GUIDELINES FOR MANAGEMENT OF PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA (CAP) AND NOSOCOMIAL (HOSPITAL ACQUIRED) PNEUMONIA (HAP)

Dorel Sandesc, Ovidiu Bedreag

OBJECTIVES

Upon completion of this article, the reader should be able to summarize epidemiology, characteristics of diagnosis and treatment of community acquired and nosocomial (hospital acquired) pneumonia and to discuss management and preventive strategies against developing nosocomial pneumonia in hospitalized patients.

COMMUNITY ACQUIRED PNEUMONIA

INTRODUCTION

This review is based on American Thoracic Society guidelines for community-acquired pneumonia, first presented in 1993, and regularly updated since then. Also a large number of clinical studies were reviewed to create a general and useful view on this pathology for the specialists and general practitioners.1,2

Community-acquired pneumonia (CAP) ranks as the 4th most common cause of death in the United Kingdom3 and the 6th as the leading infectious cause of death when combined with influenza in the United States.4 That pathology is responsible for a major portion of health care budget. Data show 3.0-5.6 million cases annually in the United States,5-7 with important costs of care.8-11 CAP mortality rates range generally from <1% to 9%, but can increase to 50% for the patients requiring admission to an intensive care unit.6,8 About 10% of patients admitted in hospital for CAP will need treatment in an intensive care unit.

An important part of this statistics is due to a better medical management of chronic diseases and to the increasing number of persons with structural lung disease. World Health Organization predicted that chronic obstructive pulmonary disease prevalence will increase from the 12th to the 5th most common chronic disease worldwide by 2020.12

Professional societies have promulgated diagnosis and treatment guidelines to aid the non-specialist practitioners who treat most patients with CAP. These guidelines are meant to reduce cost of care, inpatient days, mortality and possibly antibiotic resistance.5,7,9,10,13-15

DIAGNOSIS OF COMMUNITY-ACQUIRED PNEUMONIA

History of the patient and physical examination has low sensitivity and specificity in CAP diagnosis. The signs and symptoms relied on to confirm the clinical suspicion for CAP are; cough, purulent sputum production, dyspnea, pleuritic chest pain, fever, chills, tachypnea, tachycardia, consolidation on examination, rales, leukocytosis and presence of new or evolving infiltrate on chest x-ray.5,16,17,18 The elderly may present with fewer symptoms, including headache, malaise, diarrhea, confusion, falling, and decreased appetite.7,8

To minimize missed diagnoses and risk of clinical deterioration caused by delay in treatment, emergency
department physicians may over read chest x-rays and conservatively elect to treat patients because of the limitations of radiographic diagnosis, concerns regarding social issues, and follow-up obstacles. Consideration of additional factors, such as the patient’s age and hydration and immune status, diastolic blood pressure <60 mm Hg and elevated blood urea nitrogen can reduce the number of missed cases of CAP.

Recently published studies have called into question the routine collection of cultures on CAP patients. Culture-positive identification rates ranged from 2.1% to approximately 50%, and the presence or absence of this information did not affect outcome. All authors have found poor overall identification rates and limited utilization of the data in clinical decision making.

This may represent an opportunity to use some criteria as indices to limit culturing on lower risk patients.

**DECISION TO HOSPITALIZE PATIENTS WITH COMMUNITY-ACQUIRED PNEUMONIA**

For a good disease management is crucial to identify patients with low risk for morbidity or mortality with CAP. A scheme has been done in the Pneumonia Patient Outcomes Research Team (PORT) investigation (beginning 1997). In this clinical trial more than 55,000 patients with CAP were evaluated to determine the best predictors of a good outcome. This system uses a 2-step risk assessment. If patients are younger than 50 years of age and without comorbid disease or significant vital sign irregularities, they may be treated at home with antibiotics. Contrarily, if patients are male, come from a nursing home, or have marked laboratory abnormalities, they tend to represent the more severe end of this pathology.

Despite large numbers of patients in this model, as many as 10% of patients identified as treatable in an outpatient setting will ultimately require ICU care.

The election of the site of care is perhaps the most important clinical decision made by physicians during the initial course of illness for patients with CAP. It has a direct bearing on the intensity of laboratory testing, microbiologic evaluation, antibiotic therapy and costs of treating this illness.

Multiple studies have identified a series of risk factors that increase the risk of a complicated course for CAP. When multiple risk factors coexist, hospitalization should be strongly considered. The decision to hospitalize is not necessarily a commitment to long-term inpatient care. The patients should be observed closely until it is clear that therapy can be safely continued out of the hospital. Once it is evident on the ward that the patient’s infection is responding to therapy and may safely be continued in the outpatient setting, the patient may be discharged.

The admission decision may also be influenced by the availability of outpatient support services (home nursing, home intravenous therapy), and alternative sites for care.

A scale of risk developed by the Pneumonia Patient Outcomes Research Team (PORT) separated patients into high and low risk of death, and that scale has been extrapolated into defining the need for admission.

