Judicious Use of Antibiotics

A Guide for Oregon Clinicians

Second Edition

Oregon AWARE
Oregon Alliance Working for Antibiotic Resistance Education

DHS
Oregon Department of Human Services

Created by the Oregon Alliance Working for Antibiotic Resistance Education (AWARE) and the Oregon Department of Human Services

Judicious Use of Antibiotics SECOND EDITION

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Intended Audience

Primary care providers, including physicians, nurse practitioners and physician assistants.

Objectives

Upon completion of this activity, participants should be able to:

1. State the prevalence of pneumococcal resistance in Oregon.
2. State the risk factors for development of antibiotic resistance.
3. Apply the criteria for initiating antibiotic treatment of sinusitis, pharyngitis, bronchitis, otitis media and community-acquired pneumonia.
4. Name the first-line agents for the treatment of sinusitis, pharyngitis, bronchitis, otitis media and community-acquired pneumonia.

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I. BACKGROUND: ANTIBIOTIC RESISTANCE

In the United States, *Streptococcus pneumoniae* (SP) was universally sensitive to penicillin until the 1980s, and high-level resistance (minimal inhibitory concentration ≥ 2.0 µg/mL) was unknown until the early 1990s. Penicillin resistance among pneumococci increased in epidemic fashion during the 1990s, reaching a peak in 2000. These data come from the Emerging Infections Program (EIP) of the Centers for Disease Control and Prevention (CDC). Oregon is one of the 11 EIP sites and contributes data and isolates from cases of invasive SP disease in the Portland Tri-County area.

The decline in resistance since 2000 is felt to be a result of the introduction of the 7-valent pneumococcal conjugate vaccine (PCV-7), which was licensed in 2000 and recommended for universal infant vaccination in the US. The rate of invasive infections due to SP has declined dramatically in the age groups covered by vaccine. The vaccine covers 7 serotypes of SP that accounted for the majority of isolates recovered from children in the pre-vaccine era. These 7 serotypes were more likely to be resistant to antibiotics than the non-vaccine serotypes, so declines in the occurrence of these serotypes explain the concomitant decrease in resistance: the rate of invasive SP caused by strains not susceptible to penicillin was 35% lower in 2001 in the US than in 1999.

While this decline is an encouraging trend, public health experts continue to watch for the development of "replacement disease," the emergence of non-vaccine serotypes that could replace the serotypes now covered by vaccine. Additionally, given the rapid increase in prevalence of drug-resistant SP (DRSP) in the 1990s in the US, clinicians need to be aware of the potential for resistance to develop rapidly in the non-vaccine SP serotypes.

Another area of concern is the development of multi-drug resistant SP (MDRSP).

Figure 1: Percent of invasive *S. pneumoniae* isolates non-susceptible* to penicillin, Portland and other EIP sites, 1996-2003. CDC and Emerging Infections Program, unpublished data.

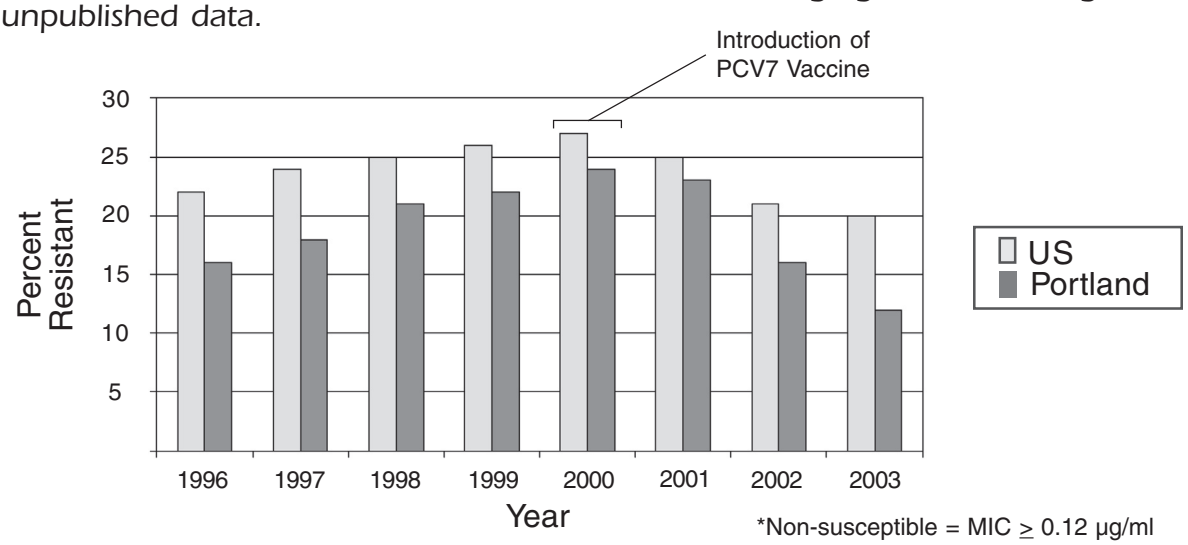

Table 1: Resistance to other antibiotics among penicillin-resistant *S. pneumoniae* isolates, Portland Tri-County area, July 1995 - December 2003 (n=320).

Antibiotic	Percent Resistant
Clindamycin	11
Erythromycin	42
Cefuroxime	63
TMP-SMX	87

Table 1 (above) shows the level of cross-resistance among penicillin-resistant SP isolates from the Portland area; most isolates that are resistant to penicillin exhibit resistance to other classes of oral antibiotics commonly used in the outpatient setting. Isolates of SP that are resistant to erythromycin are typically also resistant to other macrolides, such as azithromycin and clarithromycin, but not to telithromycin.

Multiple studies have implicated recent use of antibiotics as the most important risk factor for both carriage of DRSP and invasive disease due to DRSP. Studies measuring nasopharyngeal carriage of SP in children being treated for otitis media have documented an increase in DRSP within 3-4 days of initiating treatment. Other identified risk factors include age less than 2 years or over 65 years, daycare center attendance, exposure to young children, multiple medical comorbidities and immunosuppression.

Educational campaigns conducted by CDC and state health departments, such as the Oregon Alliance Working for Antibiotic Resistance Education (AWARE), appear to have had an impact on antibiotic prescribing trends in the US. Results from the National Ambulatory Medical Care Survey (NAMCS), an annual sample of outpatient visits to office-based community physicians, showed promising declines in the percentage of patients receiving prescriptions for upper respiratory tract infections between the periods 1991-1992 and 1998-1999. Among adults, the frequency of antibiotic prescribing decreased from 1991-1992 to 1998-1999 for the common cold (56% vs. 43% of patient visits), pharyngitis (78% vs. 64%), and acute bronchitis (76% vs. 59% of patient visits). Among children, the frequency of antibiotic prescribing decreased for the common cold (41% vs. 21% of patient visits) and pharyngitis (73% vs. 54%). However, during the same time period, use of broad-spectrum antibiotics doubled among adults, from 24% to 48% of antibiotic prescriptions; in children, broad-spectrum antibiotic use rose from 23% to 40% of antibiotic prescriptions.

Risk Factors for DRSP:

- Recent use of antibiotics
- Age <2 years or >65 years
- Daycare center attendance
- Exposure to young children
- Multiple medical comorbidities
- Immunosuppression

2. USING PHARMACOKINETIC/PHARMACODYNAMIC PRINCIPLES TO MAKE RATIONAL ANTIBIOTIC CHOICES

Traditionally, clinicians have relied on measurement of the minimal inhibitory concentration (MIC) necessary to kill the organism to determine whether an organism was susceptible to a given antibiotic. Recent guidelines addressing management of otitis media, sinusitis and pneumonia have drawn on pharmacokinetic/pharmacodynamic principles to guide rational use of antibiotics. For beta-lactams (penicillins and cephalosporins), macrolides and clindamycin, the best predictor of antimicrobial efficacy is the amount of time that the concentration of the antibiotic remains above the MIC (T>MIC). The T>MIC should be > 40%-50% of the dosing interval in immunocompetent hosts.

