Evaluation and Management of Community-Acquired Pneumonia (CAP)

Abstract: Community-Acquired Pneumonia (CAP) is a serious medical problem affecting mostly the young healthy adults, children and elderly population all over the globe and is associated with considerable mortality and morbidity. CAP is the 6th leading cause of death. Millions of people are affected by CAP world over every year from developed to developing countries, most of them needs hospitalized treatment and hence the economic burden on the society is huge. Although diagnostic techniques and antibiotic therapy have improved to a great extent yet optimal management of the disease is still problematic. Lower respiratory tract infection by atypical intracellular pathogens have made the problem of CAP more complicated. This article reviewed the current trends in the evaluation and management of CAP.

INTRODUCTION

Community acquired pneumonia is defined as pneumonia acquired in the patients home or in non hospital environment being diagnosed within 48 hours of hospital admission. Despite the availability of various diagnostic methods and potent newer antimicrobial agents and effective vaccines CAP occur throughout the globe and stands as the 6th leading cause of death. The mortality rate in hospitalized patients is 14% and in outpatient population is 1% . The morbidity rate is significantly high, lower respiratory tract infection by atypical intracellular pathogens have made the management of CAP more complicated.1

The disease affects the people of all age group but is more in healthy young adults, children and elderly. Infection is mostly spread by droplet inhalation and most patients affected are previously well.2 Cigarette smoking, alcoholism, corticosteroid therapy and immune suppression, all impair mucociliary clearance and predispose to infection.

The epidemiology of CAP is not clear, because few population based statistics on the condition alone are available.3 It is estimated that 4 million American adults suffer from CAP each year imposing a significant economic burden on the society with an annual expenditure of approximately 10 million $.4 The incidence of CAP requiring hospitalization is estimated to be 258 cases per 100,000 population and 926 cases per 100,000 persons ≥ 65 years of age.5 The incidence of CAP is highest in winter months.

EVALUATION

Clinical
Clinical presentation depends on the micro-biologic agent and host factors such as age, immune status and other comorbid conditions. A detailed history of exposure, travel, hobbies and past medical history is helpful in suggesting a microbiologic etiology. Severity and presentation of CAP ranges from mild to life threatening, although the symptoms may vary.

**Symptoms of CAP Commonly Include**

- Difficulty in breathing.
- Cough that produces yellow or greenish sputum.
- Sharp or stabbing chest pain.
- High fever that may be accompanied with sweating, chills and uncontrollable shaking.
- Rapid, shallow breathing that is often painful.

**Less Common Symptoms Include**

- Coughing out of blood
- Reduced appetite
- Headache
- Blueness of the skin
- Excessive fatigue
- Muscle aches and joint pain
- Loose motion.

*The manifestations of pneumonia might not be typical in older people. They may present with*

- Mental confusion
- Hypothermia
- Falls

*Additional symptoms for infants could include*

- Being overly sleepy
- Yellowing of the skin
- Difficulties in feeding.

**Physical Examination**

CAP should be suspected in patients with newly acquired lower respiratory symptoms (cough, sputum production, and or/dyspnoea), especially if these symptoms are accompanied by fever, altered breath sound and rales. The most common signs of CAP are tachycardia and tachypnea, temperature is usually elevated but doesn't have a specific pattern. Pulmonary auscultation reveals crepitations and rhonchi. Sign of consolidation, such as dullness to percussion, increased vocal fremitus, bronchial breath sound and egophony, may be present. A pleural effusion may be detected. Cynosis, confusion and severe tachypnoea indicate severe respiratory distress. Hypotension and circulatory collapse occur in severe cases.

**Radiography**

According to the latest American Thoracic Society (ATS) guidelines for the diagnosis and treatment of adults with CAP, “all patients with suspected CAP should have a chest radiograph to establish the diagnosis and identify the possible complications”. Chest radiograph may reveal a lobar consolidation, which is common in typical pneumonia; or it could show bilateral, more
diffuse infiltrates than those commonly seen in atypical pneumonia. However chest radiography performed early in the course of the disease could be negative. Consolidation of one or more lobes with or without pleural effusion or cavitation suggest a bacterial pneumonia. Multilobar involvement, rapidly increasing infiltrates or presence of cavities in CAP is an indicator of higher morbidity and mortality.