Risk factors have been identified that are associated with an increased risk of death or a complicated course. These factors include a number of features listed below, and those with an asterisk (*) are factors that have been identified to predict mortality in the Pneumonia Patient Outcomes Research Team (PORT) prediction rule model:

1. Age over 65 year
2. Coexisting illnesses: chronic obstructive lung disease, bronchiectasis, malignancy *, diabetes mellitus, chronic renal failure*, congestive heart failure*, chronic liver disease*, chronic alcohol abuse, malnutrition, cerebrovascular disease*, post-splenectomy status, history of hospitalization within the past year
3. Physical findings that predict either mortality, increased morbidity, or a complicated course:
   a. White blood cell count < 4,000 elements / mm³ or >10,000 elements/ mm³
   b. PaO₂ < 60 mm Hg* or PaCO₂ of > 50 mm Hg while breathing room air
   c. Evidence of abnormal renal function, manifested by serum creatinine > 1.2 mg/dl or BUN > 20 mg/dl
   d. Presence of unfavorable chest radiograph findings: more than one lobe involvement, presence of a cavity, rapid radiographic spreading (which usually cannot be determined at the time of admission), the presence of a pleural effusion*
   e. Hematocrit < 30% * or hemoglobin < 9 mg/dl;
   f. Evidence of sepsis or organ dysfunction as manifested by metabolic acidosis, or coagulopathy;
Arterial pH < 7.35*

The above-described approach is not quantitative, and in the past 10 years, multiple studies have used variates analysis to develop prediction rules for outcome in CAP that could be used to help with to decide the initial site of care.22-25 None of these rules was specifically designed to define need for hospitalization. The approach developed by the British Thoracic Society (BTS) Research Committee is used for identifying high-risk patients who not only usually require admission, but who also often require ICU care.26-27 In this model, patients with any two of the following are classified as having severe CAP:

- Respiratory rate > 30 breaths/minute,
- Diastolic blood pressure < 60 mm Hg,
- Blood urea nitrogen concentration > 20 mg/dL, or
- Confusion.

It must be defined severe CAP as any patient admitted to an ICU specifically for pneumonia. Epidemiologically, this patient population comprises approximately 10% of all ICU admissions. Patients in the ICU with pneumonia have the highest mortality of all CAP patients (35% to 40%) compared with less than 15% for general hospitalized patients with CAP.2

Under this definition, the following criteria are proposed by ATS panel to help clinicians to decide about the need for ICU care:

1. one or more major criteria (shock, need for mechanical ventilation)
2. two or more minor criteria (systolic blood pressure < 90 mm Hg, multilobar infiltrates, PaO₂/FiO₂ ratio < 250 mm Hg).

These simple criteria establish a sensitivity of 78% and specificity of 94% for identifying patients in need of ICU care (i.e., severe CAP).

These two prediction rules are complementary. The BTS rule is focused on identifying high-risk patients so that their severity of illness is not underestimated, while the Pneumonia PORT approach is focused on recognizing some patients as low risk, so that their severity of illness is not overestimated.

### ETIOLOGY

According to numerous trials the epidemiologic patterns of CAP are:
- *Streptococcus pneumoniae* (25 - 33% of cases)
- Gram-negative organisms (including *Haemophilus influenzae*) (10 - 20% of cases), with atypical organisms and Legionella comprising the remainder. In elderly patients, particularly those from...
a nursing home environment, Gram-negative organisms command a larger role, as does Staphylococcus aureus.

Despite rigorous efforts in large-scale trials, no bacteriologic diagnosis can be made in up to 50% of cases. The mentioned data imply that making an etiologic diagnosis would improve outcomes, through more directed antimicrobial therapy. This hypothesis has not been proven. In fact, one study found that outcomes appeared better in patients in whom no pathogen was isolated. With this conflicting data, it appears that isolation of the pathogenic organism does not necessarily improve outcome, particularly if early and appropriate antimicrobial therapy is instituted.

TREATMENT

Reduced inpatient and 30-day mortality has been related to antibiotic administration in less than 8 hours, and current standards require the first dose to be administered within 4 hours of arrival at the hospital. Application of empiric guidelines to antibiotic selection has been demonstrated to reduce overall costs, mortality, and length of hospital stay. Pharmaceutical costs and side effect profiles vary substantially among oral and parenteral options and must be familiar to practitioners for helping the patient to obtain the prescribed medications at discharge.

Dual coverage with β-lactam and macrolide has been demonstrated to improve response to treatment, even for abbreviated macrolide regimens. It is still subject of debate whether the bacteriostatic effect of aminoglycosides or macrolides may, in fact, detract from the bactericidal effect of β-lactam antibiotics (i.e., penicillins or cephalosporins), with most recent data suggesting there is no adverse clinical impact of these combinations. Azithromycin administration has been shown to be an independent predictor of positive outcome, particularly if early and appropriate antimicrobial therapy is instituted.

**Table 2.** Modifying factors that increase the risk of infection with specific pathogens 1

<table>
<thead>
<tr>
<th>Penicillin-resistant and drug-resistant pneumococci:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 65 years</td>
</tr>
<tr>
<td>Beta-lactam therapy within the past 3 months</td>
</tr>
<tr>
<td>Immune-suppressive illness (including therapy with corticosteroids)</td>
</tr>
<tr>
<td>Multiple medical comorbidities</td>
</tr>
<tr>
<td>Exposure to a child in a day-care center</td>
</tr>
<tr>
<td>Enteric gram-negatives</td>
</tr>
<tr>
<td>Residence in a nursing home</td>
</tr>
<tr>
<td>Underlying cardiopulmonary disease</td>
</tr>
<tr>
<td>Multiple medical comorbidities</td>
</tr>
<tr>
<td>Recent antibiotic therapy</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Structural lung disease (bronchiectasis)</td>
</tr>
<tr>
<td>Corticosteroid therapy (&gt; 10 mg of prednisone per day)</td>
</tr>
<tr>
<td>Broad-spectrum antibiotic therapy for &gt; 7 days in the past month</td>
</tr>
<tr>
<td>Malnutrition</td>
</tr>
</tbody>
</table>

**Table 3.** Outpatients, without cardiopulmonary disease, without modifying factors* 1

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumoniae</td>
<td>Advanced generation macrolide azithromycin or clarithromycin** or Doxycycline***</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td></td>
</tr>
<tr>
<td>Chlamydia pneumoniae (alone or as mixed infection)</td>
<td></td>
</tr>
<tr>
<td>Hemophilus influenzae</td>
<td></td>
</tr>
<tr>
<td>Respiratory viruses</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
</tr>
<tr>
<td>Legionella spp.</td>
<td></td>
</tr>
<tr>
<td>Mycobacterium tuberculosis</td>
<td></td>
</tr>
<tr>
<td>Endemic fungi</td>
<td></td>
</tr>
</tbody>
</table>

* Excludes patients at risk for HIV
** Erythromycin is not active against H. influenzae and the advanced generation of β-lactams.
macrolides azithromycin and clarithromycin are better tolerated.

