The LEbanese society for infectious diseases and clinical microbiology (LSIDCM) guidelines for adult community-acquired pneumonia (CAP) in Lebanon


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ABSTRACT: Adult community-acquired pneumonia (CAP) is a common cause of morbidity and mortality which is managed by different disciplines in a heterogeneous fashion. Development of consensus guidelines to standardize these wide variations in care has become a prime objective. The Lebanese Society of Infectious Diseases and Clinical Microbiology (LSIDCM) convened to set Lebanese national guidelines for the management of CAP since it is a major and a prevalent disease affecting the Lebanese population. These guidelines, besides being helpful in direct clinical practice, play a major role in establishing stewardship programs in hospitals in an effort to contain antimicrobial resistance on the national level. These guidelines are intended for primary care practitioners and emergency medicine physicians. They constitute an appropriate starting point for specialists’ consultation being based on the available local epidemiological and resistance data. This document includes the following: 1/Rationale and scope of the guidelines; 2/Microbiology of CAP based on Lebanese data; 3/ Clinical presentation and diagnostic workup of CAP; 4/Management and prevention strategies based on the IDSA/ATS Consensus Guidelines, 2007, and the ESCMID Guidelines, 2011, and tailored to the microbiological data in Lebanon; 5/ Comparison to regional guidelines. The recommendations made in this document were graded based on the strength of the evidence as in the 2007 IDSA/ATS Consensus Guidelines. Hopefully, these guidelines will be an important step towards standardization of CAP care in Lebanon and set the agenda for further research in this area.

Keywords: Lebanon, LSIDCM, adult community acquired

RATIONALE

The pandemic of antimicrobial resistance has become a serious threat globally [1]. This situation is aggravated by the paucity of antimicrobials in the pharmaceutical industry pipelines which led to the famous alarm raised by the Infectious Diseases Society of America (IDSA) of “Bad Bugs, No Drugs” situation [2]. The situation in Lebanon is not an exception as the antimicrobial resistance is a rapidly evolving situation in the country as shown by Araj et al. [3]. Susceptibility to fluoroquinolones in Escherichia coli has decreased during the past decade from 75% to 53%, and extended spectrum β-lactamase (ESBL) production in Klebsiella pneumoniae has increased from 12% to 28% [3-4]. The susceptibility of Enterobacteriaceae to trimethoprim/sulphamethoxazole has remained consistently low (50%), in addition to the emergence of extensively drug-resistant (XDR) Acinetobacter, Pseudomonas and carbapenem resistant Enterobacteriaceae [3,5].

Although antimicrobial resistance is an ancient phenomenon on the genetic level, the use of antibiotic is directly related to emergence and propagation of this resistance at the phenotypic level [6]. Antimicrobial stewardship has become a must to promote judicious use of antibiotics [7].

In this context, the Lebanese Society of Infectious Diseases and Clinical Microbiology (LSIDCM), an official society of the Lebanese Order of Physicians whose members are specialized in infectious diseases and or clinical microbiology, has initiated practice guidelines for common infectious diseases in Lebanon.

This working group started the first of these guidelines with community-acquired pneumonia, where a large armamentarium of drugs is being used and where fluoroquinolones play a major role in treatment [8].

Recommendations

The recommendations of these guidelines are based on the Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) Consensus Guidelines on the Management of CAP in Adults [9] and European
Society of Clinical Microbiology and Infectious Diseases (ESCMID) Guidelines for the Management of Adult Lower Respiratory Tract Infections (LRTI) [10-11], taking into consideration local microbiological data. Despite the fact that there is no registry for antibiotic resistance in Lebanon, the current recommendations were supported from available articles and reports that are published in the literature.

Due to the strong potential of fluoroquinolones to induce resistance and pass it on to other classes of antibiotics [12] and their high rate of resistance in Enterobacteriaceae in Lebanon [3] the LSIDCM members have decided to use them as a second choice except in indications where they are irreplaceable. The recommendations made in this document were graded based on the strength of the evidence as high-level (Level I), moderate-level (Level II), and low-level (Level III) evidence. It was adopted from the IDSA/ATS guidelines (Table I).

Scope of these Guidelines
In this article, recommendations are restricted to community-acquired pneumonia in adults in Lebanon.