**Laboratory Test**

The selection of diagnostic test is determined by the clinical severity of infection. Minimal laboratory investigation is necessary with mild disease. In critically ill patients, more extensive testing is necessary. Routine laboratory test for CAP include leukocyte count, gram-staining, cytological screening, aerobic culture of specimens, blood culture and urine antigens.

Complete blood count reveals leukocytosis or leukopenia. Thrombocytopenia and evidence of disseminated intravascular coagulation may be present in severe cases. Poor prognosis is associated with leukocyte counts < $4 \times 10^9$/L, an absolute neutrophil count < $1 \times 10^9$/L, Pa O₂ < 60 mm Hg or Pa CO₂ > 50 mm Hg at room air, hemoglobin < 9 g/dl, evidence of DIC, and elevated creatinine > 1.2 mg/dl.

**Microbiology**

Prospective studies fail to identify the causes in 40 to 60% of cases, although bacteria are more commonly identified than virus. The microbiological pattern in CAP is shown in Table 1.

**Sputum Examination**

Sputum gram stain provides a rapid and inexpensive method for a microbiologic diagnosis and aids in the selection of an appropriate management of CAP, though value of a gram stain of expectorated sputum has been debated. A satisfactory sputum specimen is one that has < 10 epithelial cell and > 25 neutrophils in a low power field. Sputum specimen that do not meet these strict criteria should be rejected for culture and the gram stain results disregarded. Gram stains should be performed rapidly to reduce unnecessary delay in therapy. Cultures should also be performed rapidly to improve accuracy. Delays from the time of specimen collection to incubation that exceed 2-5 hours may be associated with deceptive results. Abundant pathogenic bacteria with a characteristic morphology, such as the small lancet-shaped gram positive diplococci of *S. pneumoniae*, gram negative coccobacillary froms of *H. influenzae*, or gram-negative cocci of *M. catarrhalis*, may help in making the diagnosis. Special stains must be performed on specimens to identify organisms not ordinarily seen on the gram stain. Direct fluorescent antibody stains may detect legionella species; KOH preparation may be necessary to identify fungi-like Histoplasma or coccidioides. *P. carinii* is identified by using either methenamine silver staining or fluorescent calcofluor stain. In bacterimic pneumococcal pneumonia, only 40-50% of cases have a positive sputum culture for *S. pneumoniae*, *M. pneumoniae* isolation from sputum cultures is technically difficult, and it may take ≤ 30 days to grow the micro-organism.

**Serological Tests**

Serological test are usually not helpful in the initial evaluation of patients with CAP. Serologic diagnosis must be confirmed with an appropriate clinical picture and a positive 1g M or a fourfold increase or decrease in the 1g G. titer in paired sera. A negative serology does not exclude the presumptive diagnosis. The presence of cold agglutinins at a titer of ≥ 1.64 support the diagnosis of *M. pneumoniae* infection with a sensitivity of 30 to 60% but agglutination assay
have poor specificity. The merits serology test for *C. pneumoniae* have been debated. In primary infection due to *C. pneumoniae*, 1g M antibodies may take up to 3 weeks to appear and 1 g G antibodies may take up to 8 weeks to appear. Therefore, the absence of detectable antibodies several weeks after infection does not exclude the diagnosis of acute *C. pneumoniae* infection. Serologic test for legionella in the acute phase of the disease is usually negative and show a low titer if the etiology of a case remains in question, a convalescent - phase serum specimen can be obtained, and paired serological studies can be performed.