*** Many strains of S. pneumoniae are resistant to tetracycline, and it should be used only if the patient is allergic to or intolerant of macrolides.

### Table 4. Outpatient with cardiopulmonary disease and/or other modifying factors

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumonia (including DRSP)</td>
<td>Beta-lactam (oral cephalosporine, cefuroxime, high-dose amoxicillin, amoxicillin/clavulanate, or parenteral ceftriaxone followed by oral cefuroxime) plus or Macrolide or doxycycline** or Antipneumococcal fluoroquinolone (used alone)</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>Intravenous beta-lactam** (cefotaxime, ceftriaxone, ampicillin/subactam, high-dose ampicillin) plus or Intra venous or oral macrolide doxycycline*** or Intravenous antipneumococcal fluoroquinolone alone</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>Mixed infection (bacteria plus atypical pathogen)</td>
</tr>
<tr>
<td>Enteric gram-negatives</td>
<td>Intravenous beta-lactam** (cefotaxime, ceftriaxone, ampicillin/subactam, high-dose ampicillin) plus or Intra venous or oral macrolide doxycycline*** or Intravenous antipneumococcal fluoroquinolone alone</td>
</tr>
<tr>
<td>Hemophilus influenzae</td>
<td>Respiratory viruses</td>
</tr>
<tr>
<td>Enteric gram-negatives</td>
<td>Miscellaneus:</td>
</tr>
<tr>
<td>Aspiration (anaerobes)</td>
<td>Mycobacterium tuberculosis, endemic fungi</td>
</tr>
<tr>
<td>Aspiration (anaerobes)</td>
<td>Pneumocystis carinii</td>
</tr>
<tr>
<td>Miscellaneous:</td>
<td>M. tuberculosis, endemic fungi, P. carinii</td>
</tr>
</tbody>
</table>

* In 50–90% of the cases no etiology was identified

** High-dose amoxicillin is 1 g every 8 h; if a macrolide is used, erythromycin does not provide coverage of H. influenzae, and thus when amoxicillin is used, the addition of doxycycline or of an advanced-generation macrolide is required to provide adequate coverage of H. influenzae

### Table 5. Inpatients, not in ICU

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Cardiopulmonary disease and/or modifying factors</td>
<td>Intravenous beta-lactam** (cefotaxime, ceftriaxone, ampicillin/subactam, high-dose ampicillin) plus or Intra venous or oral macrolide doxycycline*** or Intravenous antipneumococcal fluoroquinolone alone</td>
</tr>
<tr>
<td>Streptococcus pneumonia (including DRSP)</td>
<td>Mixed infection (bacteria plus atypical pathogen)</td>
</tr>
<tr>
<td>Hemophilus influenzae</td>
<td>Mixed infection (bacteria plus atypical pathogen)</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>Mixed infection (bacteria plus atypical pathogen)</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>Mixed infection (bacteria plus atypical pathogen)</td>
</tr>
<tr>
<td>Enteric gram-negatives</td>
<td>Viruses</td>
</tr>
<tr>
<td>Aspiration (anaerobes)</td>
<td>Miscellaneous:</td>
</tr>
<tr>
<td>Aspiration (anaerobes)</td>
<td>M. tuberculosis, endemic fungi, P. carinii</td>
</tr>
</tbody>
</table>

* In 30–50% of the cases no etiology was identified

** Antipseudomonal agents such as ceftepime, piperacillin/tazobactam, imipenem, and meropenem are generally active against DRSP, but not recommended for routine use in this population that does not have risk factors for P. aeruginosa

*** Use of doxycycline or an advanced generation macrolide (azithromycin or clarithromycin) will provide adequate coverage if the selected beta-lactam is susceptible to bacterial beta-lactamases.

### Prevention

Because antibiotic resistance remains a major obstacle to successful patient treatment, prevention or dumping of community-acquired pneumonia is gaining increasing popularity through more aggressive pneumococcal and influenza vaccination of at risk groups, even before hospital discharge from a community-acquired pneumonia admission. Vaccination with pneumococcal polysaccharide does prevent pneumonia with an efficacy of 65%–84%. CAP prevention is even more important in geriatrics. The 23-valent pneumococcal polysaccharide vaccination is appropriate for high-risk adults to potentially cover the serotypes responsible for 85% of cases of pneumonia caused by S. pneumoniae.

This vaccination may be given simultaneously, at different sites, with the influenza vaccination without an increase in adverse reactions. Influenza vaccine has been proven to reduce disease severity, and can prevent 70 to 90% of cases in healthy persons younger than 65 years. It should be administered annually and can reduce occurrence of pneumonia, hospitalization and death.

### Hospital Acquired Pneumonia

#### Introduction

Hospital acquired pneumonia (HAP) is defined as pneumonia with onset of symptoms after more than 48 hours after admission to an acute care hospital or chronic care facility or less than 7 days after a subject is discharged from the hospital. In this case the initial hospitalization must have been more than 3 days duration. All these terms are used in order to exclude an infection being in the incubation period in this time.

There is no unity in definitions, other synonyms used for this pathology are nosocomial pneumonia (NP), ventilator-associated pneumonia (VAP) or Intensive Care Unit acquired pneumonia. HAP represents an important cause of mortality and morbidity.