Studies looking at patients with pneumococcal pneumonia have not found any adverse treatment outcomes in either children or adults with pneumococci of intermediate susceptibility. This should not be surprising, given that commonly used dosages of penicillin can achieve sufficient serum concentrations to eradicate SP in the intermediate susceptibility range, and similar levels can easily be achieved in well-perfused alveoli.

For infections that can be treated orally, amoxicillin is better absorbed than penicillin and is often effective against isolates of SP that are resistant to penicillin. Recent guidelines on the management of acute otitis media make a strong argument for continued use of amoxicillin as a first line agent based on its ability to achieve higher levels in middle ear fluid (MEF) than other commonly used oral agents. Although administration of amoxicillin in standard recommended doses (40-45 mg/kg/day) may fail to achieve peak MEF concentrations sufficient to eradicate highly-resistant DRSP in all cases, higher doses of amoxicillin or amoxicillin-clavulanate potassium (80-90 mg/kg/day) are more likely to achieve T>MIC of 40%-50% of the dosing interval in MEF. This is illustrated in Table 2 (below): the middle column shows the concentration of antibiotic needed to eradicate DRSP for several common oral antibiotics. However, only amoxicillin and ceftriaxone achieve high enough concentrations in MEF (column 3) to be effective against DRSP.

Table 2: Activity of beta-lactam drugs against drug-resistant *S. pneumoniae* (DRSP) causing acute otitis media.

Agent	MIC-90* for DRSP	Peak Middle Ear Fluid Concentration (µg/ml)
Amoxicillin (standard dose)	2 - 4	1 - 6
Amoxicillin (high dose)	2 - 4	3 - 8
Cefuroxime	4 - 16	1 - 2
Cefpodoxime	4 - 16	0.2 - 1
Cefprozil	32	2
Cefixime	64	1 - 2
Ceftriaxone (IM)	1 - 4	35

* The concentration that inhibits 90% of isolates tested.

III. TREATMENT GUIDELINES FOR UPPER RESPIRATORY INFECTIONS

Otitis Media

Diagnosis & criteria for treatment

Otitis media is the leading indication for outpatient antimicrobial use in the US. A critical step in reducing unnecessary prescribing is to identify the subset of patients who are unlikely to benefit from antibiotics. Distinguishing AOM from a simple middle ear effusion (MEE) and deferring antibiotics for MEE will accomplish this goal.

A diagnosis of AOM requires all three of the following: 1) a history of acute onset of signs and symptoms; 2) the presence of middle-ear effusion, and 3) signs and symptoms of middle-ear inflammation, as described in the box below. No clinical symptoms alone reliably predict the presence of AOM. In one study, 90% of children with AOM presented with fever, earache, and excessive crying. However, 72% of children with upper respiratory infections but not AOM also displayed the same symptoms.

Antimicrobials are not warranted for children with MEE but without any of the other hallmarks of AOM. MEE may occur as part of a viral respiratory infection, or as a prelude to or sequela of AOM. The natural history of appropriately treated AOM includes persistent MEE for several weeks: 70% of children have an effusion two weeks after the end of treatment, and 40% will still have an effusion one month following effective treatment. Traditionally, the justification for antibiotics for persistent MEE was that untreated MEE could lead to hearing loss and delays in language acquisition. Recent studies have shown that the mild conductive losses normally seen with MEE do not interfere with language development.

Definition of Acute Otitis Media (AOM)

Elements of the definition of AOM are:

1. Recent, usually abrupt, onset of signs and symptoms of middle-ear inflammation and effusion. AND

2. The presence of middle-ear effusion that is indicated by any of the following:
   a. Bulging of the tympanic membrane
   b. Limited or absent mobility of the tympanic membrane
   c. Air-fluid level behind the TM
   d. Otorrhea AND

3. Signs or symptoms of middle-ear inflammation as indicated by either:
   a. Distinct erythema of the TM, OR
   b. Distinct otalgia (discomfort clearly referable to the ear that results in interference with normal activities or sleep)

In Europe, deferring antibiotic therapy unless symptoms persist for > 2 days and treating for 5-7 days has been the standard of care for decades. In 2004, the American Academy of Pediatrics and the American Academy of Family Physicians published guidelines giving the option of observing selected children without antimicrobial treatment for 48-72 hours and limiting management to symptomatic relief. The decision to observe or treat is based on the certainty of the diagnosis, the child's age, and severity of illness (see Table 2). Observation should only be used when the child's caregiver has a means of communication with the clinician and reevaluation is possible if necessary. Clinicians may also consider the use of a "safety-net" prescription to be filled if the patient does not improve in 48-72 hours.

Table 3: Criteria for initial antibacterial agent treatment or observation in children with AOM.

Age	Certain Diagnosis	Uncertain Diagnosis
<6 months	Antibacterial therapy	Antibacterial therapy
6 months - 2 years	Antibacterial therapy	Antibacterial therapy if severe* illness; observation option if non-severe illness
>2 years	Antibacterial therapy if severe* illness; observation option if non-severe illness	Observation option

* Severe illness is defined as moderate to severe otalgia or fever > 39ºC.

Antibiotic treatment

(see algorithm, page 20)

Management of pain is an important component of managing episodes of AOM; acetaminophen and ibuprofen are effective for mild to moderate pain and provide longer-lasting effects than topical agents such as benzocaine.

Amoxicillin remains the treatment of choice for AOM for several reasons. In addition to its safety, low cost, acceptable taste, and a narrow spectrum of activity, amoxicillin is the most active of all oral beta-lactam agents against SP. Although the other common bacteria responsible for cases of AOM, *Haemophilus influenzae* and *Moraxella catarrhalis*, have high rates of beta-lactamase production, their high spontaneous resolution rate make them far less important to treat empirically.

High-dose amoxicillin (80-90 mg/kg/day, divided bid) is more likely to be active against DRSP than any other agent and is appropriate for initial treatment of children with AOM. Clinicians can consider initiating treatment with a lower dosage (45-50 mg/kg/day) for children who meet all of the following criteria: 1) age > 2 years; 2) not in day care; and 3) no antibiotics within the last 3 months.

Based on similar pharmacokinetic/pharmacodynamic data and its activity against beta-lactamase producing organisms (*H. influenza and M. catarrhalis*), amoxicillin-clavulanate is recommended as second-line therapy in cases where amoxicillin has failed. Ceftriaxone also achieves concentrations in middle ear fluid that could be expected to eradicate DRSP and may be useful when the patient is unable to tolerate an oral medication. Cefdinir, cefpodoxime and cefuroxime are oral cephalosporins with both good beta-lactamase stability and activity against *S. pneumoniae*, and may be considered as alternatives to

High-dose amoxicillin is most likely to be active against DRSP and is appropriate for initial treatment of children with AOM.

Macrolides are recommended only in patients with severe penicillin allergies.

amoxicillin and amoxicillin-clavulanate, particularly in children with mild penicillin allergies (not Type 1 hyper-sensitivity). However, treatment failures with cephalosporins have been documented in cases of AOM due to DRSP, limiting their use in children at risk for resistant infection (antibiotic use in the past 3 months, age < 2 years, and daycare attendance).

Finally, macrolides are recommended only in patients with severe penicillin allergies. Resistance to macrolides is common, and substantial cross-resistance exists between beta-lactam agents and macrolides, making patients who have failed amoxicillin treatment more likely to have an infection resistant to macrolides. Additionally, the predicted clinical response rate with macrolides is less than with recommended front-line agents. Clindamycin is another option in patients with Type I hypersensitivity to beta-lactams.

The optimal duration of therapy for AOM is uncertain; there are no clear data to justify the 10-day course in older children. Thus, a 5- to 7-day course of treatment is recommended in children 6 years of age and older with mild to moderate disease.

