# ARTICLE IN PRESS

Infectious diseases now xxx (xxxx) xxx

FISEVIER

Contents lists available at ScienceDirect

# Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now



# Guidelines

Update of guidelines for management of community acquired pneumonia in adults by the French infectious disease society (SPILF) and the French-speaking society of respiratory diseases (SPLF). Endorsed by the French intensive care society (SRLF), the French microbiology society (SFM), the French radiology society (SFR) and the French emergency society (SFMU)

ARTICLE INFO

Keywords:
Pneumonia
Antibiotic
Imagery
Biology
Corticosteroids

#### 1. Introduction

The objective of the present updating of the 2010 guidelines is to define the new modalities of initial management of community-acquired pneumonia (CAP) of presumably bacterial origin in outpatient and hospital-based care of adult patients. While this text is also applicable to cases of severe pneumonia, the authors do not propose specific recommendations for critical care management (Table 1). In this framework, the respective roles of antibiotic therapy and corticosteroid therapy are likewise considered, the reasons being that these treatments must be started as early as possible (in emergency units) and that some patients with severe CAP are not managed in critical care.

While the present recommendations deal with presumably bacterial CAP, they include neither respiratory infections with viral etiology (flu, SARS-CoV-2, respiratory syncytial virus...) without signs of bacterial superinfection, nor cases of aspiration pneumonia. Lastly, patients with bronchiectasis, related or not to cystic fibrosis, are excluded from these guidelines, and CAP prevention is not taken into consideration.

From the outset, CAP management necessitates assessment of the patient's clinical situation (past medical history, field, risk factors) and disease severity, the objective being to propose appropriate care (Tables 1 to 3).

The decision algorithm designed to identify place of intervention and severity scores have not been reconsidered; the 2010 guidelines remain as references [1].

In this text, recommendations are classified as grade A, B or C, according to the level of scientific evidence established in the recent literature (Table 4).

# 2. Antibiotic therapy and adjuvant treatment

- 2.1. Probabilistic choice of first-line antibiotic therapy (other than dual therapy and anti-Pseudomonas aeruginosa beta-lactam)
- 2.1.1. The data from the literature since 2010
- 2.1.1.1. Amoxicillin versus amoxicillin-clavulanic acid versus ceftriaxone. Two retrospective studies found no significant difference concerning the evolution of CAP patients with comorbidities hospitalized outside critical care, and treated by ceftriaxone versus ampicillin [2], or ceftriaxone versus amoxicillin-clavulanic acid [3]. A retrospective study noted that probabilistic utilization of ceftriaxone as treatment for CAP is inappropriate in nearly 96 % of lower respiratory tract infections [4]. Amoxicillin remains the reference beta-lactam in cases of non-severe CAP in outpatient or hospital-based settings for patients without comorbidities.
- 2.1.1.2. Macrolides versus doxycycline versus fluoroquinolone for atypical bacteria. Mycoplasma pneumoniae is frequent in young adults [5–7]. While macrolides are widely recognized as standard treatment [8,9], macrolide resistance in different countries is highly variable and has been spreading [10]. Fluoroquinolones and doxycycline remain active [8,11].

Treatment of *Chlamydophila pneumoniae* is based on macrolides, doxycycline and fluoroquinolones [9,12–14]. Except in the event of high antimicrobial resistance rates, macrolides remain the antibiotics of reference. There is no difference of *in vitro* activity between cyclins and fluoroquinolones.

2.1.1.3. Macrolides versus fluoroquinolones for Legionella pneumophila. Legionella pneumophila pneumonia has been considered in only a few recent publications. The results of studies and meta-analyses concerning

https://doi.org/10.1016/j.idnow.2025.105034

Received 22 January 2025; Accepted 27 January 2025

2666-9919/© 2025 Elsevier Masson SAS. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Please cite this article as: Aurélien Dinh et al., Infectious diseases now, https://doi.org/10.1016/j.idnow.2025.105034

**Table 1**Definition of severe pneumonia If one major criterium or at least three minor criteria (according to ATS/IDSA) [86–90,131].