In November 1995, a Consensus Statement was officially adopted by the American Thoracic Society Board of Directors, in order to highlight the diagnosis, assessment of severity, initial antimicrobial therapy and preventive strategies in hospital-acquired pneumonia in adults. Last years researches on etiology, pathogeny of HAP and, most of all, on antibiologic resistance updated these data, and in 2002 an International Consensus Conference in Critical Care on ICU-Acquired Pneumonia has organized by the American Thoracic Society Assembly on Critical Care (ATS), the European Respiratory Society (ERS), the European Society of Intensive Care Medicine (ESICM), and the Société de Réanimation de Langue Française (SRLF).
EPIDEMIOLOGY

As incidence, hospital acquired pneumonia (HAP) is the second nosocomial infection, after urinary tract infections, but has the greatest mortality. Incidence in USA is 5-10 patients/1000 hospital admissions. The incidence rises 6-21 times for mechanical ventilated patients in intensive care units. In these units HAP is the most frequent nosocomial infection, having an incidence that rises until 60% of patients.

Incidence of Ventilator – Associated Pneumonia (VAP) is about 7 cases for 1000 days of mechanical ventilation. The risk is at the maximum level in the 5th day of mechanical ventilation, after 15 days follows a regression, VAP being rare at chronic mechanical ventilated patients. Nosocomial bacterial pneumonia is under-recognized in ARDS, with one study finding histologically proven pneumonia at autopsy in 58% of patients, in 36% of whom it was unsuspected.

Although the crude mortality rate for patients with HAP may be as high as 70%, all of these deaths are not the direct result of infection. The mortality attributable to pneumonia has been defined as the percentage of deaths that would not have occurred in the absence of this infection. Studies have estimated that between one third to one half of all HAP deaths are the direct result of infection, but the attributable mortality may be higher if bacteremia is present or if the etiologic agent is Pseudomonas aeruginosa or Acinetobacter species.

PATHOGENY

For respiratory infection to occur, at least one of three conditions must be present: host defenses must be impaired, an inoculum of organisms of sufficient number must reach the patient’s lower respiratory tract and overwhelm the host’s defense mechanism, or a highly virulent organism must be present.

Bacterial entry into the lungs may occur by various routes, including:
- microaspiration of oropharyngeal secretions colonized with pathogenic bacteria;
- aspiration of esophageal/gastric contents;
- inhalation of an infected aerosol;
- blood-borne spread from a distant site of infection;
- exogenous penetration from an infected site (pleural space);
- direct inoculation into the airways of intubated patients from ICU personnel
- translocation from the gastrointestinal tract (uncertain)

The risk factors for respiratory tract colonization and HAP have considerable overlap and include patient-related conditions, infection control-related problems, and intervention-related alterations in host defense or bacterial exposure.

Patient-related risk factors:
- severe acute or chronic diseases;
- coma;
- malnutrition;
- prolonged hospitalization;
- arterial hypotension;
- metabolic acidosis;
- smoking, alcoholism;
- other co-morbidities: central nervous diseases, diabetes mellitus, renal failure, respiratory failure, chronic obstructive pulmonary disease (COPD)
- older patients.

Intervention-related risk factors:
- presence of an endotracheal intubation tube (endotracheal tube pneumonia) and mechanical ventilation;
- corticoid therapy or immunosuppressive therapy;
- sedation;
- prolonged thoraco-abdominal surgical interventions;
- extensive use of antibiotherapy;
- parenteral alimentation.

Infection control-related factors:
- lack of prophylactic measures (hand washing, gloves changes, facial masks etc.)
- insufficient personal in ICU team;
- contamination through medical machines, aerosols etc.

DIAGNOSIS

1. Clinical and laboratory findings

Presence of:
- fever (defined as an oral temperature > 38°C, tympanic temperature > 38.5°C, axillary temperature ≥ 38.1°C or a rectal/core body temperature ≥ 39°C) or hypothermia (defined as rectal/core body temperature < 35°C)
- leukocytosis (white blood cell count - WBC > 10,000 elements/mm³ or more than 15% immature neutrophils) or leukopenia (total WBC less than 5,000 elements/mm³);

Presence of at least 2 of the following signs:
- cough
- dyspnea, tachipnea (respiratory rate ≥ 30 breaths per minute) particularly if any or all of these are progressive;
pleuritic or inspiratory chest pain
- auscultatory findings on pulmonary examination of rales and/or evidence of pulmonary consolidation (dullness on percussion, bronchial breath sounds or egophony);
- purulent sputum production or respiratory secretion or a change in sputum character;
- hypoxemia with a \(\text{PaO}_2\) 60 mmHg or oxygen saturation <90% while the subject is breathing room air, determined by pulse-oximetry or arterial blood gas.

Presence of:
- a new or evolving infiltrate on a chest X ray film;
- the infiltrate must not be related to another disease or condition (for example congestive heart failure or acute respiratory distress syndrome)

The onset of symptoms must be after more than 48 hours after admission to an acute care hospital or chronic care facility or less than 7 days after a subject is discharged from the hospital.

A useful score for diagnosing HAP is Clinical Pulmonary Infection Score (CPIS). This score was proposed by J Pugin and modified by N Singh.35

The use of the CPIS may assist health care providers in identifying patients with a low likelihood of VAP or may serve as a tool for following clinical response to therapy. The CPIS varies from 0 to 12 points; scores higher than 6 correlate well with results from bronchoscopic diagnostic techniques for VAP, and scores of 6 or lower suggest a low probability of pneumonia. Because patients with a low CPIS have a low likelihood of pneumonia, they may be treated with a short course of ciprofloxacin.

