Chapter 45: Respiratory Tract Infections, Upper

ACUTE OTITIS MEDIA

- *Otitis media* is an inflammation of the middle ear that is most common in infants and children. There are three subtypes of otitis media: acute otitis media, otitis media with effusion, and chronic otitis media. The three are differentiated by (a) acute signs of infection, (b) evidence of middle ear inflammation, and (c) presence of fluid in the middle ear.

Pathophysiology

- Bacteria have been found in more than 90% of cases of otitis media. Common bacterial pathogens include *Streptococcus pneumoniae*, nontypeable *Haemophilus influenzae*, and *Moraxella catarrhalis*.
- 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.
- Many *S. pneumoniae* isolates in the United States are penicillin nonsusceptible, and most nonsusceptible strains have high-level penicillin resistance.
- Many *H. influenzae* isolates and nearly all *M. catarrhalis* isolates, from the upper respiratory tract, produce β-lactamases.

Clinical Presentation

- Acute otitis media is characterized as acute onset of otalgia (ear pain). Irritability and tugging on the ear are often the first clues that a child has acute otitis media.
- 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.
- Nonverbal children with ear pain might hold, rub, or tug their ear. Very young children might cry, be irritable, and have difficulty sleeping. Signs and symptoms include bulging of the tympanic membrane, otorrhea, otalgia (considered to be moderate or severe if pain lasts at least 48 hours), and fever (considered to be severe if temperature is 39°C [102.2°F] or higher).

Treatment

- Goals of Treatment: Pain management, prudent antibiotic use, and secondary disease prevention. Acute otitis media should first be differentiated from otitis media with effusion or chronic otitis media.
- Primary prevention of acute otitis media with pneumococcal conjugate vaccine and annual influenza vaccine are recommended for all children.
- Pain of otitis media should be addressed with oral analgesics. **Acetaminophen** or a nonsteroidal anti-inflammatory agent, such as **ibuprofen**, should be offered early to relieve pain of acute otitis media.
- Children 6 months–12 years of age, with moderate-to-severe ear pain or temperature of 39°C (102.2°F) or higher should receive antibiotics. Children 6–23 months of age, with nonsevere bilateral acute otitis media should also receive antibiotics. Children 6–23 months, with nonsevere unilateral acute otitis media, and children 24 months–12 years of age, with nonsevere acute otitis media, may receive initial antibiotics or initial observation without antibiotics.

- 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.
- High-dose **amoxicillin** (80–90 mg/kg/day) is recommended for most children. 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 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.
- Antibiotic treatment recommendations for acute otitis media are given in **Table 45-1**.
- If treatment failure occurs with amoxicillin, an agent should be chosen with activity against β-lactamase-producing *H. influenzae* and *M. catarrhalis*, as well as drug-resistant *S. pneumoniae*, such as high-dose amoxicillin–clavulanate (recommended) or **cefuroxime**, **cefdinir**, **cefpodoxime**, or intramuscular or intravenous **ceftriaxone**.
- Traditional recommendations call for 10 days of antibiotic therapy. In children at least 6 years old who have mild-to-moderate acute otitis media, a 5- to 7-day course of antibiotics may be used. Short-course treatment is not recommended in children younger than 2 years of age.
- Surgical insertion of tympanostomy tubes (T tubes) is an effective method for preventing recurrent otitis media. Patients with acute otitis media should be reassessed after 48–72 hours, with most children being asymptomatic at 7 days.

TABLE 45-1

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 in two divided doses), cefpodoxime (10 mg/kg/day orally in two divided doses)	Second line or nonsevere penicillin allergy
Ceftriaxone (1–3 days)	Rocephin®	50 mg/kg/day IM or IV 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 (1–3 days)	Rocephin®	50 mg/kg/day IM or IV for 3 days	First line or nonsevere penicillin allergy
Clindamycin	Cleocin®	30–40 mg/kg/day orally in three divided doses ± second- or third-generation cephalosporin	Second line or nonsevere penicillin allergy

[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.

IM, intramuscular; IV, intravenous; po, orally.

