Review Article

Current Concepts

Community-Acquired Pneumonia in Children

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COMMUNITY-ACQUIRED pneumonia is a common and potentially serious infection that afflicts children throughout the world; it is fundamentally different in children and in adults. The annual incidence of pneumonia in children younger than 5 years of age is 34 to 40 cases per 1000 in Europe and North America, higher than at any other time of life, except perhaps in adults older than 75 or 80 years of age.[1-4] In the developing world, pneumonia is not only more common than it is in Europe and North America[5-7]; it is also more severe and is the largest killer of children.[8,9]

Definitions of pneumonia vary widely. Some require only the presence of infiltrates on a chest radiograph,[2] whereas others require only certain respiratory symptoms or signs.[3] The World Health Organization has defined pneumonia solely on the basis of clinical findings obtained by visual inspection and timing of the respiratory rate.[10] Definitions are a particular problem in the case of small infants, since pneumonia and bronchiolitis are both common in this age group, and the features of these two diseases often overlap. Many studies, particularly those in the developing world, use the term "acute lower respiratory tract illness" and make no attempt to differentiate pneumonia from bronchiolitis.[7] For the purposes of this review, and particularly with respect to recommendations for treatment, pneumonia will be defined as the presence of fever, acute respiratory symptoms, or both, plus evidence of parenchymal infiltrates on chest radiography. Even this definition overlaps somewhat with that of bronchiolitis and leaves some room for disagreement among clinicians.

CAUSES

A very large number of microorganisms can cause childhood pneumonia (Tables 1 and 2), and determining the cause of an individual case may be difficult. The lung itself is rarely sampled directly, and sputum representing lower-airway secretions can rarely be obtained from children. In addition, as is the case in adults, culture of secretions from the upper respiratory tract is not useful, since the normal flora includes the bacteria commonly responsible for pneumonia.

Multiple investigations of pediatric pneumonia during the 1960s and 1970s in North America and Europe emphasized the importance of infections with respiratory viruses (respiratory syncytial virus, influenzavirus, parainfluenza viruses, and adenovirus) in preschool children, *Mycoplasma pneumoniae* in school-age children, and *Chlamydia trachomatis* in infants between two weeks and four months of age. Multiple studies have confirmed the capacity of these agents to cause pneumonia, although their role in individual cases may sometimes be unclear. More recently, *C. pneumoniae* has been found in school-age children with pneumonia,[12-15] but the strength of arguments for an etiologic role is diluted by the frequency of asymptomatic infections.[16] Similarly, the roles of cytomegalovirus, *Ureaplasma urealyticum*, *Pneumocystis carinii*,[17] and more recently, rhinoviruses[11] as causes of community-acquired pneumonia in otherwise healthy infants and children remain controversial, in view of the absence of confirmatory studies or, in some instances, the high frequency of prolonged carriage or asymptomatic infection — features that make it difficult to demonstrate a causal role.

The role of bacteria as a cause of severe pneumonia is best documented in lung-puncture studies, which have been conducted largely in the developing world.[18-26] These have confirmed the importance of *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Haemophilus influenzae*, including nontypable strains, as causes of severe pneumonia. In some studies, *S. pyogenes* and gram-negative enteric bacteria also appear.[22,23] Other series that have focused on severe or complicated disease, particularly cases involving parapneumonic effusions, have also demonstrated the importance of bacteria as causes of pneumonia.[27]

The precise role of bacteria, particularly in less severe disease, remains controversial. There have been efforts over the past decade to define this role more clearly, largely through the measurement of bacterial antigens, nucleic acid (by means of the polymerase-chain-reaction assay), antibodies, or immune complexes in blood or urine.[11,28-37] The value of these tests is, however, questionable. Antigen tests lack specificity,[38] and evidence of the sensitivity and specificity

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TABLE 1. COMMON CAUSES OF COMMUNITY-ACQUIRED PNEUMONIA IN OTHERWISE HEALTHY CHILDREN.