PHARYNGITIS

Diagnosis & criteria for treatment

A wide range of infectious agents, most commonly viruses, causes pharyngitis. Group A beta-hemolytic streptococcus (GABHS, or *Streptococcus pyogenes*)* accounts for 5%-15% of pharyngitis cases. Rationale for treatment of GABHS has traditionally included prevention of rheumatic fever, prevention of suppurative complications and relief of symptoms.

Rheumatic fever is now so rare in the US that 3,000-4,000 patients with GABHS would need to be treated to prevent a single case of acute rheumatic fever (ARF). Antibiotic therapy for pharyngitis has never been shown to prevent acute glomerulonephritis. A recent review found that treatment of pharyngitis did not reduce the risk for peritonsillar abscess, because many patients did not present for care until after the complication had developed.

Relief of suffering is often a concern of both patients and clinicians. Antibiotic therapy instituted within 2-3 days of symptom onset hastens symptomatic improvement in patients with GABHS by only 1-2 days. Antibiotics have no effect on the clinical course of patients with negative cultures.

Given the low prevalence of GABHS in cases of pharyngitis, it is important to reduce use of antibiotics for cases of pharyngitis unlikely to be due to GABHS. A combination of the Centor criteria (tonsillar exudates, tender anterior cervical lymphadenopathy, absence of cough, history of fever) and rapid antigen testing can be used to predict the presence of

* Group B streptococcus, or *Streptococcus agalactiae*, does not cause pharyngitis.

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GABHS with reasonable accuracy. Positive and negative predictive values will vary depending on the prevalence of GABHS in the population studied, but several studies have found that the presence of 3-4 of these criteria has a positive predictive value of 40%-60% (in other words, there is a 40%-60% chance that the patient actually has GABHS). For patients who have a sore throat and only one of the four symptoms, the probability that the illness is due to GABHS is only 20%.

A reasonable strategy is to defer testing and treatment in persons who meet only 1 criterion, test patients who meet 2-4 criteria with a rapid antigen test and limit antibiotic therapy to patients with positive test results.

For children and adolescents, a negative rapid antigen test should be confirmed with a throat culture result, unless the clinician has ascertained in his or her own practice that the rapid antigen test used is comparable to a throat culture. Since the risk of ARF is much lower in adults than children, diagnosis of this infection in adults can be ruled out by a negative rapid antigen test. Use of a sensitive rapid antigen test without culture confirmation has not been associated with an increase in suppurative and nonsuppurative complications of GABHS.

Treatment of pediatric & adult patients

(see algorithm, page 21)

The management of GABHS pharyngitis is straightforward. The goal is to use as narrow-spectrum an agent as possible. Since GABHS is still universally susceptible to penicillin, it remains the first choice for children and adults. Macrolides are typically recommended for patients with allergies to penicillin; in areas where resistance to GABHS among macrolides has been documented other options include cephalosporins (for patients with mild allergies) and clindamycin (severe penicillin allergies, i.e., hives or anaphylaxis). Although the prevalence of macrolide-resistant GABHS has been rare in the US, the recent report of an outbreak of erythromycin-resistant GABHS among school-children suggests that routine use of macrolides in patients without penicillin allergies should be discouraged.

SINUSITIS

Diagnosis & criteria for treatment

An estimated 20 million cases of sinusitis occur annually in the US; it is the fifth most common diagnosis for which an antibiotic is prescribed. Although the gold standard for diagnosis of bacterial sinusitis is sinus puncture, it is an invasive procedure seldom performed in primary care settings and is usually indicated only in complicated cases. Because no simple and accurate office-based test for bacterial sinusitis exists, clinicians must rely on clinical findings to make the diagnosis.

Most cases of acute sinusitis diagnosed in ambulatory care offices are caused by uncomplicated viral upper respiratory tract infections. Studies evaluating the incidence of bacterial sinusitis in persons with upper respiratory tract symptoms have estimated that only 0.5%-2% of viral upper respiratory tract infections in adults are complicated by bacterial sinusitis.

Gwaltney and colleagues studied the natural history of rhinovirus illness in young adults. Length of illness ranged from 1-33 days, and only one-fourth of the patients had symptoms lasting longer than 14 days. After 7-10 days, the respiratory symptoms generally peaked in severity in the majority of patients and began to improve. Thus, deferring antibiotic treatment until patients have symptoms beyond 10 days (that show no signs of improvement) will improve the likelihood that the illness is due to a bacterial infection.

Attempts to identify other signs and symptoms predictive of bacterial sinusitis in adults have been disappointing: no clear constellation of signs and symptoms reliably predicting bacterial infection has been identified. In general, the only patients that warrant treatment before they have had symptoms for 10 days are those who have a worsening of symptoms after 5-7 days, accompanied by more specific symptoms such as purulent nasal discharge, maxillary tooth or facial pain (especially when unilateral), and unilateral sinus tenderness. The presence of these more specific symptoms may warrant earlier initiation of antibiotic treatment.

In children, signs and symptoms that are specific for bacterial infection are high fever and purulent nasal discharge for at least 3-4 days. In uncomplicated viral infections, fever usually resolves in the first 48 hours and purulent nasal discharge does not appear for several days; concurrent presentation with fever and purulent nasal discharge increases the likelihood of bacterial sinusitis.

Other signs that are specific for bacterial sinusitis in children are unilateral facial pain and periorbital swelling. As with adults, the presence of these more severe symptoms warrants antibiotic treatment before the usual 10 days of symptoms required for patients with milder symptoms.

Although the presence of a mucopurulent discharge (thick, opaque, or discolored) is often used as an indication for antibiotic treatment, this finding (without the other features listed above) is compatible with the natural course of an uncomplicated viral URI. The color and characteristics of the discharge do not predict whether a bacterial pathogen will be isolated. Sinus radiographs are also not useful for the diagnosis of bacterial sinusitis and are technically difficult to perform in young children.

The color and characteristics of nasal discharge do not predict whether a bacterial pathogen will be isolated.

Although a normal radiograph is good evidence that the sinuses are not involved, abnormal radiographs are common even in viral URIs. Similarly, computed tomography (CT) of the sinuses is not useful in distinguishing viral from bacterial sinusitis. A study in young adults evaluated by CT in the first 48-96 hours of uncomplicated viral respiratory illnesses found that almost 90% had abnormalities of one or both maxillary sinus cavities; in two weeks the majority of the patients' CT findings had resolved in the absence of treatment.

Treatment of adult patients

(see algorithm, page 22)

Recent guidelines published by the Sinus and Allergy Health Partnership for the management of acute sinusitis point out that the diagnosis of bacterial sinusitis is made too frequently in patients with viral illnesses of a few days duration. The result is that patients receive antimicrobial therapy that not only is ineffective against viral pathogens but that also promotes resistance among respiratory tract pathogens.

Symptomatic treatment is the preferred initial management strategy for patients with mild symptoms of short duration, and antibiotic therapy should be reserved for patients with moderate to severe symptoms. Because serious intracranial and extrasinus complications of acute bacterial sinusitis usually arise secondary to SP infection, it is important for initial therapy to adequately cover SP, and DRSP if patients have recently received antibiotics.

Initial therapy depends on recent antibiotic therapy and presence of mild or moderate disease. The recent Sinus and Allergy Partnership guidelines provide no definition of the differences between mild and moderate disease; they suggest that the distinction between mild and moderate disease depends on clinical judgment and hinges on the relative degree of acceptance of clinical failure and the likelihood of spontaneous resolution of symptoms. If a patient appears ill enough that treatment failure may lead to adverse sequelae, that patient should be considered to have moderate disease and receive initial therapy that provides coverage for DRSP.

For patients with mild disease, amoxicillin (1.5-4.0 gm/day) or amoxicillin-clavulanate (1.75-4.0 gm/250mg per day) are the first-line choices. The higher dose of amoxicillin or amoxicillin-clavulanate (4 gm/day) is warranted for patients with risk factors for DRSP or in geographic areas where the prevalence of DRSP is known to be high. Other possible agents include the cephalosporins cefdinir, cefpodoxime, or cefuroxime, which provide coverage for susceptible SP and beta-lactamase producing organisms (such as *H. influenzae* and *M. catarrhalis*), although they do not provide the same coverage against DRSP that high-dose amoxicillin does. For patients with mild penicillin allergy, the cephalosporins can be used, while for patients with documented Type I hypersensitivity (hives or anaphylaxis) to beta-lactams the options are TMP/SMX, doxycycline, erythromycin, azithromycin or clarithromycin. Bacteriologic failure rates with these agents may be as high as 20%-25%, however.

