The Lebanese Society for Infectious Diseases and Clinical Microbiology (LSIDCM) guidelines for adult community-acquired pneumonia (Cap) in Lebanon

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The LEBANESE SOCIETY for INFECTIOUS DISEASES and CLINICAL MICROBIOLOGY (LSIDCM) GUIDELINES for ADULT COMMUNITY-ACQUIRED PNEUMONIA (CAP) in LEBANON

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Rima MOGHNIEH[1], Nadine YARED SAKR[2]; Souha S. KANJ[3], Umayya MUSHARRAFIEH[3]
Rula HUSNI[4], Mona JRADEH[2], Ghassan AL-AWAR[3], Madona MATAR[5], Wafa JUREIJ[6], Antoine SAAD[7]
Eid AZAR[7], Pierre ABI HANNA[8,9], Afaf MINARI[9], Jamale HAMMOUD[10], Joumana KFOURY[11]
Tahsin MAHFOUZ[12], Diaa ABOU CHAKRA[1], Mohamad ZAATARI[13], Zuhayr A. TABBARAH[3,8]

Moghnieh R, Yared Sakr N, Kanj SS, Musharrafieh U, Husni R, Jradeh M, Al-Awar G, Matar M, Jureij W, Saad A, Azar E, Abi Hanna P, Minari A, Hammoud J, Kfoury J, Mahfouz T, Abou Chakra D, Zaatari M, Tabbarah ZA. The Lebanese Society for Infectious Diseases and Clinical Microbiology (LSIDCM) Guidelines for Adult Community-Acquired Pneumonia (CAP) in Lebanon. J Med Liban 2014 ; 62 (1) : 40-47.

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 phy-sicians. 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 ß-lactamase (ESßL) 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

From Lebanon: [1]Ain Wazein Hospital, Al-Shouf; [2]Mount Lebanon Hospital, Hazmieh; [3]Department of Infectious Diseases, American University of Beirut, Beirut; [4]Lebanese American University Medical Center Rizk Hospital, Beirut; [5]Notre-Dame de Secours University Hospital, Jbeil, Holy Spirit University of Kaslik; [6]Centre Hospitalier du Nord, Zghorta; [7]University of Balamand, Saint George Hospital MUC, Ashrafieh; [8]Rafic Hariri University Hospital, Beirut; [9]Sacré-Cœur Hospital, Beirut; [10]Al-Monla Hospital, Tripoli; [11]Hayek Hospital, Beirut; [12]Nabatieh Governmental Hospital, Nabatieh; [13]Hammoud Hospital, Saida.
Correspondence: *Zuhayr A. Tabbarah, MD. Zt01@aub.edu.lb*
Infectious Diseases Society: *Rima Moghnieh, MD. amlakkis@yahoo.com*

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 etiology 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 I
LEVELS of EVIDENCE for COMMUNITY-ACQUIRED PNEUMONIA [in ADULTS]

Evidence Level	Definition
Level I (high)	Evidence from well-conducted, randomized controlled trials
Level II (moderate)	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.
Level III (low)	Evidence from case studies and expert opinion. In some instances, therapy recommendations come from antibiotic susceptibility data without clinical observations.

Adapted from: Mandell LA, Wunderink RG, Anzueto A *et al.* Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. *Clinical Infectious Diseases* 2007; 44: S27-S72.

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-meningitis *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 ß-lactam antibiotics [16]. Subsequently, it has been well mentioned in the ESCMID guidelines that adequate choice and dosing of selected ß-lactam antibiotics is still useful in the treatment of extra-meningeal pneumococcal infections where high doses of ß-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 influenza* 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).

TABLE II
PNEUMONIA SEVERITY INDEX SCORE

Patient Characteristics	Points Assigned
Demographic factors	
Age: Male	Age (years)
Female	Age (years) – 10
Nursing home resident (consider as HCAP)	Age (years) + 10
Comorbidities	
Neoplastic disease	+ 30
Liver disease	+ 20
Congestive heart failure	+ 10
Cerebrovascular disease	+ 10
Renal disease	+ 10
Physical examination findings	
Altered mental status	+ 20
Respiratory rate ≥ 30 breaths/min	+ 20
Systolic blood pressure < 90 mmHg	+ 20
Temperature < 35 °C or > 40 °C	+ 15
Pulse > 125 beats/min	+ 10
Laboratory and/or radiographic findings	
Arterial pH < 7.35	+ 30
BUN ≥ 30 mg/dl	+ 20
Sodium < 130 mmol/L	+ 20
Glucose > 250 mg/dL	+ 10
Hematocrit < 30%	+ 10
Hypoxemia by O_2 saturation:	
< 90% by pulse oximetry and/or	+ 10
60 mmHg by arterial blood gas	
Pleural effusion on baseline graph	+ 10
TOTAL POINT SCORE	

HCAP: health care-associated pneumonia **BUN**: blood urea nitrogen
Adapted from: Fine MJ, Auble TE, Yealy DM *et al.* A prediction rule to identify low-risk patients with community-acquired pneumonia. *New England Journal of Medicine* 1997; 336 (4): 243-50.

