

Common Infective Disease Upper Respiratory Tract Infection

Far Eastern Memorial Hospital
Pharmacy
Wang Ming-Shyan

Outline

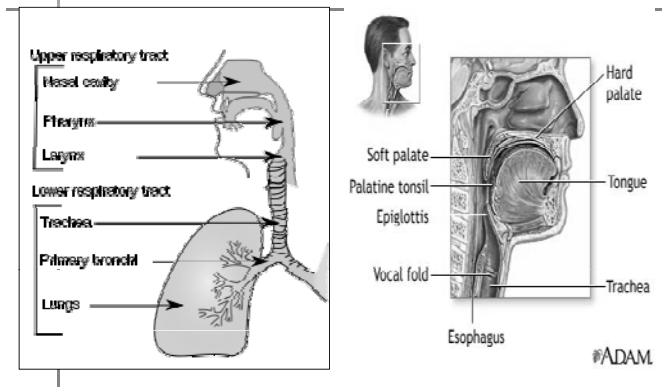
- Definitions
 - ✓ Otitis media, Sinusitis, Pharyngitis, Laryngitis(Croup), Rhinitis, Epiglottitis
- Epidemiology
- Pathophysiology and Microbiology
- Signs and Symptoms
- Treatment

Pharmacotherapy (A Pathophysiologic Approach) 7th Edition

Upper Respiratory Tract Infection

- URTI ; URI
 - ✓ Common acute illness in the outpatient
 - ✓ From the common cold (typically a mild, self-limited, catarrhal syndrome) to life-threatening illnesses (epiglottitis)
 - ✓ Include the nasal passages, sinuses, pharynx, and larynx (as gateways to the trachea)

Respiratory Anatomy



Common URI terms (Local Inflammation and Infection)

- Otitis media : middle ear
- Sinusitis : nares, paranasal sinuses, including frontal, ethmoid, maxillary, sphenoid
- Pharyngitis : pharynx, hypopharynx, uvula, tonsils
- Laryngitis(Croup) : larynx
- Rhinitis : nasal mucosa
- Epiglottitis : the superior portion of the larynx and supraglottic area

Epidemiology

- Transmission is via respiratory droplets or by contaminated hands (person-to-person)
 - ✓ facilitate the spread : inflammation causes increased secretions, rhinorrhea and results in sneezing, and coughing
- Majority of antibiotics prescribed in ambulatory practice and the cost¹
- Estimated cost of otitis media was \$3-4 billion in the USA, and \$600 million in Canada²

1. Ann Intern Med 2001;134:487-9
2. J Otolaryngol 1998;27(Suppl 2):9-16

Incidence

- Sinusitis/Rhinosinusitis
 - ✓ Common in persons with viral URIs
 - ✓ Bacterial rhinosinusitis is a complication in only approximately 2% of persons with viral URIs¹
- Epiglottitis
 - ✓ Occurs at a rate of 6-14 cases per 100,000 children²
 - ✓ Typically occurs in children aged 2-7 years and has a peak incidence in those aged 3 years³
 - ✓ Estimated to occur at annual incidence of 9.7 cases per million adults⁴
 - ✓ Decreased dramatically in USA since the introduction of the *Haemophilus influenzae* type B (Hib) vaccine

1. Centers for Disease Control and Prevention : April 30, 2009
2. Grand rounds archives: pediatric otolaryngology : 1993
3. Am Fam Physician 1999;60(8):2289-96
4. N Engl J Med 1986;314(18):1133-9

Incidence

- Otitis media
 - ✓ Common in infants and children
 - ✓ 75% of whom had at least one episode by the age of 1 year¹
- Pharyngitis
 - ✓ Acute pharyngitis accounts for 1% of all ambulatory office visits²
 - ✓ The incidence of viral and bacterial pharyngitis peaks in children aged 4-7 years
- Nasopharyngitis(common cold)
 - ✓ Incidence varies by age
 - ✓ Rates are highest in children < 5 years
 - ✓ Children who attend school or daycare are a large reservoir for URIs
 - ✓ About 3-8 viral respiratory illnesses per year

1. Pediatr Infect Dis J 1998;17:1103-13
2. National Ambulatory Medical Care Survey: 2006

Incidence

- Laryngitis and laryngotracheitis
 - ✓ Usually occurs in children aged 6 mons to 6 yrs (2-5 yrs)¹
 - ✓ Vaccination has dramatically reduced rates of pertussis, including whooping cough
 - ✓ The incidence of whooping cough cases in the United States has increased in recent years
 - 5.3 cases(adolescents and infants <5 mons) per 100,000 population in 2006²
 - ✓ In 2004, adults (19-64 yrs) accounted for 7,008 (27%) of 25,827 reported cases of pertussis in USA