Viruses
- Respiratory syncytial virus
- Influenza A or B
- Parainfluenza viruses 1, 2, and 3
- Adenovirus
- Rhinovirus*
- Measles virus†

Mycoplasma
- *Mycoplasma pneumoniae*

Chlamydia
- *Chlamydia trachomatis*
- *C. pneumoniae*‡

Bacteria
- *Streptococcus pneumoniae*
- *Mycobacterium tuberculosis*
- *Staphylococcus aureus*§
- *Haemophilus influenzae* type b¶
- Nontypable *H. influenzae*†

*Recent data from surveys that used polymerase-chain-reaction assays implicated rhinoviruses as a cause of pneumonia.[11] Some would question its etiologic role.

†Measles virus and nontypable strains of *Haemophilus influenzae* are common causes of pneumonia in the developing world, but uncommon causes in the developed world.

‡Among older schoolchildren and adolescents, *C. pneumoniae* may be a common cause of pneumonia. There is disagreement among studies and some concern about its role, however, in view of its frequent recovery in asymptomatic subjects.

§Pneumonia due to *S. aureus* is now uncommon in the United States and Europe, but it is still relatively common in other areas, particularly the developing world.

¶Pneumonia caused by *H. influenzae* type b is restricted to parts of the world where the conjugate vaccine is not widely used.

of bacterial antibody tests in children is either absent (in the case of nontypable *H. influenzae* and *Moraxella catarrhalis*) or severely limited (*S. pneumoniae*).[26] One point is clear: the more tests that are done, the more potential causes emerge. Two contrasting studies illustrate this point. In one large, early series, no serologic tests were performed, and mycoplasma or viruses were identified by culture of respiratory secretions.[3] In only 24 percent of cases was a potential cause identified, and only 0.3 percent involved combined infections. In contrast, a recent case series included antibody tests for *S. pneumoniae* and *H. influenzae*, as well as sensitive solid-phase immunoassays for respiratory viruses and a polymerase-chain-reaction assay for rhinoviruses.[11] A potential cause was identified in 85 percent of cases, and combined infections, usually bacterial and viral, were seen in 41 percent.

TABLE 2. UNCOMMON CAUSES OF COMMUNITY-ACQUIRED PNEUMONIA IN OTHERWISE HEALTHY CHILDREN.

Viruses
- Varicella–zoster virus
- Coronaviruses
- Enteroviruses (Coxsackievirus and echovirus)
- Cytomegalovirus
- Epstein–Barr virus
- Mumps virus
- Herpes simplex virus (in newborns)
- Hantavirus*†

Chlamydia
- *Chlamydia psittaci*†

Coxiella
- *Coxiella burnetii*†

Bacteria
- *Streptococcus pyogenes*
- Anaerobic mouth flora (*S. milleri,* peptostreptococcus)
- Non–type b (but typable) *Haemophilus influenzae*
- *Bordetella pertussis*‡
- *Klebsiella pneumoniae*
- *Escherichia coli*
- *Listeria monocytogenes*
- *Neisseria meningitidis* (often group Y)
- Legionella
- *Pseudomonas pseudomallei**
- *Francisella tularensis*†§
- *Brucella abortus*†
- Leptospira†

Fungi
- *Coccidioides immitis**
- *Histoplasma capsulatum**
- *Blastomyces dermatitidis**

*This organism should be included in the differential diagnosis as a cause of pneumonia only if there is a history of residence in or travel to an area of endemic infection.

†This organism should be included in the differential diagnosis only if there is a history of possible or definite exposure to particular animal reservoirs.

‡Most infants and children with clinically significant pertussis do not have pneumonia.

§This organism should be included in the differential diagnosis only if there is a history of possible or definite contact with insect vectors.

