Therapy of Pneumonia

Pneumonias

- **Pneumonia is one of the most common causes of severe sepsis, and infectious cause of death in children and adults.**
- **It affects all ages, although the clinical manifestations are most severe in the very young, the elderly, and the chronically ill.**
- **Mortality rate is high.**

Pneumonias Causative Agents

- **The most prominent pathogen causing community-acquired pneumonia (CAP) in otherwise healthy adults is *Streptococcus pneumoniae* and accounts for up to 35% (12%-68%) of all acute cases.**
- **Other common pathogens include:**

1. ***H. influenza* (2.5%-45%).**
2. **Atypical pathogens: *Mycoplasma pneumoniae*, *Legionella* sps, and *Chlamydia pneumoniae* (~20%).**
3. **A variety of viruses including influenza.**

Pneumonia Causative Agents

- **The leading causative agents in hospital-acquired pneumonia (HAP) are Gram-negative aerobic bacilli, *S. aureus*, and multidrug-resistant (MDR) pathogens.**
- **In pneumonia that follows the aspiration of gastric or oropharyngeal contents, anaerobic bacteria are the most common etiologic agents.**
- **Ventilator-associated pneumonia (VAP) is also associated with MDR pathogens.**

Pneumonia Causative Agents

- **Pneumonia in infants and children is caused by a wider range of microorganisms, and unlike adults, nonbacterial pathogens predominate.**
- **Most lung infections occurring in the pediatric age group are caused by viruses: especially RSV, parainfluenza, and adenovirus.**
- ***M. pneumoniae* is an important pathogen in older children.**

Pneumonia Causative Agents

- **Beyond the neonatal period, *S. pneumoniae* is the major bacterial pathogen in childhood pneumonia, followed by group A *Streptococcus* and *S. aureus*.**
- ***H. influenzae* type b, once a major childhood pathogen, has become an infrequent cause of pneumonia since the introduction of active vaccination against this organism in the late 1980s.**

Pneumonia Causative Agents

- **Pneumonia in non-ambulatory residents of nursing homes and other long-term care facilities is similar to hospital-acquired pneumonia and should be treated according to the HAP guidelines.**
- **Certain other patients may be better served by management in accordance with CAP guidelines.**

Therapy of Pneumonia

Treatment:

The goals of therapy are:

1. **Eradication of the offending organism through selection of the appropriate antibiotic**
2. **Achieving complete clinical cure, with minimal drug-induced toxicity.**

Therapy of Pneumonia

General Approach to Treatment:

Supportive care:

1) Humidified oxygen for hypoxemia.
2) Bronchodilators when bronchospasm is present.
3) Chest physiotherapy and postural drainage with evidence of retained secretions.
4) Adequate hydration (IV if necessary).
5) Optimal nutritional support.
6) Control of fever.

Therapy of Pneumonia

- **Appropriate sputum samples should be obtained to determine the microbiologic etiology.**
- **Selection of an appropriate antimicrobial must be made based on the patient's probable or documented microbiology.**

Pharmacologic Therapy:

- **Antibiotic concentrations in respiratory secretions in excess of the pathogen MIC are necessary for successful treatment of pulmonary infections.**

Therapy of Pneumonia

Selection of Antimicrobial Agents:

- **Treatment, initially involves the empirical use of a relatively broad-spectrum antibiotic that is effective against probable pathogens after appropriate cultures and specimens for laboratory evaluation have been obtained.**
- **Therapy should be narrowed to cover specific pathogens after the results of cultures are known.**

Management of CAP in Adults

- **This discussion is in accordance of the "Infectious Diseases Society of America / American Thoracic Society" Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults (2016).**

Antibiotic Treatment:

- **Recommendations are generally for a class of antibiotics rather than for a specific drug, unless outcome data clearly favor one drug.**

Table 6. Most common etiologies of community-acquired pneumonia.

Patient type	Etiology
Outpatient	*Streptococcus pneumoniae* *Mycoplasma pneumoniae* *Haemophilus influenzae* *Chlamydophila pneumoniae* Respiratory viruses[a]
Inpatient (non-ICU)	*S. pneumoniae* *M. pneumoniae* *C. pneumoniae* *H. influenzae* *Legionella* species Aspiration Respiratory viruses[a]
Inpatient (ICU)	*S. pneumoniae* *Staphylococcus aureus* *Legionella* species Gram-negative bacilli *H. influenzae*

NOTE. Based on collective data from recent studies [171]. ICU, intensive care unit.