MATERIALS AND METHODS

Definition of community-acquired pneumonia (CAP)
Pneumonia is an acute infection of the pulmonary parenchyma that is associated with symptom(s) of acute infection, accompanied by the presence of an acute infiltrate on a chest radiograph and/or auscultatory findings consistent with pneumonia (such as altered breath sounds and/or localized rales). CAP is a pneumonia that occurs in a patient not hospitalized or residing in a long-term care facility for more than 14 days before onset of symptoms [9].

However, it is very important to differentiate between pneumonia and other upper airway infection since their management differs [10-11].

Diagnosis of CAP
An acute febrile illness with cough and at least one new focal chest sign for four days or dyspnea/tachypnea without other obvious cause, supported by a shadow on chest radiograph is a diagnosis. In the elderly, the clinical symptoms might be very subtle [10-11]. This illness occurs in patients not hospitalized or residing in a long-term care facility for more than 14 days before onset of symptoms [9].

Microbiological considerations
The microbiological etiology of CAP has been described from a compendium of data in different studies in the UK, Europe and North America and Saudi Arabia [13-15].

In one prospective study of 507 patients treated in an ambulatory setting in Canada, the most commonly identified microorganisms were Mycoplasma pneumoniae (17%), Chlamydia pneumoniae (14%), Streptococcus pneumoniae (6%), and Haemophilus influenzae (5%) [13]. Despite considerable effort, an etiologic diagnosis could not be determined in (52%) of cases. In a prospective study from Spain that included 2521 ward patients with CAP, the most commonly identified organisms were Streptococcus pneumoniae (18%), respiratory viruses (5%), Legionella pneumophila (4%), and Haemophilus influenzae (2%) [14]. An etiologic could not be determined in 59% of cases. In the same study from Spain, among 488 patients admitted to the intensive care unit, the most commonly identified organisms were Streptococcus pneumoniae (23%), Legionella pneumophila (4%), Pseudomonas aeruginosa (3%), Chlamydia pneumoniae (2%), and Haemophilus influenzae (2%) [14]. No pathogen was identified in (47%) of patients.

A review by the ESCMID group in 2011 found out that there has been no major change in causative pathogens for lower respiratory tract infection (LRTI). More information is now available about the frequency of polymicrobial infections including viral infections [10-11]. On the other hand, Panton-Valentine leucocidin (PVL)-producing Staphylococcus aureus has emerged as a new cause, often of severe CAP, but currently remains uncommon [10-11]. Similarly the study by Memish et al. of CAP in the Middle East and North Africa showed that Streptococcus pneumoniae is the most common bacterial pathogen [15]. In one study, influenza virus was responsible for up to (53%) of the cases of CAP and Staphylococcus aureus was an important pathogen in patients with diabetes (23%) compared to (10%) in those without diabetes [15].

No data was found in the literature about the etiology

<table>
<thead>
<tr>
<th>Evidence Level</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEVEL I (high)</td>
<td>Evidence from well-conducted, randomized controlled trials</td>
</tr>
<tr>
<td>LEVEL II (moderate)</td>
<td>Evidence from well-designed, controlled trials without randomization (including cohort, patient series, and case-control studies). Level II studies also include any large case series in which systematic analysis of disease patterns and/or microbial etiology was conducted, as well as reports of data on new therapies that were not collected in a randomized fashion.</td>
</tr>
<tr>
<td>LEVEL III (low)</td>
<td>Evidence from case studies and expert opinion. In some instances, therapy recommendations come from antibiotic susceptibility data without clinical observations.</td>
</tr>
</tbody>
</table>

of CAP in Lebanon; however, the antibiotic susceptibilities of the above mentioned etiologic agents were well studied. It is noteworthy that minimal inhibitory concentration (MIC) breakpoint for resistance of non-meningeal Streptococcus pneumonia strains was changed from <2 mg/L before 2008 to > 8 mg/L after 2008, which gives a higher chance for treatment success with β-lactam antibiotics [16]. Subsequently, it has been well mentioned in the ESCMID guidelines that adequate choice and dosing of selected β-lactam antibiotics is still useful in the treatment of extra-meningeal pneumococcal infections where high doses of β-lactam antibiotic regimens should be adequate for eradicating strains with MIC ≤ 8 mg/L [10].