It is not clear what these multiple microbial associations mean. For example, in spite of the demonstration of possible pneumococcal involvement (with the use of serologic methods) in 39 percent of hospitalized children with respiratory syncytial virus infection,[39] experience dictates that antibiotics are rarely indicated in the treatment of such children.[40] Although by damaging the respiratory tract, a respiratory virus or *M. pneumoniae* might facilitate the aspiration of bacteria into the lungs or the escape of bacterial components into the lymph or bloodstream, triggering the production of antibody or immune complexes, this mechanism does not mean that these bacteria are the cause of pneumonia, nor does it mean, on a more practical level, that they need to be treated with antibiotics. In fact, the apparent 35 percent reduction in the incidence of disease associated with the use of the recently licensed pneumococcal conjugate vaccine may provide the clearest estimate of the role of *S. pneumoniae* in causing childhood pneumonia in Europe and the United States.[41,42]

In the developing world, bacteria, particularly *S. pneumoniae*, *H. influenzae*, and *S. aureus*, play a critical part in causing life-threatening pneumonia, usually with lobar consolidation. Bacteria are also the chief cause of severe or complicated pneumonias in children in Europe and North America, although widespread immunization has nearly eliminated pneumonia due to *H. influenzae* type b in the United States. In the future, immunization may reduce the frequency of pneumonia due to *S. pneumoniae*. Certain respiratory viruses, *C. trachomatis,* and *M. pneumoniae* are also important causes of disease in preschool and school-age children. Emerging evidence indicates that *C. pneumoniae* infection may be the cause of a substantial fraction of cases of pneumonia among school-age children and adolescents.[12]

DIAGNOSIS

Establishing a microbiologic diagnosis, despite its limitations, may be important in children with severe or complicated pneumonia or in those with unusual but treatable causes. A guide to preferred diagnostic procedures is presented in Table 3. As a practical matter, however, the cause of pneumonia can usually be surmised on the basis of clinical and epidemiologic data, findings on chest radiography, and a few laboratory tests such as a complete blood count, erythrocyte sedimentation rate, and levels of C-reactive protein. Although it is difficult to determine the accuracy of such nonmicrobiologic diagnostic approaches because of the lack of an etiologic gold standard, there have been many attempts to correlate them with microbiologic causes. The results of these attempts have been confusing.

For example, although the differentiation between typical (i.e., bacterial) pneumonia and atypical (i.e., viral or mycoplasmal) pneumonia may be clinically useful in the case of adolescents and adults, these syndromes are not well defined in infants and preschool children. In four large series in which investigators looked carefully at the cause of pediatric pneumonia in relation to clinical or epidemiologic findings, the signs and symptoms were surprisingly uniform throughout the etiologic spectrum.[34-36,43] In one study, pneumonias related to bacterial infection and those related to viral infection differed only with respect to the incidence of conjunctivitis (27 percent, as compared with 8 percent) and otitis media (42 percent, as compared with 22 percent).[35] In two other studies, wheezing was found more frequently in patients with viral pneumonia than in those with bacterial pneumonia (43 percent vs. 16 percent[34] and 56 percent vs. 16 percent[43]), but the features that we usually associate with viral respiratory tract infection, such as rhinorrhea, illness in family members, and myalgia, were not.[34,43]

When chest radiographs are subjected to blinded readings, they also cannot be used to differentiate between viral and bacterial disease. Several studies flatly state that there are no radiologic features that can be used to differentiate between these two major etiologic classes.[44,45] Another study concludes that radiographic findings have less discriminatory value than does measurement of C-reactive protein, erythrocyte sedimentation rate, or the white-cell count and the differential count.[46] In contrast, using data from a large Finnish series, Korppi and his colleagues[47] concluded, as would many radiologists,[48] that an alveolar (equivalent to a "lobar") infiltrate is an insensitive but reasonably specific indication of bacterial infection. And in cases at either extreme (from typical bronchiolitis with scattered infiltrates to dense lobar pneumonia with a large pleural effusion), the level of diagnostic certainty provided by radiologic findings is quite high.[48,49] In addition, there are helpful series that describe the range and frequency of radiographic findings in patients with mycoplasmal,[50] viral,[51] chlamydial,[52] and pneumococcal[53] pneumonia.