[a] Influenza A and B, adenovirus, respiratory syncytial virus, and parainfluenza.

Management of CAP in Adults

Outpatient treatment:

1. **Previously healthy and no risk factors for drug-resistant *S. pneumoniae* (DRSP) infection:**

A. **A macrolide (azithromycin, clarithromycin, or erythromycin).**

B. **Doxycycline is an alternative.**

Management of CAP in Adults

2. Presence of comorbidities (chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; use of antimicrobials within the previous 3 months, etc):

A. A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin).

B. A β-lactam plus a macrolide (High-dose amoxicillin [1g x3] or amoxicillin-clavulanate [2g x2] is preferred.

- **Alternatives include ceftriaxone, and cefuroxime.**

Management of CAP in Adults

Inpatient, non-ICU treatment:

1. **A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin.**
2. **A β-lactam plus a macrolide.**

- **(Preferred β-lactam agents include cefotaxime, ceftriaxone or ampicillin; ertapenem for selected patients). Use doxycycline as an alternative to the macrolide.**
- **A respiratory fluoroquinolone should be used for penicillin-allergic patients.**

Management of CAP in Adults

Inpatient, ICU treatment:

1. **A β-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) + either azithromycin, or a fluoroquinolone.**
2. **For *Pseudomonas* infection, use an antipseudomonal β-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) + either ciprofloxacin or levofloxacin.**

Management of CAP in Adults

3. **For community-acquired methicillin-resistant *Staphylococcus aureus* infection, add vancomycin or linezolid.**

Management of CAP in Adults

Pathogen-directed therapy:

- **Once the etiology of CAP has been identified on the basis of reliable microbiological methods, antimicrobial therapy should be directed at the specific pathogen.**

Time to first antibiotic dose:

- **For patients admitted through the emergency department (ED), the first antibiotic dose should be administered while still in the ED.**

Management of CAP in Adults

Switch from intravenous to oral therapy:

1. **Patients should be switched from intravenous to oral therapy when they are hemodynamically stable and improving clinically, are able to ingest medications, and have a normally functioning gastrointestinal tract.**
2. **Patients should be discharged as soon as they are clinically stable, have no other active medical problems, and have a safe environment for continued care. Inpatient observation while receiving oral therapy is NOT necessary.**

Management of CAP in Adults

Duration of antibiotic therapy:

1. **Patients with CAP should be treated for a minimum of 5 days, and should be afebrile for 2-3 days.**
2. **A longer duration of therapy may be needed if initial therapy was NOT active against the identified pathogen, or if it was complicated by extra-pulmonary infection such as meningitis or endocarditis.**

Management of CAP in Adults

Remember the importance of:

1. **The local pattern of causative pathogens.**
2. **The local pattern of antibiotic sensitivity and/or resistance.**

Management of HAP and VAP in Adults

- **Each hospital should generate an antibiogram as a guide for the optimal choice of antibiotics.**
- **Patients with suspected HAP (non-VAP) may be treated according to the results of microbiologic studies performed on respiratory samples obtained noninvasively, rather than being treated empirically (??).**
- **VAP may be treated empirically according to the local distribution of pathogens associated with it and their antimicrobial susceptibilities.**

Empiric Treatment of Clinically Suspected VAP

- **Cover for *S. aureus*, *Pseudomonas aeruginosa*, and other gram-negative bacilli in all empiric regimens.**
- **A regimen including piperacillin-tazobactam, cefepime, levofloxacin, imipenem, or meropenem is acceptable [This regimen covers MSSA (not MRSA)].**
- **Oxacillin, nafcillin, or cefazolin are preferred for treatment of proven MSSA, but are not necessary if one of the above agents is used.**

Empiric Treatment of Clinically Suspected VAP

- For MRSA, either vancomycin or linezolid is indicated.
- If resistance is suspected, 2 antipseudomonal antibiotics from different classes are indicated.
- If risk of resistance is low, one antibiotic active against *P. aeruginosa* is indicated.
- Avoid aminoglycosides and colistin if alternative agents with adequate gram-negative activity are available.

