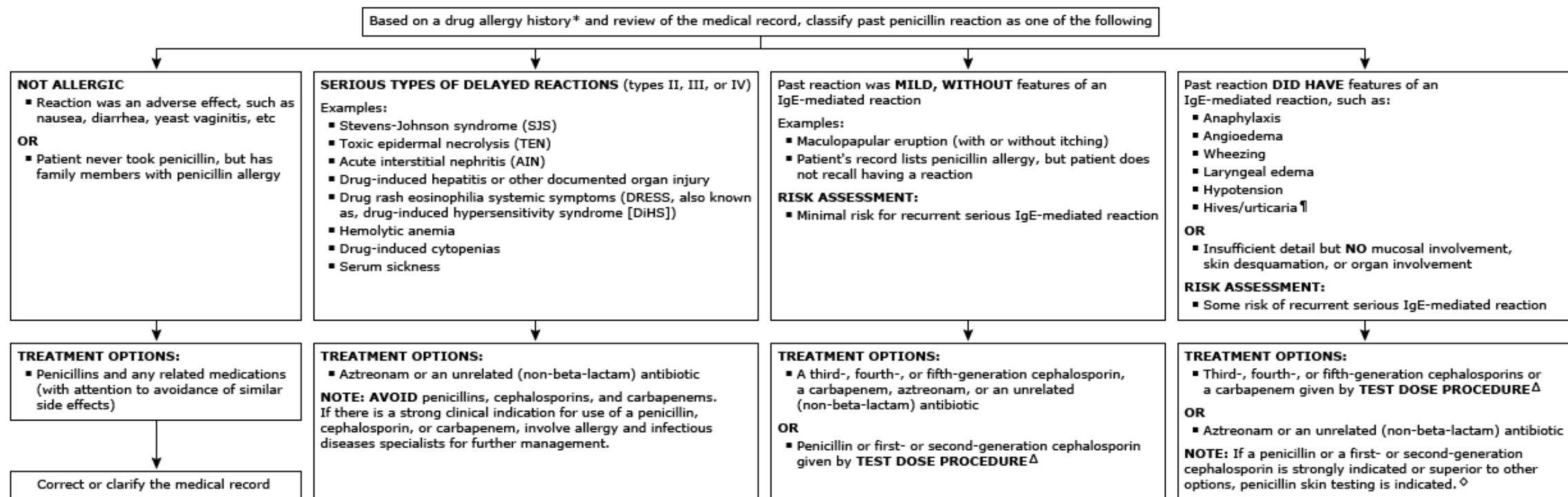
Δ Macrolide resistance varies considerably by region, with higher rates observed in Asia and Europe when compared with the United States. Knowledge of local resistance patterns should guide antibiotic selection.

◇ 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.

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?