PHARYNGITIS

- *Pharyngitis* is an acute infection of the oropharynx or nasopharynx that is responsible for 6% of visits by children to their primary care provider annually. Although viral causes are most common, group A β-hemolytic *Streptococcus* (GABHS) is the primary bacterial cause.
- Viruses (eg, rhinovirus, coronavirus, and adenovirus) cause most of the cases of acute pharyngitis. A bacterial etiology for acute pharyngitis is far less likely. Of all of the bacterial causes, GABHS is the most common (10%–30% of cases in pediatric patients and 5%–15% in adults).

- Suppurative and nonsuppurative complications include acute rheumatic fever, acute glomerulonephritis, reactive arthritis, peritonsillar abscess, retropharyngeal abscess, cervical lymphadenitis, mastoiditis, otitis media, rhinosinusitis, and necrotizing fasciitis.

Clinical Presentation

- The most common symptom of pharyngitis is sore throat of sudden onset that is mostly self-limited.
- Fever and constitutional symptoms resolve in about 3–5 days.
- Signs and symptoms of GABHS pharyngitis include sore throat; pain on swallowing; fever; headache; nausea; vomiting; and abdominal pain (especially in children); erythema/inflammation of the tonsils and pharynx with or without patchy exudates; enlarged; tender lymph nodes; red swollen uvula; petechiae on the soft palate; and a scarlatiniform rash.
- Signs suggestive of viral origin for pharyngitis include conjunctivitis, coryza, and cough.
- Diagnosis can be confirmed by throat swab and culture and a rapid antigen-detection test (RADT).

Treatment

- Goals of Treatment: Improve clinical signs and symptoms, minimize adverse drug reactions, prevent transmission to close contacts, and prevent acute rheumatic fever and suppurative complications such as peritonsillar abscess, cervical lymphadenitis, and mastoiditis.
- Antimicrobial therapy should be limited to those who have clinical and epidemiologic features of GABHS pharyngitis, preferably with a positive laboratory test.
- Because pain is often the primary reason for visiting a physician, emphasis on analgesics such as **acetaminophen** and nonsteroidal anti-inflammatory drugs (NSAIDs) to aid in pain relief is strongly recommended.
- **Penicillin** and **amoxicillin** are the treatments of choice. Antimicrobial treatment should be limited to those who have clinical and epidemiologic features of GABHS pharyngitis with a positive laboratory test (**Table 45-2**). **Table 45-3** presents antibiotics and doses for eradication of GABHS in chronic carriers. The duration of therapy for GABHS pharyngitis is 10 days, except for **benzathine penicillin** and **azithromycin**, to maximize bacterial eradication. However, 3–6 days of oral antibiotics has comparable efficacy to oral **penicillin** for 10 days.
- **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.
- Most cases of pharyngitis are self-limited; however, antimicrobial therapy will hasten resolution when given early to proven cases of GABHS. Symptoms generally resolve by 3 or 4 days even without antibiotics; however, symptoms will improve 0.5–2.5 days earlier with antibiotic therapy. Follow-up testing is generally not necessary for index cases or in asymptomatic contacts of the index patient; however, throat cultures 2–7 days after completion of antibiotics are warranted for patients who remain symptomatic or when symptoms recur despite completion of treatment.

TABLE 45-2

Antibiotics and Doses for Group A β-Hemolytic Streptococcal Pharyngitis

Antibiotic	Brand Name	Dose	Duration	Rating
Preferred antibiotics if no penicillin allergy				
Penicillin V	Pen-V	Children: 250 mg twice daily or three times daily orally; adult: 250 mg four times daily or 500 mg twice daily orally	10 days	IB
Penicillin G benzathine	Bicillin L-A	<27 kg: 0.6 million units; 27 kg or greater: 1.2 million units intramuscularly	One dose	IB
Amoxicillin[a]	Amoxil	50 mg/kg once daily (maximum 1000 mg); 25 mg/kg (maximum 500 mg) twice daily	10 days	IB
Penicillin allergy				
Cephalexin	Keflex	20 mg/kg/dose orally twice daily (maximum 500 mg/dose)	10 days	IB
Cefadroxil	Duricef	30 mg/kg orally once daily (maximum 1 g)	10 days	IB
Clindamycin	Cleocin	7 mg/kg/dose orally thrice daily (maximum 300 mg/dose)	10 days	IIaB
Azithromycin[b]	Zithromax	12 mg/kg orally once daily (maximum 500 mg) for 1 day, then 6 mg/kg orally once daily (maximum 250 mg) for 4 days	5 days	IIaB
Clarithromycin[b]	Biaxin	15 mg/kg orally per day divided in two doses (maximum 250 mg twice daily)	10 days	IIaB

[a]Standard formulation, not extended release.

