Treatment Options for Pneumonia Across the Age Spectrum

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FACULTY:

Ruben J. Rucoba, MD
Instructor in Pediatrics,
Northwestern University Feinberg School of Medicine

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Ruben J Rucoba has no actual or potential conflict of interest in relation to this program.

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Program Overview:

To provide participants with an understanding of pneumonia in a variety of age groups as well as the risks each of those groups suffer.

OBJECTIVES:

After completing this program, participants will be able to:

- Identify the most likely pathogens that cause pneumonia
- Describe the appropriate antibiotic treatment for pneumonia in the following age groups: newborns, infants/toddlers/preschoolers, school age children, teens, adults, and seniors
Treatment Options for Pneumonia Across the Age Spectrum

Pneumonia is one of the most common infections in all age groups. In the US, about 4 million cases are diagnosed every year, costing the health care system $23 billion (Glover). This monograph will summarize the most significant pathogens causing pneumonia in each age group, and review the treatment options for each of these pathogens.

Newborns

Case #1: Baby Boy Fisher is a term baby born via vaginal delivery to a mother who had a normal pregnancy. She tested negative for Hepatitis B, but positive for Group B streptococcus. Her labor progressed quickly, and she received only one dose of penicillin before her baby was born. The child is now 6 hours old, and has respiratory distress and hypoxia. He is taken to the Neonatal Intensive Care Unit (NICU), where a chest x-ray shows patchy infiltrates. He is started on empiric antibiotics while awaiting cultures of the endotracheal secretions. What is the most likely pathogen in this case, and which empiric antibiotics should be started?

Pneumonia in the neonate (an infant in the first month of life) can be acquired in the antenatal, perinatal or postnatal periods. The predominant pathogens in pneumonia contracted antenatally are viruses, especially rubella, herpes simplex virus, cytomegalovirus, adenovirus, and varicella-zoster virus. The most common pathogens in pneumonia acquired in the perinatal period are those found in the birth canal: gram positive cocci such as groups A, B, and F streptococci, Chlamydia trachomatis, and gram negative bacilli, usually Escherichia coli. Another pathogen seen in perinatally acquired pneumonia is Toxoplasma gondii. The gram-positive cocci and gram-negative bacilli are common in postnatal pneumonia, along with viruses, especially respiratory syncytial virus (RSV) (Warren and Anderson; Boyer). Case #1 above represents a neonate with group B strep pneumonia.

When these patients present to the NICU, empiric therapy is started until cultures are obtained, from either endotracheal tube secretions or blood. Initial treatment for pneumonia in neonates includes a penicillin (penicillin G or ampicillin) and either an aminoglycoside or 3rd generation cephalosporin. More directed therapy depends on the culture results (Barnett). All cases of pneumonia in neonates are treated as inpatients, at least initially (Durbin and Stille).
If *C trachomatis* pneumonia is suspected or proven, erythromycin is the treatment of choice. However, if no antibiotics are given, the infants are sick for several weeks but do not become acutely ill (Estrippeaut). There is currently no effective treatment for RSV.

In the NICU, epidemics can occur due to contaminated instruments or infected health care workers. Common pathogens in these cases are methicillin-resistant staph aureus (MRSA) and *Pseudomonas aeruginosa* (Barnett). In addition to appropriate pharmacotherapy, identification of the infected device or person is critical to preventing further spread of the microbes (McAdams et al.).

Table 1 summarizes the appropriate therapy for the most common pathogens in newborn pneumonia.

**Table 1. Common pathogens and antimicrobial therapy in newborn pneumonia**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Therapy</th>
<th>Duration of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive cocci</td>
<td>Penicillin</td>
<td>10 days</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>Aminoglycoside or 3rd generation cephalosporin</td>
<td>10 days</td>
</tr>
<tr>
<td><em>C trachomatis</em></td>
<td>Erythromycin</td>
<td>10 days</td>
</tr>
<tr>
<td>RSV</td>
<td>None</td>
<td>NA</td>
</tr>
<tr>
<td>MRSA</td>
<td>Vancomycin and linezolid (Liu et al.)</td>
<td>3-6 weeks</td>
</tr>
<tr>
<td><em>P aeruginosa</em></td>
<td>Aminoglycoside, beta-lactam congeners (Sun et al.)</td>
<td>10 days</td>
</tr>
<tr>
<td><em>T gondii</em></td>
<td>Pyrimethamine/sulfadiazine/leucovorin</td>
<td>10 days</td>
</tr>
</tbody>
</table>

(Pregnant women with acute infection can be treated prenatally with pyrimethamine and sulfadiazine) (Tamma)
Infants/Toddlers/Preschoolers

Case #2: Guadalupe G. is a 2 year-old who presents to her pediatrician with low grade fever, cough, decreased appetite, and decreased activity. Her pediatrician examines her and gets a chest x-ray. He diagnoses her with pneumonia. She is not hypoxic and not vomiting. What is the most likely cause of her pneumonia, and what is the best antibiotic to give her?