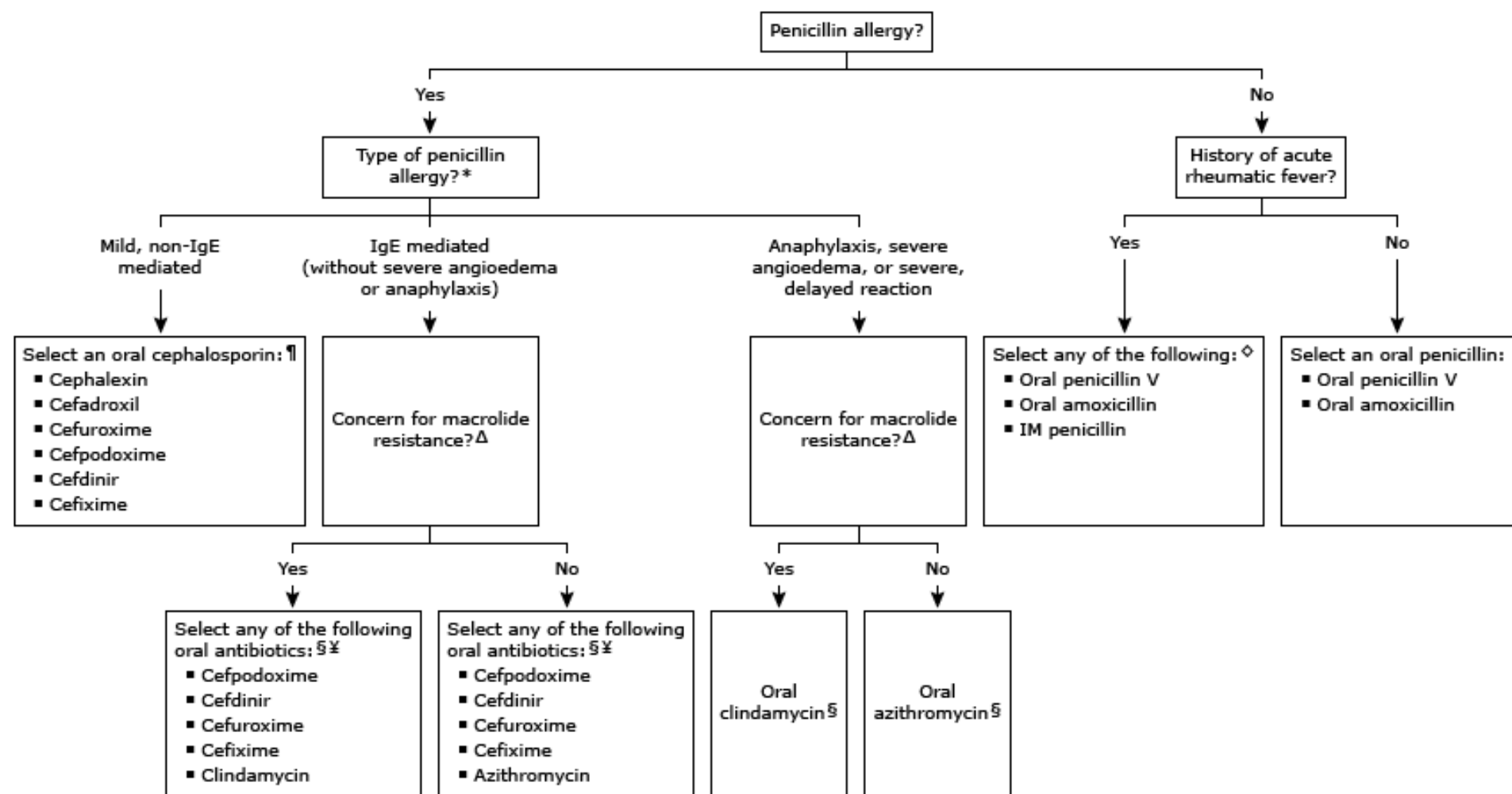
¶ Isolated mild hives, without other symptoms of an IgE-mediated reaction, can often occur in the setting of an infection. Patients with this history, especially if it occurred in childhood or >10 years ago, may also be considered to be at minimal risk for a recurrent serious reaction.

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.

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.

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.

UpToDate®

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	IM penicillin G benzathine given every 28 days
Alternative treatment in nonendemic areas where IM penicillin is unavailable or prohibitively expensive	Oral penicillin V
Confirmed penicillin allergy*	- Preferred – Oral azithromycin - Alternative – Oral sulfadiazine
Severe symptomatic RHD [¶]	- Preferred – Oral penicillin V - Alternatives – Oral azithromycin or oral sulfadiazine
Bleeding problems following IM injection that cannot be addressed	- Preferred – Oral penicillin V - Alternatives – Oral azithromycin or oral sulfadiazine
Other barriers to using the preferred treatment that cannot be resolved ^Δ	Oral penicillin V
Patients at low risk of recurrence [◇]	Oral penicillin V
Breakthrough infection while on prophylaxis	- 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.

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

* 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.

Type of drug reactions

Type of reaction	Common features
Non-allergic reaction	▪ Adverse effects (eg, diarrhea, vomiting, yeast vaginitis) ▪ Family history of penicillin allergy but no personal history
Mild non-IgE-mediated reaction	▪ Maculopapular rash (with or without itching) ▪ Medical record lists penicillin allergy but patient unaware of reaction
IgE-mediated reaction	▪ Anaphylaxis ▪ Angioedema ▪ Wheezing ▪ Laryngeal edema ▪ Hypotension ▪ Hives/urticaria
Serious delayed reactions	▪ 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.

