Chapter 130: Upper Respiratory Tract Infections

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CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Chapter 45, Respiratory Tract Infections, Upper.

KEY CONCEPTS

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1. Many upper respiratory tract infections are due to viral etiologies and will resolve spontaneously without pharmacologic therapy.
2. The most common bacterial causes are *Streptococcus pneumoniae* (acute otitis media and acute rhinosinusitis) and group A β-hemolytic *Streptococcus* (acute pharyngitis).
3. Vaccination against influenza and pneumococcus may decrease the risk of acute otitis media.
4. Distinguishing between viral and bacterial causes for upper respiratory tract infections may be difficult, and antimicrobials are often prescribed inappropriately leading to antimicrobial resistance.
5. When antimicrobials are indicated, amoxicillin or amoxicillin-clavulanate is first-line for acute otitis media, amoxicillin-clavulanate for acute rhinosinusitis, and amoxicillin or penicillin for acute pharyngitis.
6. For acute otitis media, high-dose amoxicillin (80-90 mg/kg/day in two divided doses) is recommended.

BEYOND THE BOOK

Watch the videos entitled "What is an upper respiratory infection (URI)?", "What is sinusitis?", and "Pharyngitis" in Khan Academy. These videos provide an overview of common URI. Compare and contrast infectious etiologies, diagnoses, and clinical presentation of these conditions.

INTRODUCTION

Upper respiratory tract infection is the most common reason for visits to primary care providers. There are over 25 million office visits per year for acute upper respiratory tract infections.[1] Otitis media, rhinosinusitis, and pharyngitis are the three most common upper respiratory tract infections. Although most upper respiratory tract infections typically manifest as mild illnesses, their high incidence and transmissibility places these infections as a leading cause of missed work or school days. The majority of these illnesses are caused by viruses; however, distinguishing patients with viral versus bacterial infection poses challenges as signs and symptoms are generally similar. Upper respiratory tract infections remain the leading condition for antibiotic prescribing, often inappropriately, and thereby serve as catalysts for the emergence and spread of antibiotic resistance. The prudent use of antibiotics for upper respiratory tract infections is critically important.

ACUTE OTITIS MEDIA

Acute otitis media comes from the Latin *oto-* for "ear," *itis* for "inflammation," and *medi-* for "middle"; otitis media, then, is an inflammation of the middle ear. There are three subtypes of otitis media: acute otitis media, otitis media with effusion, and chronic otitis media. Acute otitis media is the subtype with the greatest role for antibiotics and will be discussed in detail.

Epidemiology

Acute otitis media is primarily an infection during childhood and is the most common pediatric infection for prescribing an antibiotic in the United States. There are more than 709 million cases of otitis media worldwide each year; half of these cases occur in children under 5 years of age.[2] Most cases of acute otitis media occur in young children ages 6 to 24 months. Fortunately, the incidence of acute otitis media has declined over the past two decades, and a downward trend in acute otitis media healthcare visits have been observed in children younger than 5 years of age from 2001 to 2011. The introduction of routine pneumococcal vaccinations in infants may have been a major contributor to this decline, coinciding with the introduction of the seven-valent pneumococcal conjugate vaccine (PCV-7) in 2000, that was updated with PCV-13 starting in 2010.[3]

Etiology

1 Acute otitis media frequently occurs following an initial viral upper respiratory illness (eg, common cold) that often predisposes the patient to a bacterial otitis media. When comprehensive and sensitive microbiologic methods have been used in patients with a diagnosis of acute otitis media, bacteria have been found in more than 80% of cases.[4]

2 Common bacterial pathogens include *Streptococcus pneumoniae*, nontypeable *Haemophilus influenzae*, and *Moraxella catarrhalis*.[5] *S. pneumoniae* and *H. influenzae* together cause up to 60% of all pediatric cases. *Staphylococcus aureus* including methicillin-resistant *S. aureus* is uncommon in children, although it is an emerging pathogen in adult.

S. pneumoniae is an important cause of acute otitis media. Among children, there has been a dramatic shift in the microbial etiology after the introduction and widespread use of the pneumococcal conjugate vaccines. Specifically, the proportion of *S. pneumoniae* cases has declined over time, and the proportion of *H. influenzae* cases has risen.[4–6]

S. pneumoniae, *H. influenzae*, and *M. catarrhalis* can all possess resistance to β-lactams. *S. pneumoniae* develops resistance through alteration of penicillin-binding proteins, whereas *H. influenzae* and *M. catarrhalis* produce β-lactamases.

Pathophysiology

Acute otitis media usually follows a viral upper respiratory tract infection that impairs the mucociliary apparatus and causes Eustachian tube dysfunction in the middle ear. The middle ear is the space behind the tympanic membrane, or eardrum. A noninfected ear has a thin, clear tympanic membrane. In otitis media, this space becomes blocked with fluid, resulting in a bulging and erythematous tympanic membrane. Acute otitis media results when bacteria from the nasopharynx enter the inflammatory fluid in the middle ear and are not cleared properly by the mucociliary system. The bacteria proliferate and cause infection. Children tend to be more susceptible to otitis media than adults because the anatomy of their Eustachian tube is shorter and more horizontal, facilitating bacterial entry into the middle ear.[7]

Clinical Presentation

Patients or caregivers frequently characterize acute otitis media as having an acute onset of otalgia (ear pain). For parents of young children, irritability and tugging on the ear are often the first clues that a child has acute otitis media. In adults, an upper respiratory tract infection or seasonal allergic rhinitis episode often predisposes the onset of acute otitis media. In adults it is usually unilateral with ear pain and muffled hearing. If the tympanic membrane is ruptured, a sudden relief of pain followed by purulent otorrhea may be reported.

The diagnosis of acute otitis media includes demonstration of fluid in the middle ear. The American Academy of Pediatrics (AAP) guidelines have stringent diagnostic criteria to ensure accurate diagnosis. Children should be diagnosed with acute otitis media if they have middle ear effusion *and*

either (1) moderate-to-severe bulging of the tympanic membrane *or* new onset otorrhea not due to acute otitis externa, or (2) mild bulging of the tympanic membrane *and* onset of ear pain within the last 48 hours or intense erythema of the tympanic membrane. Middle ear effusion should be identified based on pneumatic otoscopy and/or tympanometry.[4]

The diagnoses of acute otitis media and otitis media with effusion are easily confused, and careful attention to history, signs, and symptoms is important. Otitis media with effusion is characterized by fluid in the middle ear without signs and symptoms of acute ear infection, such as pain and a bulging eardrum.[8]

CLINICAL PRESENTATION: ACUTE OTITIS MEDIA

General

- Cases of acute otitis media often follow viral upper respiratory tract infections or an exacerbation of seasonal allergic rhinitis. Nonverbal children with ear pain might hold, rub, or tug their ear. Infants might cry, be irritable, or have difficulty sleeping.

Signs and Symptoms

- Bulging of the tympanic membrane
- Reduced tympanic membrane mobility (pneumatoscopy)
- Otorrhea
- Otalgia (considered to be moderate or severe if pain lasts at least 48 hours)
- Diminished hearing
- Fever (considered to be severe if temperature is 39°C [102.2°F] or higher)
- Other signs reported include vertigo, nystagmus, and tinnitus

Data from Reference 3.

Treatment

Desired Outcomes

6 Treatment goals include pain management and prudent antibiotic use.

3 Pneumococcal conjugate vaccine and annual influenza vaccination should be assessed in all children according to the Advisory Committee on Immunization Practices (ACIP) schedule from the United States Centers for Disease Control and Prevention.[3] Also, because acute otitis media cases often follow influenza cases, influenza vaccination should be considered as a possible means to prevent acute otitis media.