Empiric Treatment of Clinically Suspected VAP

- **If patient has structural lung disease increasing the risk of gram-negative infection (cystic fibrosis or bronchiectasis), 2 antipseudomonal agents are recommended.**

Empiric Treatment of Clinically Suspected VAP

Role of Inhaled Antibiotic Therapy:

- **For patients with VAP due to gram-negative bacilli that are susceptible to only aminoglycosides or polymyxins (colistin or polymyxin B), It is suggested to use both inhaled and systemic antibiotics, rather than systemic antibiotics alone.**
- **Adjunctive inhaled antibiotic therapy is a last resort for patients who are NOT responding to intravenous antibiotics alone, whether the infecting organism is or is NOT multidrug resistant (MDR).**

Empiric Treatment of Clinically Suspected HAP (Non-VAP)

- When there is high risk for MRSA infection, use an antibiotic with activity against MRSA (vancomycin or linezolid).
- For patients with NO risk factors for MRSA infection, use oxacillin, nafcillin, or cefazolin.
- When empiric treatment may include coverage for MSSA (and not MRSA) use a regimen containing piperacillin-tazobactam, cefepime, levofloxacin, imipenem, or meropenem.

Empiric Treatment of Clinically Suspected HAP (Non-VAP)

- **Also use antibiotics with activity against P. aeruginosa and other gram-negative bacilli.**
- **In patients who have factors increasing the likelihood for *Pseudomonas* or other gram-negative infection, use antibiotics from 2 different classes with activity against *P. aeruginosa*.**

Empiric Treatment of Clinically Suspected HAP (Non-VAP)

- **All other patients with HAP who are being treated empirically may be prescribed a single antibiotic with activity against *P. aeruginosa*.**
- **Do not use an aminoglycoside as the sole antipseudomonal.**

Pathogen-Specific Therapy

- **Treatment for MRSA HAP/VAP: Vancomycin or linezolid.**
- **HAP/VAP Due to *P. aeruginosa*: Definitive (NOT empiric) therapy based upon the results of antimicrobial susceptibility testing.**
- **No aminoglycoside monotherapy.**

Pathogen-Specific Therapy

- **For patients with HAP/VAP due to *P. aeruginosa* who are NOT in septic shock, or NOT at a high risk for death, and for whom the results of antibiotic susceptibility testing are known, use monotherapy with an antibiotic to which the isolate is susceptible.**
- **For patients with HAP/VAP due to *P. aeruginosa* who remain in septic shock or at a high risk for death when the results of antibiotic susceptibility testing are known, use combination therapy with 2 antibiotics to which the isolate is susceptible.**

Pathogen-Specific Therapy

- **Treatment of patients with HAP/VAP due to extended-spectrum β-lactamase (ESBL) – producing gram-negative bacilli: The choice of an antibiotic for definitive (NOT empiric) therapy should be based upon the results of antimicrobial susceptibility testing and patient-specific factors (allergies and comorbidities that may confer an increased risk of adverse effects).**

Pathogen-Specific Therapy

- **Treatment of patients with HAP/VAP due to *Acinetobacter* species: use either a carbapenem or ampicillin/sulbactam if the isolate is susceptible to these agents.**
- **In patients with HAP/VAP caused by *Acinetobacter* species sensitive only to polymyxins, use intravenous polymyxin (colistin or polymyxin B), with adjunctive inhaled colistin.**
- **Do not use tigecycline.**

Pathogen-Specific Therapy

- **Treatment of patients with HAP/VAP due to carbapenem-resistant pathogens: If the pathogen is sensitive only to polymyxins, use intravenous polymyxins (colistin or polymyxin B), with adjunctive inhaled colistin.**

Length of therapy

- **For patients with VAP or HAP, a 7-day course of antimicrobial therapy rather than a longer duration is recommended.**
- **A shorter or longer duration of antibiotics may be indicated, depending upon the rate of improvement of clinical, radiologic, and laboratory parameters.**

Should Antibiotic Therapy be De-escalated or Fixed in Patients with HAP/VAP?

