

Pneumonia : Review of Guidelines



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Introduction

Many studies have been published on the topic of CAP and numerous societies have published their guidelines for the same. These groups include The IDSA, ATS, ERS, BTS and the Canadian guidelines. In view of the differences in the various guidelines and the confusion hence prevailing, the IDSA and the ATS published the Consensus guidelines which is the most widely accepted.

Epidemiology

Pneumonia is a leading cause of death in the world and the sixth most common cause of death in the United States. It is the number one cause of death from infectious diseases in the United States.¹ Every year in the United States, there are from 5-10 million cases of CAP leading to as many as 1.1 million hospitalizations and 45,000 deaths. In Europe, the overall incidence of community acquired lower respiratory tract infections (LRTIs) was found to be 44 cases per 1,000 populations per year in a single general practice. However, the incidence was two- to four-times higher in people aged over 60 yrs than in those aged 50 yrs.^{2,3} The mortality rate in both continents is less than 1% for persons with CAP who do not require hospitalization; however, the mortality rate averages from 12% to 14% among hospitalized patients with CAP. Among patients who are admitted to the intensive care unit (ICU), or who are bacteremic, or who are admitted from a nursing home, the mortality rate averages from 30% to 40%.¹⁻⁴

Definition

The IDSA defines CAP as “an acute infection of the pulmonary parenchyma that is associated with at least some symptoms of acute infection, accompanied by the presence of an acute infiltrate on a chest radiograph or auscultatory findings consistent with pneumonia (such as altered breath sounds and/or localized rales), in a patient not hospitalized or residing in a long-term care facility for more than 14 days before onset of symptoms.”¹

The most comprehensive definition² is provided by the BTS which is as follows:

- Symptoms of an acute lower respiratory tract illness (cough and at least one other lower respiratory tract symptom)
- New focal chest signs on examination
- At least one systemic feature (either a symptom complex of sweating, fevers, shivers, aches and pains and/or temperature of 38°C or more).
- No other explanation for the illness, which is treated as CAP with antibiotics.
- Definition of CAP in patients admitted to hospital (when a chest x-ray is available):
- Symptoms and signs consistent with an acute lower respiratory tract infection associated with new radiographic shadowing for which there is no other explanation (e.g. not pulmonary edema or infarction).
- The illness is the primary reason for hospital admission, and is managed as pneumonia.

Risk Factors

Patients with co-existing illnesses like COPD, Diabetes Mellitus, Renal failure, Congestive Heart Failure, Coronary Artery disease, malignancy, Chronic Neurological disease and Chronic liver disease have increased incidence of CAP.² Patients with CAP and certain co-morbidities have increased mortality.⁵ These risk factors include diabetes mellitus, coronary artery disease, CHF, immunosuppression, neurologic disease, active malignancies, alcohol consumption, increasing age, bacteremia, leukopenia, hypotension, altered mental status, tachypnea, hypoxemia, aspiration pneumonia, and infections due to gram-negative organisms.

The ATS emphasizes certain modifying factors that increase the risk of infection with drug-resistant and unusual pathogens.¹

Risk factors for drug-resistant *Streptococcus pneumoniae* (DRSP) include age greater than 65 years, beta-lactam therapy within the past 3 months, immunosuppression (either as the result of an illness or induced by treatment with corticosteroids), multiple medical co-morbidities, alcoholism, and exposure to a child in a day care center.

Risk factors for enteric gram-negative organisms are as follows: recent antibiotic therapy, underlying cardiopulmonary disease, residence in a nursing home, and multiple medical co-morbidities.

Risk factors for *P aeruginosa* are as follows: structural lung disease such as bronchiectasis, broad-spectrum antibiotic therapy that lasted for at least 7 days in the past month, corticosteroid therapy with at least 10 mg of prednisone per day, and malnutrition.⁷

Pathogenesis

Several prospective studies of CAP have failed to identify an organism in 50% of cases. When an organism is identified, however, *S pneumoniae* is the most common etiologic agent.^{1,2,3,7} It accounts for about two thirds of bacteremic pneumonia. It is the most frequent cause of lethal CAP.¹ Multidrug resistance (such as beta-lactams, macrolides, doxycycline, and recently fluoroquinolone antibiotics) is an emerging problem and complicates the management of CAP. Therefore, it is important to recognize factors that place patients at risk for DRSP.^{1,3,7}