Patients with mild disease who do not improve within 72 hours should be switched to high dose amoxicillin-clavulanate (4.0 gm/250mg per day), ceftriaxone (one gram/day IM or IV for five days), or one of the respiratory fluoroquinolones (gatifloxacin, levofloxacin and moxifloxacin). The fluoroquinolones should be considered a last resort for those patients who have failed amoxicillin or amoxicillin-clavulanate, or who are intolerant to beta-lactam antibiotics. Only by selectively

using fluoroquinolones can resistance to this important class of antibiotics be delayed.

Recommendations for patients with mild disease who have been on antibiotics in the last 3 months, or with moderate disease, are the same as for patients with mild disease who require switch therapy: high dose amoxicillin-clavulanate (4.0 gm/250mg per day), ceftriaxone (one gram/day IM or IV for five days), or one of the respiratory fluoroquinolones. For these patients, failure to respond after 72 hours should prompt a change to another agent or further evaluation with additional diagnostic procedures such as CT or sinus aspiration.

Treatment of pediatric patients

(see algorithm, page 23)

As with adults, antibiotic treatment should be reserved for patients with persistent or specific symptoms to minimize the number of children with viral URIs who receive antibiotics. In children, the most common pathogens responsible for bacterial sinusitis are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*, the same pathogens that cause AOM.

The antibiotic recommendations for sinusitis thus mirror the treatment recommendations for AOM. The first-line agent is high-dose amoxicillin, unless the child does not have any risk factors for DRSP (age < 2 years, daycare attendance, recent antibiotic use).

In cases of treatment failure, alternatives to consider are amoxicillin-clavulanate (high-dose) or ceftriaxone if the patient is unable to tolerate oral medications. For children with mild penicillin allergies (not Type 1 hypersensitivity) alternatives are cefdinir, cefpodoxime and cefuroxime. For patients with severe (hives or anaphylaxis) penicillin allergies the alternatives are azithromycin or clarithromycin. Given the risk of treatment failure of the macrolides, clindamycin may be used in severely allergic patients when DRSP is suspected.

The optimal duration of treatment for bacterial sinusitis has not been established. A treatment course of 7-10 days is commonly used and will avoid prolonged courses of antibiotics, thereby minimizing the risk of developing resistant strains of bacteria.

Cough Illness / Bronchitis

Diagnosis & criteria for treatment

Bronchitis is technically defined as inflammation of the bronchial respiratory mucosa, resulting in a cough. Although the term bronchitis does not imply a specific etiology, the application of this diagnosis often results in a prescription for antibiotics: in 1998, 59% of patients diagnosed with bronchitis in the US received an antibiotic prescription.

The vast majority of cases of acute bronchitis, however, have a non-bacterial cause. Reviews of studies in both pediatric patients and adults have implicated respiratory viruses, particularly influenza, parainfluenza and respiratory syncitial virus, as the etiology of most cases of cough illness. *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* account for a small proportion of cases in adults and children, although the likelihood of *C. pneumoniae* does increase in cases of cough lasting longer than 2 weeks. *Bordetella pertussis* should also be considered in children and adults with paroxysmal cough or any cough lasting two weeks or more.

Lack of efficacy of antibiotics in patients with cough illness is well documented. Three recent meta-analyses reviewed the published literature on acute bronchitis in adults and found no impact of antibiotic treatment on duration of illness, limitation of activity, or loss of work. Several studies have evaluated the use of antibiotics for cough illnesses in children and similarly found no benefit. Additionally, several reviews have examined the role of antibiotic treatment for prevention of bacterial complications of viral respiratory illnesses. In children and adults, antibiotics did not prevent or decrease the severity of bacterial complications subsequent to viral respiratory tract infections.

Evaluation of the patient with acute cough illness should focus on ruling out pneumonia. The absence of abnormalities in vital signs and chest examination usually reduces the likelihood of pneumonia to the point where further diagnostic testing is usually not necessary. Although the presence of purulent sputum is often used as a clinical criterion for initiating antibiotics, purulence occurs when inflammatory cells or sloughed mucosal epithelial cells are present, and it can result from either viral or bacterial infection.

Treatment of adult patients

(see algorithm, page 24)

For patients with acute bronchitis of suspected viral etiology, use of the term “viral chest cold” rather than bronchitis may help reduce patient expectations for receipt of antibiotics.

The natural history of rhinovirus includes cough for greater than 2 weeks in up to 25% of patients. In the absence of signs and symptoms of pneumonia, antibiotics are generally not warranted for cough illnesses of less than 3 weeks duration. For patients with cough

The differential diagnosis for adults includes:

- Asthma or reactive airway disease
- Second-hand smoke exposure
- Post-nasal drip syndrome
- Gastroesophageal reflux
- ACE-inhibitor drug cough
- Environmental exposure
- Chronic bronchitis
- Bronchiectasis
- Malignancy

persisting for more than 3 weeks, chest radiography is recommended in the absence of other known causes; the differential diagnosis includes asthma or reactive airway disease, second-hand smoke exposure, post-nasal drip syndrome, gastroesophageal reflux, ACE-inhibitor drug cough, environmental exposure, chronic bronchitis, bronchiectasis, and malignancy. Therapy should be directed at specific underlying causes.

Patients with exacerbations of chronic obstructive pulmonary disease (defined by a change in sputum volume or quality, with or without systemic symptoms) may benefit from short courses of antibiotics, although only patients with severe exacerbations are likely to benefit. Appropriate empiric therapies include amoxicillin, trimethoprim/sulfamethoxazole or doxycycline. These patients have also been shown to benefit from a short course of oral corticosteroids. Erythromycin or doxycycline is recommended for *M. pneumoniae, C. pneumoniae* and *B. pertussis.*

Treatment of pediatric patients

(see algorithm, page 25)

As with adults, cough illnesses of less than 3 weeks duration should seldom require treatment in a well-appearing child in the absence of signs and symptoms of serious lung disease. Once the child has had a cough for more than 3 weeks, the differential diagnosis should include allergies, habit cough, sinusitis, cystic fibrosis, foreign body aspiration, asthma or reactive airway disease, second-hand smoke exposure and gastroesophageal reflux.

The diagnosis of *B. pertussis* should be suspected in children with prolonged paroxysmal coughing with supportive associated findings such as inspiratory whoop, posttussive emesis and lymphocytosis; the diagnosis should be confirmed by nasopharyngeal culture or polymerase chain reaction. The recommended treatment is a macrolide (erythromycin, azithromycin or clarithromycin). Infections due to *M. pneumoniae* and *C. pneumoniae* are more difficult to diagnose and are unlikely in children under the age of five.

The diagnosis of *B. pertussis* should be suspected in children with prolonged paroxysmal coughing with supportive associated findings such as inspiratory whoop, posttussive emesis and lymphocytosis.

Community-Acquired Pneumonia

Diagnosis & criteria for treatment

Pneumonia is the sixth most common cause of death in the US. Annually, 2-3 million cases of community-acquired pneumonia (CAP) result in ~10 million physician visits, 500,000 hospitalizations, and 45,000 deaths in the US. Prospective studies evaluating causes of CAP in adults have failed to detect an etiology in 40%-60% of cases. The most commonly identified agent is *S. pneumoniae*, which accounts for approximately two-thirds of all bacteremic pneumonia (cases of pneumonia in which patients have a positive blood culture). Other pathogens include *H. influenzae*, *M. pneumonia*, *C. pneumoniae*, *S. aureus* (with methicillin-resistant *S. aureus* on the rise), *S. pyogenes*, *N. meningitidis*, *M. catarrhalis*, *K. pneumoniae* and other gram-negative rods, *Legionella* species, influenza virus, respiratory syncitial virus, adenovirus, parainfluenza virus, and other microbes.