Nonmicrobiologic laboratory tests have also been widely used in an attempt to differentiate bacterial from nonbacterial pneumonia. However, they are not much better than chest radiographs. Several analyses show that the C-reactive protein level and the absolute neutrophil count are the most helpful,[46,54-58] although the dividing lines are not sharp. Cutoff levels of 40 mg of C-reactive protein per liter,[56] 60 mg per liter,[57] and 100 mg per liter[46] have been used to identify bacterial infection, each with somewhat different results. In these comparisons, children with pneumococcal pneumonia were more easily identified than those with other bacterial causes, and the findings in patients with mycoplasmal pneumonia were similar to those in patients with viral infections.[46,54]

TREATMENT

Perhaps because of the many controversies that surround the etiologic process of community-acquired pneumonia in children, there have been few attempts to devise treatment guidelines in Europe or North America. In contrast, official recommendations regarding the treatment of pneumonia in adults have been published in Britain, Canada, and the United States.[59-61] An ad hoc group of Canadian experts has published guidelines,[62] and numerous recommendations address subgroups of patients with pneumonia,

TABLE 3. MICROBIOLOGIC DIAGNOSIS OF PNEUMONIA IN CHILDREN.*

MICROORGANISM	PREFERRED DIAGNOSTIC METHOD	COMMENTS
Viruses		
Respiratory syncytial virus Influenza A or B Parainfluenza viruses 1, 2, and 3 Adenovirus	Identify the virus in nasopharyngeal secretions; the best test is immunofluorescence assay, solid-phase immunoassay, or PCR assay.	Viral culture is also helpful, but results may not be available for several days. Comparison of antibody levels during the acute phase and convalescence adds little useful information. In cases of adenoviral infection, serotyping may be helpful.
Rhinovirus	Identify the virus by PCR assay of nasopharyngeal secretions.	The etiologic connection not well established.
Measles virus	Identify the virus by immunofluorescence assay of nasopharyngeal secretions, or measure at least a quadrupling of serum antibody levels between the acute phase and convalescence.	The clinical diagnosis may be quite specific.
Varicella–zoster virus	Identify the virus by immunofluorescence assay of skin lesions, or measure at least a quadrupling of serum antibody levels between the acute phase and convalescence.	The clinical diagnosis is usually quite specific.
Hantavirus	Identify virus in nasopharyngeal secretions or antibody in serum. IgM or IgG antibodies may be found at presentation.	Hantavirus infection is sufficiently uncommon that the finding of antibody in one serum sample is essentially diagnostic of acute infection.
Cytomegalovirus Epstein–Barr virus	Identify IgM antibodies in serum during the acute phase or at least a quadrupling of serum antibody levels between the acute phase and convalescence.	Finding virus in upper-airway secretions is not valuable with respect to the diagnosis, since both cytomegalovirus and Epstein–Barr virus may be found in normal subjects.
Chlamydia		
Chlamydia trachomatis	Identify virus in nasopharyngeal secretions by culture or PCR assay.	An IgM antibody test may be helpful.
Chlamydia pneumoniae	Identify the virus in nasopharyngeal secretions by culture or PCR assay, or measure at least a quadrupling of serum antibody levels between the acute phase and convalescence.	Etiologic connection in young children is not yet well established. The evidence is more convincing with respect to adolescents.
Chlamydia psittaci	The finding of at least a quadrupling of serum antibody levels between the acute phase and convalescence is diagnostic.	
Coxiella		
Coxiella burnetii	The finding of at least a quadrupling of serum antibody levels between the acute phase and convalescence is diagnostic.	
Mycoplasma		
Mycoplasma pneumoniae	The finding of cold agglutinins (titer >1:128) or IgM antibody in serum late in the acute phase or early in convalescence is helpful, as is a positive PCR assay of secretions from a throat or a nasopharyngeal swab.	The finding of at least a quadrupling of serum antibody levels between the acute phase and convalescence is diagnostic.
Bacteria *Streptococcus pneumoniae* *Haemophilus influenzae* *Streptococcus pyogenes* *Staphylococcus aureus* Gram-negative enteric bacteria Mouth anaerobes Group B streptococci *Neisseria meningitidis*	Identify bacteria in culture of blood or pleural fluid.	Culture of blood or pleural fluid is clearly an insensitive method, but there are not yet any established alternatives in children.
Bordetella pertussis	Identify bacteria in culture, immunofluorescence assay, or PCR assay of nasopharyngeal secretions.	
Francisella tularensis	The finding of at least a quadrupling of serum antibody levels between the acute phase and convalescence is diagnostic.	Culture of blood or sputum for this organism requires special medium and may pose a danger of infection to laboratory workers.
Legionella pneumophila and other legionella species	Identify bacteria in culture of sputum or tracheal aspirate or antigen in urine; or measure at least a quadrupling of serum antibody levels between the acute phase and convalescence.	Culture of the organism requires special medium. Urinary antigen tests can detect only *L. pneumophila* antigen.
Brucella abortus	Identify bacteria in culture of blood or measure at least a quadrupling of serum antibody levels between the acute phase and convalescence.	
Mycobacterium tuberculosis	Identify bacteria in culture of sputum or gastric aspirates, with or without a positive test for tuberculosis with purified protein derivative.	Culture of bronchoalveolar-lavage fluid is also specific but somewhat less sensitive. A PCR assay is more useful for the identification of the bacterium than for the detection of it.
Fungi		
Histoplasma capsulatum *Blastomyces dermatitidis* *Coccidioides immitis*	Identify organism by staining or culture of respiratory tract secretions; or measure serum IgM antibody or at least a quadrupling of serum antibody levels between the acute phase and convalescence.	Histoplasma antigen is sometimes detectable in urine.