Pneumonia is a common and often serious problem in children. The pathogens responsible for pneumonia are numerous, and often vary by age, season, geographic location, and individual patient risk factors. Infection with both viruses and bacteria are commonly seen, and in as many as 50% of cases, no etiologic pathogen is identified (Durbin and Stille).

For children aged 1 month to 3 months, viruses are the most common microbes responsible for pneumonia, with RSV and parainfluenza being the most frequent. Chlamydia trachomatis and Streptococcus pneumoniae are seen in this age group, too. Almost all children less than 3 months are initially treat as in-patients, due to the infant’s tendency to deteriorate rapidly, become hypoxemic, and have bacteremia (Durbin and Stille).

Viruses are still the dominant pathogens in children aged 3 months to 4 years. Influenza becomes a significant pathogen in this group, but there are no data on the efficacy of using the available anti-virals to treat pneumonia (Durbin and Stille). Pneumococcal pneumonia is also common, but the incidence of this disease has decreased due to the widespread use of the pneumococcal conjugate vaccine in infants (Theodoratou et al.). The incidence of Mycoplasma pneumoniae and Chlamydia pneumoniae seem to be increasing in this age group. Haemophilus influenzae type B (Hib) was an extremely frequent cause of pneumonia in this age group, but has been practically eliminated since the Hib vaccine was introduced in the early 1990s. Most patients with pneumonia in this age group can be treated as out-patients, provided the patient is not very ill, and can tolerate oral antibiotics (Durbin and Stille).

Making a distinction between bacterial and viral pneumonia is vexing for health care providers. Studies have been undertaken to identify reliable biomarkers to aid in the diagnosis of Community-Acquired Pneumonia CAP. One such study investigated C-reactive protein (CRP), serum procalcitonin (PCT), total white blood cell count and erythrocyte sedimentation rate (ESR) in relation to pneumonia in children. The results indicated that when all or most of the markers were elevated, then a bacterial pathogen was most likely the cause of pneumonia. However, low levels of these markers did not rule out a bacterial cause (Don et al.)
Like the neonates in the NICU, young children are often treated with empiric antibiotics. Young children are unlikely to give an accurate sputum culture, and treatment is directed at the most common bacterial pathogen, *S pneumoniae*. Often, the provider may give a single dose of ceftriaxone on the first day of outpatient treatment. Any child with pneumonia who is not better in 48 hours should be reassessed (Durbin and Stille).

As with other childhood infections, immunization is a cornerstone of pneumonia prevention. Vaccination against Hib and pneumococcus has already been mentioned, but other vaccines to prevent childhood pneumonia exist. Vaccination against influenza has proven to be effective in preventing hospitalization and doctor visits for pneumonia in children (Kwong et al.). Though there is no true RSV vaccine, passive immunization is achieved with the use of palivizumab, a monoclonal antibody against RSV given monthly only to high-risk children during RSV season. Palivizumab has been effective in reducing hospitalization rates among these vulnerable children. Most of these children are hospitalized for bronchiolitis, but pneumonia is a common co-diagnosis (Shadman and Wald).

Regarding Guadalupe in Case #2 above, the most likely cause of her pneumonia is viral, which means that there is no antibiotic with which to treat her.

Table 2 summarizes the most common pathogens in this group. Antibiotic therapy is usually given for 10 days in this age group.

**Table 2: Common pathogens and antimicrobial therapy in pneumonia in children aged 1 month to 4 years**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viruses</td>
<td>None</td>
</tr>
<tr>
<td><em>C trachomatis</em></td>
<td>Erythromycin</td>
</tr>
<tr>
<td><em>S pneumoniae</em></td>
<td>Beta-lactam (may use single dose of ceftriaxone on day 1 of outpatient treatment if desired)</td>
</tr>
<tr>
<td><em>M pneumoniae</em></td>
<td>Macrolide (azithromycin for 5 days commonly preferred)</td>
</tr>
<tr>
<td><em>C pneumoniae</em></td>
<td></td>
</tr>
</tbody>
</table>
**School-age children/adolescents**

Case #3: James W. is a 15 year-old boy who presents to the walk-in clinic at the local pharmacy with a 5 day gradual onset of low-grade fever, cough, and malaise. He has diffuse crackles in his lungs. The provider in the walk-in clinic diagnoses pneumonia. What is the most likely pathogen and what is the antibiotic of choice in this case?