Wakim et al. [17] carried out a 6-year prospective study in 78 hospitals throughout Lebanon. In this study, a total of 257 isolates of culture confirmed Streptococcus pneumoniae were evaluated from different sites of the country between 2005 and 2011. The isolates’ pattern of resistance was as follows: penicillin (17.4%), ceftriaxone (86.9%), erythromycin (29.3%), and levofloxacin (0.5%). The aim of this surveillance study was to obtain data about the epidemiologic characteristics, serotypes, and antibiotic susceptibilities of Streptococcus pneumoniae isolates causing invasive disease in Lebanon [17].

In a study by Daoud et al. [18], a total of 121 strains of Streptococcus pneumoniae were isolated between 2005 and 2009 from two university hospitals in Beirut. Out of 121 isolates, 58 were susceptible to penicillin, 61 were intermediate, and 2 were fully resistant to this antibiotic. Amoxicillin-clavulanic acid and cefpodoxime showed 100% activity on all tested isolates. Fifty-four percent of isolates were penicillin non-susceptible with MIC ranging between 0.004 and 2 mg/L. The isolates showed percentages of non-susceptibility to clarithromycin varying from 25.7%-41.4%, and ofloxacin susceptibility was around 94%. Other investigators found similar results where erythromycin resistance reached up to (30%) in 2010 Streptococcus pneumoniae isolates [3].

Naba et al. have described the emergence of three isolated strains of levofloxacin resistant Streptococcus pneumoniae [19]. In a study by Kanj et al., looking at the antibiogram of respiratory pathogens collected between 2003 and 2004 in a tertiary care center in Lebanon, resistance in Streptococcus pneumoniae isolates using MIC > 8 mg/L was not detected [20]. However, when using the MIC between 0.02 mg/L and 2 mg/L, resistance was detected in 30% of the strains, with Haemophilus influenzae strains sensitivity to amoxicillin/clavulanic acid reaching (95%) active against and (100%) active against Moraxella strains. No data is available from Lebanon evaluating susceptibility patterns of strains of Klebsiella pneumoniae that come only from the community and cause CAP. All published Lebanese data about Klebsiella pneumoniae come from pooled data that include nosocomial and community-acquired strains causing collectively either pneumonia, intra-abdominal, postsurgical or urinary tract infections [3].

### Diagnostic testing

#### Chest Radiograph

A chest radiograph is required for the routine evaluation of patients who are likely to have pneumonia in order to establish a proper diagnosis and to aid in differentiating CAP from other common causes of cough and fever, such as acute bronchitis (level III evidence) [9-10].

The chest radiograph does not need to be repeated prior to hospital discharge in those who have made a satisfactory clinical recovery from CAP (level I evidence). For patients who are hospitalized for suspected pneumonia but who have negative chest radiography findings, it may be reasonable to treat their condition presumptively with antibiotics and repeat the imaging in 24-48 hours [9]. A chest radiograph should be arranged after about 6 weeks for all those patients who have persistence of symptoms or physical signs or who are at higher risk of underlying malignancy [21].

#### Other tests

For outpatients: No tests are recommended other than the chest X-ray (CXR) and C-reactive protein (CRP).