*PCR denotes polymerase chain reaction.

which are usually classified according to the cause.[63-65] In contrast, given the enormous problem of undifferentiated pneumonia in the developing world, the World Health Organization issued its own treatment guidelines in the early 1980s.[10] These guidelines, however, are designed for areas where pneumonia is a major killer, bacterial pneumonia is probably more common, access to drugs is limited, and the available diagnostic tools are few.[66]

Treatment decisions should be based on diagnostic algorithms that begin with the age of the child, then consider clinical and epidemiologic factors, and finally take into account the results of chest radiography. The Canadian consensus statement,[62] which is primarily based on age, serves as an excellent introduction to a discussion of management and treatment.

The most likely causes of pneumonia according to age are given in Table 4. Pneumonia during the first three weeks after birth is uncommon, but when it does occur it is often related to perinatally associated infections. Between three weeks and three months of age, two of the most important causes of pneumonia are macrolide-sensitive organisms: *C. trachomatis* is also one of the most common, and *Bordetella pertussis* is an infrequent cause of pneumonia, although when it does occur the disease may be very severe.[68-70] These pneumonias usually have an interstitial pattern of infiltrates, with cough as a prominent feature. In children who are older than five years of age, two other macrolide-sensitive organisms, *M. pneumoniae* and *C. pneumoniae*, cause pneumonia that, on chest radiograph, is often not distinguishable from bacterial pneumonia but that is characterized by cough, a low-grade fever, and sometimes wheezing. In many surveys, *M. pneumoniae* is the most common identified cause of pneumonia among children who are 5 to 15 years of age.