### 2. Bacteriological diagnosis

It is important that biological specimen sampling to be done before the start of antibiotic therapy. Gram stain is useful for choosing the first line of antibiotic drug. There are multiple methods for bacteriological diagnosis:

- routine tracheal aspiration with culture without quantitative analysis – the easiest but with minimum specificity;
- quantitative analysis of tracheo-bronchial secretions. The diagnostically limit is for more than \(10^4\) colony-forming units (CFU)/ml
- fiber-bronchoscopic technics:
  - broncho-alveolar lavage (BAL) – diagnostically limit \(>10^4\) CFU/ml
  - protected specimen brushing (PSB) - diagnostically limit \(>10^4\) CFU/ml
  - non-bronchoscopic (blind) bronchoalveolar lavage.

At present, the greatest debate if an invasive strategy is improving patient outcomes (i.e., bronchoscopy vs. endotracheal aspirate sampling). Now it is clear that endotracheal aspirate sampling is most sensitive, while bronchoscopic sampling is most specific. Concerns persist about delays in initiating therapy while awaiting invasive testing, and about the best processing method for these samples. Furthermore, it is well known that intensivists are refractory to discontinue antibiotic therapy when culture results are negative raising the question of the importance of invasive strategies meant to determine the causative organism of VAP.29

### Treatment of HAP

#### Antibiotherapy

Once the clinical decision has been made to initiate therapy for suspected HAP, antibiotic selection should be guided by placing the patient into one of the categories listed in Tables 8-10.

HAP classification by onset:
- early onset: within 5 days from admission to hospital
- late onset: after 5 days from admission in hospital

### Table 6. Clinical Pulmonary Infection Score Calculation (CPIS)*

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 36.5°C and &lt; 38.4°C</td>
<td>0 point</td>
</tr>
<tr>
<td>≥ 38.5°C and ≤ 38.9°C</td>
<td>1 point</td>
</tr>
<tr>
<td>≥ 39°C or ≤ 36°C</td>
<td>2 points</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood leukocytes (WBC/mm³)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 4,000 and ≤ 11,000</td>
<td>0 point</td>
</tr>
<tr>
<td>&lt; 4,000 or ≥ 11,000</td>
<td>1 point + band forms ≥ 50% = add 1 point</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tracheal secretions</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence of secretions</td>
<td>0 point</td>
</tr>
<tr>
<td>Presence of non-purulent secretions</td>
<td>1 point</td>
</tr>
<tr>
<td>Presence of purulent secretions</td>
<td>2 points</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oxygenation ((\text{PaO}_2/\text{FiO}_2), mm Hg)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 240 or ARDS (ARDS defined as (\text{PaO}_2/\text{FiO}_2) &lt; 200, pulmonary arterial wedge pressure ≤ 18 mm Hg and acute bilateral infiltrates)</td>
<td>0 point</td>
</tr>
<tr>
<td>≤ 240 and no ARDS</td>
<td>2 points</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pulmonary radiography</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No infiltrate</td>
<td>0 point</td>
</tr>
<tr>
<td>Diffuse (or patchy) infiltrate</td>
<td>1 point</td>
</tr>
<tr>
<td>Localized infiltrate</td>
<td>2 points</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Progression of pulmonary infiltrate</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No radiographic progression</td>
<td>0 point</td>
</tr>
<tr>
<td>Radiographic progression (after CHF and ARDS excluded)</td>
<td>2 points</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Culture of tracheal aspirate</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenic bacteria cultured in rare or light quantity or no growth</td>
<td>0 point</td>
</tr>
<tr>
<td>Pathogenic bacteria cultured in moderate or heavy quantity</td>
<td>1 point</td>
</tr>
<tr>
<td>Same pathogenic bacteria seen on Gram stain</td>
<td>1 point</td>
</tr>
</tbody>
</table>

**Definition of abbreviations:**
- ARDS = acute respiratory distress syndrome, CHF = congestive heart failure,
- \(\text{PaO}_2/\text{FiO}_2\) = ratio of arterial oxygen pressure to fraction of inspired oxygen
- Modified from Pugin and coworkers, - Predominant organism in the culture.
In classifying patients into one of the categories in Tables 8-10, it is necessary to define the severity of illness as either mild-to-moderate or severe:

- **severe:**
  - need for admission in an intensive care unit
  - respiratory failure, (need for mechanical ventilation or the need for > 35% oxygen to maintain an arterial oxygen saturation > 90%)
  - rapid radiographic progression, multilobar pneumonia, or cavitation of a lung infiltrate
  - evidence of severe sepsis with hypotension and/or end-organ dysfunction:
    - shock (systolic blood pressure < 90 mm Hg, or diastolic blood pressure < 60 mm Hg)
    - requirement for vasopressors for more than 4 h
    - urine output < 20 ml/h or total urine output < 80 ml in 4 h (unless another explanation is available)
  - Acute renal failure requiring dialysis

- **mild-to-moderate** (not fulfilling severe HAP criteria)

Patients with mild-to-moderate illness, regardless of when pneumonia occurs, will fall into the descriptions in Tables 8 or 9, depending on the absence (Table 8) or presence (Table 9) of specific risk factors for infection.

Patients with severe HAP, usually requiring admission to the intensive care unit, will fall into the descriptions in Tables 8 or 10.
The regimens listed in Table 8 for severe HAP are directed at particularly virulent and/or drug-resistant organisms. In such cases initial antibiotic treatment relies on combination chemotherapy to provide a broader spectrum of coverage as well as possible additive or even synergistic activity against such pathogens.

Table 10. Patients with severe HAP with risk factors, early onset or patients with severe HAP, late onset

<table>
<thead>
<tr>
<th>Core Organisms, Plus</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>P. aeruginosa</td>
<td>Aminoglycoside or ciprofloxacin plus one of the following: Antipseudomonal penicillin Beta-lactam/beta-lactamase inhibitor Ceftazidime or cefoperazone Imipenem Aztreonam** +/- Vancomycin</td>
</tr>
<tr>
<td>Acinetobacter species</td>
<td>Consider MRSA</td>
</tr>
<tr>
<td>Considers MRSA</td>
<td></td>
</tr>
</tbody>
</table>

* Excludes patients with immunosuppression.
** Aztreonam efficacy is limited to enteric gram-negative bacilli and should not be used in combination with an aminoglycoside if gram-positive or Hemophilus influenzae infection is of concern.