Community-Acquired Pneumonia (CAP In school aged children and adolescents, *Mycoplasma pneumonia* and *Chlamydia* in school aged children and adolescents, *pneumoniae* are the most common pathogens (the latter more common in teens than in younger children). *S pneumoniae* is still an important cause of pneumonia in this age group, and viruses are less frequent than in the younger children. Less common causes include tuberculosis, histoplasmosis, coccidiomycosis, and Legionnaire’s disease (Durbin and Stille).

In Case #3, James most likely has *M. pneumoniae*, and should be treated with azithromycin or doxycycline.

Table 3 summarizes the most common causes of infection and the appropriate therapy in this age group. Duration of therapy for these agents is usually 7-10 days.

**Table 3: Common pathogens and antimicrobial therapy in pneumonia in children 5 years old through adolescence.**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M pneumoniae</em></td>
<td>Macrolide (azithromycin for 5 days commonly preferred)</td>
</tr>
<tr>
<td><em>C pneumoniae</em></td>
<td>Doxycycline (if &gt;8 years old)</td>
</tr>
<tr>
<td><em>S pneumoniae</em></td>
<td>Beta-lactam (may use single dose of ceftriaxone on day 1 of outpatient treatment if desired)</td>
</tr>
<tr>
<td></td>
<td>Fluoroquinolone (if &gt;18 years old)</td>
</tr>
<tr>
<td></td>
<td>May need to treat for both pneumococcus and <em>Mycoplasma/Chlamydia</em> pneumonia with beta-lactam and macrolide or doxycycline (Durbin and Stille)</td>
</tr>
</tbody>
</table>
**Adults**

*Case #4: Barbara T., a 45 year-old woman with Stage V breast cancer, is undergoing chemotherapy. She presents to her oncologist with cough, fever, and mild respiratory distress. What is the likely pathogen in this scenario, and what is the best therapeutic option?*

The most likely pathogens causing CAP in adults are *S pneumoniae, M pneumoniae, C pneumoniae* and *H influenzae*. Treatment of those first three pathogens has already been discussed. Beta-lactams or macrolides are the treatment of choice for *H influenzae* (Thiem, Heppner and Pientka). Choosing appropriate therapy is made difficult by pneumococcal resistance to beta-lactams, macrolides, and fluoroquinolones. For the hospital-based pharmacist, decision trees are available to help guide antibiotic therapy (File).

Less common pathogens that cause severe pneumonia, often hospital-acquired, are MRSA, *Legionella* species, and gram-negative bacilli (File). MRSA may be treated with vancomycin, but increasing resistance is a concern (Watkins and Lemonovich). Pneumonia caused by Legionella should be treated with a beta-lactam combined with a fluorquinolone or macrolide (Thiem, Heppner and Pientka). Those with gram-negative bacilli pneumonia can be treated with piperacillin/tazobactam or an aminoglycoside, perhaps for as little as 5 days (Pugh, Cooke and Dempsey).

Tuberculosis (TB) is always a concern in any age group, and is seen more in teens, adults and seniors than in infants or preschoolers. Risk factors for TB include close contact with a person with infectious TB, foreign birth, HIV infection, homelessness, incarceration, geography, unemployment, and occupation (Taylor, Nolan and Blumberg). Infection with *Mycobacterium tuberculosis* is a lower respiratory tract infection, and presents differently than most cases of acute pneumonia, but should be considered in those at risk or those whose respiratory symptoms are chronic.

A small but significant group of adults with pneumonia is the immunocompromised group. Immunocompromised patients include those who are undergoing cancer treatment, have recently undergone a transplant, are HIV positive, or are receiving chronic therapy with steroids or other immunosuppressants. Barbara T. in Case #4 is such a patient. The most likely pathogen in this case is *Pneumocystis jiroveci*. First line treatment is trimethoprim-sulfa (Carmona and Limper)
Adjunctive therapy for pneumonia is undergoing increased scrutiny. One review summarized the results of dozens of studies of immunomodulatory agents in the treatment of CAP (Corrales-Medina and Musher). The summary can be found in Table 4.