Other causative pathogens in CAP include *Hemophilus influenzae* (usually nontypeable strains), *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Neisseria meningitidis*, *Moraxella catarrhalis*, *Klebsiella pneumoniae*, and other gram-negative rods, *Legionella* species and influenza virus.¹⁻³

The ATS statement describes the possibility of “atypical pathogens” (*C pneumoniae*, *M pneumoniae*, and *Legionella pneumophila*) infecting or co-infecting all patients with CAP and therefore recommends therapy to account for this possibility.⁷

If patients with CAP require admission to the ICU, one must consider *S pneumoniae*, the atypical pathogens (especially *Legionella*) and enteric gram-negative organisms as the organisms responsible for the infection.^{1,3,6} *P aeruginosa* is responsible for infection in some patients with severe CAP and should be considered in patients with previously described specific risk factors because it necessitates a different treatment regimen.¹

Table 1 : Most common etiologies of community-acquired pneumonia

Patient type	Etiology
Outpatient	Streptococcus pneumoniae
	Mycoplasma pneumoniae
	Haemophilus influenza
	Chlamydia pneumoniae
	Respiratory viruses
Inpatient (non-ICU)	<i>S. pneumoniae</i>
	<i>M. pneumoniae</i>
	<i>C. pneumoniae</i>
	<i>H. influenza</i>
	<i>Legionella</i> species
	Aspiration
	Respiratory viruses
Inpatient (ICU)	<i>S. pneumoniae</i>
	<i>Staphylococcus aureus</i>
	<i>Legionella</i> species
	Gram-negative bacilli
	<i>H. influenza</i>

In India the etiologic agent for CAP varies according to the region we study. There is no cross-sectional study available. Streptococcus pneumonia is the commonest organism in Shimla⁹ and Delhi⁸ whereas Pseudomonas aeruginosa predominates in blood culture positive Pneumonia in Ludhiana. A study conducted at the Sher I Kashmir Institute of Medical Sciences, Soura looked at 100 consecutive admitted patients who had blood or sputum cultures sent for CAP. The overall etiologic agent was established in 29 patients.¹⁰ The most common etiologic agent was Pseudomonas (10), Staph aureus (7), E. coli (6), Klebsiella (3), S. pneumoniae (1), S. pyogenes (1), and Acinetobacter (1) (Table 1).

Diagnostic Studies

In addition to a constellation of suggestive clinical features, a demonstrable infiltrate by chest radiograph or other imaging technique, with or without supporting microbiological data, is required for the diagnosis of pneumonia.

Other general investigations for a patient admitted to hospital.²

- Oxygenation saturations and, where necessary, arterial blood gases.
- Chest radiograph.
- Urea and electrolytes to inform severity assessment
- C-reactive protein to aid diagnosis and as a baseline measure
- Full blood count
- Liver function tests

Microbiological tests should be performed on all patients with moderate and high severity CAP. The extent of investigation in these patients being guided by severity.¹¹

For patients with low severity CAP the extent of microbiological investigations should be guided by clinical factors (age, co-morbid illness, and severity indicators), epidemiological factors, and prior antibiotic therapy.^{11,12}

Where there is clear microbiological evidence of a specific pathogen, empirical antibiotics should be changed to the appropriate pathogen-focused agent, unless there are legitimate concerns about dual pathogen infection.^{13,14}

Microbiological investigations in the community

For patients managed in the community microbiological

investigations are not recommended routinely.¹⁵

Examination of sputum should be considered for patients who do not respond to empirical antibiotic therapy.^{13,15}

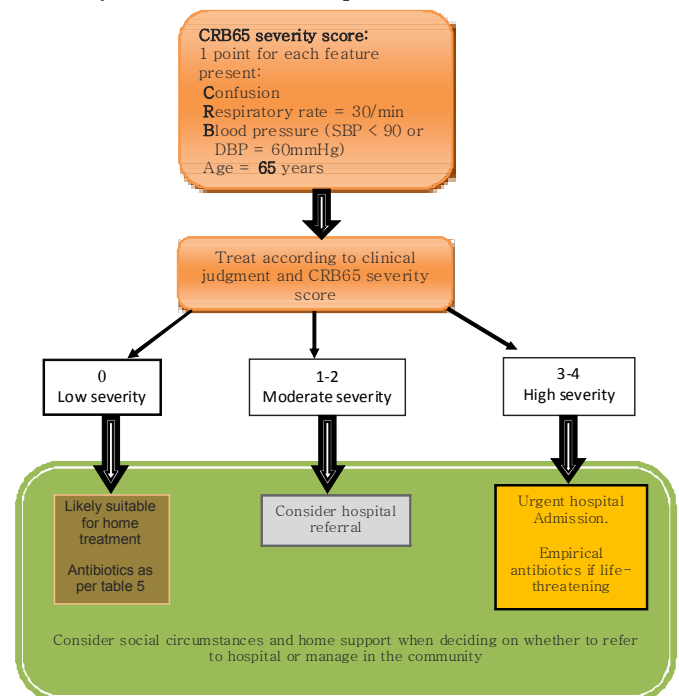
Examination of sputum for *Mycobacterium tuberculosis* should be considered for patients with a persistent productive cough, especially if malaise, weight loss or night sweats, or risk factors for tuberculosis are present.¹