Major criteria	Septic shock	
	Respiratory distress necessitating mechanical ventilation	
Minor criteria	Respiratory rate ≥ 30 cycles/min	
	$PaO_2/FIO_2 \le 250*$	
	Multilobar infiltrates (i.e., $\geq 2$ )	
	Confusion/disorientation	
	Plasma urea ≥ 3.3 mmol/L	
	Leukopenia (leukocytes < 4000/mm <sup>3</sup> )†	
	Thrombocytopenia (platelets < 100,000/mm <sup>3</sup> )	
	Hypothermia (body temperature < 36 °C)	
	Hypotension necessitating volume expansion	

<sup>\* (</sup>FiO<sub>2</sub> estimated by the formula: FiO<sub>2</sub> =  $0.21 + 0.03 \times O_2$  flow (L/min) [132]. † Due to infection alone (i.e., not cancer chemotherapy).

**Table 2** Elements leading to suspicion of community-acquired pneumonia (CAP) with atypical bacteria (low sensitivity and specificity) [133–135].

	Mycoplasma pneumoniae CAP	Legionellosis
Context	Epidemics (familial,	– At-risk situations (travel,
	institution)	exposure to water aerosols)
	No response after 48 h-72 h of	<ul> <li>No response after 48 h-72 h of</li> </ul>
	well-conducted beta-lactam	well-conducted beta-lactam
	treatment	treatment
Field	Young > aged	Comorbidities,
		immunodepression
Clinical	<ul> <li>Progressive: persistent</li> </ul>	<ul> <li>Rapidly progressive (2 to 3</li> </ul>
	feverish cough, upper	days)
	respiratory tract signs	<ul> <li>Extra-respiratory signs:</li> </ul>
	<ul> <li>Extra-respiratory signs:</li> </ul>	digestive (abdominal pain,
	cutaneous-mucosal, digestive,	diarrhea, vomiting), neurological
	neurological (headache),	(impaired consciousness,
	myalgia, arthralgia	headache), myalgia, dissociated pulse (Faget sign)
Biological	Hemolytic anemia, renal failure	Renal failure, hyponatremia, cytolysis, rhabdomyolyses
Radiological	- Unsystematized infiltrates in	Unilateral or bilateral alveolar
· ·	both lungs	opacities
	<ul> <li>Interstitial syndrome</li> </ul>	-
	micronodular centrilobular –	
	bronchiolitis $\pm$ alveolar	
	infiltrates	

the superiority of fluoroquinolones *versus* macrolides are discordant [15–19]. However, a large-scale retrospective study in intensive care settings suggests the potential benefits of fluoroquinolones [18].

2.1.1.4. *Pristinamycin*. Pristinamycin acts on the bacteria responsible for CAP, with interesting *in vitro* activity, particularly against pneumococci and atypical bacteria, with some favorable clinical outcomes [20,21]. No new results have been published since 2010.

2.1.1.5. Suspected bacterial co-infection in a context of viral respiratory tract infection. Viral respiratory tract infection can favor bacterial co/superinfection [22–24]. The bacteria identified in influenza pneumonia (Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, Streptococcus pyogenes) lead to recommendations of antibiotic therapy with the amoxicillin-clavulanic acid association. In cases of beta-lactam allergy, fluoroquinolone with anti-pneumococcal activity may be prescribed.

**Table 4** Recommendation rating scale.

Recommendation grades	Level of scientific evidence in the literature
A Established scientific evidence	Level 1  - High-powered randomized comparative trials  - Meta-analysis of randomized comparative trials  - Analysis of decisions based on well-conducted studies
B Scientific presumption	Level 2  - Low-powered randomized comparative trials  - Non-randomized, well-conducted comparative studies
C Low level of scientific	<ul><li>Cohort studies</li><li>Level 3</li><li>Case-control studies</li></ul>
evidence	Level 4  - Comparative studies with major biases  - Retrospective studies  - Case series  - Descriptive epidemiological studies (transversal, longitudinal)

# Strength of recommendations:

- 1 =the experts strongly support;
- $2 = the \ experts \ moderately \ support;$
- 3 =the experts weakly support.