Table 11. Causative agents of HAP

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Incidence</th>
<th>Onset of HAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus pneumoniae</td>
<td>10-20%</td>
<td>Early</td>
</tr>
<tr>
<td>- Penicillin-resistant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Multidrug-resistant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>5-15%</td>
<td>Early</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>20-30%</td>
<td>Early</td>
</tr>
<tr>
<td>- MSSA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- MRSA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>30-60%</td>
<td>Late</td>
</tr>
<tr>
<td>- Pseudomonas aeruginosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Enterobacteriaceae species</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Escherichia coli</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Klebsiella species</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Proteus species</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Serratia species</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Legionella pneumoniae</td>
<td>0-15%</td>
<td>Late</td>
</tr>
</tbody>
</table>

De-escalation Therapy

After clinical diagnosis and culture sampling the initial therapy should be started with a broad-spectrum antibiotic. The initial choice must be based on:
- data from updated literature;
- guidelines customized to local epidemiology, microbiology, and resistance patterns;
- classification of HAP.

After bacteriological diagnosis is available, antibiotic therapy should be reduced to a narrow-spectrum efficient antibiotic.

Some international guidelines, including the Tarragona Straegy for management of VAP are presented in the next tables.

Table 12. The Tarragona Strategy for VAP management (2001)

1. Antibiotic therapy should be started without delay.
2. Choice of antibiotic should be based on the regimen that each patient has received previously.
3. Antibiotic choice can be targeted based on direct stains.
4. The antibiotic regimen should be modified based on microbiological findings.
5. Patients with chronic obstructive pulmonary disease (COPD) or 1 week of ventilation should receive combination therapy.
6. Methicillin-susceptible Staphylococcus aureus (MSSA) should be strongly suspected if Glasgow Coma Scale (GCS) <8. Methicillin-resistant Staphylococcus aureus (MRSA) is not expected in the absence of prior antibiotic administration.
7. Vancomycin administration for MRSA ventilator-associated pneumonia (VAP) caused by S. aureus is associated with very poor outcome.
8. Antifungal therapy is not required even in the presence of Candida spp.
9. Prolonging antibiotic treatment does not prevent recurrences.
10. Guidelines should be regularly updated and customized to local patterns.

Table 13. Initial antibiotic regimens for early-onset, mild to moderate ventilator-associated pneumonia

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Initial antibiotics</th>
<th>General comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus</td>
<td>Third-generation cefalosporin</td>
<td>Drug resistance</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>(such as ceftriaxone) or</td>
<td>uncommon, except</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>extended-spectrum quinolone</td>
<td>for S pneumoniae</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>(such as levofloxacin)</td>
<td>Prognosis good</td>
</tr>
<tr>
<td>Klebsiella species</td>
<td></td>
<td>and mortality</td>
</tr>
<tr>
<td>Enterobacteriaceae species</td>
<td></td>
<td>low</td>
</tr>
<tr>
<td>Serratia species</td>
<td></td>
<td>Other equivalent</td>
</tr>
<tr>
<td>- Pseudomonas aeruginosa</td>
<td></td>
<td>antibiotics could</td>
</tr>
<tr>
<td>- Enterobacteriaceae species</td>
<td></td>
<td>be used</td>
</tr>
<tr>
<td>- Escherichia coli</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Klebsiella species</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Proteus species</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Serratia species</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Applies to patients with ventilator-associated pneumonia who have no risk factors, who have had no previous antibiotic treatment, and who do not reside in an acute- or chronic-care facility.

Antibiotics rotation

Antimicrobial resistance is a major worldwide public health concern. The emergence of methicillin-resistant Staphylococcus aureus and new patterns of resistance in Gram-negative bacteria (e.g., Pseudomonas aeruginosa, Enterobacter species, Escherichia coli, and Klebsiella pneumoniae) have the potential for major public health consequences. The increase in antimicrobial resistance is most seen in intensive care units. Several factors contribute to increased antimicrobial resistance: the sicker inpatient population, the larger immunocompromised population, new procedures and instrumentation, emerging pathogens, ineffective infection control and compliance and the increase in antibiotic use. Some factors are related to patients and others are related to the antibiotic.

Improving antibiotic control precautions could decrease antimicrobial resistance in hospitalized patients and a good method is rotation of empirical antibiotic therapy. Continuous changes in selection pressure by rotating antibiotic therapy reduce the emergence of resistance and the associated morbidity.
The implementation of a quarterly, empirical antibiotic rotation schedule in an ICU is associated with significant reductions in the incidence of infection, antibiotic-resistant organism infection, and infectious mortality without increases in antibiotic cost.

**Table 15. A model of an antibiotic rotation schedule**

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Pneumonia</th>
<th>Peritonitis or sepsis of unknown origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan-Mar</td>
<td>Ciprofloxacin + clindamycin**</td>
<td>Ceftazidime or cefepime plus ciprofloxacin or aminoglycoside</td>
</tr>
<tr>
<td>Apr-Jun</td>
<td>Piperacillin/tazobactam</td>
<td>Carbapenem (such as imipenem) ampicillin/sulbactam</td>
</tr>
<tr>
<td>Jul-Sep</td>
<td>Ceftazidime</td>
<td>Carbapenem</td>
</tr>
<tr>
<td>Oct-Dec</td>
<td>Cefepime + clindamycin**</td>
<td>Cefepime + metronidazole***</td>
</tr>
</tbody>
</table>

* add clindamycin for pneumonia if aspiration is suspected
** imipenem or meropenem
*** add ampicillin or vancomycin if Enterococcus sp. Is suspected

**Peculiarities on treatment of HAP**

1. **HAP and anaerobes germs**
   If in 1995 ATS guidelines the clindamycine was used as routine, today medical evidences shows that anaerobes can be copathogens in early stages of HAP but without worsening the outcome. Metronidazol and Clindamycine is no more used as routine, and could lead to apparition of Vancomycin resistant Enterococci (VRE). Antianaerobes therapy is justified only on alcoholic patients, with a poor oral hygiene or with history or tracheo-bronchial aspiration syndrome.