Table 4: Summary of immunomodulatory agents in the treatment of CAP

<table>
<thead>
<tr>
<th>Agent</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrolides</td>
<td>Use together with beta-lactams in pneumococcal pneumonia</td>
</tr>
<tr>
<td></td>
<td>Study their role as adjuvant therapy in all-cause pneumonia</td>
</tr>
<tr>
<td>Statins</td>
<td>Encourage their prophylactic use in patients at high risk of pneumonia and who otherwise have an indication for statin use</td>
</tr>
<tr>
<td>Glitazones</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Encourage their prophylactic use in patients at high risk of pneumonia and who otherwise have an indication for aspirin use</td>
</tr>
<tr>
<td>Other NSAIDS</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Steroids</td>
<td>Further study needed to determine value of treating pneumonia</td>
</tr>
</tbody>
</table>

Seniors

Case #5: Jacob C. is a 70 year-old man whose status is post-coronary artery bypass graft surgery. While on the ventilator, he develops a fever of 102, has crackles throughout all lung fields, and requires higher settings on the ventilator. What are some likely pathogens in this case, and how should he be treated?

Seniors are discussed separately from other adult patients because some pneumonia situations are more common in senior citizens. One such type of pneumonia is ventilator-associated pneumonia (VAP). VAP can occur in any age group, but is especially prominent in seniors. Jacob C. in Case #5 has VAP.

The pathogens most frequently seen in VAP are *P aeruginosa*, MRSA, *Klebsiella pneumoniae*, and *Acinetobacter baumannii*. Choice of antimicrobial therapy should depend on local resistance patterns and individual patient factors (Gupta et al.). Table 5 lists possible therapeutic options for these pathogens. Shorter duration of antibiotic therapy has been noted to be equal to longer term therapy, and research is continuing in the areas of prevention and treatment of VAP (Rewa and Muscedere).
Table 5: Pathogens and suggested therapy in VAP

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. aeruginosa</em></td>
<td>Carbapenems, Polymyxin B, Colistin (intravenous), Aminoglycosides, Third generation cephalosporins</td>
</tr>
<tr>
<td>MRSA</td>
<td>Vancomycin, Linezolid, Carbapenems, Clindamycin</td>
</tr>
<tr>
<td><em>K. pneumoniae</em></td>
<td>Carbapenems, Polymyxin B, Colistin (intravenous), Aminoglycosides, Third generation cephalosporins</td>
</tr>
<tr>
<td><em>A. baumannii</em></td>
<td>Carbapenems, Polymyxin B, Colistin (intravenous), Aminoglycosides, Third generation cephalosporins</td>
</tr>
</tbody>
</table>

Of course, the usual pathogens for CAP in adults (discussed in the previous section) are also seen in seniors. Mortality is high in the elderly with pneumonia, often due to co-morbid conditions, poor nutrition, and the tendency to get severely ill with CAP (Ma, Tang and Woo).

As with the other age groups, vaccination is key to preventing pneumonia in the elderly. Vaccination against influenza is recommended for everyone older than 6 months, but especially so in high-risk groups, such as those older than 65 years. Interestingly, one study demonstrated that childhood vaccination against flu was associated with lower rates of hospitalization for pneumonia and influenza in seniors. Vaccination of the seniors themselves, however, was not associated with lower rates of hospitalization for pneumonia and influenza. These results suggest that herd immunity may be more effective in the elderly than direct vaccination (Cohen, Chui and Naumova). Another study found higher hospitalization rates in those >50 years in areas of high childhood vaccination rates, but decreased hospitalization rates among those aged 5-49 years (King et al.).

A study in Spain compared the outcomes in a group of elderly patients admitted to the hospital with CAP. One group was vaccinated against pneumococcus and influenza, and the other group was not. Researchers found no difference in clinical outcomes between the two groups (Manzur et al.).

Even with conflicting data, the official recommendation of the Centers for Disease Control and Prevention (CDC) is to give an influenza vaccination everyone over the age of 6 months. However, the elderly often have poor immunologic response to influenza vaccination, which may explain the many studies that demonstrate little effectiveness of the vaccine in this age group. A relatively newer vaccine
specifically designed for the elderly has a higher antigenic load. It is unclear if this vaccine will have any effect on flu morbidity or mortality in the elderly (Centers for Disease Control and Prevention).

**Summary**

Pneumonia is common in all age groups. Pathogens vary by age and risk factors, however, and antibiotic therapy needs to be individualized for each patient. Vaccination against some pathogens is a preventive measure that can be utilized by retail-based or hospital-based pharmacists.
References


