Pharmacotherapy 2

Upper Respiratory Tract Infections

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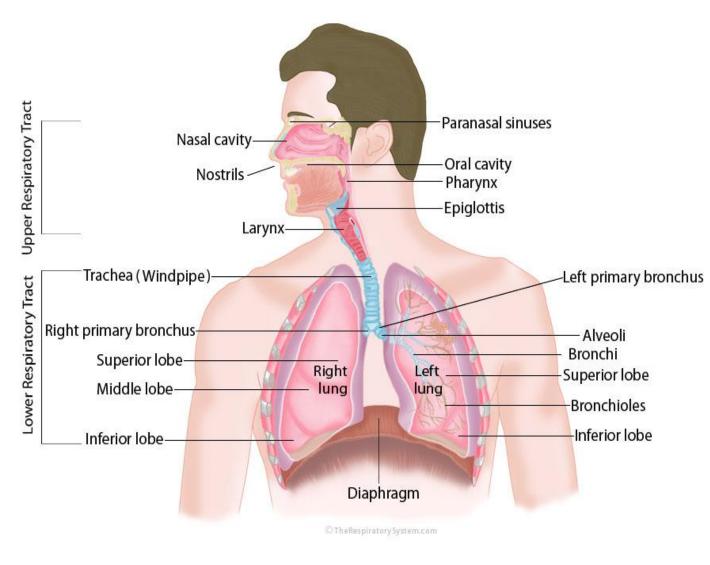
Topic Outline

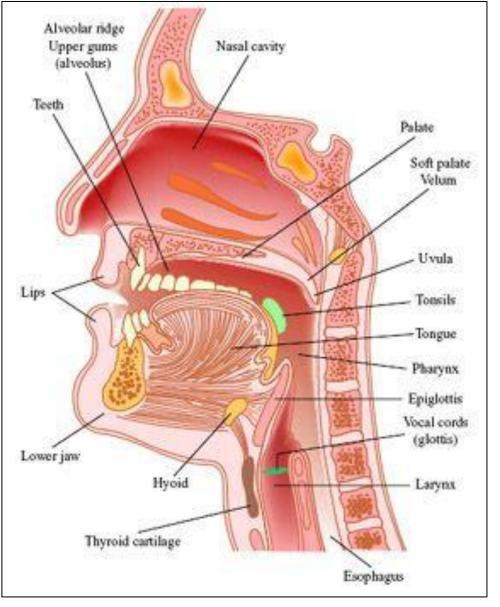
- Pharyngitis (general principles, diagnosis, treatment)
- Rhinosinusitis (general principles, diagnosis, treatment)
- Otitis Media (general principles, diagnosis, treatment)
- Influenza Virus Infection (general principles, diagnosis, treatment, complications)