**Antigen Detection**

Antigen detection by EIA, counterimmunoelectrophoresis, bacterial antigen test or radioimmunoassay may be used for identifying microorganisms in sputum and in other body fluids. Presence of *S pneumoniae, H influenzae* or *C pneumophila* can be detected using these test. Pneumococcal antigen detection has the highest yield in sputum and persists for an extended period of time after an acute infection. Rapid EIA detection of RSV, influenza virus or para-influenza viruses has a sensitivity of > 80%. Urine antigen tests have been shown to be sensitive and specific for detecting legionella serogroup 1, which accounts for 70%. A negative laboratory test does not exclude legionnaires disease, particularly if it is caused by other than *L pneumophila* serogroup 1, but a positive culture or urine antigen assay is virtually diagnostic.

**Blood Culture**

Current ATS guidelines recommend that patients hospitalized for suspected CAP should receive two sets of blood culture. Blood cultures are particularly useful in chronically ill, immunocompromised patients and in patients with history of alcoholism and malignancies. Prior studies have indicated that an average of 11% of hospitalized patients with CAP have positive blood culture. Some studies cast doubt on the clinical utility of obtaining blood culture from patient with suspected CAP. In a study of CAP cases in 19 Canadian hospitals over a six-months period, positive blood cultures were obtained in only 5.2 to 6.2% of patients, including those with the most severe disease. Based on these findings, other researchers concluded that a positive blood culture had no correlation with the severity of the illness or outcome. Blood cultures, however, are not necessary for outpatient diagnosis.

**DNA Probes and Amplification**

Several rapid diagnostic tests with use of nucleic acid amplification for the evaluation of respiratory secretion or serum are presently under development, especially for detecting species of Chlamydia, Mycoplasma and Legionella. Their greatest potential utility is anticipated for the detection of *M. pneumoniae*, Legionella species and selected pathogens that infrequently colonize the upper airways in the absence of disease.

**Invasive diagnostic tests:** Bronchoscopy, transtracheal aspiration (TTA), Percutaneous lung needle aspiration (PLNA), Thoracentesis.

Bronchoscopy is impractical for routine use because it is expensive, requires technical expertise and may be difficult to perform in a timely manner. Bronchoscopy is specially useful for detecting selected pathogens such as *P. carinii*, Mycobacterium species and cytomegalovirus. Some authorities favor its use in patients with fulminant clinical course who required admission to the ICU or have complex pneumonia that are unresponsive to therapy. For recovery of common bacterial pathogens, quantitative culture of BAL fluid or a protected brush catheter specimen is considered superior. BAL specimen is considered diagnostic if it has $10^3 - 10^5$ cfu/ml growth of bacteria, especially if the gram stains shows > 25 neutrophils and < 1% squamous cell.
The diagnostic yield of transtracheal aspiration (TTA) is low. It is now infrequently performed because of concern for adverse affects. TTA was previously used to obtain uncontaminated lower respiratory secretions that were valid for culture of anaerobic organisms and common aerobic pathogens.19

The used of PLNA for diagnosing CAP has been limited in the past because of potential complications, specially bleeding and pneumothorax. The more recent introduction of thinner needles has reduced the frequency of complications. The diagnostic yield ranges from 40 to 80%.20

Thoracentesis should be performed in patients with a pleural effusion who are not responding to appropriate antibiotics, or in seriously ill patients who are suspected to have empyema. Pleural fluid should be promptly analyzed for pH, glucose, protein and LDH and should be gram stained and cultured for bacteria mycobacteria and fungi.

Finally open lung biopsy may be necessary when other procedures fail to make a diagnosis. Open-lung biopsy is important in seriously ill, immunocompromised patients or in patients not responding to empiric therapy. The diagnostic yield varies from 60 to 100%.8 The lung tissue can also be subjected to molecular analysis by DNA probes or PCR techniques for rapid diagnosis.

MANAGEMENT

The primary aim of pharmacotherapy for patients with CAP include eradicating the causative pathogens, resolving the clinical sign and symptoms, minimizing hospitalization and preventing reinfection.21 Physicians should choose a medication based on the pharmacokinetic profile, adverse reactions, drugs interaction, and cost - effectiveness.22 Consensus guidelines from ATS, Infectious Disease Society of America, and Canadian Guidelines for the initial management of CAP recommend initial empiric therapy with macrolides, fluoroquinolones or doxycycline.23 A fourth guideline developed by the Therapeutic Working Group of the CDC, however, recommends using fluoroquinolones sparingly because of resistance concerns.23

Following points to be kept in mind by the physician before initiating treatment for CAP to get a better results:

1. Rational use of the microbiology laboratory.
2. Antimicrobial treatment should be initiated promptly.
3. Decision regarding hospitalization should be based on prognostic criteria.
4. An attempt should be made to administer pathogen directed antimicrobial therapy to hospitalized patients.