The IDSA and the ATS differ in their recommendations of microbiologic studies to determine the etiology of CAP. The IDSA recommends routine sputum culture with Gram stain to optimize antibiotic therapy for each individual patient as well as to monitor drug-resistance among pathogens.¹ The ATS, however, does not recommend routine sputum culture with Gram stain (in the absence of suspected drug resistance) because studies have shown that a pathogen is not identified in 40% to 50% of all patients.⁴

The ATS and the IDSA both recommend drainage of any significant pleural effusion (defined as greater than 10-mm thickness on a radiograph taken with the patient in the lateral decubitus position) to rule out the possibility of an empyema or a parapneumonic effusion.^{1,4}

Decision to admit/categorization of risk

Severity-of-illness scores, such as the CURB-65 criteria (confusion, uremia, respiratory rate, low blood pressure, age 65 years or greater), or prognostic models, such as the Pneumonia Severity Index (PSI), can be used to identify patients with CAP who may be candidates for outpatient treatment.¹



For patients with CURB-65 scores 2, more-intensive treatment i.e., hospitalization or, where appropriate and available intensive in-home health care services—is usually warranted.²

Direct admission to an ICU is required for patients with septic shock requiring vasopressors or with acute respiratory failure requiring intubation and mechanical ventilation. In addition to the 2 major criteria (need for mechanical ventilation and septic shock), an expanded set of minor criteria (respiratory rate, 130 breaths/min; arterial oxygen pressure/fraction of inspired oxygen (PaO₂/FiO₂) ratio, <250; multi-lobe infiltrates; confusion; blood urea nitrogen level, 120 mg/dL; leukopenia resulting from infection; thrombocytopenia; hypothermia; or hypotension

Table 2 : Criteria for severe community-acquired pneumonia

Minor criteria	Major criteria
Respiratory rate ≥ 30 breaths/min	Invasive mechanical ventilation
PaO ₂ /FiO ₂ ratio ≤ 250	Septic shock with the need for vasopressors
Multilobar infiltrates	
Confusion/disorientation	
Uremia (BUN level, ≥ 20 mg/dL)	
Leukopenia (WBC count, < 4000 cells/mm ³)	
Thrombocytopenia (platelet count, $< 100,000$ cells/mm ³)	
Hypothermia (core temperature, ≤ 36 °C)	
Hypotension requiring aggressive fluid resuscitation	

requiring aggressive fluid resuscitation) is proposed (Table 2). The presence of at least 3 of these criteria suggests the need for ICU care but will require prospective validation.^{16,17}

Management of CAP

IDSA guidelines (Table 3)

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

- A. A macrolide (azithromycin, clarithromycin, or erythromycin)
- B. Doxycycline (weak recommendation; level III evidence)¹

Presence of comorbidities, such as 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 (in which case an alternative from a different class should be selected); or other risks for DRSP infection:
- A. A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg])
- B. A b-lactam plus a macrolide (High-dose amoxicillin [e.g., 1 g 3 times daily] or amoxicillin-clavulanate [2gm 2 times daily] is preferred; alternatives include ceftriaxone, cefpodoxime, and cefuroxime [500 mg 2 times daily]; doxycycline is an alternative to the macrolide.)^{1,18}

Inpatient, non-ICU treatment

A respiratory fluoroquinolone

A b-lactam plus a macrolide (Preferred b-lactam agents include cefotaxime, ceftriaxone, and ampicillin; ertapenem for selected patients; with doxycycline as an alternative to the macrolide. A respiratory fluoroquinolone should be used for penicillin-allergic patients.)

Inpatient, ICU treatment

A b-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) plus either azithromycin (level II evidence) or a fluoroquinolone.