1. Am Fam Physician 1999;60(8):2289-96
2. Health United States, 2008 With Chartbook

Incubation Period

- Rhinoviruses and group A streptococci : 1-5 days
- Influenza and parainfluenza : 1-4 days
- Respiratory syncytial virus (RSV) : for a week
- Epstein-Barr virus (EBV) : 4-6 weeks
- Pertussis : 7-10 days or even as long as 21 days before causing symptoms
- Diphtheria : 1-10 days

Pathophysiology and Microbiology

- Most nonspecific upper respiratory tract infections have a viral, not bacterial^{1,2}
 - ✓ Resolve spontaneously
 - ✓ Limiting unnecessary antibiotic use
- Otitis media, sinusitis, pharyngitis
 - ✓ Bacterial in origin
 - ✓ Appropriate antibiotic treatment can minimize morbidity and potentially prevent complications

1. Ann Intern Med 2001;134:490-4
2. Drugs 2001;61:2065-77

Otitis Media

- Diagnosis of acute otitis media
 - ✓ Includes signs and symptoms of infection (otalgia, fever, presence of fluid)
 - ✓ In otitis media with effusion, but signs and symptoms of infection are absent
 - ✓ Risk factors for bacterial otitis media caused by resistant pathogens
 - Day-care attendance
 - Recent antibiotic exposure
 - Age younger than 2 yrs
 - Frequent bouts of otitis media

Risk Factors for Otitis Media

- Winter season/outbreaks of respiratory syncytial or influenza virus
- Attendance at day care centers
- Lack of breast-feeding in infants
- Aboriginal or Inuit origin
- Early age of first diagnosis
- Nasopharyngeal colonization with middle ear pathogens
- Genetic predisposition
- Siblings in the home
- Lower socioeconomic status
- Exposure to tobacco smoke
- Use of a pacifier
- Male gender
- Immunodeficiency
- Allergy
- Urban population

1. *Pediatr Infect Dis J* 1998;17:1103-13
2. *Clin Pediatr* 2002;41:373-90

Pathophysiology

- Acute otitis media (AOM)
 - ✓ Viral upper respiratory tract infection
 - Eustachian tube dysfunction and mucosal swelling in the middle ear
 - ✓ Bacteria (by mucociliary system¹)
 - Colonize the nasopharynx thus enter the middle ear
 - Effusion (bacteria proliferate and infection)
 - ✓ Children are more susceptible than adults
 - The anatomy of their eustachian tube is shorter and more horizontal²

1. *N Engl J Med* 2002;347:1169-74
2. *Clin Pediatr* 2002;41:373-90

Microbiology

- Most common bacterial cause of AOM
 - ✓ *S. pneumoniae* : 20-35%¹
 - ✓ *Haemophilus influenzae* : 20-30%
 - ✓ *Moraxella catarrhalis* : 20%
- No bacterial pathogen is found (in 20-30% of cases)²
 - ✓ A viral etiology is found with or without concomitant bacteria

1. *Pediatr Infect Dis J* 1999;18:1-9
2. *N Engl J Med* 2002;347:1169-74

Clinical Presentation of Acute Bacterial Otitis Media

General

The acute onset of signs and symptoms of middle ear infection following cold symptoms of runny nose, nasal congestion, or cough

Signs and symptoms

Pain that can be severe (more than 75% of patients)
Children may be irritable, tug on the involved ear, and have difficulty sleeping
Fever is present in less than 25% of patients and, when present, occurs more often in younger children
Examination shows a discolored (gray), thickened, bulging eardrum
Pneumatic otoscopy or tympanometry demonstrates an immobile eardrum; 50% of cases are bilateral
Draining middle ear fluid occurs (less than 3% of patients) that usually reveals a bacterial etiology

Laboratory tests

Gram stain, culture, and sensitivities of draining fluid or aspirated fluid if tympanocentesis is performed

Treatment of AOM

- Desired outcome
 - ✓ Reduction in signs and symptoms
 - ✓ Eradication of the infection
 - ✓ Prevention of complications
- Avoidance of unnecessary antibiotic prescribing
 - ✓ Because of increasing resistance of *S. pneumoniae*
 - ✓ Antibiotics provide resolution of symptoms in approximately 95% of patients¹
 - 80% of placebo also have a resolution of symptoms
- An appropriate management strategy in correctly diagnosed bacterial AOM