> Empiric treatment of pneumonia should be discouraged, especially in the era of antibiotic resistance. The CXR, in addition to confirming the diagnosis, may shed light on the etiology and prognosis of the patient as well as identify alternative diagnoses.

When a pathogen has been identified, the nature of the organisms has reflected the population studied and types of diagnostic tests performed. With sputum culture, pneumoccocus is the most commonly identified pathogen (9%-20% of all episodes) in adults, while *M. pneumoniae* is the most common organism (13%-37%) identified when serologic testing is performed. *C. pneumoniae* has been reported in up to 17% of outpatients with CAP.

Although recent national guidelines make it very clear that all episodes of pneumonia need to be confirmed by chest radiography (CXR), the guidelines do not provide specific objective criteria for the decision to obtain a chest radiograph, and the decision to obtain a CXR remains a clinical decision. No single criterion, such as presence of cough or tachypnea, is clinically useful in predicting the presence of pneumonia. Decision rules based on combinations of these findings are also imperfect. A patient with an acute cough but no additional signs or symptoms has a probability of 1%-13% of having pneumonia (the wide range is due to the fact that studies have reached conflicting conclusions about whether normal vital signs rule out pneumonia). On the other hand, a patient with acute cough, fever, tachycardia, and crackles on chest examination has a probability of pneumonia of 18%-42%.

Given the lack of predictive value of findings on physical examination, empiric treatment should be discouraged, especially in the era of antibiotic resistance. The CXR, in addition to confirming the diagnosis, may shed light on the etiology and prognosis of the patient as well as identify alternative diagnoses, such as congestive heart failure or pulmonary malignancy. CXR does not detect all infiltrates; a heightened level of scrutiny may be required for elderly or immunocompromised patients.

Treatment of adult patients

(see algorithm, pages 26-27)

Although mortality has ranged from 2% to 30% among hospitalized patients in different studies, the average is ~14%. Mortality is estimated to be 1% among outpatients. Since the costs of inpatient management of CAP are 20-fold higher than outpatient treatment, identifying the patient most likely to benefit from hospitalization is one of the single most important decisions made by clinicians in managing CAP. The following guidelines are only applicable to patients in the outpatient setting not HIV-infected or immunocompromised who are over the age of 18 years.

The predictive value of the Pneumonia Outcomes Research Team (PORT) Severity Index (PSI) has been well-validated, and the PSI is endorsed by both the Infectious Diseases Society of America and the American Thoracic Society. Calculation of the index is based on age, sex, comorbidities, physical exam findings, and laboratory and radiographic results (see algorithm, pages 26-27). Patients in risk classes I and II usually do not require hospitalization, patients in risk class 3 may require brief hospitalization, and those in risk classes IV and V require hospitalization. Although designed to assist clinical decision making, these prediction rules are meant to contribute to and not supersede clinical judgment. Patients in lower risk classes may have contraindications to outpatient care, such as cognitive impairments, the inability to tolerate oral medications, or poor social supports, that may make hospitalization the only feasible management option.

The predictive value of the Pneumonia Outcomes Research Team (PORT) Severity Index (PSI) has been well-validated, and the PSI is endorsed by both the Infectious Diseases Society of America and the American Thoracic Society.

Although patients treated as outpatients require no diagnostic testing beyond CXR, hospitalized patients require the following work-up: complete blood cell count and differ-

Table 4: Risk of mortality by PIS risk class.

Risk Class	No. of Points	No. of Patients	Mortality, %	Recommended Site of Care
I	Not applicable	3034	0.1	Outpatient
II	≤70	5778	0.6	Outpatient
III	71-90	6790	2.8	Outpatient or brief inpatient
IV	91-130	13,104	8.2	Inpatient
V	>130	9333	29.2	Inpatient

ential, routine chemistries, measurement of oxygen saturation (oximetry or arterial blood gas), two pre-treatment blood cultures, and sputum gram stain and culture. For selected patients, especially those aged 15-24 years, HIV testing should be considered, and patients with specific risk factors should be tested for *Legionella* species and tuberculosis.

Treatment should be pathogen-specific if the etiology is known or strongly suspected, with an emphasis on choosing the agent that is most cost-effective, least toxic and with the narrowest spectrum possible. Recommendations for empirical treatment are based on severity of illness, pathogen probabilities, resistance patterns of *S. pneumococcus* (the most common and most lethal agent), and co-morbid conditions.

For patients treated as outpatients, previously healthy adults should receive a macrolide or doxycycline unless they have been on antibiotics recently (within the past 3 months); recently treated patients require an advanced macrolide (clarithromycin or azithromycin) plus either high-dose amoxicillin or high-dose amoxicillin-clavulanate. A second option for these patients would be a respiratory fluoroquinolone alone, although fluoroquinolones should be reserved for patients who have failed initial therapy or have a known allergy to first-line agents. For patients with co-morbidities (COPD, diabetes, renal or congestive heart failure, or malignancy), an advanced macrolide is the initial choice for untreated patients, followed by a respiratory fluoroquinolone. Those recently on antibiotics should receive either an advanced macrolide plus a beta-lactam (high dose amoxicillin, high dose amoxicillin-clavulanate, cefpodoxime, cefprozil, or cefuroxime) or a respiratory fluoroquinolone alone.

The recommendation for inpatients not previously treated is an advanced macrolide plus a beta-lactam (in this case, cefotaxime, ceftriaxone, ampicillin-sulbactam or ertapenem), again with a respiratory fluoroquinolone alone as a second choice. Essentially the same regimen is recommended for inpatients recently on antibiotics, but the actual choice (advanced macrolide plus a beta-lactam vs. a respiratory fluoroquinolone alone) will be dictated by the nature of their recent therapy.

For patients requiring intensive care, the initial empiric therapy depends largely on the patient's risk factors for *Pseudomonas*. If no risk factors for *Pseudomonas* are present, administration of a beta-lactam (cefotaxime, ceftriaxone, ampicillin-sulbactam or ertapenem) and an advanced macrolide or a respiratory fluoroquinolone is appropriate. When *Pseudomonas* infection is a possibility (in patients with severe structural lung disease [e.g., bronchiectasis], recent antibiotic therapy or hospital stay), treatment options include: 1) an antipseudomonal agent plus ciprofloxacin, or 2) an antipseudomonal agent plus an aminoglycoside plus a respiratory fluoroquinolone or macrolide.

Treatment of pediatric patients

Studies investigating the etiology of pneumonia in children have been even less satisfying than those conducted in adults, and no national body in Europe or the US has attempted to develop evidence-based official recommendations on the management of pneumonia in children. Despite these limitations, there are a few clinical and epidemiological findings that can aid clinicians caring for children with possible pneumonia. Pneumonia in the first 3 weeks of life is uncommon, and management should follow guidelines for management of sepsis in this age group. Between 3 weeks and 3 months of age, additional pathogens to consider would be

C. trachomatis and *B. pertussis* (although pertussis is still a rare cause of pneumonia, it can be very severe and warrants detection to prevent further spread in the community). SP and *H. influenzae* used to be the dominant bacterial pathogens in children under 5 years of age, but vaccination against these two bacteria has now made them relatively uncommon. *M. pneumoniae* and *C. pneumoniae* are typically seen in children over 5 years of age.

Other clinical clues are localized chest pain, which suggests bacterial pneumonia, and wheezing, which is more common with *M. pneumoniae* and *C. pneumoniae* or viruses such as respiratory syncitial virus (RSV). Outbreaks of RSV and influenza are uncommon outside winter and spring. The presence of signs and symptoms of sepsis should always suggest bacterial infection in children.

