

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

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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.^{4,6-8} 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

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department physicians may over read chest x-rays^{5,19} and conservatively elect to treat patients because of the limitations of radiographic diagnosis,¹⁶ concerns regarding social issues, and follow-up obstacles.¹⁸ 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 nitrogen³ 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%,⁷⁻⁹ 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.^{7,15,16} 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).²⁰ 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^{21,22}. 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.²

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.²²

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:²²

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:
 - respiratory rate < 30 breaths/min*;
 - diastolic blood pressure < 60 mm Hg or systolic blood pressure < 90 mm Hg*;
 - pulse < 125/min*;
 - fever < 35 or > 40C*;
 - confusion or decreased level of consciousness*;
 - evidence of extrapulmonary sites of infection.
4. Laboratory findings that predict increased morbidity or mortality:
 - 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;

g. 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

Table 1. Epidemiologic conditions related to specific pathogens in patients with community-acquired pneumonia¹

Condition	Commonly Encountered Pathogens
Alcoholism	<i>Streptococcus pneumoniae</i> (including DRSP), anaerobes, gram-negative bacilli, tuberculosis
COPD/smoker	<i>S. pneumoniae</i> , <i>Hemophilus influenzae</i> , <i>Moraxella catarrhalis</i> , <i>Legionella</i>
Nursing home residency	<i>S. pneumoniae</i> , gram-negative bacilli, <i>H. influenzae</i> , <i>Staphylococcus aureus</i> , anaerobes, <i>Chlamydia pneumoniae</i> , tuberculosis Anaerobes
Poor dental hygiene	Legionnaire's disease <i>Legionella</i> species
Epidemic	<i>Histoplasma capsulatum</i>
Exposure to bats	<i>Chlamydia psittaci</i> , <i>Cryptococcus neoformans</i> , <i>H. capsulatum</i>
Exposure to birds	<i>Francisella tularensis</i>
Exposure to rabbits	Coccidioidomycosis
Travel to Southwest United States	<i>Coxiella burnetii</i> (Q fever)
Exposure to farm animals or parturient cats	Influenza, <i>S. pneumoniae</i> , <i>S. aureus</i> , <i>H. influenzae</i>
Influenza active in community	Anaerobes, chemical pneumonitis or obstruction
Suspected large-volume aspiration	<i>P. aeruginosa</i> , <i>Pseudomonas cepacia</i> or <i>S. aureus</i>
Structural disease of lung (bronchiectasis, cystic fibrosis, etc.)	<i>S. aureus</i> , anaerobes, tuberculosis, <i>Pneumocystis carinii</i>
Injection drug use	Anaerobes
Endobronchial obstruction	Drug-resistant pneumococci, <i>P. aeruginosa</i>
Recent antibiotic therapy	

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.²

Application of empiric guidelines to antibiotic selection has been demonstrated to reduce overall costs, mortality, and length of hospital stay.^{6,9,13,15} 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 beta-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 and reduced length of hospital stay in mild to moderate CAP.²

Guideline options for monotherapy with antipneumococcal fluoroquinolones have also been well received by practitioners and patients because of once-daily dosing of a single medication. However, concerns have been raised regarding increasing resistance, particularly among immunocompromised individuals in the few months after fluoroquinolone use.²

As antibiotic resistance increases in prevalence, it becomes critical that practitioners educate their patients. Antibiotics should be limited to use in bacterial infections and not provided when demanded for common cold symptoms, despite patient pressures to do so. When prescribed, it must be reinforced to patients that subjective improvement does not mark

the end of bacterial infection and antibiotic courses must be taken to completion.

Regarding severe CAP, the ATS statement has focused on *Pseudomonas aeruginosa* as an important factor in the treatment algorithm. In this decision tree, if patients with severe CAP are suspected of having *P. aeruginosa* infection, combination therapy with a beta-lactam plus anti-Pseudomonal quinolone or a beta-lactam with an aminoglycoside \pm a macrolide or quinolone is recommended. For patients without suspicion of *P. aeruginosa*, a second- or third-generation cephalosporin plus intravenous administration of a macrolide or quinolone is recommended. Because of many concerns, quinolone monotherapy is not recommended for at least moderately ill patients with CAP.