CAP patients can be divided in two groups for better treatment:

I. Patients who do not require hospitalization (out patient therapy).
II. Patients who require hospitalization (in patient therapy).

**Out patients therapy:** Patients without any underlying comorbidity and with normal or mildly abnormal physical findings represents low risk individuals who may be treated with antimicrobial therapy as out patient. In addition to risk factors and objective findings, patient compliance and competence and the presence of a care giver at home should be considered in making the decisions for outpatient versus in patient care.

**In patient therapy:** The presence of coexisting illness, immunosuppression. Respiratory rate > 30/min, hypotension, multiobar involvement, hypoxemia, acidosis, electrolyte abnormalities, leukopenia (leukocytes <4.0/mm³) or leukocytosis (leukocytes > 20 / mm³) are indices of severe CAP that warrant hospitalization.8 This assessment should be conducted expeditiously, because these patients can progress rapidly to circulatory collapse and respiratory distress necessitating mechanical ventilation. They should receive immediate antimicrobial therapy because delay in antimicrobial therapy may increase morbidity and mortality.
Empirical antibiotic treatment decision: The selection of empiric antibiotics therapy depends on the severity of disease, host factors, epidemiological factors, likely micro-organisms and local antimicrobial patterns. Suggested regimens for empirical use in patients for CAP are summarized in Tables 2 to 4.

**ANTIBIOTIC CONSIDERATION**

**β-lactams and related agents:** The β-lactams are inactive against all strains of *M. pneumoniae* and *C. pneumoniae* and they are ineffective against legionella infections. β-lactams exert their antibacterial effects by interfering with synthesis of the peptidoglycan component of the bacterial cell wall. Parenteral penicillin G and oral penicillin V or amoxicillin are generally viewed as the β-lactam drugs of choice for penicillin susceptible strains of *S. pneumoniae*. Penicillins combined with β-lactamase inhibitors - amoxicillin clavulanate, ticarcillin/ clavulanate, ampicillin / sulbactam and piperacillin/tazobactum are active against β - lactamase producing organisms, *H. influenzae*, anaerobes, methicillin - susceptible stains of *S. aureus* and *M. catarrhalis*. Alternative to penicillin are generally preferred for infections involving *S. pneumoniae* resistant to penicillin.

**Macrolides:** All three macrolides—Erythromycin, azithromycin and clarithromycin appear to be effective in the treatment of infections caused by *M. pneumoniae*, *C. pneumonia* and legionella species. Approximately 10 -15% of *S. pneumonia* isolates are resistant to macrolides in vitro, so that caution is necessary when these agents are used empirically in suspected cases of *P. pneumonia*. Of the three macrolides, azithromycin is most active in vitro against legionella species, *H. influenzae* and *M. pneumoniae*, whereas clarithromycin is the most active against *S pneumoniae* and *C. pneumoniae*. A recent multicenter prospective study of patients with CAP showed that use of Erythromycin is a cost effective treatment. CAP strains of *S. aureus* are usually susceptible to macrolides. Erthromycin is relatively inactive against *H. influenzae*. Clarithromycin also has relatively limited in vitro activity against *H. influenzae*, however its 14-OH metabolite augments the activity of the parent compound.