General Approach to Treatment

The first step in treatment is to differentiate acute otitis media from otitis media with effusion or chronic otitis media, as the latter two types do not necessitate antibiotic therapy. Risk factors and disease severity of acute otitis media are assessed when considering initiation of antibiotic therapy. Amoxicillin is the mainstay of therapy and can overcome penicillin resistance, in many cases, with higher doses. The therapeutic strategy should be changed if complications develop or if symptoms fail to resolve within 3 days.

Pharmacologic Therapy

National clinical practice guidelines for diagnosis and management of acute otitis media (updated in 2013) are focused on children 6 months to 12

years of age with uncomplicated cases and without underlying conditions that may alter the natural course of the disease.[4] The decision to administer antibiotics or initially observe the patient ("watchful waiting") depends on patient age, symptom severity, laterality, and joint decision-making.

- Antibiotic therapy should be initiated for:
  - Children 6 months and older with acute otitis media showing severe symptoms (ie, toxic-appearing, persistent ear pain lasting more than 48 hours, or temperature of 39°C [102.2°F] or higher)
  - Children 6 months and older with acute otitis media with otorrhea
  - Children 6 to 23 months of age, with bilateral acute otitis media
- Observation without initial antibiotic treatment can be considered for:
  - Children 6 months and older with nonsevere unilateral acute otitis media without otorrhea
  - Children 24 months and older with bilateral acute otitis media without otorrhea

Initial observation (watchful waiting) should be based on joint decision-making with parents/caregivers, and must include a plan to initiate antibiotics if the child's symptoms worsen or decline within 48 to 72 hours of symptom onset.[4] The central principle is to administer antibiotics quickly when the diagnosis is certain, but to withhold antibiotics, at least initially, when the diagnosis is uncertain.

4 Antibiotic therapy for upper respiratory diseases must be balanced with possible increases in adverse drug events and increased antibiotic pressure to cause bacterial resistance. Systematic reviews and randomized controlled trials suggest a moderate benefit of antibiotics for the treatment of acute otitis media, including a marked decline in suppurative complications, and improved outcomes in both early- and late-phases.[9,10] On the other hand, rates of adverse effects, such as diarrhea and diaper rash are higher for children who receive antibiotics for acute otitis media.

There are no national guideline recommendations for the treatment of acute otitis media among adults. Data regarding the etiologies and safety of withholding antibiotics are limited for adults. Because acute otitis media is unusual among adults without underlying risk factors where complications might be significant, the general recommendation is to treat adults with empiric antibiotic therapy.[5] Choice of antibiotic regimens should be based on (1) coverage of the common bacterial pathogens (see Etiology), and (2) allergy, tolerance, previous exposure to antibiotics, costs, and resistance levels. Table 130-1 lists antibiotic recommendations for acute otitis media.

TABLE 130-1

Antibiotics and Doses for Acute Otitis Media

Antibiotic	Brand Name	Dose	Comments[a]
Initial Diagnosis			
Amoxicillin	Amoxil®	80-90 mg/kg/day orally divided twice daily	First-line
Amoxicillin-clavulanate	Augmentin®	90 mg/kg/day orally of amoxicillin plus 6.4 mg/kg/day orally of clavulanate, divided twice daily	First-line if certain criteria are present[b]
Cefdinir, Cefuroxime, Cefpodoxime	Omnicef®, Ceftin®, Vantin®	Cefdinir (14 mg/kg/day orally in 1-2 doses), Cefuroxime (30 mg/kg/day orally divided in two daily, Cefpodoxime (10 mg/kg/day orally divided in two daily doses)	Second-line or nonsevere penicillin allergy
Ceftriaxone	Rocephin®	50 mg/kg/day IM or IV once daily for 3 days	Second-line or nonsevere penicillin allergy
Failure at 48-72 Hours			
Amoxicillin-clavulanate[b]	Augmentin®	90 mg/kg/day orally of amoxicillin plus 6.4 mg/kg/day orally of clavulanate, divided twice daily	First-line
Ceftriaxone	Rocephin®	50 mg/kg/day IM or IV once daily for 3 days	First-line or nonsevere penicillin allergy

IM, intramuscular; IV, intravenous

[a]Amoxicillin-clavulanate 90:6.4 or 14:1 ratio is available in the United States; 7:1 ratio is available in Canada (use amoxicillin 45 mg/kg for one dose, amoxicillin 45 mg/kg with clavulanate 6.4 mg/kg for second dose).

[b]If a patient has received amoxicillin in the last 30 days, has concurrent purulent conjunctivitis, or has a history of recurrent infection unresponsive to amoxicillin.

Data from Reference 4.

5 Amoxicillin is the first-line therapy for most children.[4] Exceptions include: children who have received amoxicillin in the last 30 days, have concurrent purulent conjunctivitis, or have a history of recurrent infection unresponsive to amoxicillin. These patients should receive amoxicillin-clavulanate instead of amoxicillin. Patients with otitis conjunctivitis syndrome are more likely to be infected with nontypeable *H. influenzae*, hence the need for a β-lactamase inhibitor (such as clavulanate).[4] Clinicians should reassess the plan if the child's symptoms worsen or decline within 48 to 72 hours of symptom onset.[4]

High-dose amoxicillin (80-90 mg/kg/day in two divided doses) is recommended for most pediatric patients with acute otitis media. Amoxicillin has the best pharmacodynamic profile against drug-resistant *S. pneumoniae* of all available oral antibiotics. In addition, amoxicillin has a long record of safety, possesses a narrow spectrum of activity, is inexpensive, and is more palatable than other options. Higher middle ear fluid concentrations of

amoxicillin, as a result of higher dosing, overcome most drug-resistant *S. pneumoniae*.[3] Its excellent efficacy against *S. pneumoniae* outweighs the issue of β-lactamase-producing *H. influenzae* and *M. catarrhalis*, against which amoxicillin may not be effective. This is because both *H. influenzae* and *M. catarrhalis* are more likely than *S. pneumoniae* to lead to a spontaneous resolution of the infection.

A patient who has received amoxicillin in the last 30 days, has concurrent purulent conjunctivitis, or has a history of recurrent infection unresponsive to amoxicillin should receive high-dose amoxicillin-clavulanate (90 mg/kg/day of amoxicillin, with 6.4 mg/kg/day of clavulanate, in two divided doses) instead of amoxicillin. Amoxicillin-clavulanate has activity against β-lactamase-producing *H. influenzae* and *M. catarrhalis* as well as drug-resistant *S. pneumoniae*.[4]

In most adults, the first-line treatment is amoxicillin-clavulanate 875 mg with clavulanate 125 mg orally twice daily. A higher dose of the amoxicillin component (2,000 mg) with clavulanate is recommended for patients with clinical or epidemiologic risk for severe infections or infections due to penicillin nonsusceptible *S. pneumoniae* (those who live in regions with >10% penicillin nonsusceptible *S. pneumoniae*, 65 years and older, immunocompromised, recent hospitalizations, or have used antibiotics in the past month).[5]

Other antibiotic choices include cefdinir, cefuroxime, cefpodoxime, and intramuscular or intravenous ceftriaxone.[4] Second-generation cephalosporins, though β-lactamase stable, are expensive, have an increased incidence of side effects, and may increase selective pressure for resistant bacteria. Furthermore, most cephalosporins do not achieve adequate middle ear fluid concentrations against drug-resistant *S. pneumoniae* for the desired duration of the dosing interval. Amoxicillin and intramuscular ceftriaxone and amoxicillin are the only antibiotics that achieve middle ear fluid concentrations above the minimal inhibitory concentration (MIC) for greater than 40% of the dosing interval. Although single doses of ceftriaxone have been used, daily doses for 3 days are recommended to optimize clinical outcomes.[4] Ceftriaxone is more expensive than amoxicillin, and the intramuscular injections are painful.