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**TABLE II**

<table>
<thead>
<tr>
<th>PNEUMONIA SEVERITY INDEX SCORE</th>
<th>PATIENT CHARACTERISTICS</th>
<th>POINTS ASSIGNED</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic factors</strong></td>
<td>Age: Male</td>
<td>Age (years)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>Age (years) – 10</td>
</tr>
<tr>
<td></td>
<td>Nursing home resident (consider as HCAP)</td>
<td>Age (years) + 10</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td>Neoplastic disease</td>
<td>+ 30</td>
</tr>
<tr>
<td></td>
<td>Liver disease</td>
<td>+ 20</td>
</tr>
<tr>
<td></td>
<td>Congestive heart failure</td>
<td>+ 10</td>
</tr>
<tr>
<td></td>
<td>Cerebrovascular disease</td>
<td>+ 10</td>
</tr>
<tr>
<td></td>
<td>Renal disease</td>
<td>+ 10</td>
</tr>
<tr>
<td><strong>Physical examination findings</strong></td>
<td>Altered mental status</td>
<td>+ 20</td>
</tr>
<tr>
<td></td>
<td>Respiratory rate ≥ 30 breaths/min</td>
<td>+ 20</td>
</tr>
<tr>
<td></td>
<td>Systolic blood pressure &lt; 90 mmHg</td>
<td>+ 20</td>
</tr>
<tr>
<td></td>
<td>Temperature &lt; 35 ºC or &gt; 40 ºC</td>
<td>+ 15</td>
</tr>
<tr>
<td></td>
<td>Pulse &gt; 125 beats/min</td>
<td>+ 10</td>
</tr>
<tr>
<td><strong>Laboratory and/or radiographic findings</strong></td>
<td>Arterial pH &lt; 7.35</td>
<td>+ 30</td>
</tr>
<tr>
<td></td>
<td>BUN ≥ 30 mg/dl</td>
<td>+ 20</td>
</tr>
<tr>
<td></td>
<td>Sodium &lt; 130 mmol/L</td>
<td>+ 20</td>
</tr>
<tr>
<td></td>
<td>Glucose &gt; 250 mg/dL</td>
<td>+ 10</td>
</tr>
<tr>
<td></td>
<td>Hematocrit &lt; 30%</td>
<td>+ 10</td>
</tr>
<tr>
<td></td>
<td>Hypoxemia by O₂ saturation:</td>
<td>+ 10</td>
</tr>
<tr>
<td></td>
<td>&lt; 90% by pulse oximetry and/or</td>
<td>+ 10</td>
</tr>
<tr>
<td></td>
<td>60 mmHg by arterial blood gas</td>
<td>+ 10</td>
</tr>
<tr>
<td></td>
<td>Pleural effusion on baseline graph</td>
<td>+ 10</td>
</tr>
</tbody>
</table>

**TOTAL POINT SCORE**

HCAP: health care-associated pneumonia  
BUN: blood urea nitrogen  
Routine diagnostic tests for an etiologic diagnosis are optional (level III evidence) [9].

For inpatients, the following tests are required: complete blood count with differential (CBCD), CRP, blood cultures, sputum cultures, Gram staining for both, urinary antigen tests for Legionella pneumophila and Streptococcus pneumoniae, and expectorated sputum samples collected for culture. For intubated patients, endotracheal aspirate sample should be obtained (level II evidence) [9]. Yet, these recommendations are considered of level III evidence in the ESCMID guidelines [10-11].

### TABLE III
**PNEUMONIA SEVERITY INDEX (PSI) with POINT TOTAL, SUGGESTED THERAPY and MORTALITY**

<table>
<thead>
<tr>
<th>PSI Risk Class</th>
<th>Characteristic points</th>
<th>Mortality</th>
<th>Site of Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>I - Low*</td>
<td>&lt; 51</td>
<td>0.1%</td>
<td>Outpatient</td>
</tr>
<tr>
<td>II - Low</td>
<td>51-70</td>
<td>0.6%</td>
<td>Outpatient</td>
</tr>
<tr>
<td>III - Low</td>
<td>71-90</td>
<td>0.9%</td>
<td>Outpatient/Inpatient (Brief)</td>
</tr>
<tr>
<td>IV - Moderate</td>
<td>91-130</td>
<td>9.5%</td>
<td>Inpatient</td>
</tr>
<tr>
<td>V - High</td>
<td>&gt; 130</td>
<td>26.7%</td>
<td>Inpatient</td>
</tr>
</tbody>
</table>

*Younger than 51 years of age and no coexisting illnesses or abnormal physical examination findings.


**PSI** is a tool that helps to classify patients into five risk categories (I–V). Mortality and site of care are suggested based on the PSI score. Mortality predictions are estimated for each risk category.