2. **HAP in head injured and severe trauma patients**
   Trauma is the major cause of death in the under-45 age group and the third leading cause of death in all populations. Trauma deaths have a trimodal distribution. Late deaths, occurring between 3 days and 3 weeks postinjury, represent 25% of the total. In this group, infection is the cause of death in 80% of cases.

   Pneumonia occurring in patients with trauma and head injury is caused by S. aureus, Haemophilus influenzae, or other gram-positive cocci, and by gram-negative bacilli in only 20% of cases. Methicillin-sensitive *Staphylococcus Aureus* (MSSA) is the predominant pathogen in multiple-trauma patients in coma, and nasal MSSA colonization at time of severe injury may increase the risk of MSSA pneumonia. In the remaining patients, gram-negative bacilli are responsible for the majority of cases.

   Cardiopulmonary resuscitation, GCS < 9, and the need for intubation are the most important risk factors for HAP during the first 48 hours after tracheal intubation. Prolonged mechanical ventilation, continuous enteral feeding, and craniotomy are also risk factors for developing HAP in trauma patients. A higher pulmonary complication rate was associated with a higher injury severity score (ISS). In this category of patients, factors that influence the development of bacterial infections are also: upper airway colonization, alteration of the natural antimicrobial barrier, surgical treatment, the immunosuppressive effect of sedatives and barbiturates administered to patients with cerebral edema, and massive blood loss resulting in a marked decrease in immunodefense proteins. Blood transfusion is also a possible source: there is a dose-dependent relationship between the number of units transfused and infection risk.

   Diagnosis of HAP in these patients is difficult because radiographic infiltrates may not highlight any infection. The diagnosis of ventilator-associated pneumonia (VAP) remains controversial; many patients having a clinical diagnosis of VAP may have also a noninfectious etiology for their fever and purulent sputum in the setting of a new or progressive pulmonary infiltrate. Radiographic infiltrates in trauma patients may reflect noninfectious problems: atelectasis, pulmonary contusion, pleural effusions, pulmonary edema, and acute lung injury that can mimic pneumonia.

   Initial antibiotic choice should be based on the likelihood of the presence of potential pathogens. In patients in coma, coverage against MSSA is mandatory; drugs with antipseudomonal coverage and vancomycin are not considered adequate. Amoxicillin/
clavulanate, cefuroxime, or a third-generation cephalosporin are recommended because most of the infections occur soon after hospital admission, often in patients who have not previously received antibiotic treatment. In late-onset NP broad spectrum antimicrobial that is effective against both gram-negative and -positive bacteria should be administered as soon as infection is suspected.38

3. HAP in patients with COPD

In this class of patients bacterial resistance is common, making failure of eradication a frequent problem when serial bronchial samples are examined. For this reason direct (bronchoscopic) quantitative cultures should be taken in all patients admitted to the ICU with COPD, presenting HAP. This is particularly true in higher-risk patients, who experience higher rates of bacterial resistance and different pathogen patterns (i.e., increased Gram-negative organisms). Recognized indications for antibiotics in COPD exacerbations include at least 2 of the following 3 criteria: increased dyspnea, increased sputum volume, or sputum purulence.40

PROFILAXY OF INTENSIVE CARE UNIT-ACQUIRED PNEUMONIA - GUIDELINES AND RECOMMENDATIONS

Presence of endotracheal tube (ETT)

Endotracheal tubes bypass normal upper airway reflexes and prevent effective coughing. Oral secretions pool above the tube cuff and tend to “trickle” down the airway. Since invasive mechanical ventilation is a risk factor for intensive care unit acquired pneumonia (ICU-AP) strategies that reduce its duration (i.e., weaning protocols) might reduce its incidence.41

Reintubation

Reintubation secondary to unplanned or failed extubation is an independent risk factor for ICU-AP. This may occur because such patients frequently have their upper airways colonized with pathogens and aspirate during the reintubation procedure. Avoiding reintubation (for example with non-invasive ventilation techinics) may prevent pneumonia.42

Route of ETT (i.e., nasal or oral)

Nasal intubation is associated with a higher incidence of sinusitis.43

Oro-/naso-gastric feeding tubes

Enteral feeding via nasogastric tubes may promote reflux and aspiration of stomach contents, especially when patients are lying supine. The risk of aspiration is unaltered by the size of the feeding tube, and inconsistently affected by pro-motility agents and different feeding regimes. Post-pyloric placement of feeding tubes decreases neither the risk of aspiration nor of ICU-AP.44

Body position

Patients receiving mechanical ventilation should be in a semi-recumbent position (30–45°), especially when enterally fed, to decrease the occurrence of aspiration of gastric contents. Some studies have identified supine positioning to be associated with pneumonia, even for a short period during transportation out of the intensive care unit.45

Ventilator management

The condensate in the ventilator tubing can become contaminated with bacteria and could lead to VAP. However, the frequency of ventilator tubing changes does not alter the risk of VAP. There is no evidence that active (wick or cascade) humidifiers increase the risk of ICU-AP. There is little evidence to suggest that closed suction systems lower the risk of VAP even though open systems are associated with increased environmental contamination. When closed systems are used, infrequent changes do not appear to increase the risk for ICU-AP. There is no data to suggest that frequency of suctioning impacts on ICU-AP.46,47