Despite their limitations, clinical and epidemiologic findings may be useful. The presence of symptoms and signs of sepsis, even in the absence of severe respiratory symptoms, suggests bacterial infection. Localized chest pain (unlike the retrosternal pain of tracheitis, which tends to occur in viral or mycoplasma infections) usually signifies pleural irritation, and pleural irritation in an otherwise healthy child is rarely found in any type of pneumonia other than bacterial. A child with pneumonia who is wheezing is likely to have a viral, *M. pneumoniae*, or *C. pneumoniae* infection.[34,43] In most series, conjunctivitis has not been found to be characteristic of any type of pneumonia except in the case of infants less than three months of age; in this age group, *C. trachomatis* infection is included in the differential diagnosis.[71] The presence of otitis media or diarrhea cannot be used to help make the diagnosis.

Epidemiologic factors are important considerations for the identification of geographically restricted or exposure-related pneumonias (Tables 1 and 2). In temperate climates, seasonality is a major determinant. Respiratory syncytial virus infection and influenza are uncommon outside their winter–spring epidemics. Although *M. pneumoniae* epidemics are less predictable, cases do occur in community-wide clusters during the winter.[3,72]

There is ample evidence that a chest radiograph is useful to confirm the diagnosis of pneumonia. Several studies have demonstrated the lack of both sensitivity[73] and specificity[74,75] of the findings on history taking and physical examination. The signs and symptoms that have a high degree of sensitivity (e.g., fever and tachypnea) lack specificity, and those with a high degree of specificity (e.g., rales and pleuritic pain) lack sensitivity. Chest radiographs that show consolidative lobar infiltrates, particularly if either a large pleural effusion or any parenchymal necrosis is present, are indicative of a bacterial cause. When the white-cell count, differential count, and C-reactive protein level are very abnormal, they also have predictive value with respect to bacterial pneumonia and can corroborate a diagnosis that is based on clinical and historical information.

These considerations, in conjunction with the knowledge of prevailing antimicrobial-susceptibility patterns, can be used to determine the necessity for and the nature of empirical drug treatment (Table 5). In infants who are 3 weeks to 3 months of age and in those who are 5 to 15 years of age, a macrolide antibiotic is the most reasonable first choice,[69] unless the child appears to have sepsis or the chest radiograph shows lobar infiltrates (with or without effusion). The choice of macrolide can be based on availability, cost, tolerability, and convenience, since in comparative trials they have similar efficacy.[15,76] A second- or third-generation cephalosporin should be used for children with sepsis, except for infants, who should receive both ampicillin and gentamicin, as well as a third-generation cephalosporin in severe cases. Although staphylococcal pneumonia is now quite rare in Europe and North America,[77] it is still a possibility in some instances, and in these circumstances, oxacillin or, in areas where methicillin-resistant strains of *S. aureus* have appeared,[78] vancomycin should then be added to the regimen. If the condition of school-age children does not improve with the use of cephalosporin or if the findings on the chest radiograph or the clinical findings are ambiguous, a macrolide should be added, since patients who have either a *M. pneumoniae* or *C. trachomatis* infection can present with radiographic and clinical findings similar to those associated with an infection caused by pyogenic bacteria.