As with adults, a CXR should be obtained for every child suspected of having pneumonia. Children under the age of two years require careful history, physical examination and diagnostic evaluation (blood culture and complete blood count, in addition to CXR) to identify the etiology and rule out other possible underlying conditions (such as cardiac disease, immunodeficiency, anatomic abnormality, etc.). In children 3-4 years of age treated as an outpatient, oral amoxicillin, focusing on SP, is the initial empiric choice, while hospitalized children should receive intravenous cefuroxime or cefotaxime. Above age 5 years, outpatient management would consist of either a macrolide or doxycycline (if the patient is over age 8). The initial choice for hospitalized patients in this age group would be a macrolide plus cefuroxime, cefotaxime, or ceftriaxone.

Recommended Reading

Principles of judicious use of antimicrobial agents in pediatric upper respiratory infections. *Pediatrics* 1998;101:163-184.

Principles of appropriate antibiotic use for treatment of acute respiratory tract infections in adults. *Annals of Internal Medicine* 2001;134:479-529.

Subcommittee on Management of Sinusitis and Committee on Quality Improvement. Clinical Practice Guideline: Management of Sinusitis. *Pediatrics* 2001;108:798-808.

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Bisno AL, Gerber MA, Gwaltney JM, Jr., Kaplan EL, and Schwartz RH. Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis. *Clinical Infectious Disease* 2002;35:113-25.

American Academy of Pediatrics Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. *Pediatrics* 2004;113:1451-65.

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IV. PROMOTING JUDICIOUS USE OF ANTIBIOTICS

Although the development and promotion of evidence-based consensus guidelines is an important component of promoting judicious use of antibiotics, curtailing inappropriate use of antibiotics will ultimately require substantial commitment to educating the public as well.

Multiple studies have found that patient expectations and demands for antibiotics drive antibiotic prescriptions; other studies have found that rates of antibiotic prescription rise with increasing patient volume and shorter visits. Factors influencing antibiotic prescribing habits are complex, and it is not surprising that interventions that focus purely on clinician education to decrease unnecessary antibiotic use have been ineffective.

Interventions that have included patient education as a component have been more successful. A recent study evaluated the impact of a combined approach of clinician education, the mailing of brochures and refrigerator magnets to patients, and office education (waiting room fact sheets and posters) on prescribing rates for adults with bronchitis. Compared to the control clinics that received usual care, rates of antibiotic prescriptions at the clinic receiving the intervention were significantly lower, and patients interviewed 2-3 weeks after their visit at the intervention clinic did not report any differences in duration of symptoms, return visits, or satisfaction with the visit compared to patients seen at control clinics.

The success of the program was publicized throughout the health system the following fall and at a single staff meeting at the intervention clinic. That following winter, not only did antibiotic prescription rates for acute bronchitis remain low at the intervention clinic compared to the control clinics, but patients seen for acute bronchitis the first winter at the intervention clinic were less likely to seek care the following winter than patients seen in the control clinic.

Evidence suggests that patient satisfaction with the office encounter depends less on receipt of antibiotics than on the nature of the interaction between patient and clinician, such as the amount of time that the clinician spent explaining the diagnosis and treatment plan. The following suggestions may be useful for clinicians caring for patients with uncomplicated upper respiratory tract illnesses:

1. Provide realistic expectations for the duration of the patient's symptoms. It is not unusual for URI symptoms from viral infections to last 10-14 days.

2. Personalize the risk of unnecessary antibiotic use. Educate patients that antibiotic use increases the risk of carriage of and infection with resistant bacteria that may be difficult to treat and require more expensive antibiotics or even hospitalization. Also point out that antibiotics commonly have side effects such as gastrointestinal symptoms and that rare reactions may occur, such as anaphylaxis.

3. Utilize materials developed by the Centers for Disease Control and Prevention or your state health department to assist in patient education. Brochures, fact sheets, or posters in your waiting room may be useful adjuncts in informing patients about the risk of misuse of antibiotics. CDC materials may be viewed at http://www.cdc.gov/drugresistance/community/tools.htm; Oregon AWARE's materials may be viewed, downloaded or ordered in bulk at http://www.healthoregon.org/antibiotics/pubs.cfm.

4. Promote non-antibiotic measures for relief of viral respiratory symptoms (see algorithms on following pages).

Otitis Media

Differentiate acute otitis media from middle ear effusion

Acute Otitis Media (AOM)

Diagnosis requires all three of the following:

1. Recent onset of symptoms;
2. Middle ear effusion (bulging TM), limited mobility of TM, air fluid level behind TM, otorrhea);
3. Signs or symptoms of inflammation (erythema of TM or otalgia).

Management - AOM

For children with mild cases of uncomplicated AOM, >2 years of age, consider treating symptomatically with topical or systemic analgesia (acetaminophen or ibuprofen) and reassessing if not improved in 48-72 hours.

Amoxicillin remains as efficacious as newer drugs: 80–90 mg/kg/day, divided bid (maximum dose 2–3 gm/day) for 5 days (10 days if <6 years).

If no improvement in 48–72 hours, ceftriaxone or amoxicillin-clavulanate* 80–90 mg/kg/day, divided bid.

Other treatment alternatives: cefdinir, cefpodoxime, cefuroxime.

For severe penicillin allergies (hives or anaphylaxis): azithromycin or clarithromycin.

For repeated treatment failure consider:
1. Tympanocentesis for culture/susceptiblity,
2. Consultation with ENT.

*May use standard formulation of amoxicillin-clavulanate mixed with additional amoxicillin, or high-dose amoxicillin formulation of amoxicillin-clavulanate.

Middle Ear Effusion (MEE)

Signs/symptoms:

- Effusion present
- Immobility of tympanic membrane
- No symptoms or signs of acute infection
- Non-specific symptoms and signs (rhinorrhea, low-grade fever, cough, diarrhea, etc.) may be present

Management - MEE

Antibiotics are not indicated.

Meta-analysis of all known studies showed only marginal short-term benefit of antibiotics.

Antibiotic prophylaxis contributes to resistance and should be used infrequently.

For persistent effusion ≥3 months consider: 1. Hearing evaluation, 2. Consultation with ENT.

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Pharyngitis in Children & Adults

Signs and symptoms:

1. Tonsillar exudate 2. Tender anterior cervical lymph nodes
3. Absence of cough 4. Fever

2-4 CRITERIA PRESENT

OBTAIN RAPID STREPTOCOCCAL ANTIGEN TEST

POSITIVE

Group A Streptococcal Pharyngitis Management

Adults: single-dose benzathine penicillin 1.2 m.u. IM *or* penicillin V 500 mg po bid x 10 days.
Pen-allergic adults: erythromycin.

Children <12 years: single-dose benzathine penicillin 25,000 units/kg IM (max. dose 1.2 million units) *or* amoxicillin or penicillin V 45 mg/kg/day po divided bid or tid x 10 days.
Pen-allergic children: erythromycin.

Macrolide use should be discouraged for initial therapy in patients that can tolerate beta-lactams.

Children with streptococcal pharyngitis should not return to school or child care during the first 24 hours after beginning antimicrobial therapy. Follow-up throat culture is not recommended.

NEGATIVE

< 2 CRITERIA PRESENT

DO NOT TEST

Viral Pharyngitis Management

90% of pharyngitis is viral in origin.

Antibiotics benefit only the 10% of cases caused by Group A beta-hemolytic streptococcus.

Symptomatic treatments:
- Avoid cigarette smoke
- Gargle with dilute salt water
- Acetaminophen or ibuprofen as needed for fever or pain
- Throat lozenges (age-appropriate)
- Hydration—drink plenty of liquids
- Adequate rest

*For children, a negative rapid antigen test should be confirmed with a throat culture. Due to the lower incidence of strep infection and acute rheumatic fever in adults, a negative rapid test alone is sufficient to rule out Group A strep infection in adults.**

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*According to Clinical Laboratory Improvement Amendments (CLIA) guidelines, throat culture should be performed if required by the manufacturer.

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Acute Sinusitis / Rhinosinusitis – Adults

URI symptoms with mucopurulent discharge

<10 DAYS DURATION (UNLESS SEVERE SYMPTOMS)

Purulent nasal secretions or sputum do not predict bacterial infection.