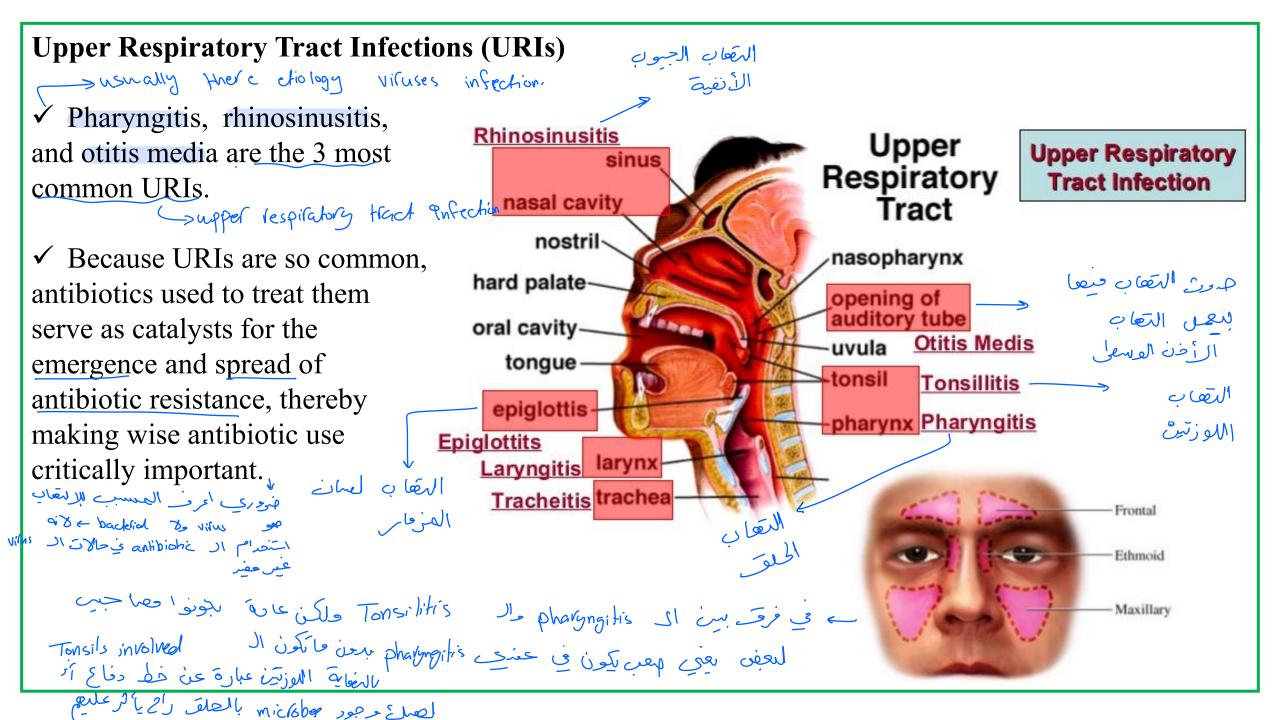


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Upper and Lower Respiratory Tract







Pharyngitis → Tonsilitis = 50le aein is tonsilities — Tonsilities 11 manigment 11 > 1. tonsils enlarged 2. pass on the tonsils 1. Rechess in oral General Principles: Pharyngs. 3. redness 2. dylation (inflammation) ✓ An acute infection of oropharynx or nasopharynx. 4. mucousy (secteations) 3. Conjestion Viral Streptococcal ✓ Viruses [rhinovirus (20%), coronavirus Pharyngitis **Pharyngitis** (5%), adenovirus (5%), HSV (4%), influenza virus (2%), parainfluenza virus (2%), Epstein-Barr virus (1%)] are the most pharyngilis common cause of pharyngitis. \checkmark GABHS (group A β-hemolytic Streptococcus) pharyngitis: primary bacterial cause, 5–15% of cases in adults, 15-30% in children need Original image by James Heilman, MD / CC BY-SA 3.0 Original image Dake~commonswiki / CC BY-SA 2.5 antibiohic therapy GI symptoms: diarria ✓ Children 5 to 15 years of age are most susceptible (At increased risk: parents of school-age children and those who work with children) لے یکون اگریف عندہ تھوے من: > sore Hovoat 1. que p is Ilye Mildren younger than 3 years old. cavity display! و gas pharyngihi العدد عن طريق الـ العدام عن طريق الله العدام عن الع 2. ألم قي الملق واللوزين

Diagnosis:

- Clinical Presentation:
 - Fever, cervical lymphadenopathy, tonsillar exudates & throat pain > most common clinical manifestations المهمول عنف الم hode ألموجودة في الرصه

• 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.

microbiological test

not recommended.

gas
Backfiel
infection.

* Viral Infection of phayings -> self limited * GABHS Infection of pharyngs -> need antibiotic specific type of bacteria. * another bacterial infection -> self limited.

CLINICAL PRESENTATION: Group A B-hemolytic 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 GAS Pharyngitis

- Sore throat, usually with sudden onset
- Pain on swallowing
- Fever
- Headache, nausea, vomiting, and abdominal pain (especially in children)
- Erythema/inflammation of the tonsils and pharynx
- Patchy exudates
- 7 Enlarged, tender anterior cervical lymph nodes
- Red swollen uvula
- Petechiae or purple spots on the soft palate
- Scarlatiniform rash (papular, blanching, and erythematous rash often affecting neck then spreads along the trunk and limbs).