- **For patients with HAP/VAP, antibiotic therapy should be de-escalated rather than fixed.**
- **De-escalation therapy means changing an empiric broad-spectrum antibiotic regimen to a narrower antibiotic regimen by changing the antimicrobial agent or changing from combination therapy to monotherapy.**
- **Fixed antibiotic therapy refers to maintaining a broad-spectrum antibiotic regimen until therapy is completed.**

Neonatal Pneumonia

Onset:

1) **May be within hours of birth, and as part of a generalized sepsis syndrome.**
2) **After 7 days (most commonly in neonatal ICUs among infants who require prolonged endotracheal intubation because of lung disease).**

Neonatal Pneumonia

Organisms are acquired from the maternal genital tract or the nursery, and include:

a) **Gram-positive cocci (groups A and B streptococci, both methicillin-sensitive and methicillin-resistant *Staphylococcus aureus*)**
b) **Gram-negative bacilli (*E. coli, Klebsiella* sp, *Proteus* sp).**
c) ***Pseudomonas, Citrobacter, Bacillus,* and *Serratia* in infants who have received broad-spectrum antibiotics.**

Neonatal Pneumonia

Treatment:

- **Antimicrobial therapy in early-onset disease is similar to that for neonatal sepsis: Vancomycin and a broad-spectrum β-lactam drug such as meropenem, piperacillin/tazobactam, or cefepime are the initial treatment of choice.**
- **This regimen treats sepsis as well as pneumonia with typical hospital-acquired pathogens including *P. aeruginosa*.**

Neonatal Pneumonia

- **Local patterns of infection and bacterial resistance should always be used to help guide empiric choices of antimicrobials.**
- **More specific antibiotics are substituted after sensitivity results are available.**

Neonatal Pneumonia

Chlamydial pneumonia:

- **Exposure to chlamydial organisms (*Chlamydia trachomatis*) occurs during delivery.**
- **May result in development of chlamydial pneumonia at 2 to 18 wk.**

Treatment:

- **Erythromycin or azithromycin lead to rapid resolution.**
- **Erythromycin may cause hypertrophic pyloric stenosis in neonates.**
- **The mother and father should also be treated for chlamydia.**

Community-Acquired Pneumonia in Children

- **The most likely etiology depends on the age of the child.**
- **Viral and *Streptococcus pneumoniae* infections are most common in preschool-aged children, whereas *Mycoplasma pneumoniae* is common in older children.**

Community-Acquired Pneumonia in Children

- **Preschool-aged children with uncomplicated bacterial pneumonia should be treated with amoxicillin.**
- **Macrolides are first-line agents in older children.**
- **Immunization with the 13-valent pneumococcal conjugate vaccine is important in reducing the severity of childhood pneumococcal infections.**

CAP Etiologies in Children

Age	*Common etiologies*	*Less common etiologies*
2 to 24 months	Respiratory syncytial virus Human metapneumovirus Parainfluenza viruses Influenza A and B Rhinovirus Adenovirus Enterovirus *Streptococcus pneumoniae* *Chlamydia trachomatis*	*Mycoplasma pneumoniae* *Haemophilus influenzae* (type B and nontypable) *Chlamydophila pneumoniae*

CAP Etiologies in Children

2 to 5 years	Respiratory syncytial virus Human metapneumovirus Parainfluenza viruses Influenza A and B Rhinovirus Adenovirus Enterovirus *S. pneumoniae* *M. pneumoniae* *H. influenzae* (B and nontypable) *C. pneumoniae*	*Staphylococcus aureus* (including methicillin-resistant *S. aureus*) Group A streptococcus

CAP Etiologies in Children

Older than 5 years	*M. pneumoniae* *C. pneumoniae* *S. pneumoniae* Rhinovirus Adenovirus Influenza A and B	*H. influenzae* (B and nontypable) *S. aureus* (including methicillin-resistant *S. aureus*) Group A streptococcus Respiratory syncytial virus Parainfluenza viruses Human metapneumovirus Enterovirus

Recommended Empiric Outpatient Treatment of Childhood CAP

60 days to 5 years of age:

- **Preferred regimens: Amoxicillin for 7-10 days.**
- **Alternative regimens for patients allergic to penicillin or beta-lactam antibiotics: Azithromycin (5 days), clarithromycin (7-10 days), or erythromycin (7-10 days).**

5 to 16 years of age: Azithromycin (5 days).

Recommended Empiric Inpatient Treatment of Childhood CAP

60 days to 5 years of age:

- **Cefuroxime for 10-14 days.**
- **In critically ill patients: Cefuroxime + erythromycin 10-14 days, or cefotaxime + cloxacillin for 10-14 days**

5 to 16 years of age: Cefuroxime + erythromycin 10-14 days, or azithromycin for 5 days.