Most cases of acute rhinosinusitis seen as outpatients are caused by uncomplicated viral upper respiratory infection.

Antibiotic treatment of adults with non-specific URI does not improve symptoms or prevent complications.

Management

Symptomatic measures include:

- Avoid cigarette smoke
- Drink plenty of liquids
- Steam (e.g., showers or baths) to loosen secretions
- Warm facial packs for 5-10 minutes 3-4 times a day to promote drainage
- Saline nasal spray or drops may provide some relief
- Acetaminophen or ibuprofen as needed for fever or pain
- Adequate rest
- Elevate head of bed to promote sinus drainage

SPECIFIC SYMPTOMS OF SINUSITIS OF ANY DURATION OR SYMPTOMS >10 DAYS WITHOUT IMPROVEMENT

Purulent nasal discharge for 3-4 days
Unilateral facial pressure/pain
Maxillary toothache
Worsening of symptoms after initial improvement

Management

Mild disease, no recent antibiotic use*: amoxicillin (1.5 - 4 gm/day**); amoxicillin-clavulanate (1.75 - 4 gm/day**); cefdinir, cefpodoxime or cefuroxime.

Moderate disease or mild disease with recent antibiotic use*:** amoxicillin-clavulanate (4 gm/day); ceftriaxone; gatifloxacin, levofloxacin, or moxifloxacin.

For Type 1 pen-allergic patients (hives or anaphylaxis) : TMP/SMX, doxycycline, erythromycin, azithromycin or clarithromycin.

* For paiients with no improvement after 72 hours, consider drugs listed under moderate disease.

** Use higher dose when patient has risk factors for DRSP or in geographic areas where prevalence of DRSP is known to be high.

***For patients with no improvement after 72 hours, consider imaging studies, sinus aspirate or ENT consultation.

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Acute Sinusitis / Rhinosinusitis – Children

URI symptoms with mucopurulent discharge

<10 DAYS DURATION (UNLESS SEVERE SYMPTOMS)

Purulent nasal secretions or sputum do not predict bacterial infection.

Most cases of acute rhinosinusitis seen as outpatients are caused by uncomplicated viral upper respiratory infection.

Antibiotic treatment of children with non-specific URI does not improve symptoms or prevent complications.

Management

Symptomatic measures include:

- Avoid cigarette smoke
- Drink plenty of liquids
- Steam (e.g., showers or baths) to loosen secretions
- Warm facial packs for 5-10 minutes 3-4 times a day to promote drainage
- Saline nasal spray or drops may provide some relief
- Acetaminophen or ibuprofen as needed for fever or pain
- Adequate rest
- Elevate head of bed to promote sinus drainage

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SPECIFIC SYMPTOMS OF SINUSITIS OF ANY DURATION OR SYMPTOMS >10 DAYS WITHOUT IMPROVEMENT

High (>39°C) or persistent fever

Purulent nasal discharge for 3-4 days in a child who appears ill

Unilateral facial pressure/pain

Postnasal drainage

Periorbital swelling

Management

Amoxicillin remains as efficacious as newer drugs: 80-90 mg/kg/day, divided bid for 7-10 days* (maximum dose 2-3 gm/day).

If no improvement in 48-72 hours, ceftriaxone or amoxicillin-clavulanate 80-90 mg/kg/day, divided bid for 7-10 days.

Other treatment alternatives, or for pen-allergic patients (*not Type 1 hypersensitivity*): cefdinir, cefpodoxime, cefuroxime.

For severe allergies (hives or anaphylaxis): azithromycin** or clarithromycin.

Consider imaging studies or ENT consult in persistent or unclear cases.

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* Patients with severe or prolonged symptoms may require up to 14 days of treatment.

** Not FDA-approved for sinusitis in children.

Cough Illness / Bronchitis* – Adults

Cough without evidence of pneumonia

Acute / < 3 weeks cough

Evaluation should focus on ruling out serious illness; normal vital signs and chest exam effectively rule out pneumonia. Cough illness/ bronchitis is caused by viral pathogens in >90% of cases.

Antibiotics are not effective in treating cough illness/bronchitis in patients without chronic lung disease.

Antibiotic treatment *does not* prevent bacterial complications such as pneumonia.

The presence of sputum and its characteristics are not helpful in distinguishing bacterial from viral infections.

Management

Do not use antibiotics for cough less than 21 days in a well-appearing adult without clinical evidence of pneumonia.

Therapeutic measures include: avoid cigarette smoke, consider bronchodilators, drink plenty of liquids, steam (e.g., from shower or bath) to loosen secretions, acetaminophen or ibuprofen as needed for fever or pain, adequate rest, and guaifenesin/ antitussive for symptom relief.

Chronic / > 3 weeks cough

Adults with prolonged cough or recurrent episodes can be evaluated for:

- Asthma or reactive airway disease
- Smoking or second-hand smoke exposure
- Post-nasal drip syndrome
- Gastroesophageal reflux disease (GERD)
- ACE-inhibitor drug cough
- Environmental exposures
- Chronic bronchitis
- Bronchiectasis
- Malignancy

Other infectious agents rarely causing prolonged cough include *B. pertussis, M. pneumoniae* or *C. pneumoniae.*

Management

Obtain CXR.

Treat COPD exacerbation (fever, leukocytosis and purulent sputum) with amoxicillin, TMP/SMX or doxycycline, and a short course (10–14 days) of oral corticosteroids.

Treat confirmed *B. pertussis* with a macrolide (erythromycin, azithromycin, or clarithromycin).

Treat confirmed *M. pneumoniae* or *C. pneumoniae* with a macrolide or doxycycline.

For other etiologies, direct therapy to the specific underlying cause.

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* The term *bronchitis* triggers an expectation for antibiotics and should be avoided or carefully explained. Other terms, such as “chest cold,” may be preferable.

Cough Illness / Bronchitis* – Children

Cough without evidence of pneumonia

Acute / < 3 weeks cough

Most cough illness in children is caused by viral pathogens.

Antibiotic treatment does not prevent bacterial complications such as pneumonia.

Rhinovirus often triggers a cough that lasts up to 2 weeks.

The presence of sputum and its characteristics are not helpful in distinguishing bacterial from viral infections.

Management

Do not use antibiotics for cough less than 3 weeks in a well-appearing child without clinical evidence of pneumonia.

Therapeutic measures include: avoid cigarette smoke, consider bronchodilators, drink plenty of liquids, steam (e.g., from shower or bath) to loosen secretions, acetaminophen or ibuprofen as needed for fever or pain, and adequate rest.

Chronic / > 3 weeks cough

Consider pertussis in children with paroxysmal cough, inspiratory whoop, or history of exposure.

In children >5 years of age, consider *M. pneumoniae* or *C. pneumoniae.*

Non-infectious causes that need to be ruled out:

- Allergies
- Habit cough
- Sinusitis
- Cystic fibrosis
- Foreign body aspiration
- Reactive airway disease
- Second-hand smoke exposure
- Gastroesophageal reflux disease (GERD)

Management

Treat confirmed *B. pertussis* with a macrolide (erythromycin, azithromycin, or clarithromycin).

Treat *M. pneumoniae* or *C. pneumoniae* with a macrolide, or, if >8 years of age, tetracycline.

For other etiologies, direct therapy to the specific underlying cause.

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Community-Acquired Pneumonia (CAP) in Adults

Outpatient treatment of adults not HIV-infected or immunocompromised

Clinical Considerations

CAP should be suspected in patients with newly-acquired lower respiratory tract symptoms (cough, sputum production, or dyspnea) especially if accompanied by fever, altered breath sounds, and rales. A CXR is required to make the diagnosis.

The initial site of care is the single most important decision made by clinicians during an episode of CAP. This decision involves 3 steps: 1) assessment of any preexisting conditions that compromise the safety of home care; 2) calculation of the PSI (see verso); and 3) clinical judgement.