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Signs Suggestive of Viral Origin for Pharyngitis

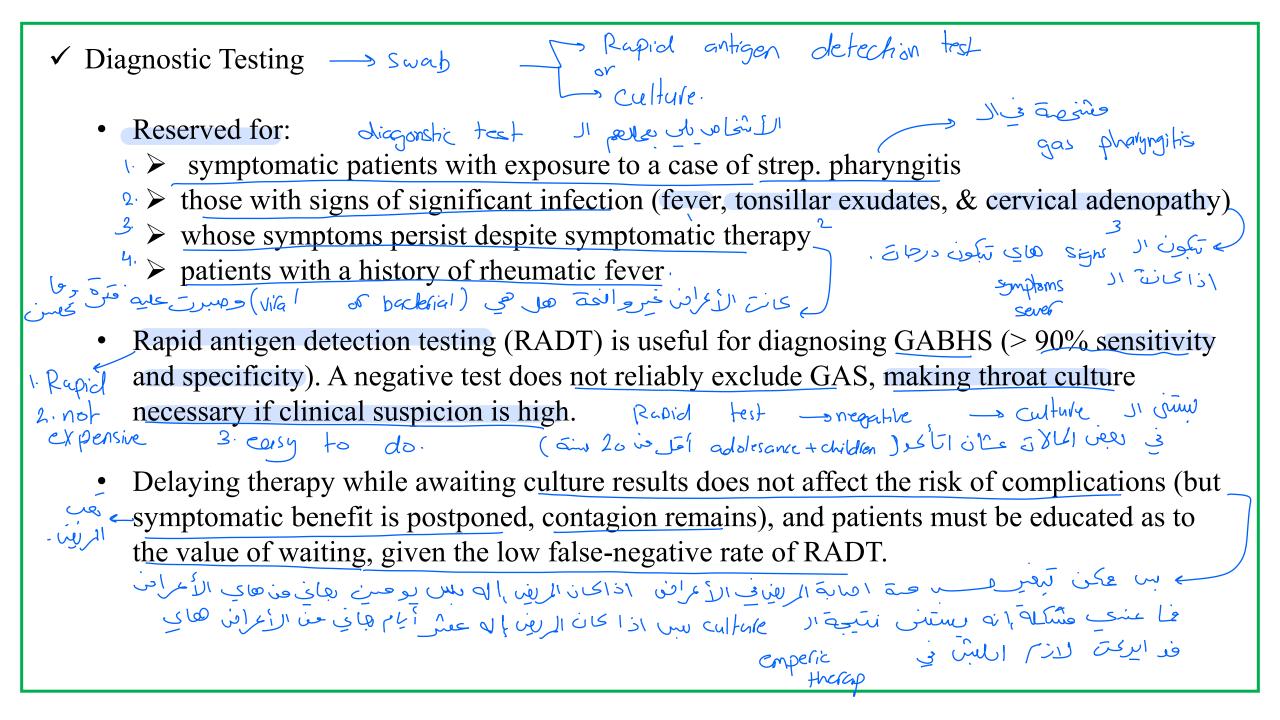
- · Conjunctivitis eye envolvment
- امراره که فی اکانف (آعراف اُنفیه) در ایس Coryza Coryza Coryza Coryza کیسلان ر عطیس)
- الحوف الغم حـ Anterior stomatitis
- 5 Viral exanthem -> fash. wide splead

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Laboratory Tests

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

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Complications of gos pharyngitis Non suppletive -> (joint) Kidney, heart, bkin)

Autrimmune responce Suppretive L spread the intection to 1. Acute rhamatic fever -> rhamatic Heart distance. another area and cause 2. problem in the joints.
2. problem in the problem in the kidney
2. med Joint College of Lablate gas phalyngitis II is men step complications))
antihistic ... another intection such as: stitis media, Rhinosinositis عامل محيح بيني عكن كانت الم الريق العادم عنى كافته الم الريق الم الريق الم الريق الم الريق الم الريق الم الريق الم المريق العادم عنى كافته الم المريق المراق المرا

antigen II (so antigen = gas phalogopitis) de sie is e autoimme l'espance must a le a le autoimme l'espance ontigen de le a per antigen (joint, blain, heart) must is a per antigen II de a per antigen II de a per antigen II comp ontibodies à sur Acut Meumatic fever sie per e self antigen II pleu une gas phalogopitis d'en sie le cour sie le comp antibodies à sur d'en sie le cour sie le comp antibodies à sur d'en sie le cour sie le comp a phalogopités disease.