1. *J Pediatr* 1994;124:355-67(meta-analysis)

Delayed Antimicrobial Therapy

- Delayed treatment (wait-and-see)
 - ✓ decreases antibiotic use (30%)
 - ✓ Decreases side effects
 - ✓ Minimizes bacterial resistance
- Eligible population¹
 - ✓ Children ages 6 mons to 2 yrs (not severe)
 - ✓ Others should receive antibiotic therapy
 - severe symptoms, recent antimicrobial exposure, when underlying conditions exist

1. *Pediatrics* 2004;113(5):1451-65

Delayed Antimicrobial Therapy

- Antibiotics should be started
 - ✓ If no improvement in 48-72 hrs
 - ✓ Recommend reevaluation in 24 hrs (in children ages 6 mos to 2 yrs)
- Appropriate pain medication
 - ✓ Oral ibuprofen or acetaminophen
 - ✓ Aware of the symptoms of deterioration, and has easy access to follow up

Antimicrobial Therapy

- Effusion in AOM tends to continue after antimicrobial therapy is completed
 - ✓ BUT does not require retreatment
- The drug of choice – Amoxicillin
 - ✓ Safety, narrow spectrum, inexpensive
 - ✓ High dose (80 to 90 mg/kg/day)
 - Risk for a penicillin-resistant pneumococcal infection
 - ✓ Time above the MIC in the middle ear fluid for more than 40% of the dosing interval

Antimicrobial Therapy

- Amoxicillin
 - ✓ Excellent efficacy against *S. pneumoniae*
 - ✓ Poor to beta-lactamase-producing *H. influenzae* and *M. catarrhalis*
 - BUT easy to a spontaneous resolution
- Amoxicillin-clavulanate
 - ✓ For moderate-severe illness (severe otalgia, and temperature $>39^{\circ}\text{C}$)

Treatment Failure for Amoxicillin

- Against beta-lactamase-producing *H. influenzae* and *M. catarrhalis*, *S. pneumoniae*
 - ✓ High-dose amoxicillin-clavulanate
 - ✓ Cefuroxime, cefdinir, cefpodoxime, cefprozil
 - Expensive
 - Increased incidence of side effects
 - increase selective pressure for resistant bacteria
 - Not adequate middle ear fluid concentrations

Treatment Failure for Amoxicillin

- Intramuscular ceftriaxone
 - ✓ Achieves middle ear fluid concentrations above the MIC for more than 40% of the dosing interval¹
 - ✓ Single doses or daily doses for 3 days
 - 3-day regimen optimizes clinical outcomes²
 - ✓ For severe and unresponsive infections
 - Expensive, IM is painful, possible non-adherence
- Discouraged (high rates of resistance)
 - ✓ Trimethoprim-sulfamethoxazole and erythromycin

Alternative Therapy

- Tympanocentesis
 - ✓ Relieving pain and pressure
 - ✓ Collect fluid to identify causative agents

Patients with Penicillin Allergy

- Not type I hypersensitivity
 - ✓ Cefdinir, cefpodoxime, or cefuroxime¹
- Type I
 - ✓ macrolide (azithromycin) or clarithromycin
- Clindamycin
 - ✓ Coverage of penicillin resistant *S. pneumoniae* (inactive against *H. influenzae*, *M. catarrhalis*)
- High incidence of resistance
 - ✓ Only clindamycin is recommended by the Centers for Disease Control and Prevention (CDC) and American Academy of Pediatrics guidelines

1. Pediatrics 2004;113(5):1451-65

Acute Otitis Media Treatment Recommendations

First Line	Penicillin Allergy	Treatment Failure ^a
Amoxicillin high dose 80-90 mg/kg/day divided twice daily	Non-type I: Cefdinir 14 mg/kg/day once or twice daily Cefuroxime 30 mg/kg/ day divided twice daily Cefpodoxime 10 mg/kg/ day once daily Cefprozil 50 mg/kg/day divided twice daily	Amoxicillin-clavulanate ^a
	Type I: Azithromycin 10 mg/kg/ day 1, then 5 mg/kg/ day for days 2-5 Clarithromycin 15 mg/ kg/day divided twice daily	Ceftriaxone 50 mg/kg/ day IM/IV for 3 days
If severe symptoms (severe otalgia and temperature above 39°C [102.2°F])		Alternatives: Clindamycin 30-40 mg/ kg/day in 3 divided doses
Amoxicillin-clavulanate ^a		Tympanocentesis