Patients with a penicillin allergy can be treated with several alternative antibiotics, including a cephalosporin in patients without history of severe or type 1 penicillin allergy. Use of trimethoprim-sulfamethoxazole and erythromycin-sulfisoxazole is discouraged because of high rates of resistance. Notably, clindamycin lacks efficacy against *H. influenzae*. Cefdinir or azithromycin (Zithromax) should be the first-line antibiotic in those with penicillin allergy based on risk of cephalosporin allergy.

There is ongoing debate regarding the optimal duration of therapy for acute otitis media. Duration is based on age and severity of symptoms. Traditional recommendations call for 10 days of antibiotic therapy; however, some experts have speculated that patients can be treated for as little as 5 to 7 days. Short-course treatment is not recommended in children younger than 2 years of age.[11] In children at least 6 years of age who have uncomplicated acute otitis media, a 5- to 7-day treatment course may be used.[4]

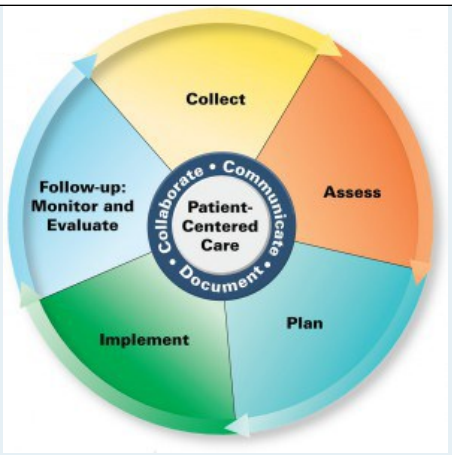
Recurrent acute otitis media is defined as at least three episodes in 6 months or four episodes in 1 year, with one episode in the preceding 6 months. Recurrent episodes are of concern because children younger than 3 years of age are at high risk for hearing loss and language and learning disabilities. Clinicians should avoid prophylactic antibiotics against recurrent episodes, but they may offer tympanostomy tubes (T tubes).[4]

Adjunctive Therapy

Children with acute otitis media should be assessed and treated for pain. Those with pain should be recommended analgesics to reduce pain regardless of the decision to administer antibiotics.[4] This is largely because antibiotics do not reduce pain in the first 24 hours. Furthermore, some children may experience some pain up to 3 to 7 days even after antibiotics are started. Choice of pain treatment depends on possible benefits and risks to the individual patient. Acetaminophen and ibuprofen are mainstays of treatment, are effective analgesics for mild-to-moderate pain, and are readily available. Eardrops with a local anesthetic may offer additional, but brief, benefit over acetaminophen in patients at least 5 years of age.[4] Finally, several studies have documented the large risk reductions in pediatric pneumococcal acute otitis media.[12,13] Thus, routine assessment of vaccination schedules is essential for prevention.

Patient Care Process

Patient Care Process for Acute Otitis Media



Collect

- Patient characteristics (eg, age, weight)
- Patient history (eg, past infections, current and past antibiotic/antiviral use noting previous failures, medication allergies)
- Determine whether patient has concurrent purulent conjunctivitis
- Objective data:
  - Temperature
  - Signs and symptoms (see Clinical Presentation)
  - Presence of congestion, fullness, purulent discharge, or pain in the ear
  - Presence of redness, fullness, bulging, or limited/absent mobility of the tympanic membrane

Assess

- Infection status, including presence of signs and symptoms
- Determine which symptoms may need additional therapy (eg, ongoing ear pain)
- Use information collected, patient factors (eg, patient age, symptom severity, laterality), 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
  - Determine if the patient meets criteria for high-dose amoxicillin-clavulanate
  - Determine whether a short-course of therapy (5-7 days) may be appropriate

Plan

- Select drug therapy regimen including specific antibiotic, dose, route, frequency, and duration; specify the continuation and discontinuation of existing therapies (see Table 130-1)
- 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

Implement*

- 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 ear pain, if present

Follow-up: Monitor and Evaluate

- Improvement/resolution of signs and symptoms; reassess the plan if the child's symptoms worsen or decline within 48 to 72 hours of symptom onset
- Presence of adverse effects, particularly allergic reactions and diarrhea
- Patient adherence to treatment plan using multiple sources of information
- Recommend pneumococcal conjugate vaccine (PCV) and annual influenza vaccination

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

Evaluation of Therapeutic Outcomes

Patients with acute otitis media should be reassessed after 48 to 72 hours. By this time, there should be clinical improvement in the signs and symptoms of infection, including pain, fever, and erythema/bulging of the tympanic membrane. If the patient has not responded and antibiotics were withheld initially, they should be instituted now.[14] If the patient initially received an antibiotic, then the antibiotic should be changed (Table 130-1). A switch in regimen is recommended if there is no clinical improvement by the third day of therapy, given the possibility of infection with a β-lactamase-producing strain of *H. influenzae* or *M. catarrhalis* or with a strain of penicillin-resistant *S. pneumoniae.* Most children will become asymptomatic within 7 days. Tympanocentesis for culture of middle ear fluid can be considered for treatment failure or persistent acute otitis media. It has a therapeutic effect of relieving pain and pressure and can be used to collect fluid to identify the causative agent.

Early reevaluation of the eardrum when signs and symptoms are improving can be misleading because effusions persist. Over a period of 1 week, changes in the eardrum normalize, and the pus becomes serous fluid. Air-fluid levels are apparent behind the eardrum, at which point the stage is now referred to as *otitis media with effusion*. This does not represent ongoing infection, nor are additional antibiotics required.[4]

Immediate reevaluation is appropriate if hearing loss results from persistent middle ear effusions following infection. Complications of otitis media are infrequent but include mastoiditis, bacteremia, meningitis, and auditory sequelae with the potential for speech and language impairment.[4]

ACUTE BACTERIAL RHINOSINUSITIS

Sinusitis is an inflammation and/or infection of the paranasal sinuses, or membrane-lined air spaces, around the nose.[15] The term *rhinosinusitis* is preferred because sinusitis typically also involves the nasal mucosa.[15] Even though the majority of rhinosinusitis infections are viral in origin, antibiotics are frequently prescribed. It is important to differentiate between viral and bacterial rhinosinusitis to avoid unnecessary antibiotic use.

The most current clinical practice guidelines for acute bacterial rhinosinusitis were published in 2012 by the Infectious Diseases Society of America (IDSA) and 2015 by the American Academy of Otolaryngology—Head and Neck Surgery Foundation (AAO-HNSF).[15,16]

Epidemiology

1 Nearly 30 million cases of rhinosinusitis are diagnosed annually in the United States.[17] Adults with rhinosinusitis miss an average of 1 to 2

workdays/year with these infections and experience significant activity, work, and social limitations.[16] Most episodes of acute sinusitis are caused by viral upper respiratory tract infection; however, the lack of clinical criteria to accurately differentiate bacterial from viral infections leads to inappropriate use of antibiotics and remains the fifth leading diagnosis for which antibiotics are prescribed.[14,18]

Etiology

2 Acute bacterial rhinosinusitis is caused, most often, by the same bacteria implicated in acute otitis media: *S. pneumoniae* and nontypeable *H. influenzae*. These organisms are responsible for approximately 50% to 70% of bacterial causes of acute bacterial rhinosinusitis in both adults and children.[15] *M. catarrhalis* is also sometimes implicated in children (approximately 8%-16%) and less commonly in adults.[15] *Streptococcus spp.*, *S. aureus*, gram-negative bacilli, atypical bacteria, and anaerobes are associated less frequently with acute bacterial rhinosinusitis.[15] Healthcare-associated cases can be attributable to pathogens prevalent in the healthcare environment including *S. aureus*, methicillin-resistant *S. aureus* (MRSA), *P. aeruginosa*, *K. pneumoniae*, and other gram negatives; and often are polymicrobial.