Treatment: prevention Secondary Les and a supple tive complication Secondary Les and a supple tive complication Secondary Les and a supple tive complication Les a supple tive complicatio

- ✓ 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.

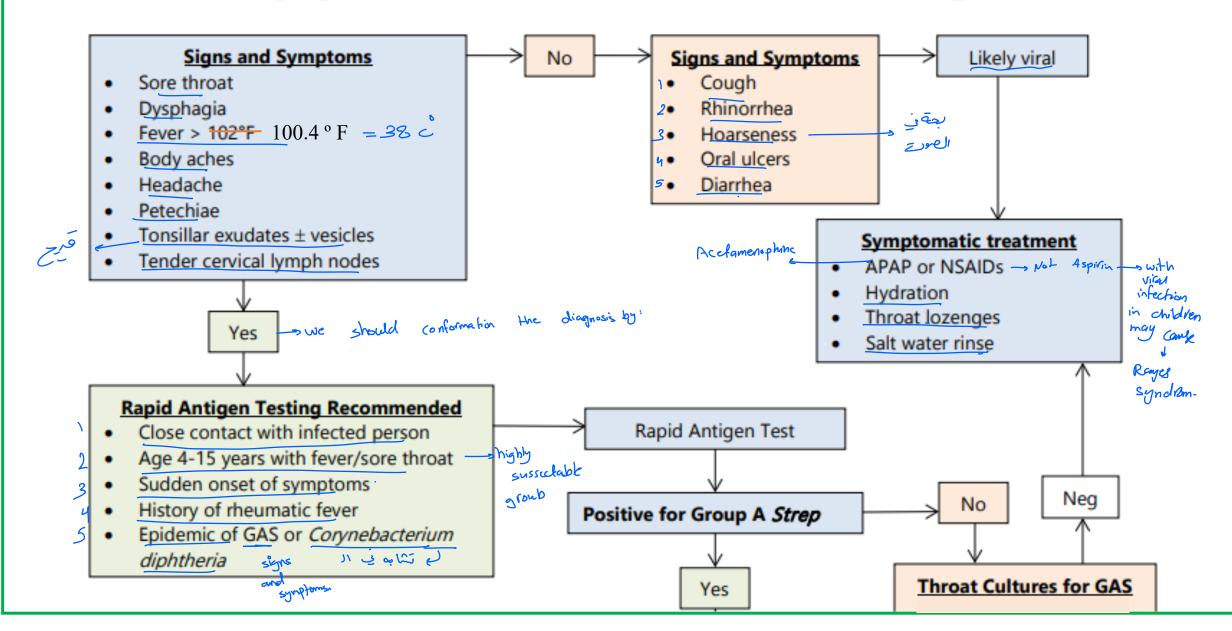
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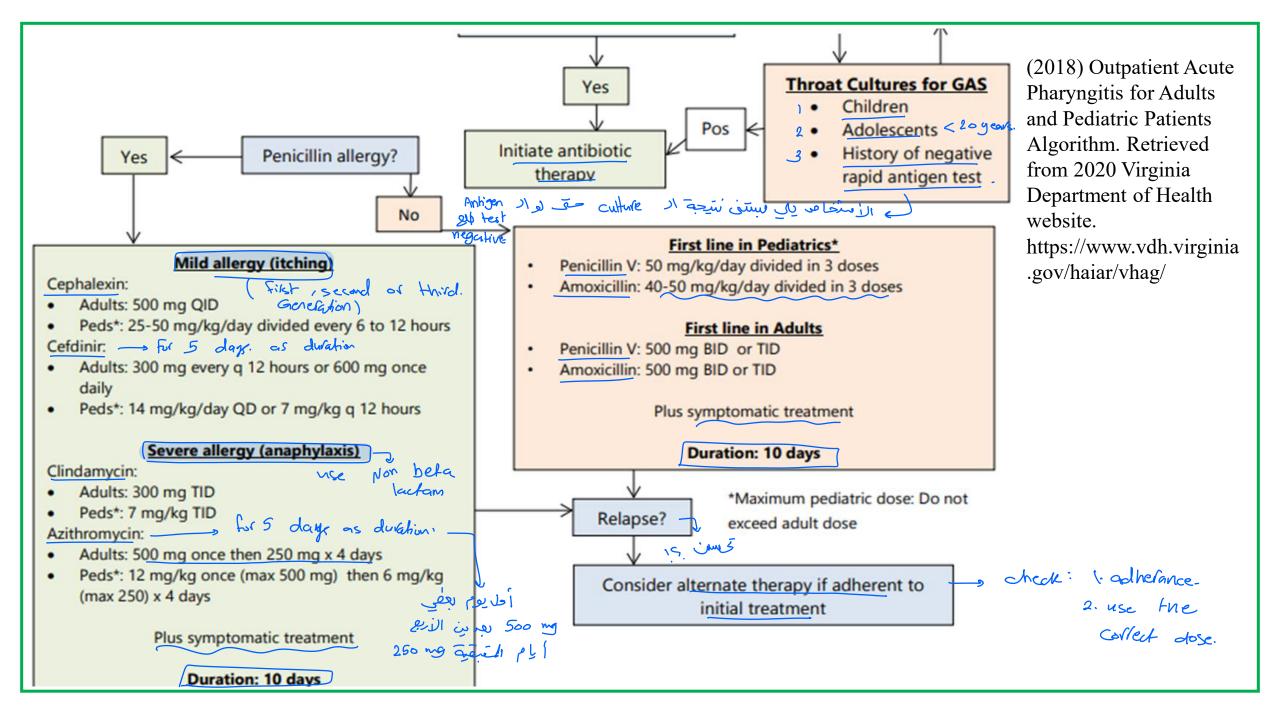
- ✓ Supportive care should be offered to all patients with acute pharyngitis (antipyretic medications,
- ² analgesics, and nonprescription lozenges and sprays containing menthol and topical anesthetics for temporary relief of pain).
- ✓ GABHS carriers (33% of household contacts of acute case) do not need antimicrobial therapy due to low risk of spreading GABHS pharyngitis or developing complications.