Short Courses of Therapy

- Short courses of antibiotics
 - ✓ No difference in cure rates after short (<7 days) and usual durations (≥7 days) in children (meta-analysis of 32 trials)¹
- Limitations
 - ✓ Inadequate study sample sizes, lack of use of standardized diagnostic criteria, and sub-therapeutic doses
- The advantages of short-term therapy
 - ✓ Increased likelihood the patient will adhere to the full course of treatment
 - ✓ Decreased side effects and cost
 - ✓ Decreased bacterial selective pressure for both the individual and the community
- In children at least 6 yrs old (mild to moderate AOM), a 5- to 7-day course may be used
 - ✓ Not recommended in <2 yrs old

1. Cochrane Database Syst Rev 2000;(2):CD001095

Antibiotic Prophylaxis of Recurrent Infections

- Recurrent otitis media
 - ✓ Defined as at least 3 episodes in 6 mons or at least 4 episodes in 12 mons
 - ✓ <3 yrs old is at high risk for hearing loss and language and learning disabilities¹
- A meta-analysis demonstrated that prophylaxis prevents one infection each time one child is treated for 9 mons²

1. Pediatr Infect Dis J 1996;15:854-8
2. JAMA 1993;270:1344-51

Vaccination

- Vaccination against influenza and pneumococcus
 - ✓ Immunization with the influenza vaccine
 - 36% reduction in the incidence of AOM¹
 - ✓ Conjugate pneumococcal vaccine
 - 6% reduction in the frequency of AOM in infants and children²
 - ✓ 10-26% decrease in otitis media episodes in children who experienced 3-10 infections per year³
 - ✓ Do not benefit from later vaccination⁴
 - Previously unvaccinated children who are > 1 yr old and who have recurrent otitis media infections

1. Am J Dis Child 1991;145:445-8
2. N Engl J Med 2001;344:403-9
3. Pediatr Infect Dis J 2003;22:10-5
4. Lancet 2003;361:2189-95

Sinusitis

- Sinusitis
 - ✓ Inflammation and/or infection of the paranasal sinus mucosa
 - ✓ Viral and bacterial sinusitis are difficult to differentiate (similar presentations)
 - Viral infections resolve by 7-10days
 - Bacterial infection : persistence of symptoms or worsening of symptoms¹
 - ✓ Acute bacterial sinusitis lasts less than 30 days with complete resolution of symptoms
 - ✓ Chronic sinusitis : inflammation lasting >3 mons with persistence of respiratory symptoms

Clinical Presentation and Diagnosis of Bacterial Sinusitis

- No one sign can accurately diagnose
 - ✓ Gold standard-sinus aspiration
 - >10⁵ organisms/mL
 - ✓ 5-13% of viral URI in children are complicated by bacterial sinusitis
 - Only 0.5-2% in adults
- Other factors associated with sinus disease
 - ✓ Allergic inflammation, systemic diseases, trauma, environmental exposures, and anatomic abnormalities

Clinical Presentation and Diagnosis of Bacterial Sinusitis

General

A nonspecific upper respiratory tract infection that persists beyond 7 to 14 days

Signs and symptoms

Acute

Adults

Nasal discharge/congestion

Maxillary tooth pain, facial or sinus pain that may radiate (unilateral in particular) as well as deterioration after initial improvement

Severe or persistent (beyond 7 days) signs and symptoms are most likely bacterial and should be treated with antimicrobials

Children

Nasal discharge and cough for greater than 10 to 14 days or severe signs and symptoms such as temperature above 39°C (102.2°F) or facial swelling or pain are indications for antimicrobial therapy

Chronic

Symptoms are similar to acute sinusitis but more nonspecific

Rhinorrhea is associated with acute exacerbations

Chronic unproductive cough, laryngitis, and headache may occur

Chronic/recurrent infections occur three to four times a year and are unresponsive to steam and decongestants

Pathophysiology

- Bacterial sinusitis
 - ✓ Usually precede by a viral respiratory tract infection that causes mucosal inflammation
 - Lead to obstruction of the sinus ostia (pathways that drain the sinuses)
 - Mucosal secretions become trapped
 - Local defenses are impaired and bacteria from adjacent surfaces begin to proliferate
- Chronic sinusitis
 - ✓ Caused by more persistent pathogens or there is a subtle defect in the host's immune function
 - ✓ Some patients develop chronic symptoms after their acute infection