Treatment of pneumonia due to *S. pneumoniae* has

TABLE 4. MICROBIAL CAUSES OF COMMUNITY-ACQUIRED PNEUMONIA IN CHILDHOOD, ACCORDING TO AGE.*

AGE GROUPING AND CAUSE†	SALIENT CLINICAL FEATURES
Birth to 20 days	
Group B streptococci	Pneumonia part of early-onset sepsis; disease usually very severe, bilateral, diffuse
Gram-negative enteric bacteria	Infection often nosocomial, therefore often not seen until after 1 week of age
Cytomegalovirus	Pneumonia part of systemic cytomegalovirus infection; other signs of congenital infection usually present
Listeria monocytogenes	Pneumonia part of early-onset sepsis
3 Weeks to 3 months	
Chlamydia trachomatis	Caused by maternal genital infection; causes afebrile, progressive, subacute interstitial pneumonia
Respiratory syncytial virus	Peak incidence at 2 to 7 months of age; usually characterized by wheezing (hard to differentiate bronchiolitis from pneumonia); rhinorrhea typically profuse; midwinter or early spring
Parainfluenza virus 3	Very similar to disease caused by respiratory syncytial virus infection, but affects slightly older infants and is not epidemic in the winter
Streptococcus pneumoniae	Probably the most common cause of bacterial pneumonia, even in this young age group
Bordetella pertussis	Primarily causes bronchitis, but also causes pneumonia in severe cases
Staphylococcus aureus	A much less common cause of pneumonia now than in former years; causes severe disease, often with complicated effusion
4 Months to 4 years	
Respiratory syncytial virus, parainfluenza viruses, influenzavirus, adenovirus, rhinovirus	Most common cause of pneumonia in the younger children in this age group
Streptococcus pneumoniae	Most likely cause of lobar or segmental pneumonia, but may cause other forms as well
Haemophilus influenzae	Type b infection almost eliminated in areas with wide vaccine use; type b, other types, and nontypable forms common in the developing world
Mycoplasma pneumoniae	Causes pneumonia primarily in the older children in this age group
Mycobacterium tuberculosis	Important cause of pneumonia in areas with a high prevalence of infections with this organism
5 to 15 years	
Mycoplasma pneumoniae	Chief cause of pneumonia in this age group; radiographic appearance variable
Chlamydia pneumoniae	Still controversial, but probably an important cause in older children in this age group
Streptococcus pneumoniae	Most likely cause of lobar pneumonia, but probably causes other forms as well
Mycobacterium tuberculosis	Pneumonia particularly common in areas with a high prevalence of infections with this organism; may be exacerbated at the onset of puberty and by pregnancy

*Data were modified from McIntosh and Harper.[67]

†Causes are listed roughly in the descending order of frequency.

been the subject of several studies,[79-81] as well as of consensus guidelines issued by the American Academy of Pediatrics.[64] The emergence of strains of *S. pneumoniae* that are not susceptible to penicillin has had less of an effect on the treatment of pneumonia than on the treatment of meningitis, and satisfactory rates of recovery can be achieved with the use of high doses of many β-lactam antibiotics.[80] For most nonsusceptible strains, a second-generation cephalosporin (cefuroxime) or a third-generation cephalosporin (cefotaxime or ceftriaxone) is somewhat more effective than either ampicillin or penicillin, although a high dose of amoxicillin (80 to 100 mg per kilogram of body weight per day) is the preferred treatment for pneumonia in outpatients. The addition of a beta-lactamase inhibitor conveys no advantage, since the mechanism of resistance in this organism does not involve this enzyme. Vancomycin is rarely needed to treat pneumococcal pneumonia, even severe cases.

Use of the recently licensed pneumococcal conjugate vaccine appears likely to prevent the majority of cases of pneumococcal pneumonia in the United States,[41] but the high cost of this vaccine will preclude its use in the parts of the world where pneumococcal pneumonia is most common and severe. Moreover, there is already some evidence in vaccinated persons that pneumococcal serotypes not represented in the vaccine are replacing the serotypes covered by the vaccine and are causing otitis media.[82] The World Health Organization's approach to the treatment of pneumonia, despite its success,[83] may well aggravate the problem of antibiotic resist-

TABLE 5. SUGGESTED DRUG TREATMENTS FOR COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN, ACCORDING TO WHETHER THEY ARE HOSPITALIZED.*