Pathophysiology

Acute bacterial rhinosinusitis is often preceded by a viral respiratory tract infection that causes mucosal inflammation. This can lead to obstruction of the sinus ostia—the pathways that drain the sinuses. Mucosal secretions become trapped, local defenses are impaired, and bacteria from adjacent surfaces begin to proliferate. The maxillary and ethmoid sinuses are most frequently involved. The pathogenesis of chronic rhinosinusitis has not been well studied. Whether it is caused by more persistent pathogens or a subtle defect in the host's immune function, some patients develop chronic symptoms after their acute infection. Rarely, life-threatening complications of sinusitis can include meningitis, epidural, or cerebral abscess.

Clinical Presentation

CLINICAL PRESENTATION: ACUTE BACTERIAL RHINOSINUSITIS

General

The diagnosis of acute bacterial sinusitis involves assessing signs and symptoms, distinguishing bacterial from viral infection with temporal patterns of the illness. Patients manifest with focused sinonasal symptoms compared to those with viral URIs. Acute sinusitis manifests with up to 4 weeks of purulent nasal drainage.

Signs and Symptoms

- Purulent anterior nasal discharge, purulent or discolored posterior nasal discharge, nasal congestion or obstruction, facial congestion or fullness, facial pain or pressure, fever, headache, ear pain/pressure/fullness, halitosis, dental pain, cough, and fatigue
- Clinical presentations (any of 3) that are most consistent with acute bacterial versus viral rhinosinusitis:

  i) Onset with *persistent* signs or symptoms compatible, lasting for ≥10 days without any evidence of clinical improvement

  ii) Onset with *severe* signs or symptoms of high fever (≥39°C [102.2°F]) and purulent nasal discharge or facial pain lasting for at least 3 to 4 consecutive days at the beginning of illness

  iii) Onset with *worsening* signs or symptoms characterized by new-onset fever, headache, or increase in nasal discharge following a typical viral URI that lasted 5 to 6 days and were initially improving ("double sickening")

Data from Reference 15.

Treatment

Desired Outcomes

The goals of treatment for acute bacterial rhinosinusitis are to reduce signs and symptoms, achieve and maintain patency of the ostia, limit antibiotic treatment to those who may benefit, eradicate the bacterial infection with appropriate antibiotic therapy, minimize the duration of illness, prevent complications, and prevent progression from acute disease to chronic disease.

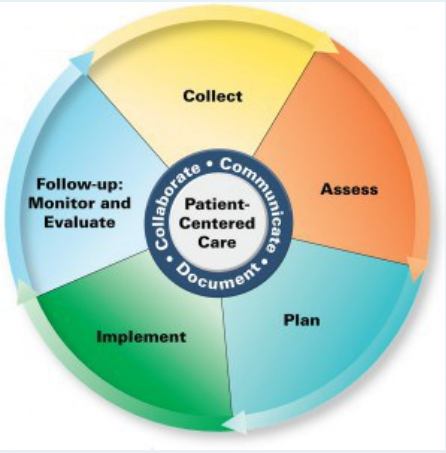
General Approach to Treatment

4 The first step is to differentiate viral and bacterial rhinosinusitis. This is based on disease duration, initial severity of illness, and worsening symptomatology. Viral rhinosinusitis typically improves in 7 to 10 days. In contrast, acute bacterial rhinosinusitis symptoms persist for 10 days or greater without improvement or with worsening symptoms after 10 days, or can manifest worsening after initial improvement ("double-sickness" pattern).[16] Acute bacterial rhinosinusitis may also be suspected if the patient has severe symptoms at the beginning of his/her illness. Management involves antibiotic therapy or watchful waiting based on shared decision making. Amoxicillin-clavulanate is the first-line antibiotic therapy for patients with acute bacterial rhinosinusitis.[15]

"Urgent early referral to a specialist is essential for patients exhibiting complicated acute bacterial rhinosinusitis. Indications for referral include high, persistent fevers, periorbital edema or inflammation, mental status changes, visual disturbances, severe headache, immunosuppressive illness, healthcare-associated infections, anatomic defects causing obstruction, unusually severe symptoms, multiple recurrent episodes (three to four times per year), unilateral findings, significant coexisting illnesses, risk factors for unusual or resistant pathogens, and history of antibiotic failure." The specialist may perform computed tomography to assess the severity and extent of disease and identify the underlying causes.

Patient Care Process

Patient Care Process for Acute Bacterial Rhinosinusitis



Collect

- Patient characteristics (eg, age, weight, comorbidities)
- Patient history (eg, past infections, current and past antibiotic/antiviral use noting previous failures, medication allergies, history of allergic rhinitis)
- Recent healthcare exposures or procedures
- Temporal patterns of symptoms
- Determine whether patient is in daycare, is a daycare worker, or has a child in daycare
- Objective data:
    - Temperature

- Signs and symptoms (see Clinical Presentation)
- Presence of congestion, fullness, or pain in the nose, face, or ear
- Presence of purulent or discolored nasal discharge
- Other diagnostic tests, when indicated (eg, computerized tomography scan (CT), sinus puncture)

Assess

- Infection status, including presence and severity of signs and symptoms
- Determine which symptoms may need additional therapy (eg, ongoing nose pain)
- Decide if referral is needed (eg, mental status changes, visual disturbances, immunosuppressive illness, nosocomial infections, anatomic defects, unilateral findings)
- 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
  - Determine if the patient meets criteria for high-dose amoxicillin-clavulanate

Plan*

- Select drug therapy regimen including specific antibiotic, dose, route, frequency, and duration; specify the continuation and discontinuation of existing therapies (see Tables 126-2 and 126-3)
- 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

Implement

- 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 symptomatic measures to reduce nose pain and inflammation

Follow-up: Monitor and Evaluate

- Improvement/resolution of signs and symptoms; reassess the plan if the patient's symptoms worsen or decline within 48 to 72 hours of symptom onset
- Presence of adverse effects, particularly allergic reactions and diarrhea
- Patient adherence to treatment plan using multiple sources of information

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

Pharmacologic Therapy

The IDSA published clinical practice guidelines in 2012 that are the primary source for many of the statements in this chapter.[15] Additional guidance and recommendations come from a 2015 update of the 2007 guidelines from AAO-HNSF.[16] There are two major differences in the IDSA and AAO-HNSF guidelines. The AAO-HNSF guidelines endorse watchful waiting, without antibiotics, unless symptoms fail to improve within 7 days.[16] When antibiotics are given, the AAO-HNSF endorses amoxicillin as first-line treatment, instead of amoxicillin-clavulanate.[16] In contrast, the IDSA guidelines support initiating empiric therapy as soon as the clinical diagnosis of acute bacterial rhinosinusitis is established and amoxicillin-clavulanate rather than amoxicillin alone as first-line treatment.[15]