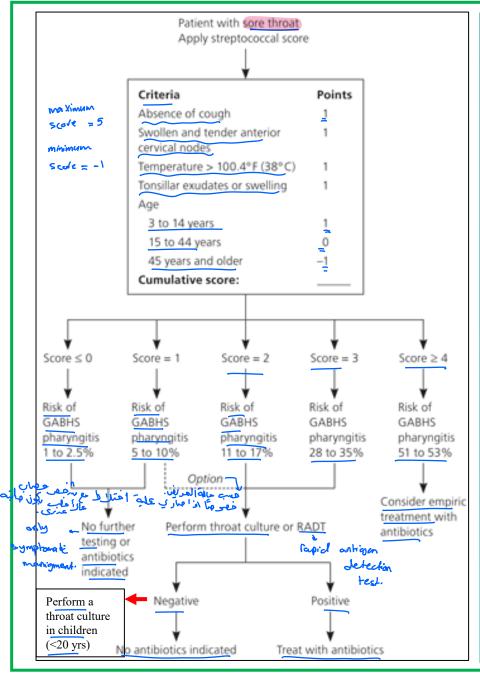
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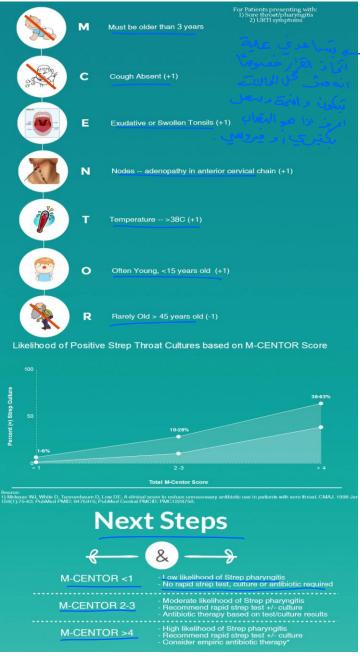
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Acute Pharyngitis for Adult and Pediatric Patients Algorithm