AGE GROUPING	OUTPATIENT	INPATIENT, WITHOUT LOBAR OR LOBULAR INFILTRATE, PLEURAL EFFUSION, OR BOTH	INPATIENT, WITH SIGNS OF SEPSIS, ALVEOLAR INFILTRATE, LARGE PLEURAL EFFUSION, OR ALL THREE
Birth to 20 days	Admit patient.	Administer ampicillin and gentamicin, with or without cefotaxime.	Administer IV ampicillin and gentamicin, with or without IV cefotaxime.†
3 Weeks to 3 months	If patient is afebrile, give oral erythromycin (30–40 mg/kg of body weight/day in 4 divided doses) or oral azithromycin (1 dose of 10 mg/kg, then 5 mg/kg/day for 4 days). Admit patient if fever or hypoxia is present.	If patient is afebrile, administer IV erythromycin (40 mg/kg/day in 4 divided doses given 6 hours apart).‡ If patient is febrile, add cefotaxime (200 mg/kg/day in 3 divided doses given 8 hours apart).	Administer IV cefotaxime (200 mg/kg/day in 3 divided doses given 8 hours apart).†§
4 Months to 4 years	Administer oral amoxicillin (80–100 mg/kg/day in 3 or 4 divided doses).	In cases of apparent viral pneumonia, no antibiotics should be given. Otherwise, consider treatment with IV ampicillin (200 mg/kg/day in 4 divided doses given 6 hours apart).	Administer IV cefotaxime (200 mg/kg/day) or IV cefuroxime (150 mg/kg/day in 3 divided doses given 8 hours apart).†§
5 to 15 years	Administer oral erythromycin (30–40 mg/kg/day in 4 divided doses), oral clarithromycin (15 mg/kg/day in 2 divided doses), or oral azithromycin (1 dose of 10 mg/kg, then 5 mg/kg/day for 4 days). In children older than 8 years of age, consider oral doxycycline (4 mg/kg/day in 2 divided doses).	Administer IV erythromycin (40 mg/kg/day in 4 divided doses given 6 hours apart) or IV azithromycin (5 mg/kg/day in 2 divided doses given 12 hours apart). In children older than 8 years of age, consider IV doxycycline (4 mg/kg/day in 2 divided doses given 12 hours apart). If there is strong evidence of a bacterial cause (e.g., high white-cell count, chills, or no response to outpatient therapy with a macrolide), add ampicillin.	Administer IV cefotaxime (200 mg/kg/day) or IV cefuroxime (150 mg/kg/day in 3 divided doses given 8 hours apart).§ Consider adding IV azithromycin if patient is not doing well.†

*Data were modified from McIntosh and Harper.[67] IV denotes intravenous.

†Staphylococcal pneumonia is unusual; however, if cultures of blood or pleural fluid grow *Staphylococcus aureus* or, in other exceptional circumstances, oxacillin or, in areas where methicillin-resistant *Staph. aureus* is a reasonable possibility, vancomycin should be added.

‡In infants younger than six weeks of age, treatment with azithromycin (5 mg per kilogram per day in two divided doses given 12 hours apart) should be considered in view of reports of hypertrophic pyloric stenosis in infants who received erythromycin.

§Some experts suggest treatment with ampicillin (200 to 300 mg per kilogram per day intravenously in four divided doses given 6 hours apart) in patients who have lobar, and therefore most likely pneumococcal, pneumonia.

ance in communities that have the highest rates of death from pneumonia. The development of an affordable pneumococcal vaccine for infants and children should be a high priority, as should efforts to reduce the risk factors that lead to a high incidence of severe pneumonia, such as malnutrition, crowding, and air pollution.

CONCLUSIONS

Perhaps because of its etiologic complexity, pneumonia in children has been relatively refractory to efforts to reduce its incidence and severity and improve the prognosis. The use of treatment algorithms in the developing world has led to lower mortality rates,[82] but the future of this approach, given the rate of development of antimicrobial resistance, is uncertain. The wider use of new pneumococcal conjugate vaccines over the next few years may represent an important advance in countries that can afford it, but the public health effects of universal immunization, particularly over the long run, are not clear. There is still room for improvements in the diagnosis of pneumonia and in the elucidation of its cause in individual cases. Finally, regional consensus guidelines for management and antimicrobial treatment should be developed, refined over time, and used by practitioners in their offices and in hospitals.

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