A significant number of treatment failures have been documented for *S. pneumoniae* resistant to macrolides.

Fluoroquinolones should be used for outpatients only when the patient has failed first-line therapy, has known allergy to first-line agents, or where highly resistant pneumococcus (penicillin MIC > 4 mcg/ml) is prevalent.

Management of Outpatients

Previously healthy, no recent (within 3 months) antibiotic therapy: 1) azithromycin, clarithromycin, erythromycin or doxycycline.

Previously healthy, antibiotics within past 3 months: 1) azithromycin or clarithromycin, **plus** high-dose amoxicillin (4 gm/day) or amoxicillin-clavulanate (4 gm/day); 2) a respiratory fluoroquinolone alone.

Comorbidities (COPD, diabetes, renal or congestive heart failure, malignancy), no recent antibiotic therapy: 1) azithromycin or clarithromycin; 2) a respiratory fluoroquinolone alone.

Comorbidities, antibiotics within past 3 months: 1) azithromycin or clarithromycin, **plus** high-dose amoxicillin, amoxicillin-clavulanate, cefpodoxime, cefprozil or cefuroxime; 2) a respiratory fluoroquinolone alone.

Further Guidelines on Management of Inpatients with CAP

Mandell LA, Bartlett JG, Dowell SF, File TM, Musher DM, Whitney C. Update of practice guidelines for the management of community-acquired pneumonia for immunocompetent patients. CID 2003;37:1405-33.

Bartlett JG, Dowell SF, Mandell LA, File TM, Musher DM, Fine MJ. Practice guidelines for the management of community-acquired pneumonia in adults. CID 2000;31:347-82.

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Adult CAP PSI Risk Calculator

Risk Class I *(usually outpatient care)*

Outpatients <50 years old with no cardiopulmonary disease and none of the following risk factors:

- Comorbidities: neoplastic disease, heart failure, cerebrovascular, chronic pulmonary, renal or hepatic disease, bronchiectasis, diabetes, alcoholism, malnutrition
- Hospitalization within past year
- Physical exam findings: Altered mental status, pulse ≥ 125/minute, respiratory rate ≥ 30/minute, systolic BP < 90mmHg, temperature < 35°C or ≥ 40°C

Risk Classes II-V *(see table below right for site of care)*

Add up point score for patients not qualifying for Class I according to the following list:

Characteristic	Points
Demographic factors:	
Age (men)	1 point/year
Age (women)	Age (yr) - 10
Nursing home resident	10
Comorbidities:	
Neoplastic disease	30
Liver disease	20
Congestive heart failure	10
Cerebrovascular disease	10
Renal disease	10
Physical exam findings:	
Altered mental status	20
Respiratory rate ≥ 30/minute	20
Systolic BP < 90 mmHg	20
Temperature < 35°C or ≥40°C	15
Pulse ≥ 125/minute	10
Lab and Radiographic Findings:	
Arterial pH < 7.35	30
Na < 130 mEq/L	20
Partial pressure of arterial 0_2< 60mmHg	10
BUN ≥ 30 mg/dL (14 mmol/L)	10
Hematocrit < 30	10
Pleural effusion	10

Risk Class Point Assignment and Site of Care

Class	Points	Site of Care
I	(see above)	Outpatient care
II	≤70	Outpatient care
III	71-90	Brief inpatient observation
IV	91-130	Traditional inpatient care
V	>130	Traditional inpatient care

Adapted from Bartlett et al., CID 2000;31:347-82. The calculator above can be downloaded for PDA at http://pda.ahrq.gov/clinic/psi/psi.htm.

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http://www.healthoregon.org/antibiotics.cfm
oregon.aware@state.or.us 4/2005

HELP SPREAD THE WORD ABOUT JUDICIOUS ANTIBIOTIC USE!

General Brochure

Warning: Unnecessary Antibiotics Can Be Harmful

Explains how taking unnecessary antibiotics leads to development of resistant bacteria. Lists which types of illnesses respond to antibiotic treatment.

Parent Brochure

Antibiotics Aren't Always the Answer

Encourages the appropriate use of antibiotics and answers parents' questions about common childhood URIs.

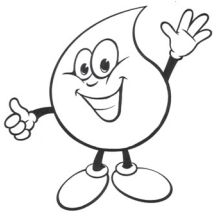
Spanish Brochure

¡La Penicilina No Sirve Para Todo!

Clarifies the role of antibiotics in treating upper respiratory infections, and suggests a number of home-care options for common viral illnesses.

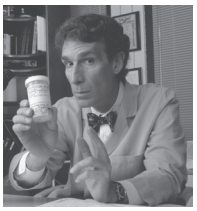
Children's Activity Kit

An eight-page booklet of educational coloring sheets and word games for kids ages 2-10. Reinforces the importance of handwashing and taking antibiotics as directed. Info for parents explains how families can use antibiotics safely and reduce their risk of developing resistant infections. Available in English and Spanish.



Bilingual Poster

Featuring Bill Nye "The Science Guy," the English side explains the dangers of inappropriate antibiotic use while discouraging the hoarding and sharing of antibiotic medications.



The Spanish side reinforces the importance of using antibiotics safely to protect the whole family's health.

Viral Rx Pad

50 pre-formatted sheets "prescribe" home treatment to relieve the symptoms of viral URIs.

Childcare Advice Letter Pad

50 pre-formatted letters to childcare providers explain that your pediatric patient's viral URI does not require antibiotics.

Bilingual Question & Answer Sheets

Three separate sheets answer common questions about the treatment of upper respiratory illnesses. Bilingual English/Spanish on three topics: Ear Infections, Runny Noses, and Colds.

All materials are written at a seventh grade reading level. They may be viewed and downloaded in .pdf format at http://www.healthoregon.org/antibiotics/pubs.cfm.

For bulk orders, use the form on page 30 or call (503) 731-4024. We charge minimal fees to cover printing and shipping. Fees are waived for rural and safety net clinics, in-home child care providers, public schools and other publicly funded organizations.

Safe Use of Antibiotics
EDUCATIONAL MATERIALS ORDER FORM

Oregon Alliance Working for Antibiotic Resistance Education

Item	Indicate desired amount of packets/pads	Price
Brochures (packets of 50 for $5.00)	____ Antibiotics Are Not Always the Answer (for parents) ____ Warning: Unnecessary Antibiotics May Be Harmful (general) ____ La Penicilina No Sirve Para Todo (Spanish)	
Bilingual Question & Answer Sheets English/Spanish (packets of 50 for $3.50)	____ Child Ear Infection ____ Child Runny Nose ____ Adult Viral Upper Respiratory Infection	
Posters (.50 each)	____ English/Spanish Think You Need Antibiotics? / La Penicilina No Sirve Para Todo	
Children's Activity Kit (packets of 50 for $5.00)	____ English ____ Spanish	
Viral "Prescription" Pad for health care providers (pads of 50 for $1.00 each)	____ English ____ Spanish	
Child Care Advice Letter for health care providers (pads of 50 for $1.00 each)	____ English ____ Spanish	
	TOTAL = $	

SHIP TO: (please print or type clearly)

Name

Street Address (no P.O. boxes)

City	State	Zip
Phone	Fax	E-mail

Please indicate payment method below. Allow 4-6 weeks for delivery. Prices include shipping. *Sorry, no credit cards accepted.*

☐ CHECK ENCLOSED
Mail order form with check payable to **Office of Health Services** to:
Oregon DHS Health Services
Cashier's Office
P.O. Box 14260
Portland, OR 97293-0260

☐ BILL ME
Fax or mail order form to:
Oregon AWARE
800 NE Oregon, Suite 772
Portland, OR 97232
Fax: 503-731-4798
Phone: 503-731-4024

☐ ELIGIBLE FOR FREE MATERIALS
Rural and safety net clinics, in-home child care providers, public schools and other publicly funded organizations: send order form to "Bill Me" address.

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Produced in collaboration with

DHS
Oregon Department
of Human Services
Office of Disease Prevention & Epidemiology