Microbiology

- Viruses are responsible for most cases of acute sinusitis
 - ✓ Persistent symptoms (≥7 days) or severe
 - Primary or secondary bacteria infection
- Bacterial in origin (the same in AOM)
 - ✓ *S. pneumoniae* and *H. influenzae*
 - Approximately 70% of bacterial causes of acute sinusitis in both adults and children¹
 - 25% of bacterial causes in children are *M. catarrhalis*
- *S. pyogenes*, *S. aureus*, *fungi*, and anaerobes are associated less frequently

Treatment of Sinusitis

- The goals of treatment of acute sinusitis
 - ✓ Reduction in signs and symptoms
 - ✓ Achieving and maintaining patency of the ostia
 - ✓ Eradicating bacterial infection with appropriate antimicrobial therapy
 - ✓ Minimizing the duration of illness
 - ✓ Preventing complications
 - ✓ Preventing progression from acute to chronic
- Approximately 65% of patients with acute sinusitis (viral) will recover spontaneously

Supportive Therapy

- Nasal decongestant sprays
 - ✓ Reduce inflammation by vasoconstriction
 - ✓ Phenylephrine and oxymetazoline
 - ✓ To limit duration of the product in order to prevent rebound congestion
- Irrigation of nasal cavity with saline and steam inhalation
 - ✓ Increase mucosal moisture and mucolytics
 - ✓ Decrease the viscosity of nasal secretions

Ann Intern Med 2001;134:498-505
Update on Acute Bacterial Rhinosinusitis. Summary, Evidence Report/Technology Assessment: June 2005

Supportive Therapy

- Antihistamines
 - ✓ NOT be used for acute bacterial sinusitis¹
 - Anticholinergic effects that can dry mucosa and disturb clearance of mucosal secretions
 - ✓ Second-generation antihistamines may play a role in chronic sinusitis (allergy)
- Intranasal glucocorticoids
 - ✓ Decrease inflammation causing headache, nasal congestion, and facial pain²
 - ✓ There is little data in acute sinusitis

1. Am Fam Phys 2004;70:1697-1704, 1711-12
2. J Allergy Clin Immunol 2005;116:1289-95

Antimicrobial Therapy

- Antimicrobial therapy (vs placebo)¹
 - ✓ Superior in reducing or eliminating symptoms in acute sinusitis
 - ✓ Reduction in clinical failure of 25-30%
 - ✓ No difference between cure rates, clinical improvement, or relapse rates was noted between different antibiotics
- Amoxicillin is first-line treatment for acute bacterial sinusitis

Patients with Penicillin Allergy

- Alternative antibiotics
 - ✓ Trimethoprim-sulfamethoxazole, doxycycline, azithromycin, clarithromycin
- Respiratory fluoroquinolone
 - ✓ Increasing resistance to trimethoprim-sulfamethoxazole and macrolides
 - ✓ Fluoroquinolones also should be restricted¹
 - Recently received antibiotics, those with severe disease, drug-resistant *S. pneumoniae*
- Not IgE-mediated reaction (hives or anaphylaxis)
 - ✓ A second-generation cephalosporin is initially recommended (cefprozil, cefuroxime, cefpodoxime)

1. Med Lett Drugs Ther 2005;47(1218):78-80
2. Pediatrics 2001;108:798-808

Treatment Failure with Amoxicillin

- Treatment failure
 - ✓ No improvement in symptoms 72 hrs after therapy or received antibiotics in the prior 4-6 wks (coverage of *H. influenzae* and *M. catarrhalis*)
 - ✓ High-dose amoxicillin plus clavulanate or a beta-lactamase-stable cephalosporin¹
 - ✓ Other alternatives : trimethoprim-sulfamethoxazole, cefdinir, azithromycin, clarithromycin²
- Local-area resistance must be considered

1. Otolaryngol Head Neck Surg Suppl 2004;130(1):S1-45
2. Am Fam Phys 2004;70:1697-1704, 1711-2

Duration of Therapy for Treatment of Sinusitis

- Duration of therapy
 - ✓ 10-14 days of antimicrobial therapy or at least 7 days after signs and symptoms are under control¹
 - ✓ A 3-day course of azithromycin was approved for use in sinusitis in both Canada and USA
- Antibiotics reduce the median duration of illness from 17-9 days (amoxicillin)²
- Surgery
 - ✓ Considered in more complicated patients