**Cephalosporins:** Among this class most active against strains of *S. pneumoniae* are cefotaxime and ceftriaxone, and the clinical relevance of in vitro resistance to these drugs is unclear. The rank order of in vitro activity of oral cephalosporins against *S. pneumoniae* is as follows: cefpodoxime > cefotaxime > cefoxitin > cefaclor = loracarbef > cefadroxil = cephalaxin. But none of these oral agents have established clinical efficacy in cases involving strains *S. pneumoniae* with reduced penicillin susceptibility. Most second and third generation cephalosporins show moderate-to-good activity against *H influenzae*. *M. catarrhalis*. Activity against *S. aureus* is variable, cefazolin and cefuroxime are the most active and cefixime and cefazidime are least active.

**Quinolones:** All the Quinolones are active in vitro against aerobic gram positive cocci, gram negative bacilli, *M pneumoniae*, *M. catarrhalis*, *H. influenzae*, *C. pneumoniae* and legionella species. Although there is limited published experience with these drugs in patients with serious CAP, initial clinical trials have shown good result. Ciprofloxacin and trovafloxacin are most active against *P. aeruginosa* and trovafloxacin is the most active against anaerobes.

**Carbapenems:** Imipemem and Meropenem are active against broad spectrum of aerobic and anaerobic gram positive and gram negative organism, most strains of *S. pneumoniae*, *P. aeruginosa*, *H. influenzae*, *M catarrhalis* and methicillin - susceptible *S. aureus*.

**Aminoglycosides:** These agent are active in vitro against the aerobic and facultative gram negative bacilli, including *P. aeruginosa* and methicillin - susceptible *S. aureus*. Aminoglycosides should not be used as single agent for treatment of gram negative bacillary pneumonia.
**Vancomycin:** It is the only currently available drug which has universal activity against *S. pneumoniae*.[27] It also acts against methicillin-resistant *S. aureus*.

**Trimethoprim-Sulfamethoxazole:** There is growing concern over increasing resistance against this combination, particularly among strains of *S. pneumoniae* and *H. influenzae*.32 But this drug is active against such diverse pathogens such as Nocardia asteroids and *P. carinii*.33

**Clindamycin:** Many authorities consider clindamycin to be the preferred drug for treatment of anaerobic pulmonary infections including putrid lung abscess.34 This drug shows good activity against gram positive cocci, *S. pneumoniae* but inactive against *H. influenzae* and atypical agents.

**Tetracyclines:** In respiratory tract infections tetracyclines are active against *M pneumoniae*, *C. pneumoniae* and legionella species.35 Among these members doxycycline most frequently used in clinical practice today because of tolerability and good bioavailability, but there is concern about occasional resistance, including resistance to *S. pneumoniae* in 5-8% of cases.[27,32]

**DURATION OF TREATMENT**

Datas are limited on duration of CAP therapy. The decision is usually based on the pathogen's response to treatment, comorbid condition and complications. Current research[36] recommends 7-10 days of therapy for *S. pneumoniae* and 10-14 days therapy for *M. pneumoniae* and *C. pneumoniae*. After hospitalization when patients are clinically stable, i.e. temperature < 37.80°C, pulse < 100 / min, respiratory rate < 24 / min, systolic blood pressure > 90 mm Hg and blood oxygen saturation > 90% and able to tolerate oral food, the patients may be treated with oral antibiotics for the rest of the course of therapy course. This can minimize hospitalization and reduce the risk of hospital acquired infection.3

**REFERENCES**

MULTIPLE CHOICE QUESTIONS

1. Urine antigen tests have been shown to be sensitive and specific for detecting:
   A. Legionella pneumophila.
   B. M. pneumoniae
   C. P. carinii

2. Infectious Diseases Society of America and Canadian Guidelines for the initial management of CAP recommend initial empiric therapy with:
   A. Clindamycin
   B. Fluoroquinolones
   C. Carbapenems

3. In CAP bronchoscopy is especially useful for detecting selected pathogens such as:
   A. Chlamydia
   B. Legionella
   C. Mycobacterium species

4. All patients with suspected CAP should have a:
   A. Chest radiography
   B. Antigen detection
   C. DNA probes and amplifications

5. Community acquired pneumonia can effect:
   A. Children
   B. Old age people
   C. All ages

6. In CAP blood culture is done in:
   A. All suspected patients
   B. Hospitalized patients
   C. Outpatients