(For penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam are recommended.)¹⁹

For *Pseudomonas* infection, use an anti-pneumococcal, anti-pseudomonal b-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin (750-mg dose)

Or

The above b-lactam plus an aminoglycoside and azithromycin

Table 3 : Recommended empirical antibiotics for community acquired pneumonia

Outpatient treatment
Previously healthy and no use of antimicrobials within the previous 3 months
A macrolide (strong recommendation; level I evidence)
Doxycycline (weak recommendation; level III evidence)
Presence of comorbidities such as chronic heart, lung, liver or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; or use of antimicrobials within the previous 3 months (in which case an alternative from a different class should be selected).
A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg]) (strong recommendation; level I evidence)
A b-lactam plus a macrolide (strong recommendation; level I evidence)
In regions with a high rate (125%) of infection with high-level (MIC ≥ 16 mg/mL) macrolide-resistant <i>Streptococcus pneumoniae</i> , consider use of alternative agents listed above in (2) for patients without comorbidities (moderate recommendation; level III evidence)
Inpatients, non-ICU treatment
A respiratory fluoroquinolone (strong recommendation; level I evidence)
A b-lactam plus a macrolide (strong recommendation; level I evidence)
Inpatients, ICU treatment
A b-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) plus either azithromycin (level II evidence) or a respiratory fluoroquinolone (level I evidence) (strong recommendation) (for penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam are recommended)
Special concerns
If <i>Pseudomonas</i> is a consideration
An antipneumococcal, antipseudomonal b-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin (750 mg)
Or
The above b-lactam plus an aminoglycoside and azithromycin
Or
The above b-lactam plus an aminoglycoside and an antipneumococcal fluoroquinolone (for penicillin-allergic patients, substitute aztreonam for above b-lactam). (moderate recommendation; level III evidence)
If CA-MRSA is a consideration, add vancomycin or linezolid (moderate recommendation; level III evidence)

Or

The above b-lactam plus an aminoglycoside and an antipneumococcal fluoroquinolone (for penicillin-allergic patients, substitute aztreonam for the above b-lactam).²⁰

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

Pathogen-directed therapy: Once the etiology of CAP has been identified on the basis of reliable microbiological methods, antimicrobial therapy should be directed at that pathogen.¹⁴

Switch from intravenous to oral therapy: 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.³

Duration of antibiotic therapy: Patients with CAP should be treated for a minimum of 5 days (level I evidence), should be afebrile for 48–72 h, and should have not more than 1 CAP-associated sign of clinical instability before discontinuation of therapy

A longer duration of therapy may be needed if initial therapy was not active against the identified pathogen or if it was

complicated by extrapulmonary infection, such as meningitis or endocarditis.²¹

Patients with CAP who have persistent septic shock despite adequate fluid resuscitation should be considered for treatment with Drotrecogin alfa activated within 24h of admission.^{4,3}

Patients with hypoxemia or respiratory distress should receive a cautious trial of noninvasive ventilation unless they require immediate intubation because of severe hypoxemia (PaO₂/FiO₂ ratio < 150) and bilateral alveolar infiltrates.

Low-tidal-volume ventilation (6 cm³/kg of ideal body weight) should be used for patients undergoing ventilation who have diffused bilateral pneumonia or acute respiratory distress syndrome.

NOTE. CA-MRSA, community-acquired methicillin-resistant *Staphylococcus aureus*; ICU, intensive care unit.

Prevention

Influenza and pneumococcal vaccination

Department of Health guidelines in relation to influenza and pneumococcal immunization of at-risk individuals should be followed. All patients aged >65 years or at risk of invasive pneumococcal disease who are admitted with CAP, and who have not previously received pneumococcal vaccine should receive 23-valent pneumococcal polysaccharide vaccine (23-PPV) at convalescence in line with the Department of Health Guidelines.^{22,23}

Smoking cessation

Smoking cessation advice should be offered to all patients with CAP who are current smokers according to smoking cessation guidelines issued by the Health Education Authority

Comment and Summary

Antibiotic management of nonresponsive in CAP has not been studied. The overwhelming majority of cases of apparent nonresponsive are due to the severity of illness at presentation or a delay in treatment response related to host factors. Other than the use of combination therapy for severe bacteremic pneumococcal pneumonia, there is no documentation that additional antibiotics for early deterioration lead to a better outcome. The presence of risk factors for potentially untreated microorganisms may warrant temporary empirical broadening of the antibiotic regimen until results of diagnostic tests are available.

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