1. N Engl J Med 2004;351:902-10
2. BMJ 1996;313:325-9

Treatment of Acute Bacterial Sinusitis

Uncomplicated Sinusitis	Amoxicillin
Uncomplicated sinusitis, penicillin-allergic patient	<i>Non-immediate-type hypersensitivity:</i> β -lactamase-stable cephalosporin <i>Immediate-type hypersensitivity:</i> Clarithromycin or azithromycin or trimethoprim-sulfamethoxazole or doxycycline or respiratory fluoroquinolone
Treatment failure or prior antibiotic therapy in past 4 to 6 weeks	High-dose amoxicillin with clavulanate or β -lactamase-stable cephalosporin Second choice: respiratory fluoroquinolone
High suspicion of penicillin-resistant <i>Streptococcus pneumoniae</i>	High-dose amoxicillin or clindamycin Second choice: respiratory fluoroquinolone

Pharyngitis

➤ Pharyngitis

- ✓ Acute infection of oropharynx or nasopharynx
- ✓ Viral causes are most common acute pharyngitis
 - Rhinovirus (20%), coronavirus ($\geq 5\%$), adenovirus (5%), herpes simplex (4%), influenza virus (2%), parainfluenza virus (2%), and Epstein-Barr virus ($< 1\%$)
- ✓ Primary bacterial cause : group A beta-hemolytic *Streptococcus* (10-30%), *S. pyogenes*
- ✓ Group A *Streptococcus*
 - 15-30% of cases of pharyngitis in the pediatric population
 - 5-15% of all symptomatic episodes of pharyngitis in adults

Clinical Presentation and Diagnosis of 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 as well as nonstreptococcal bacterial causes

Signs and symptoms

Sore throat
Pain on swallowing
Fever
Headache, nausea, vomiting, and abdominal pain (especially 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
Several symptoms that are not suggestive of group A *Streptococcus* are cough, conjunctivitis, coryza, and diarrhea

Laboratory tests

Throat swab and culture or rapid antigen detection testing

Treatment of Pharyngitis

➤ The goals of treatment of pharyngitis

- ✓ Improve clinical signs and symptoms
- ✓ Minimize adverse drug reactions
- ✓ Prevent transmission to close contacts
- ✓ Prevent acute rheumatic fever and suppurative complications
 - Peritonsillar abscess, cervical lymphadenitis, mastoiditis

Pharmacologic Therapy

➤ Pain relief

- ✓ Pain is often the primary reason for visiting
- ✓ Analgesics (acetaminophen, NSAIDs) is strongly recommended
- ✓ Acetaminophen is a better option
 - NSAIDs may increase the risk for necrotizing fasciitis/toxic shock syndrome

➤ Supportive care

- ✓ Rest, fluids, lozenges, saltwater gargles
- ✓ Symptoms may resolve 1-2 days sooner with such interventions

N Engl J Med 2001;344:1479-80

Antimicrobial Treatment of Pharyngitis

➤ Antimicrobial treatment

- ✓ Decreases the duration of signs and symptoms by 1-2 days¹⁻²
- ✓ Decreases the severity of symptoms when initiated within 2-3 days of onset in patients with proven group A *Streptococcus*²
- ✓ Microbiologic eradication will occur in 48 -72 hrs
 - Decreasing transmission
- Antimicrobial treatment should be limited to those who have clinical and epidemiologic features of group A *streptococcal* pharyngitis with a positive laboratory test
- Penicillin is the drug of choice²⁻³

1. Cochrane Rev 2000:2
2. Ann Intern Med 2001;134:506-8
3. Clin Infect Dis 2002;35:113-25

Dosing Guidelines for Pharyngitis

Drug	Adult Dosage	Pediatric Dosage	Duration
Penicillin VK	250 mg three or four times daily or 500 mg twice daily	50 mg/kg/day divided in three doses	10 days
Penicillin benzathine	1.2 million units intramuscularly	0.6 million units for weight < 27 kg (50,000 units/kg)	One dose
Penicillin G procaine and benzathine mixture	Not recommended in adolescents and adults	1.2 million units (benzathine 0.9 million units, procaine 0.3 million units)	One dose
Amoxicillin	500 mg three times daily	40-50 mg/kg/day divided in three doses	10 days
Erythromycin			10 days
Estate	20-40 mg/kg/day divided two to four times daily (max 1 g/day)	Same as adults	
Stearate	1 g daily divided two to four times daily (adolescents, adults)	-	
Ethylsuccinate	40 mg/kg/day divided two to four times daily (max 1 g/day)	Same as adults	
Cephalexin	250-500 mg orally four times daily	25-50 mg/kg/day divided in four doses	10 days