Modified Centor score and management options using clinical decision rule

Baised on clinical presentation t

Used to calculate the risk of streptococcal pharyngitis and to decide whether RADT and antimicrobial therapy should be initiated in online 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 are at risk of complications (immunocompromised or frail), or if they appear clinically unwell. Other factors should be considered (e.g., a score of 1, but recent family contact with documented streptococcal infection).

Yuchen (Richard) Tang, MD candidate 20218, McMaster University

Choby B. Diagnosis and Treatment of Streptococcal Pharyngitis – American Family Physician. American Academy of Family Physicians. 2009 http://www.aafp.org/afp/2009/0301/p383.html.

Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America.

http://cid.oxfordjournals.org/content/early/2012/09/06/cid.cis629.full_pdf+html

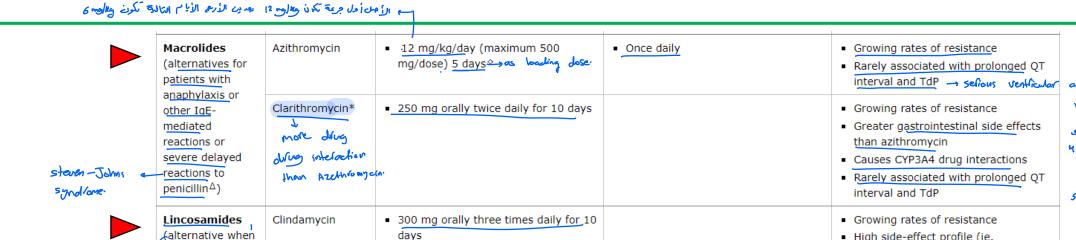
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Antibiotic class	Drug	Dosing in adults*	Advantages Coduce field of fesistance.	Disadvantages
Penicillins (preferred) drug d whatce	Penicillin V	500 mg orally two to three times daily for 10 days	Narrow spectrumNo documented resistanceLow cost	 Three-times-daily dosing; however, twice-daily regimen appears to be as effective as thrice daily^[1]
	A <u>moxicillin*</u>	 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 1	
	Penicillin G benzathine* (Bicillin L-A)	• 1.2 million units IM as a single dose no plablem in adhelance. advantag	 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	<u>Cephalexin*</u> (<u>first generation</u>)	• 500 mg orally twice daily for 10 days penecilin المرابعة المرا	High efficacy rate Narrower spectrum than later- generation cephalosporins .	Broader spectrum than penicillin Greater potential to induce antibiotic resistance,
penicillin [∆])	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 dailyHigh efficacy rate	 Broader spectrum than penicillin Greater potential to induce antibiotic resistance

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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 <u>3-d</u>ay course is approved and widely prescribed in Europe and other regions.

Reference:

macrolide

resistance is a concern and penicillins and cephalosporins cannot be used)

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.

· High side-effect profile (ie,

gastrointestinal)

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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 availabilityHigh costInjection 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	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
delayed reactions to penicillin ^(*)	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 \leq 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.

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- 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.
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 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, Sawuer MH (Eds), American Academy of Pediatrics 2015. p.694.