### TABLE IV
**CURB-65 SEVERITY SCORES for COMMUNITY-ACQUIRED PNEUMONIA**

**METHOD**

**Score 1 point for each of the following features:**
- Confusion (mental test score ≤ 8 new disorientation in person, place or time)
- Uremia (BUN > 20 mg/dl)
- Respiratory rate ≥ 30 breaths/min
- Blood pressure (systolic < 90 mmHg, or diastolic ≤ 60 mmHg)
- Age ≥ 65 years

**INTERPRETATION:**

<table>
<thead>
<tr>
<th>CURB-65</th>
<th>Mortality</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>(%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.6</td>
<td>Low risk; consider home treatment</td>
</tr>
<tr>
<td>1</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6.8</td>
<td>Short inpatient hospitalization or closely supervised outpatient treatment</td>
</tr>
<tr>
<td>3</td>
<td>14.0</td>
<td>Severe pneumonia; hospitalize and consider admittance to intensive care</td>
</tr>
<tr>
<td>4 or 5</td>
<td>27.8</td>
<td></td>
</tr>
</tbody>
</table>


**Site of care**

Almost all decisions about investigation and management of CAP, including the selection of site of care, depend on the initial assessment of the severity of the illness. The selection of the site of care (outpatient, or inpatient in a ward, or in an intensive care unit) is the most important clinical decision in managing patients with CAP. So the choice of antimicrobial therapy, the intensity of medical observation, and the need for other resources depend largely on the selected site of care [9-11].

CURB-65 [22] (Table IV) and/or PSI (Pulmonary severity index) scores [23] (Tables II & III) can be used for the decision of inpatient or outpatient management (Strong recommendation; level I evidence), and objective criteria should always be supplemented by subjective factors like the availability of support at home and the ability to take oral medication (Strong recommendation; level II evidence) [9-11].

Inpatients with a PSI of classes IV and V (> 90), and/or a CURB-65 of ≥ 2, hospitalization should be seriously considered (Moderate recommendation; level III evidence) [9-11].

If admission is not indicated as per risk assessment and where home care is planned, patients are advised on self-care such as using analgesia, staying well hydrated and on quitting smoking provided that they receive the necessary support and treatment with suitable antibiotics [10-11, 24].

Direct admission to an intensive care unit is recommended for patients presenting with CURB ≥ 3, or with PSI > 90, or with CAP with one major or three of the minor criteria for severe CAP (level II evidence) [9] (Table V).
TREATMENT (Table VI)

Outpatients (with or without comorbidities)
- In both cases, same management is followed because of high macrolide resistance in *Streptococcus pneumoniae* [9, 17, 20, 25]. A β-lactam plus a macrolide is preferred (strong recommendation; level I evidence).
- For the β-lactam, a high-dose amoxicillin (1 g 3 times daily) or amoxicillin-clavulinate (1.2 g twice daily) is preferred; alternatives would include ceftriaxone (2 g IM or IV once daily), cefpodoxime (200 mg twice per day) or cefuroxime (500 mg twice per day) (level I evidence).
- As for macrolides, azithromycin (500 mg daily for 3 days) or clarithromycin (500 mg twice per day or 1 g once daily for the extended release formulation) can be used.
- Doxycycline can be used as an alternative to the macrolides (100 mg twice per day).
- Monotherapy with a macrolide or doxycycline is not recommended because of the high incidence of *Streptococcus pneumoniae* resistance in Lebanon [17, 20].
- In order to decrease the effect of collateral damage [26-27], fluoroquinolones are to be used only as an alternative to the above regimen [9, 10-11]: levofloxacin (750 mg once daily), gemifloxacin (320 mg once daily), or moxifloxacin (400 mg once daily).