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

PSI Risk Class	Characteristic points	Mortality	Site of Care
I - Low*	< 51	0.1%	Outpatient
II - Low	51-70	0.6%	Outpatient
III - Low	71-90	0.9%	Outpatient / Inpatient (Brief)
IV - Moderate	91-130	9.5%	Inpatient
V - High	> 130	26.7%	Inpatient

*Younger than 51 years of age and no coexisting illnesses or abnormal physical examination findings.
Adapted from: Fine MJ, Auble TE, Yealy DM *et al*: A prediction rule to identify low-risk patients with community-acquired pneumonia. *New England Journal of Medicine* 1997; 336 (4): 243-50.

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 V
CRITERIA for SEVERE COMMUNITY-ACQUIRED PNEUMONIA

Major Criteria
Invasive mechanical ventilation
Septic shock with the need for vasopressors
Minor Criteria[a]
Respiratory rate[b] ≥ 30 breaths/min
PaO_2/FiO_2 ratio[b] ≤ 250
Multilobar infiltrates
Confusion/Disorientation
Uremia (BUN level ≥ 20 mg/dl)
Leukopenia[c] (WBC count < 4000 cells/mm^3)
Thrombocytopenia (platelet count <100,000 cells/mm^3)
Hypothermia (core temperature < 36 °C)
Hypotension requiring aggressive fluid resuscitation

BUN: blood urea nitrogen **WBC**: white blood cell
PaO_2/FiO_2: arterial oxygen pressure/fraction of inspired oxygen;
a. Other criteria to consider include hypoglycemia (in non-diabetic patients), acute alcoholism/alcoholic withdrawal, hyponatremia, unexplained metabolic acidosis or elevated lactate level, cirrhosis, and asplenia.
b. A need for noninvasive ventilation can substitute for a respiratory rate > 30 breaths/min or a PaO_2/FiO_2 ratio < 250.
c. As a result of infection alone.
Adapted from: Mandell LA, Wunderink RG, Anzueto A *et al*. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. *Clinical Infectious Diseases* 2007; 44: S27-S72.

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

METHOD

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

INTERPRETATION:

CURB-65 Score	Mortality (%)	Recommendation
0	0.6	Low risk; consider home treatment
1	2.7	
2	6.8	Short inpatient hospitalization or closely supervised outpatient treatment
3	14.0	Severe pneumonia; hospitalize and consider admitting to intensive care
4 or 5	27.8	

Adapted from: Lim WS; Van der Eerden MM, Laing R *et al.* Defining community-acquired pneumonia severity on presentation to hospital: an international deviation and validation study. *Thorax* 2003; 58 (5): 377-82.

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 ß-lactam plus a macrolide is preferred (strong recommendation; level I evidence).
- For the ß-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).
- 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 ß-lactam (amino-penicillin/clavulanic acid) + a macrolide (level I evidence) [9]. The ß-lactam can be [10]:

- Ampicillin 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 ceftizoxime (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 ß-lactam (Non-antipseudomonal 3rd generation cephalosporin, e.g.: cefotaxime, ceftriaxone, or ceftriaxone ceftizoxime,) + azithromycin or clarithromycin (level II evidence) OR ß-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 antipneumococcal antipseudomonal ß-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].
- OR the above ß-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, metapneumo virus, 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

TABLE VI
EMPIRICAL TREATMENT of COMMUNITY-ACQUIRED PNEUMONIA[a] THERAPEUTIC GUIDELINES:

SITE OF CARE	FIRST LINE	*ALTERNATIVE*
Outpatients		
Young and otherwise healthy & patients with comorbidities	A ß-lactam plus a macrolide[b]. For the ß-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]	*Respiratory fluoroquinolones in case of intolerance or penicillin allergy*[d] *Doxycycline*[c] *[level II evidence]*
Hospitalized patients		
Regular Ward	A ß-lactam plus a macrolide[b] [level I evidence)]. A ß-lactam like Aminopenicillin + clavulanic acid + macrolide[b] [level I evidence]. The ß-lactam can be: 1. Amoxicillin/Clavulanic acid with Ampicillin dose equivalent to 4 g/day [level I evidence] 2. A 3rd generation cephalosporin including cefotaxime (1-2 g every 8 hours), ceftriaxone (2 g once daily), or ceftizoxime (1-2 g every 8 hours)	*Respiratory fluoroquinolones in case of intolerance or penicillin allergy*
CAP with MRSA[f]	Same as ICU patient with Vancomycin or Teicoplanin Linezolid [level III evidence]	
ICU Patients (No *Pseudomonas* risk)	A ß-lactam (Non-antipseudomonal 3rd generation cephalosporin, e.g: cefotaxime, ceftriaxone, or ceftizoxime,) + azithromycin or clarithromycin [level II evidence] OR ß-lactam (Non-antipseudomonal 3rd generation cephalosporin + respiratory fluoroquinolones[d] [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 > 8 mg/L among the *Streptococcus pneumoniae* isolates in Lebanon [level I evidence].	*Respiratory fluoroquinolones*[d] *+ Aztreonam in case of intolerance or penicillin allergy [level I evidence]*
ICU Patients (With *Pseudomonas* risk[e])	An anti-pneumococcal anti-pseudomonal ß-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 ß-lactams + an aminoglycoside (amikacin 20 mg/kg/day) and a macrolide[b] [level III evidence].	*Respiratory fluoroquinolones*[d] *+ Aztreonam in case of intolerance or penicillin allergy [level I evidence]*

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[1] based on FDA warning[2] and of note is the antimicrobial activity of the clarithromycin metabolites.[3-4]
c. Doxycycline can be used as an alternative to the macrolides (100 mg twice per day) in the ß-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

1. Ray WA, Murray KT, Hall K et al. Azithromycin and the risk of cardiovascular death. *New England Journal of Medicine* 2012; 366: 1881-90.
2. FDA Drug Safety Communication: Azithromycin (Zithromax or Zmax) and the risk of potentially fatal heart rhythms.
3. D. Honeybourne, F. Kees, J.M. Andrews, D. Baldwin, R. Wise. The levels of clarithromycin and its 14-hydroxy metabolite in the lung. *European Respiratory Journal* 1994; 7: 1275-80.
4. Martin SJ, Garvin CG, McBurney CR, Sahloff EG. The activity of 14-hydroxy clarithromycin, alone and in combination with clarithromycin, against penicillin- and erythromycin-resistant *Streptococcus pneumonia.Journal of Antimicrobial Chemotherapy* 2001; 47: 581-7.

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, abcess 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

It is essential to advise patients to:

- 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.
- Observe the frequency and color of urine. Fluid intake should be increased if urine is passed infrequently and is dark in color.
- 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 (Prevnar13®, PCV13) has been approved by the FDA in Decem-ber 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 ß-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