TABLE 126-5 Antibiotics and Doses for Eradication of Group A β-Hemolytic Streptococcal Pharyngitis in Chronic Carriers

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igitis in Chronic Carriers Reccurent	pharyngitis	intection

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i ilai yiigitis iii		i ilai yiigidis i	i Cilionic 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); and rifampin: 20 mg/kg/day orally in one dose for the last 4 days of treatment (maximum 600 mg/day)	
	P <u>enicillin</u> G <u>benzathine</u> <u>and rifamp</u> in	Bicillin L-A®, Rifadin®	Penicillin G benzathine: <27 kg—0.6 million units, 27 kg or greater—1.2 million units intramuscularly; and rifampin: 20 mg/kg/day orally in two doses during last 4 days of treatment with penicillin (maximum 600 mg/day)	

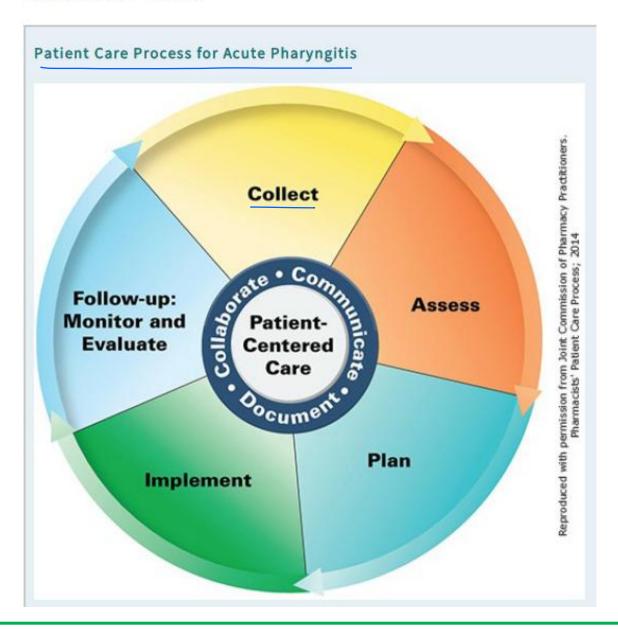
Several alternative antibiotics are preferred over penicillin or amoxicillin with GABHS carriers and recurrent pharyngitis.

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- 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.

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Patient Care Process



تحيع معلومات عن حالاً المرلين

Collect

Patient characteristics (eg, age, weight)

 Patient history (eg, past infections including rheumatic fever and rheumatic heart disease, current and past antibiotic/antiviral use noting previous failures, medication allergies)

• Determine whether the patient is a school-age child, parent/caregiver of a school-age child, or works with school-age children

Objective data:

Temperature

Signs and symptoms (see "Clinical Presentation")

Other diagnostic tests, when indicated (eg, RADT, throat culture, microbiologic testing)



Assess -> Viral or backerial infection.

Infection status, including presence of signs and symptoms

• Determine which symptoms may need additional therapy (eg, ongoing throat pain)

• Use information collected, patient factors (eg, patient age, symptom severity), and joint decision-making with parents/caregivers to determine whether antibiotics are needed

• If antibiotics are appropriate, determine proper choice of antibiotic, dose, duration, and dosage form

Plan* - a soesment Il como

- Select drug therapy regimen including specific antibiotic, dose, route, frequency, and duration; specify the continuation and discontinuation of existing therapies (see Tables 135-4 and 135-5)
- Monitor efficacy (eg, temperature, pain), safety (eg, medication-specific adverse effects), and time frame
- Educate patient and/or caregiver (eg, purpose of treatment, drug therapy) emphasizing adherence to treatment regimen
- Recommend self-monitoring of body temperature

*<u>Implement</u>

- Provide patient education regarding the infection and all elements of treatment plan
- Use motivational interviewing and coaching strategies to maximize adherence
- Schedule follow-up, when indicated
- · Recommend measures to reduce throat pain if present

Follow-up: Monitor and Evaluate

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- Presence of adverse effects, particularly allergic reactions
- Patient adherence to treatment plan using multiple sources of information
- Inquire if there have been infections among household contacts

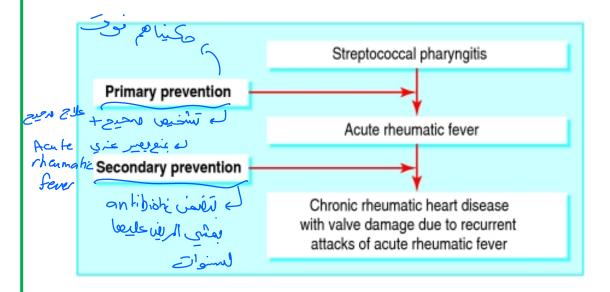
^{*}Collaborate with patient, caregiver(s), and other healthcare professionals.