Inpatients
- **With advanced chronic obstructive pulmonary disease (COPD), and/or on home oxygen, and/or on steroids, presenting with CAP, levofloxacin is the preferred fluoroquinolone regimen to cover for possible *Pseudomonas* infection pending culture results.**
- **Admitted to non-ICU ward**
  A β-lactam (amino-penicillin/clavulanic acid) + a macrolide (level I evidence) [9]. The β-lactam can be [10]:
  - Amoxicillin 4 g/day is preferred (level I evidence).
  - A 3rd generation cephalosporin including cefotaxime (1-2 g every 8 hours), ceftriaxone (2 g once daily), or cefixime (1-2 g every 8 hours). Doses of macrolides are as above. Doxycycline can be used as an alternative to macrolides [9-10]. Respiratory fluoroquinolones are used only as an alternative in case of allergy or intolerance in order to decrease its collateral damage nationwide [26-27].
- **Inpatients admitted to an ICU**
  **PATIENT STRATIFICATION**
  It is necessary to assess the risk of *Pseudomonas aeruginosa* infection in patients admitted to an ICU in order to promptly choose the proper treatment regimen (level III evidence) [10].
  The presence of two of the following four risk factors for *Pseudomonas aeruginosa* infection warrants including antipseudomonal antimicrobial agents in the treatment regimen (level III evidence) [10]:
  1. Recent hospitalization (level III evidence).
  2. Frequent (more than four courses per year) or recent administration of antibiotics (in the last 3 months) (level III evidence).
  3. Severe disease (forced expiratory volume in one second (FEV1) of < 30%), oral steroids intake (level III evidence).
  4. Previous isolation or colonization of *Pseudomonas aeruginosa* during an exacerbation of chronic bronchitis.

**TREATMENT REGIMEN**

**ICU patient with no risk for Pseudomonas infection**
- A β-lactam (Non-antipseudomonal 3rd generation cephalosporin, e.g.: cefotaxime, ceftriaxone, or ceftriaxone ceftizoxime,) + azithromycin or clarithromycin (level II evidence) or β-lactam (Non-antipseudomonal 3rd generation cephalosporin + respiratory fluoroquinolones e.g. moxifloxacin or levofloxacin) is recommended (level I evidence). Doses are same as above [9].
- It is preferable to add a respiratory fluoroquinolone or vancomycin in septic patients because of the 17% prevalence of penicillin resistance with MIC > 8 mg/L among the *Streptococcus pneumoniae* isolates in Lebanon (level I evidence) [9, 17].
- For penicillin-allergic patients, a respiratory fluoroquinolone is recommended + aztreonam (level I evidence) [9].

**ICU patient at risk for Pseudomonas infection**
- An antipseudomoccal antipseudomonal β-lactam (piperacillin/tazobactam 4.5 g every 6 hours or cefepime (2 g every 8 hours ) or meropenem (1 g every 8 hours) or imipenem (1 g every 8 hours) plus either ciprofloxacin (400 mg IV every 12 hours) or levofloxacin (750 mg once daily) (level III evidence) [9].
- On the above β-lactams + an aminoglycoside (amikacin 20 mg/kg/day) and a macrolide (azithromycin or clarithromycin) (level III evidence) [9].

**N.B.** For CAP with MRSA, add vancomycin or linezolid (level III evidence) [9].

**Antiviral therapy**
Viral pneumonia can be due to influenza virus, para influenza virus, RSV, adenovirus, metapneumovirus, the SARS agent, Hantavirus or Middle East Respiratory Syndrome Corona virus. Antiviral therapy is of proven value in influenza pneumonia, varicella zoster pneumonia or herpes zoster pneumonia and not in all other viral etiologies. For all patients with viral pneumonias, a high clinical suspicion of bacterial superinfection should be maintained. Parenteral acyclovir is indicated for treatment of varicella-zoster virus infection or herpes simplex virus pneumonia [9].
- The empirical use of antiviral agents in patients suspected of suffering from influenza is usually not recommended. Antiviral treatment should be considered only:
  - In high-risk patients who have typical influenza
symptoms (fever, muscle ache, general malaise and respiratory tract infection) for 2 days.
- During a known influenza epidemic.
- Early treatment (within 48 hours of the onset of symptoms) is recommended for influenza A (level I evidence) [9].
- The use of oseltamivir and zanamivir is not recommended for patients with influenza with symptoms of more than 48 hours (level I evidence), but these drugs may be used to reduce viral shedding in hospitalized patients or for influenza pneumonia treatment (level III evidence) [9].
- The treatment is oseltamivir (75 mg twice per day or 150 mg twice per day) in severe illness or zanamivir (10 mg twice daily for 5 days). The 10 mg dose is provided by 2 inhalations (one 5-mg blister per