5 Amoxicillin-clavulanate is considered the first-line treatment for acute bacterial rhinosinusitis in children and adults according to IDSA guidelines (Tables 130-2 and 130-3).[15] In contrast, prior guidelines, and the AAO-HNSF guidelines,[16] list amoxicillin as the first-line treatment option due to its safety, narrow spectrum of activity, good tolerability, and favorable cost. The IDSA guidelines support the choice of amoxicillin-clavulanate based on (a) the emergence of *H. influenzae* as a more common cause of upper respiratory tract infections in children than in the past,[5] and (b) the high prevalence of β-lactam-producing respiratory pathogens in acute bacterial rhinosinusitis (particularly *H. influenzae* and *M. catarrhalis*). The advantage of using amoxicillin-clavulanate, as compared with amoxicillin, is a greater spectrum of coverage. The disadvantages are increased cost, greater risk of adverse effects including diarrhea, and an added risk of hypersensitivity to the clavulanate component.[15]

TABLE 130-2

Antibiotics and Doses for Acute Bacterial Rhinosinusitis in Children

Antibiotic	Brand Name	Dose	Comments
Initial Empirical Therapy			
Amoxicillin-clavulanate	Augmentin®	45 mg/kg/day orally twice daily	First line
Amoxicillin-clavulanate	Augmentin®	90 mg/kg/day orally twice daily	Second line
β-Lactam Allergy			
Clindamycin plus cefixime or cefpodoxime	Cleocin®, Suprax®, Vantin®	Clindamycin (30-40 mg/kg/day orally three times daily) cefixime (8 mg/kg/day orally twice daily) or efpodoxime (10 mg/kg/day orally twice daily)	Non-type 1 allergy
Levofloxacin	Levaquin®	10-20 mg/kg/day orally every 12-24 hours	Type 1 allergy
Risk for Antibiotic Resistance or Failed Initial Therapy			
Amoxicillin-clavulanate	Augmentin®	90 mg/kg/day orally twice daily	
Clindamycin plus cefixime or cefpodoxime	Cleocin®, Suprax®, Vantin®	Clindamycin (30-40 mg/kg/day orally three times daily) plus Cefixime (8 mg/kg/day orally twice daily) or Cefpodoxime (10 mg/kg/day orally twice daily)	
Levofloxacin	Levaquin®	10-20 mg/kg/day orally every 12-24 hours	
Severe Infection Requiring Hospitalization			
Ampicillin-sulbactam	Unasyn®	200-400 mg/kg/day IV every 6 hours	
Ceftriaxone	Rocephin®	50 mg/kg/day IV every 12 hours	
Cefotaxime	Claforan®	100-200 mg/kg/day IV every 6 hours	
Levofloxacin	Levaquin®	10-20 mg/kg/day IV every 12-24 hours	

Data from Reference 15.

TABLE 130-3

Antibiotics and Doses for Acute Bacterial Rhinosinusitis in Adults

Antibiotic	Brand Name	Dose	Comments
Initial Empirical Therapy			
Amoxicillin-clavulanate	Augmentin®	500 mg/125 mg orally three times daily, or 875 mg/125 mg orally twice daily	First-line
Amoxicillin-clavulanate	Augmentin®	2,000 mg/125 mg orally twice daily	Second- line
Doxycycline		100 mg orally twice daily or 200 mg orally once daily	Second- line
β-Lactam Allergy			
Doxycycline		100 mg orally twice daily or 200 mg orally once daily	
Levofloxacin	Levaquin®	500 mg orally once daily	
Moxifloxacin	Avelox®	400 mg orally once daily	
Risk for Antibiotic Resistance or Failed Initial Therapy			
Amoxicillin-clavulanate	Augmentin®	2,000 mg/125 mg orally twice daily	
Levofloxacin	Levaquin®	500 mg orally once daily	
Moxifloxacin	Avelox®	400 mg orally once daily	
Severe Infection Requiring Hospitalization			
Ampicillin-sulbactam	Unasyn®	1.5-3 g IV every 6 hours	
Levofloxacin	Levaquin®	500 mg orally once daily	
Moxifloxacin	Avelox®	400 mg orally once daily	
Ceftriaxone	Rocephin®	1-2 g IV every 12-24 hours	
Cefotaxime	Claforan®	2 g IV every 4-6 hours	

Data from Reference 15.

Symptomatic Management

Symptomatic management for acute rhinosinusitis aims to relieve symptoms due to nasal drainage and obstruction such as pain with use of analgesics. The following are recommended as adjunct to therapy in patients with acute bacterial rhinosinusitis[15]:

- Intranasal saline irrigation with either physiologic or hypertonic saline
- Intranasal corticosteroids as adjunct to antibiotics in the empiric treatment of acute bacterial rhinosinusitis, primarily in patients with a history of allergic rhinitis

Topical or oral decongestants or antihistamines are generally not recommended as adjunctive treatment for acute bacterial rhinosinusitis. These agents can dry mucosa and disturb clearance of mucosal secretions.

High-dose amoxicillin-clavulanate (eg, 2,000 mg twice daily or 90 mg/kg/day twice daily) is recommended in the following situations: (a) geographic regions with high endemic rates (10% or greater) of invasive penicillin-nonsusceptible *S. pneumoniae*, (b) severe infection, (c) attendance at daycare, (d) age less than 2 or greater than 65 years, (e) recent hospitalization, (f) antibiotic use within the last month, and (g) immunocompromised persons.[15] Severe infections are those with "evidence of systemic toxicity with fever of 39°C (102.2°F) or higher, and threat of suppurative complications."[15]

For those with a history of β-lactam allergy, levofloxacin monotherapy is recommended for children or combination therapy with clindamycin plus cefixime or cefpodoxime.[15] Adults with a penicillin allergy may receive doxycycline (not suitable for children), levofloxacin, or moxifloxacin monotherapy.[15] The ISDA guidelines also provide several options for patients at risk for antibiotic resistance, who failed initial therapy, or who have a severe infection requiring hospitalization (Tables 130-2 and 130-3).[15] Notably, cephalosporins are no longer recommended as monotherapy due to variable rates of resistance against *S. pneumoniae*.[15] Combination therapy with a third-generation oral cephalosporin plus clindamycin may be used in regions with high endemic rates of penicillin nonsusceptible *S. pneumoniae*. Macrolides are not recommended because of high rates of *S. pneumoniae* resistance (~30%).[15] Trimethoprim-sulfamethoxazole has not been recommended for some time due to resistance among *S. pneumoniae* and *H. influenzae* (~30-40%).[15]

The duration of therapy for the treatment of uncomplicated acute bacterial rhinosinusitis is 5 to 7 days for most adults. A longer duration of 10 to 14 days is still recommended for children.[15]

Evaluation of Therapeutic Outcomes

If symptoms persist or worsen after 48 to 72 hours of appropriate antibiotic therapy, then the patient should be reevaluated and alternative antibiotics should be considered.[15] Patients who do not respond to first- or second-line therapies should be referred to a specialist and evaluated more aggressively, potentially with direct sinus aspiration or contrast-enhanced computed tomography.[15]

ACUTE PHARYNGITIS

1 2 Pharyngitis is an acute infection of the oropharynx or nasopharynx.[19] The most common presenting symptom is sore throat. It is responsible for 6% of visits by children to their primary care provider annually.[20] Although viral causes are most common, group A β-hemolytic *Streptococcus* (GAS, also known as *S. pyogenes*) is the primary bacterial cause[19]; pharyngitis due to GAS is commonly known as "strep throat," accounting for 20% to 30% of cases among children and 5% to 15% among adults.

Epidemiology

Acute pharyngitis accounts for approximately 15 million healthcare visits per year, resulting in an economic burden of up to $539 million for children alone.[19]

Although all age groups are susceptible, the frequency is much greater in the pediatric population. Children 5 to 15 years of age are most susceptible; parents of school-aged children and those who work with children are also at increased risk.