With the knowledge of typical bacterial pathogens, the recommendation can be made that empiric initial therapy is started immediately upon presentation and/or hospitalization with CAP. Gram stain and culture of collected sputum should be performed. Empiric antibiotic therapy should be targeted to local, regional, or institution-specific organism and resistance patterns. Furthermore, the need for ICU care can be reasonably predicted by a few clinical criteria.

Table 2. Modifying factors that increase the risk of infection with specific pathogens¹

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

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

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

* Excludes patients at risk for HIV

** Erythromycin is not active against *H. influenzae* and the advanced generation

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*¹

Organisms	Therapy
Streptococcus pneumoniae (including DRSP)	Beta-lactam (oral cefpodoxime, cefuroxime, high-dose amoxicillin, amoxicillin/clavulanate; or parenteral ceftriaxone followed by oral cefpodoxime) plus Macrolide or doxycycline** or Antipneumococcal fluoroquinolone (used alone)
Mycoplasma pneumoniae	
Chlamydia pneumoniae	
Mixed infection (bacteria plus atypical pathogen or virus)	
Hemophilus influenzae	
Enteric gram-negatives	
Respiratory viruses	
Miscellaneous	
Moraxella catarrhalis, Legionella spp., aspiration (anaerobes), Mycobacterium tuberculosis, endemic fungi	

* 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*¹

Organisms	Therapy
a. Cardiopulmonary disease and/or modifying factors	Intravenous beta-lactam** (cefotaxime, ceftriaxone, ampicillin/sulbactam, high-dose ampicillin) plus Intravenous or oral macrolide or doxycycline*** or Intravenous antipneumococcal fluoroquinolone alone
Streptococcus pneumoniae (Including DRSP)	
Hemophilus influenzae	
Mycoplasma pneumoniae	
Chlamydia pneumoniae	
Mixed infection (bacteria plus atypical pathogen)	
Enteric gram-negatives	
Aspiration (anaerobes)	
Viruses	
Legionella spp.	
Miscellaneous:	Intravenous azithromycin alone If macrolide allergic or intolerant: Doxycycline and a beta-lactam or Monotherapy with an antipneumococcal fluoroquinolone
Mycobacterium tuberculosis, endemic fungi, Pneumocystis carinii	
b. No cardiopulmonary disease, no modifying factors	
<i>S. pneumoniae</i>	
<i>H. influenzae</i>	
<i>M. pneumoniae</i>	
<i>C. pneumoniae</i>	
Mixed infection (bacteria plus atypical pathogen)	
Viruses	
Legionella spp.	
Miscellaneous:	M. tuberculosis, endemic fungi, P. carinii
M. tuberculosis, endemic fungi, P. carinii	

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

** Antipseudomonal agents such as cefepime, 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.⁵ 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.²

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.²⁸ Last years researches on etiology, pathogeny of HAP and, most of all, on antibiotal 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).²⁹

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.³⁰ 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.³¹

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.³²⁻³⁴ 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.²⁸

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 PO_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

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

Temperature (°C)

$\geq 36.5^\circ\text{C}$ and $\leq 38.4^\circ\text{C}$ = 0 point

$\geq 38.5^\circ\text{C}$ and $\leq 38.9^\circ\text{C}$ = 1 point

$\geq 39^\circ\text{C}$ or $\leq 36^\circ\text{C}$ = 2 points

Blood leukocytes (WBC/mm³)

$\geq 4,000$ and $\leq 11,000$ = 0 point

$< 4,000$ or $> 11,000$ = 1 point + band forms $\geq 50\%$ = add 1 point

Tracheal secretions

Absence of tracheal secretions = 0 point

Presence of non-purulent tracheal secretions = 1 point

Presence of purulent tracheal secretions = 2 points

Oxygenation (PaO₂/FIO₂, mm Hg)