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

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).

TABLE 45-3

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

Antibiotic	Brand Name	Dose
Clindamycin	Cleocin	20–30 mg/kg/day orally in three divided doses (maximum 300 mg/dose)
Amoxicillin–clavulanate	Augmentin	40 mg/kg/day orally in three divided doses (maximum 2000 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 2000 mg/day); *and* rifampin: 20 mg/kg/day orally in one dose for the last 4 days of treatment (maximum 600 mg/day)
Penicillin G benzathine and rifampin	Bicillin L-A, Rifadin	Penicillin G benzathine: <27 kg—0.6 million units; 27 kg or greater: 1.2 million units intramuscularly; *and* rifampin: 20 mg/kg/day orally in two doses during last 4 days of treatment with penicillin (maximum 600 mg/day)

ACUTE BACTERIAL RHINOSINUSITIS

- *Sinusitis* is an inflammation and/or infection of the paranasal sinuses, or membrane-lined air spaces, around the nose. The term *rhinosinusitis* is now preferred, because sinusitis typically also involves the nasal mucosa. The majority of these infections are viral in origin. It is important to differentiate between viral and bacterial sinusitis to aid in optimizing treatment decisions.
- Acute bacterial sinusitis is most often caused by the same bacteria implicated in acute otitis media: *S. pneumoniae* and *H. influenzae.* These organisms are responsible for ~50%–70% of bacterial causes of acute sinusitis in both adults and children.

Clinical Presentation

- There are three clinical presentations that are most consistent with acute bacterial vs viral rhinosinusitis: 1) Onset with *persistent* signs or symptoms compatible with acute rhinosinusitis, lasting for ≥10 days without any evidence of clinical improvement; 2) 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 3–4 consecutive days at the beginning of illness; 3) Onset with *worsening* signs or symptoms characterized by new-onset fever, headache, or increase in nasal discharge following a typical viral URI that lasted 5–6 days and were initially improving (“double sickening”).
- Signs and symptoms of bacterial rhinosinusitis include 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.

Treatment

- Goals of Treatment: Reducing signs and symptoms, achieving and maintaining patency of the ostia, limiting antimicrobial treatment to those who may benefit, eradicating bacterial infection with appropriate antimicrobial therapy, minimizing the duration of illness, preventing complications, and preventing progression from acute disease to chronic disease.
- Nasal decongestant sprays such as **phenylephrine** and **oxymetazoline** that reduce inflammation by vasoconstriction are often used in nonbacterial rhinosinusitis. Use should be limited to the recommended duration of the product (no more than 3 days) to prevent development of tolerance and/or rebound congestion. Oral decongestants may also aid in nasal or sinus patency. Irrigation of the nasal cavity with saline and steam inhalation may be used to increase mucosal moisture, and mucolytics (eg, guaifenesin) may be used to decrease the viscosity of nasal

secretions. Antihistamines and oral decongestants should not be used for acute bacterial sinusitis in view of their anticholinergic effects that can dry mucosa and disturb clearance of mucosal secretions.

- **Amoxicillin–clavulanate** is first-line treatment for acute bacterial rhinosinusitis. The approach to treating acute bacterial rhinosinusitis in children and adults is given in **Tables 45-4** and **45-5**.
- High-dose amoxicillin–clavulanate is preferred 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. Doxycycline is also second line for adults but should be avoided in children.
- The duration of antimicrobial therapy for acute bacterial rhinosinusitis is not well established. Most trials have used 10- to 14-day antibiotic courses for uncomplicated rhinosinusitis. For adults, the recommended duration is 5–7 days.
- If symptoms persist or worsen after 48–72 hours of appropriate antibiotic therapy, then the patient should be reevaluated and alternative antibiotics should be considered.

TABLE 45-4

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) plus cefixime (8 mg/kg/day orally twice daily) or cefpodoxime (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	

TABLE 45-5

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®	2000 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®	2000 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	

See Chapter 126, Upper Respiratory Tract Infections, authored by Christopher Frei and Bradi Frei, for a more detailed discussion of this topic.