**Table 3**List of comorbidities to be considered when choosing probabilistic antibiotic therapy for CAP.

# Comorbidities modifying the choice of probabilistic antibiotic therapy for CAP Hospitalization during the preceding three months Antibiotic therapy during the preceding month\* Chronic alcoholism Swallowing difficulties Severe neurological disease with risk of swallowing "the wrong way"\*\* Active neoplasia Immunodepression\*\*\* Severe COPD (FEV1 < 50 %) or chronic respiratory failure (LTOT or NIV) Congestive heart failure Hepatic failure Chronic renal failure (GFR < 30 mL/min)

 $<sup>^{\</sup>ast}$  except nitrofurantoin, oral fosfomycin, pivmecillinam.

<sup>\*\*(</sup>CVA, Parkinson, Dementia, MS, etc.).

<sup>\*\*\*(</sup>systemic corticosteroids  $\geq 10 \text{ mg/d}$ , other immunosuppressant treatments, asplenia, agranulocytosis, HIV infection with lymphocyte count T CD4  $\leq 200/\text{mm}^3$ , primary immunodeficiency, etc.).

NB 1: Presence of one of the above-mentioned comorbidities suffices to modify the choice of amoxicillin as probabilistic antibiotic therapy for a CAP.

NB 2: In and of itself, asthma is not a comorbidity justifying antibiotic therapy different from first-line amoxicillin. That said, it is important when choosing a treatment to consider other parameters, such as recent antibiotic prescription.

NB 3: Age without comorbidity is not a criterium to take into account.

#### 2.1.2. The 2025 guidelines

# 2.1.2.1. The ambulatory patient (Table 5).

- First-line probabilistic antibiotic therapy:
- Patient without comorbidities: amoxicillin (Grade B-1); in case of allergy: pristinamycin (Grade B-3)
- Patient with at least one comorbidity (Table 3): amoxicillinclavulanic acid (Grade B-1); in case of non-severe allergy: parenteral 3GC (3rd generation cephalosporine) (Grade B-1); only in the event of allergy contraindicating the use of betalactam: levofloxacin (Grade B-1)
- In case of suspected bacterial co/superinfection of an influenza virus infection: probabilistic first-line antibiotic therapy covering *Staphylococcus aureus* and *Streptococcus pneumoniae*: amoxicillin-clavulanic acid (**Grade C-1**); in case of allergy: pristinamycin (**Grade C-1**)
- In case of suspected atypical bacterial pneumonia: first-line macrolide therapy, pristinamycin or doxycycline as alternatives (Grade C-1).
- In case of failed first-line beta-lactam antibiotic therapy, at H72 reevaluation: macrolide therapy relay (**Grade C-1**).
- In case of failed macrolide antibiotic therapy, at H72 reevaluation: beta-lactam (amoxicillin or amoxicillin-clavulanic acid or parenteral 3GC depending on comorbidities) relay (Grade C-1).

Remark: Given their poor bioavailability and ecological impact (selection of resistant strains), oral cephalosporins have no role to play in CAP treatment.

# 2.1.2.2. The patient hospitalized with non-severe CAP (Table 6).

- Probabilistic first-line antibiotic therapy:
  - Patient without comorbidities: parenteral or oral amoxicillin per os (Grade A-1); in the event of penicillin allergy: parenteral 3GC (Grade B-1).
  - 2. Patient with comorbidities (*cf.* Table 3) (without risk factor for *Pseudomonas aeruginosa* infection, *cf.* corresponding chapter): either oral or parenteral amoxicillin-clavulanic acid, or parenteral 3GC (**Grade B-1**)
- In case of suspected bacterial co/superinfection of influenza virus infection: probabilistic first-line antibiotic therapy covering Staphylococcus aureus and Streptococcus pneumoniae: amoxicillin-clavulanic acid (Grade C-1)

**Table 5**Probabilistic antibiotic therapy for CAP in ambulatory adults.

	1 <sup>er</sup> choix	Alternative
Without comorbidities	Amoxicillin	Pristinamycin
With at least one comorbidity*	Amoxicillin- clavulanic acid	Parenteral 3GC
Suspicion of co/superinfection of a	Amoxicillin-	Parenteral 3GC
viral bacterial infection (flu)	clavulanic acid	Or pristinamycir
Clinical picture suggesting infection or highlighting atypical bacteria	Macrolide	Pristinamycin or doxycycline
Reevaluation at 72 h		

<sup>\*</sup>cf. Table 3.