> 240 or ARDS (ARDS defined as $PaO_2/FIO_2 \leq 200$, pulmonary arterial wedge pressure ≤ 18 mm Hg and acute bilateral infiltrates) = 0 point

≤ 240 and no ARDS = 2 points

Pulmonary radiography

No infiltrate = 0 point

Diffuse (or patchy) infiltrate = 1 point

Localized infiltrate = 2 points

Progression of pulmonary infiltrate

No radiographic progression = 0 point

Radiographic progression (after CHF and ARDS excluded) = 2 points

Culture of tracheal aspirate

Pathogenic bacteria-cultured in rare or light quantity or no growth = 0 point

Pathogenic bacteria cultured in moderate or heavy quantity = 1 point

Same pathogenic bacteria seen on Gram stain = add 1 point

Definition of abbreviations:

ARDS = acute respiratory distress syndrome, CHF = congestive heart failure,

PaO_2/FIO_2 = ratio of arterial oxygen pressure to fraction of inspired oxygen

* Modified from Pugin and coworkers, - Predominant organism in the culture.

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 diagnostic limit is for more than 10^5 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 7. Current methods for diagnosis of VAP: advantages and disadvantages:³⁶

120	Advantages	Disadvantages
Clinical	Easy to perform; Gram stain may be helpful	Poor specificity, especially in patients with chest radiograph abnormalities
Nonquantitative cultures	Noninvasive Inexpensive Gram stain may be helpful for initial antibiotic treatment and interpretation of culture results	May increase antibiotic use or alter outcome compared with quantitative microbiology
Clinical Pulmonary Infection Score	May help identify patients at low risk for VAP Useful for short-course therapy May be useful for assessing clinical response	Not validated
Quantitative endotracheal aspirate analysis	Simple and easy to perform; Gram stain may be helpful Less expensive than bronchoscopy and non-bronchoscopic BAL 65% correlation with bronchoscopy with PSB or BAL, but less specific Good negative predictive value	Threshold for diagnosis varies among studies; difficulty with sputum processing
Nonbronchoscopic (blind) BAL/PSB	Simpler and less expensive than bronchoscopy with PSB or BAL Correlates with bronchoscopic BAL	Costs of quantitative cultures Special skills required Limited data for comparison
Bronchoscopic BAL/PSB	Can observe sampling site Specificity > 95% Greater sensitivity for $\geq 10^3$ CFU/mL for PSB and $\geq 10^4$ CFU/mL for BAL Cytocentrifugation may be helpful for early identification of cause May decrease antibiotic use and development of resistance May be associated with better patient outcomes Useful in immunocompromised and nonresponding patients	Antibiotic use in last 24 hours may decrease sensitivity False-negative results in early cases Need quantitative bacteriology and meticulous and prompt processing of specimens Costly, not widely available Complication rate greater for BAL than PSB

BAL, bronchoalveolar lavage; PSB, protected specimen brush; CFU, colony-forming unit.

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:**

- o need for admission in an intensive care unit
- o respiratory failure, (need for mechanical ventilation or the need for > 35% oxygen to maintain an arterial oxygen saturation > 90%)
- o rapid radiographic progression, multilobar pneumonia, or cavitation of a lung infiltrate
- o 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)

- o 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.

Table 8. Patients with mild-to-moderate HAP, no unusual risk factors, onset any time or patients with severe HAP with early onset*²⁸

Core Organisms	Core Antibiotics
Enteric gram-negative bacilli Enterobacter species Escherichia coli	Second generation Cephalosporin or Non-anti-pseudomonal third generation Beta-lactam / beta-lactamase inhibitor combination
Klebsiella species Proteus species Serratia marcescens	If allergic to penicillin:
Hemophilus influenzae Methicillin-sensitive Staphylococcus aureus Streptococcus pneumoniae	Fluoroquinolone or Clindamycin + aztreonam

*Excludes patients with immunosuppression.