Seasonal outbreaks occur, and the incidence of GAS is highest in winter and early spring.[19] The incubation period is 2 to 5 days, and the illness often occurs in clusters.[19] Spread occurs via direct contact (usually from hands) with droplets of saliva or nasal secretions, and transmission is thus worse in institutions, schools, families, and crowded areas.[19] Untreated patients with streptococcal pharyngitis are infectious during the acute illness and for

another week thereafter. Effective antibiotic therapy reduces the infectious period to about 24 hours.

Acute rheumatic fever is rarely seen in developed countries. In the United States, acute rheumatic fever secondary to GAS infection was a cause of concern in the 1950s and was the major reason for penicillin therapy, but the annual incidence of this disease today is extremely rare (one case or more per 1 million population). Outbreaks have been reported in the United States as recently as the late 1980s and early 1990s. In developing countries, acute rheumatic fever and rheumatic heart disease is widespread affecting an estimated 20 million people worldwide making this a leading cause of cardiac death during the first five decades of life. This risk can be reduced by timely therapy.

Etiology

1 Viruses cause the majority of acute pharyngitis cases. Specific etiologies include rhinovirus (20%), coronavirus (5%), adenovirus (5%), herpes simplex virus (4%), influenza virus (2%), parainfluenza virus (2%), and Epstein–Barr virus (1%) and less frequently coxsackievirus A, cytomegalovirus, and acute human immunodeficiency virus (HIV) infection.[19]

4 GAS is the most common cause of pharyngitis (10%-30% of persons of all ages with pharyngitis) and is the only commonly occurring form of acute pharyngitis for which antibiotic therapy is indicated.[19] In the pediatric population, GAS causes 15% to 30% of pharyngitis cases. In adults, GAS is responsible for 5% to 15% of all symptomatic episodes of pharyngitis.[19] Pharyngitis in a child younger than 3 years of age is rarely caused by GAS.[19]

Other less common causes of acute pharyngitis are groups C and G *Streptococcus*, *Corynebacterium diphtheriae*, *Neisseria gonorrhoeae*, *Mycoplasma pneumoniae*, *Arcanobacterium haemolyticum*, *Yersinia enterocolitica*, and *Chlamydia pneumoniae*.[19] Treatment options for these organisms are not addressed in this chapter.

Pathophysiology

Streptococcal pharyngitis results from GAS proliferating in the pharynx, although exact mechanisms are not well defined. Asymptomatic pharyngeal carriers of the organism may have an alteration in host immunity (eg, a breach in the pharyngeal mucosa) and the bacteria of the oropharynx may migrate to cause an infection. Pathogenic factors associated with the organism itself, pyrogenic toxins, hemolysins, streptokinase, and proteinase, may also play a role.

Clinical Presentation

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 GAS 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 or purple spots 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.

The primary goal of diagnosis is accurate differentiation of GAS from pharyngitis due to other agents (eg, viral). There is broad overlap between the signs and symptoms of pharyngitis from GAS versus viral or nonstreptococcal agents, and thus rarely can be differentiated based on clinical grounds alone even among the most experienced clinicians.

Guidelines from IDSA and the American Heart Association recommend swabbing the throat and testing for GAS in patients with signs and symptoms of streptococcal pharyngitis.[19] Only those with a positive test for GAS require antibiotic treatment.[19] Diagnostic studies are not indicated for children <3 years old because the incidence of streptococcal pharyngitis is uncommon in this age. Laboratory tests should not be performed in patients with clinical features that strongly suggest a viral etiology. This is because a positive test does not necessarily indicate disease. A positive test may simply indicate that the patient is a carrier for GAS and is not actively infected. Approximately 20% of children are carriers of GAS; the prevalence is lower among adults.[19]

Testing for GAS can be performed using a throat swab that can be sent for culture or used for the RADT. Cultures are the gold standard, but they require 24 to 48 hours for results. The RADT is more practical in that it provides results quickly, it can be performed at the bedside, and it is less

expensive than culture. If RADT is positive, it does not require a follow-up throat culture.[19] If RADT yields negative test results, it is generally recommended to follow up with a throat culture to confirm the results for children and adolescents, but not necessary in adults.[19] Delaying therapy while awaiting culture results does not affect the risk of complications (though some argue that symptomatic benefit is postponed, and contagion remains), and patients must be educated as to the value of waiting, given the low false-negative rate of RADT.[19] The accurate diagnosis of streptococcal pharyngitis followed by appropriate antimicrobial therapy is important for the prevention of suppurative and nonsuppurative complications including acute rheumatic fever, acute glomerulonephritis, reactive arthritis, peritonsillar abscess, retropharyngeal abscess, cervical lymphadenitis, mastoiditis, otitis media, rhinosinusitis, and necrotizing fasciitis. In addition, accurate diagnosis would allow to improve outcomes, decrease transmission, and minimizing potential inappropriate antimicrobial therapy.

Treatment

Desired Outcomes

The goals of treatment for pharyngitis are to improve clinical signs and symptoms, minimize adverse drug reactions and overuse of antibiotics, prevent transmission to close contacts, and prevent acute rheumatic fever and suppurative complications, such as peritonsillar abscess, cervical lymphadenitis, and mastoiditis.[19]

General Approach to Treatment

Once the diagnosis of GAS pharyngitis has been made, the clinician must decide appropriate supportive care, when to initiate antibiotic therapy, the appropriate antibiotic, and the duration of therapy. The selection of appropriate antibiotic therapy will involve careful consideration of cost, safety, efficacy, potential for regimen adherence, and bacterial resistance rates. Clinicians should be aware of local resistance patterns, which may differ from the national patterns.

4 Inappropriate antibiotic use for acute pharyngitis has been a major contributor to the development antimicrobial resistance.[19] Approximately 60% of patients who visit their provider with a complaint of “sore throat are prescribed an antibiotic.”[21,22] This rate is well above the incidence of GAS pharyngitis. Antibiotic therapy should be reserved for those patients with clinical and epidemiologic features of GAS pharyngitis, preferably with a positive laboratory test. 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.

Pharmacologic Therapy

The clinical practice guidelines published by the IDSA in 2012 are the primary source for many of the recommendations in this section.[19] Tables 130-4 and 130-5 outline dosing for acute GAS pharyngitis and chronic carriers of GAS.

TABLE 130-4

Antibiotics and Doses for Group A β-Hemolytic Streptococcal Pharyngitis

Antibiotic	Brand Name	Dose	Route / Duration	Rating
Preferred Antibiotics				
Penicillin V	Pen-V®	Children: 250 mg twice daily or three times daily. Adolescents and Adults: 250 mg four times daily or 500 mg twice daily	Orally 10 days	IB
Penicillin G benzathine	Bicillin L-A®	<27 kg: 0.6 million units; ≥ 27 kg : 1.2 million units	IM One dose	IB
Amoxicillin[a]	Amoxil®	50 mg/kg once daily (maximum 1 g); 25 mg/kg (maximum 500 mg) twice daily	Orally 10 days	IB
Penicillin Allergy				
Cephalexin	Keflex®	20 mg/kg/dose (maximum 500 mg)	Orally 10 days	IB
Cefadroxil	Duricef®	30 mg/kg once daily (maximum 1 g)	Orally 10 days	IB
Clindamycin	Cleocin®	7 mg/kg/dose three times daily (maximum 300 mg/dose)	Orally 10 days	IIaB
Azithromycin[b]	Zithromax®	12 mg/kg once daily (maximum 500 mg) for one day, then 6 mg/kg orally once daily (maximum 250 mg) for four days	Orallly 5 days	IIaB
Clarithromycin[b]	Biaxin®	7.5 mg/kg per (maximum 250 mg) twice daily	Orally 10 days	IIaB

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).