<p>| TABLE VI  |
| EMPIRICAL TREATMENT of COMMUNITY-ACQUIRED PNEUMONIA* THERAPEUTIC GUIDELINES: |</p>
<table>
<thead>
<tr>
<th>SITE OF CARE</th>
<th>FIRST LINE</th>
<th>ALTERNATIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young and otherwise healthy &amp; patients with comorbidities</td>
<td>A β-lactam plus a macrolide®. For the β-lactam, a high-dose amoxicillin (1 g 3 times daily) or amoxicillin-clavulanate (1.2 g twice daily) is preferred; alternatives would include ceftriaxone (2 g IM or IV once daily), cefpodoxime (200 mg twice per day) or cefuroxime (500 mg twice per day) [level I evidence]</td>
<td>Respiratory fluoroquinolones in case of intolerance or penicillin allergy®</td>
</tr>
<tr>
<td>Hospitalized patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular Ward</td>
<td>A β-lactam plus a macrolide® [level I evidence]. A β-lactam like Aminopenicillin + clavulanic acid + macrolide® [level I evidence]. The β-lactam can be:</td>
<td>Respiratory fluoroquinolones in case of intolerance or penicillin allergy®</td>
</tr>
<tr>
<td></td>
<td>1. Amoxicillin/Clavulanic acid with Ampicillin dose equivalent to 4 g/day [level I evidence]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. A 3rd generation cephalosporin including cefotaxime (1-2 g every 8 hours), ceftriaxone (2 g once daily), or cefotizoxime (1-2 g every 8 hours)</td>
<td></td>
</tr>
<tr>
<td>CAP with MRSA®</td>
<td>Same as ICU patient with Vancomycin or Teicoplanin Linezolid [level III evidence]</td>
<td></td>
</tr>
<tr>
<td>ICU Patients (No Pseudomonas risk)</td>
<td>A β-lactam (Non-antipseudomonal 3rd generation cephalosporin, e.g: cefotaxime, ceftriaxone, or cefozaxime,) + azithromycin or clarithromycin [level II evidence] or β-lactam (Non-antipseudomonal 3rd generation cephalosporin + respiratory fluoroquinolones® [level I evidence]. Doses are same as above. It is preferable to add a respiratory fluoroquinolone or Vancomycin or Teicoplanin in septic patients because of the 17% prevalence of penicillin resistance with MIC &gt; 8 mg/L among the Streptococcus pneumoniae isolates in Lebanon [level I evidence].</td>
<td>Respiratory fluoroquinolones® + Aztreonam in case of intolerance or penicillin allergy [level I evidence]</td>
</tr>
<tr>
<td>ICU Patients (With Pseudomonas risk®)</td>
<td>An anti-pneumococcal anti-β-lactam (piperacillin/tazobactam 4.5 g every 6 hours or cefepime (2 g every 8 hours) or meropenem (1 g every 8 hours) or imipenem (1 g every 8 hours) + either ciprofloxacin (400 mg IV every 12 hours) or levofloxacin (750 mg once daily) [level III evidence]. or the above β-lactams + an aminoglycoside (amikacin 20 mg/kg/day) and a macrolide® [level III evidence].</td>
<td>Respiratory fluoroquinolones® + Aztreonam in case of intolerance or penicillin allergy [level I evidence]</td>
</tr>
</tbody>
</table>

a. Regimen should be tailored upon the results of microbiological testing.
b. Macrolides: Azithromycin (500 mg daily for 3 days) or clarithromycin (500 mg twice per day or once daily for the extended release formulation). Azithromycin should be avoided in cardiac patients at risk of arrhythmias® based on FDA warning® and of note is the antimicrobial activity of the clarithromycin metabolites.14
c. Doxycycline can be used as an alternative to the macrolides (100 mg twice per day) in the β-lactam macrolide combination.
d. Fluoroquinolones: levofloxacin (750 mg once daily), gemifloxacin (320 mg once daily), or moxifloxacin (400 mg once daily).
e. Pseudomonas risk:
   5. Recent hospitalization [level III evidence].
   6. Frequent (more than four courses per year) or recent administration of antibiotics (in the last three months) [level III evidence].
   7. Severe disease (forced expiratory volume in one second (FEV1) of < 30%), oral steroids intake [level III evidence].
   8. Previous isolation or colonization of Pseudomonas aeruginosa during an exacerbation of chronic bronchitis.
f. MRSA CAP: Post influenza severe pneumonia, or MRSA proven by culture.