Table 9. Patients with mild-to-moderate HAP with risk factors, onset any time*²⁸

Core Organisms Plus:	Core Antibiotics Plus:
Anaerobes (recent abdominal surgery, witnessed aspiration)	Clindamycin or beta-lactam/beta-lactamase inhibitor (alone)
Staphylococcus aureus (coma, head trauma diabetes mellitus, renal failure)	+/- Vancomycin (until MRSA is ruled out)
Legionella (high-dose steroids)	Erythromycin +/- Rifampicin**
Pseudomonas aeruginosa (prolonged ICU stay, steroids, antibiotics, structural lung disease)	Treat as severe hospital-acquired pneumonia (Table 3)

*Excludes patients with immunosuppression.

** Rifampicin may be added if *Legionella* species is documented.

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*¹

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

* 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 HAP³⁶

Microorganism	Incidence	Onset of HAP
Streptococcus pneumoniae - Penicillin-resistant - Multidrug-resistant	10-20%	Early
Haemophilus influenzae	5-15%	Early
Staphylococcus aureus - MSSA - MRSA	20-30%	Early Late
Gram-negative bacilli - Pseudomonas aeruginosa - Enterobacter species - Escherichia coli - Klebsiella species - Proteus species - Serratia species	30-60%	Late
Legionella pneumoniae	0-15%	Late

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 Taragona 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. colonization.
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*³⁶

Organisms	Initial antibiotics	General comments
Streptococcus Haemophilus influenzae Staphylococcus aureus Escherichia coli Klebsiella species Enterobacter species Serratia species	Third-generation cephalosporin (such as ceftriaxone) or extended-spectrum quinolone (such as levofloxacin)	Drug resistance uncommon, except for <i>S pneumoniae</i> Prognosis good and mortality low Other equivalent antibiotics could be used

*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.³⁷

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.

Table 14. Initial antibiotic regimens for late-onset or severe ventilator-associated pneumonia*³⁶

MDR organisms	Recommended antibiotics	General comments
Gram-negative bacilli		
<i>Pseudomonas aeruginosa</i>	Ceftazidime or cefepime plus ciprofloxacin or aminoglycoside	
<i>Acinetobacter</i> species	Carbapenem (such as imipenem) ampicillin/sulbactam	Antibiotic selection should be based on local epidemiologic data Initial antibiotic coverage should include all potential pathogens Antibiotics should be streamlined based on clinical response and microbiologic data
ESBL <i>Klebsiella</i> species	Carbapenem	
Gram-positive cocci		
Methicillin-resistant <i>Staphylococcus aureus</i>	Linezolid or vancomycin	
<i>Legionella pneumophila</i>	Azithromycin or quinolone (such as ciprofloxacin)	Legionella rates vary among hospitals

MDR, multidrug-resistant; ESBL, extended-spectrum β -lactamase-producing. *Applies to patients with risk factors.

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 schedule³⁷

Quarter	Pneumonia	Peritonitis or sepsis of unknown origin
Jan - Mar	Ciprofloxacin \pm clindamycin*	Carbapenem**
Apr - Jun	Piperacillin/tazobactam	Cefepime + metronidazole***
Jul - Sep	Carbapenem**	Ciprofloxacin + clindamycin***
Oct - Dec	Cefepime \pm clindamycin*	Piperacillin/tazobactam

* 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.³⁸

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.³⁹

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 noni-invasive ventilation technics) 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:^{1,2}