[a]Standard formulation, not extended release.

[b]Resistance of group A β-hemolytic *Streptococcus* (GAS) to these agents may vary and local susceptibilities should be considered with these agents.

Data from Reference 19.

TABLE 130-5

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) for 10 days
Amoxicillin-clavulanate	Augmentin®	40 mg/kg/day orally in three divided doses (maximum 2,000 mg/day of amoxicillin) for 10 days
Penicillin V and rifampin	Pen-V®, Rifadin®	Penicillin V: 50 mg/kg/day orally in four divided doses for 10 days (maximum 2,000 mg/day); Rrifampin: 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 once IM, ≥ 27 kg 1.2 million units once intramuscularly; *and* Rifampin: 20 mg/kg/day orally in two divided doses during last 4 days of treatment with penicillin (maximum 600 mg/day)

Data from Reference 19.

5 In the United States there have been no reported cases of penicillin-resistant GAS.[19] Because penicillin and amoxicillin have a narrow spectrum of activity and are readily available, safe, and inexpensive, they are considered to be the treatments of choice.[19]

Amoxicillin often used in place of penicillin V for children with GAS pharyngitis because the suspension is more palatable.[19] Gastrointestinal (GI) adverse effects and rash are more common with amoxicillin. A once-daily, extended-release formulation of amoxicillin has been approved for treatment of GAS pharyngitis in adults and children aged 12 years and older.[19] In addition, a number of antibiotics have been effective against GAS pharyngitis (Table 130-4). Most oral regimens are administered for 10 days.

In patients with nonanaphylactic penicillin allergy, a first-generation cephalosporin such as cephalexin is recommended for 10 days. For patients with type I immunoglobulin E (IgE)–mediated penicillin allergies, azithromycin, clarithromycin, or clindamycin is recommended for a duration of 10 days except 5 days with azithromycin. Clindamycin resistance among GAS is ~1% and 5% to 8% for macrolides in the United States, but is higher in some other areas of the world.[19]

A few antimicrobials are not recommended for GAS pharyngitis including tetracyclines due to high prevalence of resistance as well as sulfonamides and trimethoprim-sulfamethoxazole due to poor eradication rates for GAS.[19] Older fluoroquinolones such as ciprofloxacin have poor activity against GAS while newer fluoroquinolones have activity against GAS, but are expensive and have an unnecessarily broad spectrum of activity for this treatment for GAS pharyngitis.[19] Treatment early in the course leads to more rapid clinical response in symptoms, decreases contagiousness to others, and can prevent suppurative and nonsuppurative complications. The immediate therapy can be postponed up to 9 days without major nonsuppurative sequela.[19] Clinical guidelines recommend withholding antibiotics unless the patient has a positive laboratory result.[19]

The severity of pharyngitis symptoms and communicability of the disease is less after 24 hours of antibiotic therapy. The duration of therapy for GAS pharyngitis is 10 days, except for benzathine penicillin and azithromycin, to maximize bacterial eradication.[19] A systematic review of short- versus long-course therapies concluded that oral penicillin for 10 days (long course) remains first-line therapy.[23] Although some studies have suggested shorter courses of treatment for pharyngitis, confounding factors from these studies, such as the lack of strict entry criteria or differentiation between new and failed infections, limit the widespread application of short-antibiotic courses now.[19]

Approximately 33% of household contacts of a person with acute GAS pharyngitis harbor GAS in their upper respiratory tracts.[19] Routine testing and/or treating of asymptomatic household contacts of an index patient is not recommended.[19] GAS carriers do not need antimicrobial therapy due to

low risk of spreading GAS pharyngitis or developing suppurative or nonsuppurative complications.[18] If tested, it is not necessary to treat asymptomatic carriers. It is difficult to ascertain the cause of symptomatic pharyngitis in carriers of GAS if they do develop symptoms. Clinicians need to differentiate whether the patient is experiencing a repeat GAS infection or a chronic carrier of GAS because laboratory tests will be positive in these patients.[19]

When acute GAS pharyngitis occurs in a carrier, a treatment course of appropriate antibiotics is recommended.[19] Table 130-5 outlines antimicrobials for the eradication of GAS in chronic carriers experiencing symptomatic episodes. In the treatment of recurring episodes of culture-positive GAS pharyngitis, there are several alternative antibiotics which are preferred over penicillin or amoxicillin with GAS carriers. 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.[19]

Factors that should be considered when personalizing therapy for a patient include allergy status, prior antibiotic use, and adherence. Those with a history of antibiotic use for acne may be at higher risk for resistant strains of GAS. Short-course antibiotics or penicillin G benzathine may be considered in patients with a history of nonadherence. Supportive care should be offered to all patients with acute pharyngitis including antipyretic medications, analgesics, and nonprescription lozenges and sprays containing menthol and topical anesthetics for temporary relief of pain.[19] There are limited data for use of corticosteroids to reduce the symptoms of GAS pharyngitis, and given the risk of adverse effects, their use is not recommended.[19] Because pain is often the primary reason for visiting a physician, emphasis on analgesics such as acetaminophen and nonsteroidal anti-inflammatory drugs to aid in pain relief is strongly recommended.

Patient Care Process

Patient Care Process for Acute Pharyngitis

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 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

- 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*

- Select drug therapy regimen including specific antibiotic, dose, route, frequency, and duration; specify the continuation and discontinuation of existing therapies (see Tables 130-4 and 130-5)
- 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

Implement*

- 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

- 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.***

Evaluation of Therapeutic Outcomes

Most pharyngitis cases are self-limited; however, antibiotics hasten resolution when given early for proven cases of GAS pharyngitis.[19] Generally, fever and other symptoms resolve within 3 to 4 days of onset without antibiotics; however, symptoms will improve 0.5 to 2.5 days earlier with antibiotic therapy.[19] Follow-up testing is generally not necessary for index cases or asymptomatic contacts[19]; however, throat cultures 2 to 7 days after completion of antibiotics are warranted for patients who remain symptomatic or when symptoms recur despite completion of treatment.[19]

ABBREVIATIONS

AAO-HNSF	American Academy of Otolaryngology—Head and Neck Surgery Foundation
AAP	American Academy of Pediatrics
ACIP	Advisory Committee on Immunization Practices
GAS	group A β-hemolytic streptococci
GI	gastrointestinal
IDSA	Infectious Diseases Society of America
IgE	immunoglobulin E
IM	intramuscular
IV	intravascular
MIC	minimal inhibitory concentration
MRSA	methicillin-resistant *Staphylococcus aureus*
PCV7	seven-valent pneumococcal conjugate vaccine
RADT	rapid antigen-detection test
T tube	tympanostomy tube
URI	upper respiratory infection

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SELF-ASSESSMENT QUESTIONS

1. Which of the following are recommended before taking an *initial observation* approach in a patient with acute otitis media?

   A. Temperature less than 39°C (102.2°F).

   B. Joint decision-making with patients and caregivers.

   C. Action plan to administer antibiotics if symptoms worsen within 48 to 72 hours.

   D. All of the above must be in place before recommending initial observation.

2. Which of the following characteristics can help differentiate between acute otitis media and otitis media with effusion?

   A. Middle ear effusion.

   B. Cough.

   C. Ear pain.

   D. Two of the above are correct.

3. Which of the following is considered to be a first-line recommendation for the treatment of a 1-year-old child with acute otitis media and a fever of 103°F (39.4 °C)?