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

Antibiotic class	Drug	Dosing in adults*	Advantages	Disadvantages
Penicillins (preferred)	Penicillin V	500 mg orally two to three times daily for 10 days	- Narrow spectrum - No documented resistance - Low cost	Three-times-daily dosing; however, twice-daily regimen appears to be as effective as thrice daily^[1]
	Amoxicillin*	500 mg orally twice daily for 10 days 1000 mg (immediate release) once daily for 10 days	Also available as once-daily extended-release tablet[¶]	
	Penicillin G benzathine* (Bicillin L-A)	1.2 million units IM as a single dose	- Can be given as a single dose - Ensured adherence - Only drug studied for prevention of acute rheumatic fever	- Variable availability - High cost - Injection site pain
Cephalosporins (potential alternatives for mild reactions to penicillin ^Δ)	Cephalexin* (first generation)	500 mg orally twice daily for 10 days	- High efficacy rate - Narrower spectrum than later-generation cephalosporins	- Broader spectrum than penicillin - Greater potential to induce antibiotic resistance
	Cefadroxil* (first generation)	1 g orally daily for 10 days	- Once daily - High efficacy rate - Narrower spectrum than later-generation cephalosporins	- Broader spectrum than penicillin - Greater potential to 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
	Cefixime (third generation)	400 mg orally once daily for 10 days	- Once daily - High efficacy rate	- Broader spectrum than penicillin - Greater potential to induce antibiotic resistance

Macrolides (alternatives for patients with anaphylaxis or other IgE-mediated reactions or severe delayed reactions to penicillin ^Δ)	Azithromycin	12 mg/kg/day (maximum 500 mg/dose) 5 days[◇]	Once daily	- Growing rates of resistance - Rarely associated with prolonged QT interval and TdP
	Clarithromycin*	250 mg orally twice daily for 10 days		- Growing rates of resistance - Greater gastrointestinal side effects than azithromycin - Causes CYP3A4 drug interactions - Rarely associated with prolonged QT interval and TdP
Lincosamides (alternative when macrolide resistance is a concern and penicillins and cephalosporins cannot be used)	Clindamycin	300 mg orally three times daily for 10 days		- 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.

¶ 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. An extended-release preparation of amoxicillin is also available. The dose in adults is 775 mg orally once daily for 10 days.

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.

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.
-

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	▪ 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	▪ Narrow spectrum ▪ No documented resistance ▪ Low cost	▪ Thrice-daily dosing; however, twice-daily regimen appears to be as effective as thrice daily^[1]
	Amoxicillin*	▪ 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	▪ Taste of suspension more palatable than penicillin, often preferred for children ▪ Available as once-daily extended-release tablet[¶]	
	Penicillin G benzathine (Bicillin L-A)	▪ If ≤ 27 kg: Penicillin G benzathine (Bicillin L-A) 600,000 units IM as a single dose^Δ ▪ If > 27 kg: Penicillin G benzathine (Bicillin L-A) 1.2 million units IM as a single dose	▪ Can be given as a single dose ▪ Ensured adherence ▪ Only drug studied for prevention of acute rheumatic fever	▪ Variable availability ▪ High cost ▪ Injection site pain
Cephalosporins (potential alternatives for mild reactions to penicillin [◇])	Cephalexin* (first generation)	▪ 40 mg/kg/day divided twice daily for 10 days (maximum 500 mg/dose)	▪ High efficacy rate ▪ Narrower spectrum than later-generation cephalosporins	▪ Broader spectrum than penicillin ▪ Greater potential to induce antibiotic resistance
	Cefuroxime* (second generation)	▪ 10 mg/kg/dose orally twice daily for 10 days (maximum 250 mg/dose)	▪ 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)	▪ 5 mg/kg/dose orally every 12 hours (maximum 100 mg/dose) 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)	▪ 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)	▪ High efficacy rate ▪ FDA approved for 5-day course when dosed twice daily	▪ 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 delayed reactions to penicillin [◇])	Azithromycin	12 mg/kg/day (maximum 500 mg/dose) for 5 days	Can be given as a 5-day course due to extended half-life	- Growing rates of resistance - Rarely associated with prolonged QT interval and Tdp
	Clarithromycin*	7.5 mg/kg/dose (maximum 250 mg per dose) orally twice daily for 10 days		- Growing rates of resistance - Greater gastrointestinal side effects than azithromycin - Causes CYP3A4 drug interactions - Rarely associated with prolonged QT interval and TdP
Lincosamides (alternative when macrolide resistance is a concern and penicillins and cephalosporins cannot be used)	Clindamycin	7 mg/kg/dose (maximum 300 mg per dose) orally 3 times daily for 10 days		- 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.

¶ Once-daily extended-release amoxicillin is recommended by the 2009 American Heart Association guidelines but is not available in all regions. It is noninferior to immediate release amoxicillin administered in multiple daily doses. The dose in adolescents 12 years and older is 775 mg orally once daily for 10 days.

Δ 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.

◇ 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.