- 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

1. American Thoracic Society. Guidelines for the management of adults with community-acquired pneumonia: diagnosis, assessment of severity, antimicrobial therapy and prevention. ATS Board of Directors, March 9, 2001.
2. Alves DV, Kennedy MT. Community-acquired pneumonia in casualty: etiology, clinical features, diagnosis, and management. *Curr Opin Pulm Med* 2004;10(3):166-70.
3. Kamath A, Pasteur MC, Slade MG, et al. Recognizing severe pneumonia with simple clinical and biochemical measurements. *Clin Med* 2003;3:54-6.
4. Andrews J, Nadjm B, Gant V, et al. Community-acquired pneumonia. *Curr Opin Pulm Med* 2003;9:175-80.
5. Merchant S, Mullins CD, Shih YT. Factors associated with hospitalization costs for patients with community-acquired pneumonia. *Clin Ther* 2003;25:593-610.
6. Ramirez JA: Community-acquired pneumonia in adults. *Prim Care* 2003;30:155-71.
7. Pimentel LP, McPherson SJ. Community-acquired pneumonia in the emergency department: a practical approach to diagnosis and management. *Emerg Med Clin North Am* 2003;21:395-420.
8. Niederman MS, Ahmed QA. Community-acquired pneumonia in elderly patients. *Clin Geriatr Med* 2003;19:101-120.
9. Oosterheert JJ, Bonten MJ, Hak E, et al. Severe community-acquired pneumonia: what's in a name? *Curr Opin Infect Dis* 2003;16:153-159.
10. Brown RB, Iannini P, Gross P, et al. Impact of initial antibiotic choice on clinical outcomes in community-acquired pneumonia-analysis of a hospital claims-made database. *Chest* 2003;123:1503-11.
11. Arnold FW, Ramirez JA, McDonald LC, et al. Hospitalization for community-acquired pneumonia: the Pneumonia Severity Index vs. clinical judgment. *Chest* 2003;124:121-4.
12. Trends in COPD. Lung & Asthma Information Agency: Public Health Sciences Department, St. George's Hospital Medical School, London. Fact sheet, 2003/1.
13. Barlow GD, Lamping DL, Davey PG, et al. Evaluation of outcomes in community-acquired pneumonia: a guide for patients, physicians, and policy-makers. *Lancet Infect Dis* 2003;3:478-88.
14. Drummond MF, Becker DL, Hux M, et al. An economic evaluation of sequential IV/po moxifloxacin therapy compared to IV/po Co-amoxiclav with or without clarithromycin in the treatment of community-acquired pneumonia. *Chest* 2003;124:526-35.
15. Feldman RB, Rhew DC, Wong JY, et al. Azithromycin monotherapy for patients hospitalized with community-acquired pneumonia: a 3-1/2 year experience from a Veterans Affairs hospital. *Arch Intern Med* 2003;163:1718-1726.
16. Cazzola M, Matera MG, Page CP. Novel approaches to the treatment of pneumonia. *Trends Pharmacol Sci* 2003. 24:306-14.
17. Mabie M, Wunderink RG. Use and limitations of clinical and radiologic diagnosis of pneumonia. *Semin Respir Infect* 2003; 18:72-79.
18. Espana PP, Capelastegui A, Quintana JM, et al. A prediction rule to identify allocation of inpatient care in community-acquired pneumonia. *Eur Respir J* 2003, 21:695-701.
19. Kariuki S, Muyodi J, Mirza B, et al. Antimicrobial susceptibility in community-acquired bacterial pneumonia in adults. *East Afr Med J* 2003;80:213-7.
20. Marrie TJ, Durant H, Yates L. Community-acquired pneumonia requiring hospitalization: a 5 year prospective study. *Rev Infect Dis* 1989;11:586-99.
21. Fine MJ, Smith MA, Carson CA, 1996. Prognosis and outcomes of patients with community-acquired pneumonia: a meta-analysis. *JAMA* 1996;275:134-41.
22. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997;336:243-50.
23. Ortqvist A, Hedlund J, Grillner L, et al. Aetiology, outcome and prognostic factors in community-acquired pneumonia requiring hospitalization. *Eur Respir J* 1990;3:1105-13.
24. Black ER, Mushlin AI, Griner PF, et al. Predicting the need for hospitalization of ambulatory patients with pneumonia. *J Gen Intern Med* 1991;6:394-400.
25. Dean NC. Use of prognostic scoring and outcome assessment tools in the admission decision for community-acquired pneumonia. *Clin Chest Med* 1999;20:521-9.
26. Farr BM, Sloman AJ, Fisch MJ. Predicting death in patients hospitalized for community-acquired pneumonia. *Ann Intern Med* 1991;115:428-36.
27. Neill AM, Martin IR, Weir R, et al. Community-acquired pneumonia: etiology and usefulness of severity criteria on admission. *Thorax* 1996;51:1010-6.
28. American Thoracic Society. Hospital-acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial therapy, and preventative strategies. A consensus statement. *Am J Resp Crit Care Med* 1995;153:1711-25.
29. Hubmayr RD. Statement of the 4th International Consensus Conference in Critical Care on ICU-Acquired Pneumonia - Chicago, May 2002. *Intensive Care Med* 2002;28:1521-36.
30. Torres A, Aznar R, Gatell JM, et al. Incidence, risk, and prognosis factors of nosocomial pneumonia in mechanically ventilated patients. *Am Rev Respir Dis* 1990;142:523-8.
31. Chastre J, Tronillet JL, et al. Nosocomial pneumonia in patients with acute respiratory distress syndrome. *Am J Resp Crit Care Med* 1998;157:1165-72.
32. Fagon JY, Chastre J, Domart Y, et al. Nosocomial pneumonia in patients receiving continuous mechanical ventilation. *Am Rev Respir Dis* 1989;139:877-84.
33. Fagon JY, Chastre J, Hance A, et al. Nosocomial pneumonia in ventilated patients: a cohort study evaluating attributable mortality and hospital stay. *Am J Med* 1993;94:281-8.
34. Leu HS, Kaiser DL, Mori M, et al. Hospital-acquired pneumonia attributable mortality and morbidity. *Am J Epidemiol* 1989; 129:1258-67.
35. Pugin J, et al. Diagnostic of ventilator-associated pneumonia. *Am Rev Resp Dis* 1991;143:1121-9.
36. De Rosa FG, Craven DE. Ventilator-associated pneumonia: current management strategies. *Infect Med* 2003;20(5):248-59.
37. Raymond DP, Pelletier SJ, Crabtree TD. Impact of a rotating empiric antibiotic schedule on infectious mortality in an intensive care unit. *Crit Care Med* 2001;6(29):1101-8.