1. Spellberg B, Guidos R, Gilbert D et al. The epidemic of antibiotic-resistant infections: A call to action for the medical community from the Infectious Diseases Society of America. Clinical Infectious Diseases 2008; 46: 155-64.
2. Boucher HW, Talbot GH, Bradley JS et al. Bad Bugs, No Drugs: No ESKAPE! An update from the Infectious Diseases Society of America. Clinical Infectious Diseases 2009; 48: 1-12.
3. Araj GF, Avedissian AZ, Ayyash NS et al. A reflection on bacterial resistance to antimicrobial agents at a major tertiary care center in Lebanon over a decade. Lebanese Medical Journal 2012; 60 (3): 125-35.
4. Baroud M, Dandache I, Araj GF et al. Underlying mechanisms of carbapenem resistance in extended-spectrum ß-lactamase-producing *Klebsiella pneumoniae* and *Escherichia coli* isolates at a tertiary care centre in Lebanon: role of OXA-48 and NDM-1 carbapenemases. International Journal of Antimicrobial Agents 2013; 41: 75-9.
5. El-Herte RI, Kanj SS, Matar GM, Araj GF. The threat of carbapenem-resistant *Enterobacteriaceae* in Lebanon: An update on the regional and local epidemiology. Journal of Infection and Public Health 2012; 5: 233-43.
6. Galán JC, González-Candelas F, Rolain JM, Cantón R. Antibiotics as selectors and accelerators of diversity in the mechanisms of resistance: from the resistome to genetic plasticity in the ß-lactamases world. Frontiers in Microbiology 2013; 4: 1-17.
7. Dellit TH, Owens RC, McGowan JE et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship. Clinical Infectious Diseases 2007; 44: 159-77.
8. Cherfan AJ, Bizri AR, Steitieh SW, Moukhachen OE. Management of community-acquired pneumonia at a tertiary care medical center in Lebanon. American Journal of Health-System Pharmacy 2003; 60: 934-9.
9. Mandell LA, Wunderink RG, Anzueto A et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. Clinical Infectious Diseases 2007; 44: S27-S72.
10. Woodhead M, Blasi F, Ewig S et al. Guidelines for the management of adult lower respiratory tract infections. Clinical Microbiology and Infection 2011; 17 (Suppl. 6): E1-E59.
11. Woodhead M, Blasi F, Ewig S et al. Guidelines for the management of adult lower respiratory tract infections. European Respiratory Journal 2005; 26: 1138-80.
12. Jacoby GA. Mechanisms of resistance to quinolones. Clinical Infectious Diseases 2005; 41: S120-S126.
13. Marriea TJ, Poulin-Costello M, Beecroft MD, Herman-Gnjidic Z. Etiology of community-acquired pneumonia treated in an ambulatory setting. Respiratory Medicine 2005; 99: 60-5.
14. Cilloniz C, Ewig S, Polverino E et al. Microbial etiology of community-acquired pneumonia and its relation to severity. Thorax 2011; 66: 340-6.
15. Memish ZA, Shibl AM, Ahmed QAA and The Saudi Arabian Community-Acquired Pneumonia Working Group (SACAPWG). Guidelines for the management of community-acquired pneumonia in Saudi Arabia: a model for the Middle East region. International Journal of Antimicrobial Agents 2002; 20: S1-S12.
16. Effects of New Penicillin Susceptibility Breakpoints for *Streptococcus pneumoniae*-United States, 2006-2007. MMWR Dec 19, 2008; 57 (50): 1353-5.
17. Wakim RH,Chehab H, Mahfouz I et al. Epidemiologic characteristics, serotypes, and antimicrobial susceptibilities of invasive *Streptococcus pneumoniae* isolates in a nationwide surveillance study in Lebanon. Vaccine 2012; 30S: G11-G17.
18. Daoud Z, Kourani M, Saab R, Abi-Nader M, Hajjar M. Resistance of S*treptococcus pneumoniae* isolated from Lebanese patients between 2005 and 2009. Rev Esp Quimioter 2011; 24 (2): 84-90.
19. Naba M, Araj GF, Baban T, Tabbarah Z, Awar G, Kanj SS. Emergence of fluoroquinolone resistant *Streptococcus pneumoniae* in Lebanon: A report of three cases. Journal of Infectious Public Health 2010; 3 (3): 113-17.
20. Kanj SS, El-Dbouni O, Kanafani Z, Araj GF. Antimicrobial susceptibility of respiratory pathogens at the American University of Beirut Medical Center. International Journal of Infectious Diseases 2007; 11 (6): 554-6.
21. Lim WS, Baudouin SV, George RC et al. British Thoracic Society guidelines for the management of community-acquired pneumonia in adults: update 2009. Thorax 2009; 64 (Suppl III): iii1–iii55.
22. Lim WS, Van der Eerden MM, Laing R et al. Defining community-acquired pneumonia severity on presentation to hospital: an international deviation and validation study. Thorax 2003; 58 (5): 377-82.
23. Fine MJ, Auble TE, Yealy DM et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. New England Journal of Medicine 1997; 336 (4): 243-50.
24. Suchyta MR, Dean NC, Narus S, Hadlock CJ. Effects of a practice guideline for community-acquired pneumonia in an outpatient setting. American Journal of Medicine 2001; 110: 306-9.
25. Dbaibo G, Chehab H. Epidemiologic characteristics, serotypes and antimicrobial susceptibilities of invasive *Streptococcus pneumoniae* isolates in nationwide surveillance study in Lebanon. Abstract Presentation. American University of Beirut Research Day 2012.
26. Paterson DL. "Collateral damage" from cephalosporin or quinolone antibiotic therapy. Clinical Infectious Diseases 2004; 38 (Suppl 4): S341-S345.
27. Hoban DJ. Antibiotics and collateral damage. Clinical Cornerstone 2003; (Suppl.3): S12-S20.
28. Prevention and Control of Iinfluenza with Vaccines: Interim Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2013. MMWR May 10, 2013; 62 (18): 356.
29. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Oct 12, 2012; 61 (40): 816-19.
30. Memish ZA, Arabi YM, Ahmed QA, Shibl AM, Niederman MS, the GCC CAP Working Group (GCC-CAPWG). Executive summary of the Gulf Cooperation Council practice guidelines for the management of community-acquired pneumonia. Journal of Chemotherapy 2007; 19: S7-S11.