Levofloxacin: only if severe allergy to beta-lactamases and no other therapeutic possibility.

3GC: Third generation cephalosporin

- Suspicion of atypical bacterial pneumonia: macrolides (Grade C-1) (Table 7)
- In case of failed beta-lactam antibiotic therapy at H72 reevaluation, full work-up is recommended, with search for complication and/or bacteria resistant to first-line antibiotic therapy. Following which, several options are possible:
- 1. Pleural drainage in case of effusion;
- Extended spectrum beta-lactam according to context and microbiological results;
- Macrolide relay in case of strongly suspected atypical bacteria (Grade C-1).
- Pristinamycin has no role in hospitalized patients (**Grade C-1**).
- As an alternative, only in case of allergy contraindicating the use of beta-lactam: levofloxacin (Grade B-1).

# 2.1.2.3. Hospitalized patients with severe CAP (Tables 8 and 9).

- First-line probabilistic antibiotic therapy (in the absence of risk factor for *Pseudomonas aeruginosa* infection, *cf.* corresponding chapter): parenteral 3GC associated with a macrolide or, in case of allergy to one of the two drug classes: monotherapy by antipneumococcal fluoroquinolone (levofloxacin) (Grade B-1).
- Probabilistic antibiotic therapy for suspected or confirmed CAP caused by *Staphylococcus aureus* producing Panton-Valentine leukocidin (PVL) requires the use of a molecule with antitoxin activity (Table 9) (Grade B-1).

Table 10 details the usual dosages of the molecules recommended during CAP treatment.

#### 2.2. Duration of antibiotic CAP treatment

# 2.2.1. The data from the literature

In the literature, three meta-analyses have compared long (> 7 days) and short (3–7 days) antibiotic treatments and found no difference in terms of efficacy [25–27].

In addition, two randomized double-blind trials have evaluated 3-day *versus* 8-day beta-lactam CAP treatment [28,29].

The first trial compared the efficacy of 3-day *versus* 8-day amoxicillin treatment of patients admitted to hospital for moderately severe pneumonia and who improved (apyrexia, decreased respiratory signs) following the first three days of treatment [28]; the short treatment was found to be non-inferior. The population was composed of persons with

 Table 6

 Probabilistic antibiotic therapy for non-severe CAP in hospitalized adults.

	1st choice	Alternative
Without comorbidities	Amoxicillin	Parenteral
With comorbidities	Amoxicillin-	3GC
	clavulanic acid	
Suspected bacterial co/superinfection of	Amoxicillin-	
a viral infection (influenza)	clavulanic acid	
Clinical picture suggestive of atypical bacterial infection	Macrolide	Levofloxacin

Reevaluation at 72 h and de-escalation according to clinical evolution and microbiological examinations.

Levofloxacin: only if severe beta-lactam allergy, or contraindication to macrolides in case of suspected atypical bacteria.

Guidelines Infectious Diseases Now xxx (xxxxx) xxx

**Table 7**Probabilistic and directed antibiotic therapy for CAP in cases of suspected or diagnosed atypical bacteria in adults.

	Molecule (s)	Allergy / alternative
Legionellosis	Macrolide	If severe form or contraindication to macrolides: levofloxacin
Mycoplasma pneumoniae	Macrolide	Cyclin
		If contraindication to macrolides and cyclins: levofloxacin
Chlamydophila pneumoniae	Macrolide	Cyclin
		If contraindication to macrolides and cyclins: levofloxacin

Macrolides: azithromycin, clarithromycin, roxithromycin, spiramycin

met on D3, a three-day antibiotic regimen is recommended (**Grade A-1**).  $^{1}$ 

- If clinical stability criteria are met between three and five days of treatment, a 5-day antibiotic regimen is recommended (**Grade B-1**).
- In the other cases of uncomplicated CAP, a 7-day antibiotic regimen is recommended (**Grade A-1**).
- Duration of treatment exceeding 7 days must be justified by a complication (lung abscess, significant pleural fluid effusion...).