38. Sirgo G, Bodi M, Diaz E, et al. Pneumonia in head-injured and severe trauma patients. *Semin Respir Crit Care Med* 2002; 23(5):435-441.
39. Leal SR, de Luis JC, Marquez JA, et al. Transfusion as a risk factor for infection in ICU. *Clin Pulm Med* 1999;6:236-40.
40. Saint S, Bent S, Vittinghoff E, et al. Antibiotics in chronic obstructive pulmonary disease exacerbations. A meta-analysis. *JAMA* 1995;273:957-60.
41. Nava S, Ambrosino N, Clini E, et al. Noninvasive mechanical ventilation in the weaning of patients with respiratory failure due to chronic obstructive pulmonary disease: a randomized, controlled trial. *Ann Intern Med* 1998;128:721-8.
42. Torres A, Gatell JM, Aznar E, et al. Re-intubation increases the risk of nosocomial pneumonia in patients needing mechanical ventilation. *Am J Respir Crit Care Med* 1995;152:137-41.
43. Rouby JJ, Laurent P, Gosnach M, et al. Risk factors and clinical relevance of nosocomial maxillary sinusitis in the critically ill. *Am J Respir Crit Care Med* 1994;150:776-783.
44. Kearns PJ, Chin D, Mueller L, et al. The incidence of ventilator-associated pneumonia and success in nutrient delivery with gastric versus small intestinal feeding: a randomized clinical trial. *Crit Care Med* 2000;28:1742-6.
45. Torres A, Serra-Batllés J, Ros E, et al. Pulmonary aspiration of gastric contents in patients receiving mechanical ventilation: the effect of body position. *Ann Intern Med* 1992;116:540-3.
46. Dreyfuss D, Djedaini K, Gros I, et al. Mechanical ventilation with heated humidifiers or heat moisture exchangers: effects on patient colonization and incidence of nosocomial pneumonia. *Am J Respir Crit Care Med* 1995;151:986-92.
47. Kirton O, DeHaven B, Morgan J, et al. A prospective randomized comparison of an in-line heat moisture exchange filter and heated wire humidifiers: rates of ventilator-associated earlyonset (community-acquired) or late-onset (hospital-acquired) pneumonia and incidence of endotracheal tube occlusion. *Chest* 1997;112:1055-9.
48. Doebbeling BN, Stanley GL, Sheetz CT, et al. Comparative efficacy of alternative hand-washing agents in reducing nosocomial infections in intensive care units. *N Engl J Med* 1992;327:88-93.