Other factors:

General preventive measures: hand washing and oral antiseptics

Hand washing is an important, often overlooked, measure to prevent nosocomial infections. Strict hand-washing techniques by the ICU personnel, combined with other measures to control infection, including the use of gloves when dealing with specific antibiotic-resistant pathogens, reduce the rate of acquired nosocomial infections. The specific impact on ICU-AP is unknown. Accumulated bacteria in the dental plaque of intubated patients have been implicated as a source of pathogens in ICU-AP. Oropharyngeal decontamination with chlorhexidine solution has been shown to reduce the occurrence of ICU-AP in patients undergoing cardiac surgery.48

Subglottic secretion drainage

Secretions that accumulate above an inflated ETT cuff may be a source of aspirated material. These secretions may be removed by irrigation and drainage or by continuous suctioning above the cuff of the ETT, using a specially designed ETT. Others have questioned whether drainage of subglottic secretions are likely to have a major impact on VAP, since in most cases, the pathogens have already adhered to the lower airway mucosa before suctioning begins.

Current state of knowledge and unresolved controversies:12

- Coma, prolonged mechanical ventilation
through an endotracheal tube, repeated intubations, the supine posture, and long-term antibiotic use increase the risk of ICU-AP.

- The only established preventive measure is avoidance of the supine posture.

- Safe, inexpensive, logical, but unproven interventions include routine handwashing, avoidance of indiscriminate antibiotic use, limiting stress ulcer prophylaxis to high-risk patients, and the use of non-invasive mechanical ventilation whenever feasible.

- More data are needed concerning the potential benefit from postpyloric placement of feeding tubes, kinetic/physiotherapy, subglottic drainage, the use of oral and digestive tract decontamination in specific patient populations, early tracheostomy, the placement of oral as opposed to nasotracheal tubes, and the use of endotracheal tube material that inhibits biofilms.

REFERENCES


GUIDELINES FOR MANAGEMENT OF PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA (CAP) AND NOSOCOMIAL (HOSPITAL ACQUIRED) PNEUMONIA (HAP)

Dorel Sandesc, Ovidiu Bedreag

1. HAP diagnosis includes:
   a) onset of symptoms within 48 h after admission in hospital
   b) onset after more than 7 days after the subject is discharged from the hospital
   c) hypothermia (core body temperature < 35°C)
   d) leucopenia (total WBC less than 5,000 elements/mm³)
   e) anemia (Hb < 7g/dl)

2. CAP diagnosis includes:
   a) cough, purulent sputum production and dyspnea
   b) thorax hyper-sonority at percussion
   c) signs of consolidation on examination
   d) leukocytosis
   e) nausea and vomiting

3. Patients presenting diagnosed CAP should be:
   a) always treated at home
   b) always admitted in a hospital
   c) admitted in an intensive care unit if they have a respiratory rate < 30 breaths/minute and a serum creatinine > 1.2g/dl
   d) admitted in an intensive care unit if they present shock or need for mechanical ventilation
   e) discharged as soon as possible if they were admitted in hospital for preventing nosocomial infection risk

4. For diagnosing HAP:
   a) specimen sampling to be done before the start of antibiotic therapy
   b) Gram stain is not useful in HAP management
   c) chest xRay film is not always necessary
   d) fiber-bronchoscopic technics should be routinely performed
   e) non-bronchoscopic (blind) bronchoalveolar lavage has a very low specificity

5. In CAP etiology:
   a) patients with structural lung disease (bronchiectasis) have a high risk for infection with *Pseudomonas aeruginosa*
   b) patients with Beta-lactam therapy within the past year have a high risk for infection with drug-resistant pneumococci
   c) anaerobes are frequent
   d) after exposure to farm animals, *Coxiella burnetii* (Q fever) is frequent encountered
   e) *H. Influenzae* is encountered in a low percent of CAP cases

6. Treatment for outpatients with CAP, without cardiopulmonary disease, without modifying factors, should be started with:
   a) penicillin
   b) erythromycin
   c) doxycycline
   d) azithromycin or clarithromycin
   e) ciprofloxacin

7. Treatment for outpatient with CAP, cardiopulmonary disease and other modifying factors should be done with:
   a) ceftriaxone plus clarithromycin
   b) ceftriaxone plus doxycycline
   c) ciprofloxacin alone
   d) high-dose amoxicillin,
   e) amoxicillin/clavulanate

8. Patients with mild-to-moderate HAP, no unusual risk factors, allergic to penicillin should be treated with:
   a) fluoroquinolone
   b) clindamycin + aztreonam
   c) cefpodoxime
   d) cefuroxime
   e) amoxicillin/clavulanate

9. De-escalation therapy:
   a) could be started with imipenem
   b) should be started with a broad-spectrum antibiotic
   c) should be started with a narrow-spectrum antibiotic
   d) its duration must be at least 5 days
   e) after bacteriological diagnosis is available, antibiotherapy should be changed

10. For preventing Intensive Care Unit - Acquired Pneumonia:
    a) endotracheal tubes should never be used
    b) nasal intubation is associated with a lower risk of ICU AP
    c) supine position is better
    d) hand-washing techniques on the ICU personnel are useful
    e) subglottic secretion drainage prevents ICU-AP.

To complete the examination for CME evaluation turn the page for instructions and the response form.

Correct answers for CME: Type 2 Diabetes Mellitus in Children and Adolescents (TMJ 2004;3:308-14):
1 - b; 2 - b, c,d; 3 - b,c,d; 4 - a,b,c; 5 - d; 6 - c; 7 - b,c,d,e; 8 - b; 9 - c,d,e; 10 - c,d