# 2.3. Indications for antibiotic combinations

#### 2.3.1. The data from the literature

Four meta-analyses of observational and randomized studies have reported discordant results on the prognostic impact of initial dual antibiotic therapy (beta-lactam and macrolide) for hospitalized CAP patients [30–33]. The beneficial effects of this strategy seem limited to

Table 8
Probabilistic antibiotic therapy for severe cases of CAP in hospitalized adults.

	Molecule(s)	Allergy / alternative	
Initial	Parenteral C3G + Macrolide	Levofloxacin (only if allergy contraindicating the use of beta-lactam)	
De-escalation	As early as possible according to clinical e	As early as possible according to clinical evolution and microbiological documentation	

**Table 9**Probabilistic and directed antibiotic therapy for suspected\* or confirmed severe CAP with *Staphylococcus aureus* producing Panton-Valentine leukocidin (PVL) toxin in adults.

Empirical and directed antibiotic therapy for suspected\* or confirmed severe necrotizing CAP with *Staphylococcus aureus* producing PVL toxin

	Molecule(s)	Allergy / alternative
Initial (probabilistic)	Parenteral 3GC	Parenteral 3GC (cefotaxime
	(cefotaxime or	or ceftriaxone)
	ceftriaxone)	+ Vancomycin
	+ Macrolide	+ Clindamycin**
	+ Linezolid	-
		In case of beta-lactamase
		allergy:
		Levofloxacin + linezolid
De-escalation during		
documentation		
MSSA PVL+	Penicillin M (IV) or	1) Vancomycin +
	cefazoline	clindamycin or rifampicin
	+ Clindamycin or	or
	rifampicin	2) Linezolid
MRSA PVL+	Linezolid	Vancomycin + clindamycin
		or rifampicin

<sup>\*</sup> Post-influenza context, severity, suggestive presentation: hemoptysis, leukopenia, cutaneous rash and necrotizing pneumonia (multiple nodules, excavated images).

a mean age of 55 years, and few comorbidities [28].

The second trial involved older (mean age: 73 years), comorbid and more severely ill patients meeting stability criteria at D3 (Table 11). It compared 3 days of beta-lactam (parenteral 3GC or amoxicillinclavulanic acid) *versus* 8 days. The trial demonstrated the non-inferiority of the 3-day treatment [29].

#### 2.2.2. The 2025 guidelines

 In non-severe (outpatient) and moderately severe (hospitalization outside critical care) cases of CAP, if all clinical stability criteria are

Table 10
Antibiotic dosage during CAP (without renal failure).

Antibiotics	Not in critical care	In critical care
Amoxicillin	1 g × 3/d	2 g × 3/d
Pristinamycin	1 g × 3/d	No
Amoxicillin-clavulanic acid	1 g × 3/d	1 or 2 g $\times$ 3/d
Cefotaxime	1 g × 3/d	80–100 mg/kg/d
Ceftriaxone	$1 \text{ g} \times 1/d$	$2 \text{ g} \times 1/d$
Levofloxacin	500 mg/d	500 mg à 1000 mg/d
Azithromycin	500 mg/d (D1), then 250 mg/d	500 mg/d (D1), then 250 mg/d
Clarithromycin	500 mg × 2/d	500 mg × 2/d
Spiramycin	1.5 MUI to 3 MUI × 3/d	3 MUI × 3/d
Doxycycline	100 mg × 2/d	100 mg × 2/d
Cefazoline	80-100 mg/kg/d	80-100 mg/kg/d*
Penicillin M	80 to 100 mg/kg/d	100 mg/kg/d*
Linezolid	600 mg × 2/d	600 mg × 2/d

<sup>\*</sup>in three daily infusions or continuous infusion after a loading dose of 30 mg/kg in one hour.