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

Dorel Sandesc, Ovidiu Bedreag

- HAP diagnosis includes:
 - onset of symptoms within 48 h after admission in hospital
 - onset after more than 7 days after the subject is discharged from the hospital
 - hypothermia (core body temperature $< 35^{\circ}\text{C}$)
 - leucopenia (total WBC less than 5,000 elements/ mm^3)
 - anemia (Hb $< 7\text{g/dl}$)
- CAP diagnosis includes:
 - cough, purulent sputum production and dyspnea
 - thorax hiper-sonority at percussion
 - signs of consolidation on examination
 - leukocytosis
 - nausea and vomiting
- Patients presenting diagnosed CAP should be:
 - always treated at home
 - always admitted in a hospital
 - admitted in an intensive care unit if they have a respiratory rate < 30 breaths/minute and a serum creatinine $> 1.2\text{g/dl}$
 - admitted in an intensive care unit if they present shock or need for mechanical ventilation
 - discharged as soon as possible if they were admitted in hospital for preventing nosocomial infection risk
- For diagnosing HAP:
 - specimen sampling to be done before the start of antibiotic therapy
 - Gram stain is not useful in HAP management
 - chest xRay film is not always necessary
 - fiber-bronchoscopic technics should be routinely performed
 - non-bronchoscopic (blind) bronchoalveolar lavage has a very low specificity
- In CAP etiology:
 - patients with structural lung disease (bronchiectasis) have a high risk for infection with *Pseudomonas aeruginosa*
 - patients with Beta-lactam therapy within the past year have a high risk for infection with drug-resistant pneumococci:
 - anaerobes are frequent
 - after exposure to farm animals, *Coxiella burnetii* (Q fever) is frequent encountered
- H. Influenzae* is encountered in a low percent of CAP cases
- Treatment for outpatients with CAP, without cardiopulmonary disease, without modifying factors, should be started with:
 - penicillin
 - erythromycin
 - doxycycline
 - azithromycin or clarithromycin
 - ciprofloxacin
- Treatment for outpatient with CAP, cardiopulmonary disease and other modifying factors should be done with:
 - ceftriaxone plus clarithromycin
 - ceftriaxone plus doxycycline
 - ciprofloxacin alone
 - high-dose amoxicillin,
 - amoxicillin/clavulanate
- Patients with mild-to-moderate HAP, no unusual risk factors, allergic to penicillin should be treated with:
 - fluoroquinolone
 - clindamycin + aztreonam
 - cefepodoxime
 - cefuroxime
 - amoxicillin/clavulanate
- De-escalation therapy:
 - could be started with imipenem
 - should be started with a broad-spectrum antibiotic
 - should be started with a narrow-spectrum antibiotic
 - its duration must be at least 5 days
 - after bacteriological diagnosis is available, antibioterapy should be changed
- For preventing Intensive Care Unit - Acquired Pneumonia :
 - endotracheal tubes should never be used
 - nasal intubation is associated with a lower risk of ICU AP
 - supine position is better
 - hand-washing techniques on the ICU personnel are useful
 - 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