References
2. FDA Drug Safety Communication: Azithromycin (Zithromax or Zmax) and the risk of potentially fatal heart rhythms.
inhalation). Zanamivir is not recommended for the treatment of patients with underlying airways disease [9].

Treatment timing issues
- Treatment of CAP should be started as soon as the diagnosis is made (level I evidence) [10].
- In hospitalized patients, the first dose should be given in Emergency Department (level I evidence) [9] and in septic patients antibiotic treatment should not be delayed more than one hour after diagnosis (level I evidence) [10].
- Treatment duration ranges between 5 to 8 days and can be extended in case of complications like empyema, abscess formation or if the patient is immunocompromised (level I evidence) [9].
- Treatment can be switched from IV to PO when the patient is stable and after resolution of the most prominent symptoms (level III evidence) [10].

Additional therapies
- Low molecular weight heparin is indicated in patients with acute respiratory failure.
- The use of noninvasive ventilation may be considered particularly in patients with COPD [9].
- Steroids have no place in the treatment of CAP in the absence of COPD, unless septic shock is present [9].

Additional Recommendations
- Use paracetamol or ibuprofen as required thus reducing temperature and symptoms of malaise.
- To rest and drink a sufficient amount of fluids to prevent dehydration.
- Avoid cough suppressant medicines.
- Quit smoking. Physician might need to offer support and guidance for smoking cessation [9-11].

PREVENTION OF CAP

Influenza
Inactivated influenza vaccine is recommended for persons aged > 6 months of age, as recommended by the Advisory Committee on Immunization Practices (ACIP), and the Center for Disease Control and Prevention (level I evidence) [28]. Healthcare workers in inpatient, outpatient, or long-term care facilities should receive annual anti-influenza immunization [28].

Pneumococci
- Pneumococcal polysaccharide vaccine (23-valent polysaccharide vaccine) (Pneumovax23®, PPSV23) is recommended for persons aged ≥ 65 years and those with selected high-risk concurrent diseases, according to ACIP guidelines (level I evidence). [29]. It is worth mentioning that (Prevenar13®, PCV13) has been approved by the FDA in December 2011 for use in adults aged 50 or above [28-29].
- A CDC advisory committee on immunization practices recommended lately that adults with immunocompromised conditions should receive the 13-valent pneumococcal conjugate vaccine followed 8 weeks later with the 23-serotype polysaccharide vaccine [29].

Smoking cessation should be a goal in general and particularly for hospitalized patients with CAP [9-11].

Respiratory etiquette: Hand hygiene and cough etiquette should be taught in schools and well advertised to become integrated social habits.

COMPARISON TO REGIONAL GUIDELINES

These are the first CAP guidelines in the MENA (Middle East, North Africa) region; however, Saudi Arabia CAP Guidelines Working Group has put the Saudi CAP guidelines in 2002 [15] that were reviewed and updated by the Gulf Cooperation Council in 2007 [30]. Our guidelines follow the same subdivisions as the Saudi and GCC guidelines, but the empiric treatment recommendations do differ. In our guidelines, we recommend fluoroquinolones to be used in ICU patients with severe pneumonia like in the Saudi and GCC guidelines [30], however, outside the ICU, we have put fluoroquinolones only as an alternative not a primary choice, in order to decrease collateral damage and hopefully curb antibiotic resistance trends. On the other hand, the Saudi and GCC guidelines [30] recommend macrolide monotherapy in outpatients with no comorbidities; yet due to macrolide resistance in the Lebanese microbiology data, we recommend adding a β-lactam antibiotic to macrolides in this category of patients. Our recommendation is based on that of the IDSA guidelines, which clearly state that if macrolide resistance is ≥ 30% in a community, macrolide monotherapy should be avoided (level I evidence) [9].

CONCLUSION

The LSID members consider these guidelines as a first step in a long journey that should be followed immediately by the initiation of a national antimicrobial resistance surveillance system. This system will monitor resistance patterns in target strains both in community and health care settings which will allow us to perform a periodic review of the guidelines and update them according to new research and official national trends of antimicrobial resistance.

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REFERENCES