   A. Azithromycin

   B. Amoxicillin

   C. Ceftriaxone

   D. Cefuroxime

4. A child with moderate symptoms of acute otitis media returns to clinic after taking amoxicillin for 4 days without improvement, which of these alternatives would you recommend?

   A. Amoxicillin-clavulanate

   B. Trimethoprim-sulfamethoxazole

   C. Ceftriaxone

   D. Erythromycin-sulfisoxazole

5. Which of the following vaccines can help prevent episodes of acute otitis media?

   A. Pneumococcal conjugate vaccine.

   B. Seasonal influenza vaccine.

C. Tetanus, diphtheria, and pertussis vaccine.

D. Two of the above are correct.

6. Which of the following patients should receive amoxicillin-clavulanate instead of amoxicillin for acute otitis media?

A. Patient who received amoxicillin for another infection 2 weeks prior to this visit.

B. Patient with purulent conjunctivitis and acute otitis media.

C. Both of these patients should receive amoxicillin-clavulanate instead of amoxicillin.

D. Neither of these patients should receive amoxicillin-clavulanate instead of amoxicillin.

7. Which of the following is the most common pathogen in acute rhinosinusitis?

A. Viruses

B. Streptococcus pneumoniae

C. Haemophilus influenzae

D. Moraxella catarrhalis

8. Which of the following is suggestive of bacterial versus viral rhinosinusitis?

A. Persistent symptoms for 10 days or more.

B. Worsening of symptoms after 7 days.

C. Lack of symptomatic response to nonprescription nasal decongestants.

D. Two or more of the above are correct.

9. Which of the following is considered to be a first-line recommendation for the treatment of a 68-year-old man with a 2-week history of persistent nasal congestion and sinus pain? The man received 10 days of clindamycin when he was hospitalized for a skin abscess 2 months ago.

A. Amoxicillin-clavulanate

B. Clarithromycin

C. Levofloxacin

D. Amoxicillin

10. Which of the following nonprescription medications is recommended for the management of patients with acute bacterial rhinosinusitis?

A. Nasal antihistamine.

B. Oral antihistamine.

C. Nasal decongestant.

D. None of the above are recommended for a patient with acute bacterial rhinosinusitis.

11. A 10-year-old male presents to the pediatrician's office with severe throat pain and dysphagia. His highest temperature was 99.9°F (37.7°C). During the physical exam, he is found to have swollen tonsils but no swelling of the anterior cervical nodes. Based on the above information, when is antibiotic therapy recommended?

A. Clinical criteria present

B. Clinical criteria present and RADT test positive

C. Clinical criteria present and laboratory results pending

D. B and C

12. Which of the following is NOT consistent with the clinical presentation of GABHS pharyngitis.

A. Enlarged, tender lymph nodes

B. Sore throat

C. No cough

D. Conjunctivitis

13. A local daycare reports several cases of GABHS pharyngitis. How many days must pass before the risk of additional cases is no longer a concern?

A. 1 day

B. 5 days

C. 10 days

D. 14 days

14. The most appropriate therapy for a young adult (weighing 70 kg) diagnosed with GABHS pharyngitis and has a penicillin allergy (anaphylaxis) is:

A. Tetracycline 500 mg PO BID for 10 days

B. Levofloxacin 750 mg PO daily for 10 days

C. Penicillin V 500 mg PO twice daily for 10 days

D. Azithromycin 500 mg PO once daily for one day, then 250 mg once daily for 4 days

15. A 9-year-old female (weighing 30 kg) is diagnosed with pharyngitis. Which of the following is most appropriate?

A. Amoxicillin suspension 400 mg / 5 mL: Take 12.5 mL PO once daily for 10 days

B. Clindamycin hydrochloride 75 mg capsules: Take three capsules PO thrice daily for 10 days

C. Sulfamethoxazole-trimethoprim 200 mg / 40 mg per 5 mL oral suspension: Take three teaspoonfuls PO twice daily for 5 days

D. Penicillin benzathine 0.6 million units IM: Administer one dose

SELF-ASSESSMENT QUESTION-ANSWERS

1. **D.** Initial observation approach for acute otitis media should all be based on join decision making with patients/caregivers, have a plan to initiate antibiotics if symptoms worsen or decline within 48 to 72 hours of symptom onset, and can be considered for:
    - Children 6 months and older with nonsevere unilateral acute otitis media without otorrhea
    - Children 24 months and older with bilateral acute otitis media without otorrhea

- Patients with temperatures of less than 39°C (102.2°F)

2. **C.** Otitis media with effusion is characterized by fluid in the middle ear without signs and symptoms of acute ear infection, such as pain and a bulging eardrum.

3. **B.** High-dose amoxicillin (80-90 mg/kg/day in two divided doses) is recommended for most pediatric patients with acute otitis media.

4. **A.** Clinicians should reassess all plans if the child's symptoms worsen or decline within 48 to 72 hours. First-line treatment for treatment failure at 48-72 hours is amoxicillin-clavulanate.

5. **D.** The pneumococcal conjugate vaccine and annual influenza vaccination have shown to decrease risk of acute otitis media.

6. **C.** Children who have received amoxicillin in the last 30 days, have concurrent purulent conjunctivitis, or have a history of recurrent infection unresponsive to amoxicillin should receive amoxicillin-clavulanate instead due to likely resistant infection with the presence of a β-lactamase.

7. **A.** Majority of acute rhinosinusitis infectious are viral in origin.

8. **D.** Viral rhinosinusitis typically improves in 7 to 10 days. In contrast, acute bacterial rhinosinusitis symptoms persist for 10 days or greater without improvement or with worsening symptoms after 10 days or can manifest worsening after initial improvement ("double-sickness" pattern). Acute bacterial rhinosinusitis may also be suspected if the patient has severe symptoms at the beginning of his/her illness.

9. **A.** Amoxicillin-clavulanate is considered the first-line treatment for acute bacterial rhinosinusitis in children and adults according to IDSA guidelines. The patient is also likely to be experiencing a resistant bacterial rhinosinusitis infection due to recent antibiotic treatment and hospitalization with a 2-week history of persistent symptoms.

10. **D.** Topical or oral decongestants or antihistamines are generally not recommended as adjunctive treatment for acute bacterial rhinosinusitis. These agents can dry mucosa and disturb clearance of mucosal secretions.

11. **B.** Patient presents symptoms meeting clinical criteria for acute pharyngitis per severe throat pain, dysphagia, fever, and swollen tonsils. Antibiotic therapy is recommended only for those with a positive test for GAS usually confirmed by a RADT.

12. **D.** GAS pharyngitis symptoms:

    - Soar 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 or purple spots on the soft palate and scarlatiniform rash

    Signs of viral origin pharyngitis

    - Conjunctivitis
    - Coryza
    - Cough

13. **B.** The incubation period of GAS pharyngitis ranges from 2 to 5 days; therefore, the risk of additional cases is no longer a concern after 5 days.

14. **D.** Due to prevalence of resistance, tetracyclines, sulfonamides, and trimethoprim-sulfamethoxazole are not recommended for GAS pharyngitis. Newer fluoroquinolones have activity against GAS but are expensive and have an unnecessarily broad spectrum of activity. Azithromycin is an appropriate treatment for patients with penicillin allergy; however, local susceptibilities should be considered before recommending this medication.

15. **A.** Penicillin V and amoxicillin are the treatment of choice for acute pharyngitis due to having a narrow spectrum of activity and are readily available, safe, and inexpensive. However, amoxicillin is often used instead of penicillin V due to the suspension being more palatable. Penicillin benzathine is also an option but not favored due to causing more pain from administrating intramuscularly.