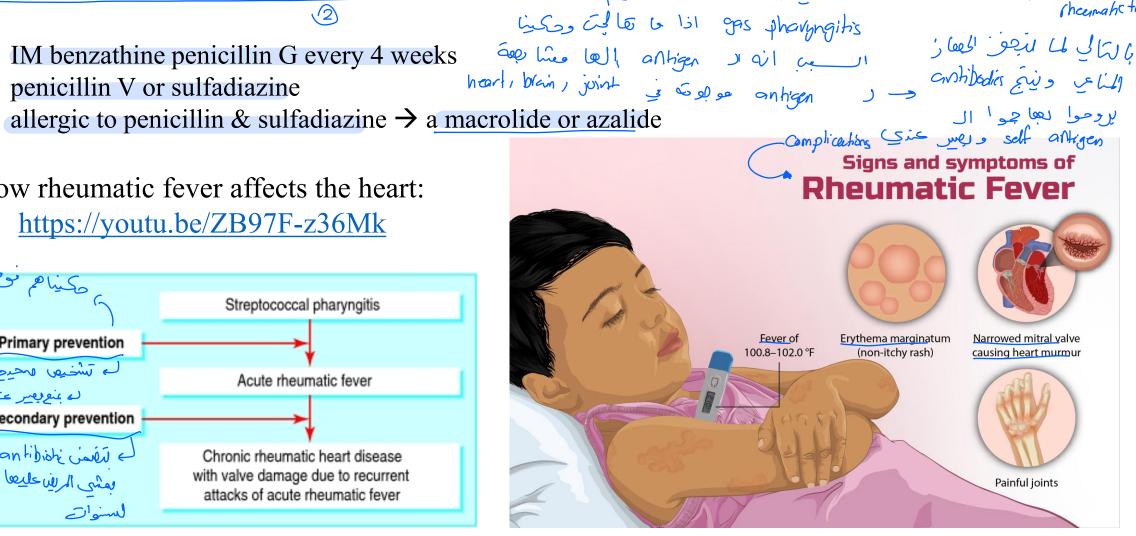
✓ Secondary prophylaxis of recurrence of rheumatic fever and/or rheumatic heart disease: patients should receive continuous antibiotic prophylaxis initiated as soon as the patient is diagnosed and the initial infection has been treated lie complications les sur co

penicillin V or sulfadiazine

allergic to penicillin & sulfadiazine → a macrolide or azalide

How rheumatic fever affects the heart: https://youtu.be/ZB97F-z36Mk





بالكالي لما ليجو الحفار

Secondary prophylaxis for rheumatic fever -Duration of therapy

Category	Duration after last attack
Rheumatic fever with carditis and residual heart disease	10 years or until 40 years of age (whichever is longer) Sometimes lifelong prophylaxis (refer to
(persistent valvular disease*)	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	10 years or until 21 years of age (whichever is longer) الأفعل.
(no valvular (a disease*)	ا2 له والعير عر ١2 له م
Rheumatic fever without carditis	5 years or until 21 years of age (whichever is longer)

Rhymatic heart disease may be reversable

or irreversable of symptoms: fatige, shortness of breath,

symptoms: fatige, shortness of breath,

cough

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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

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* Clinical or echocardiographic evidence.

Sever sever

Type of drug reactions



Type of reaction	Common features	
<u>Non-allerg</u> ic r <u>eacti</u> on	 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 — dizzines , Hypotension Angioedema — على الله الله الله الله الله الله الله ال	→ Po peneci Cephalospo
Serious delayed reactions delay reachion	 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 	-suse mace

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IgE: immunoglobulin E.



✓ Patient Education Tips

self reading +self learning.

• 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.