**Table 11**Clinical stability criteria during CAP [136].

Clinical stability criteria	Levels
Temperature	≤37.8 °C
Systolic blood pressure	$\geq$ 90 mmHg
Heart rate	≤100/min
Respiratory rate	≤24/min
$SpO_2$	≥90 % in room air
or PaO <sub>2</sub>	$\geq$ 60 mmHg in room air

severe cases.

We have found no recent study conclusively demonstrating the benefits of dual antibiotic therapy other than probabilistic treatment of CAP with bacteriological documentation, particularly in cases of *Legionella pneumophila* [18,19,34]; that much said, a single retrospective study pointed to the benefits of adding an antibiotic with anti-toxin

<sup>\*\*</sup> Clindamycin acts on most atypical bacteria, but not on all strains of legionella.

No data concerning immunosuppressed patients or patients with severe chronic respiratory, hepatic or renal insufficiency.

Infectious Diseases Now xxxx (xxxxx) xxx

effects (clindamycin or rifampicin) in cases of community-acquired necrotizing pneumonia due to methicillin-sensitive *Staphylococcus aureus* (MSSA) producing Panton Valentine leukocidin (PVL) and treated with anti-staphylococcal beta-lactam [35].

# 2.3.2. The 2025 guidelines

Guidelines

- In non-severe CAP cases, a probabilistic combination therapy associating beta-lactam and macrolide or fluoroquinolone is not recommended; monotherapy with a macrolide in case of suspected atypical bacteria, particularly *L. pneumophila*, is to be preferred (Grade A-1).
- In severe CAP cases necessitating hospitalization, probabilistic combination therapy associating beta-lactam (3GC) and macrolide is recommended. De-escalation to monotherapy by beta-lactam should immediately be considered in the absence of any clinical or biological argument suggesting atypical bacterial CAP (Grade B-1).
- In CAP with bacteriological documentation (including *L. pneumophila*), dual therapy is not recommended, with the exception of severe CAP involving PVL-producing strains, for which combination therapy associating an anti-staphylococcus beta-lactam and an antibiotic with antitoxin effects (clindamycin, rifampicin) can be considered (**Grade B-1**). In the event of severe cases of CAP due to methicillin-resistant, PLV-producing *Staphylococcus aureus*, monotherapy with linezolid is recommended.

# 2.4. Indications for anti-Pseudomonas aeruginosa beta-lactam

### 2.4.1. The data from the literature

A bibliographic search did not identify any study specifically evaluating the relationship between preliminary antibiotic therapy and risk of *P. aeruginosa* CAP. However, recent antibiotic therapy (according to the different studies, in the one or three months preceding pneumonia onset) was found to be an independent risk factor for CAP due to multidrug-resistant bacteria (MDR) or to potentially antibiotic-resistant bacteria, including *P. aeruginosa* [36–39].

Moreover, recent antibiotic therapy is associated with a heightened risk of infection from resistant or multidrug-resistant strains in patients with a lower respiratory tract infection involving *P. aeruginosa*, particularly those with severe COPD (chronic obstructive pulmonary disease) [40–43]. Hospitalization during the 60 to 90 days preceding CAP [38,44], admission to critical care [45,46], immunodepression [47] and chronic hemodialysis [48,49] have been associated with heightened risk of *P. aeruginosa* CAP; however, after adjustment, this risk seems limited to other predisposing factors (exposure to antibiotics and history of *P. aeruginosa* infection during hospitalization...).

Delayed initiation of adequate antibiotic therapy is associated with an unfavorable prognosis in severe infections [50–53], including *P. aeruginosa* CAP [54,55].

# 2.4.2. The 2025 guidelines

- Probabilistic antibiotic therapy including an anti-Pseudomonas betalactam is recommended for hospitalized patients with severe or non-severe CAP and presenting with a history of colonization or recent respiratory infection (< 1 year) by this pathogen (Grade B-1).</li>
- Probabilistic antibiotic therapy including an anti-Pseudomonas betalactam is recommended for hospitalized patients with severe CAP admitted to critical care and presenting with at least one of the following risk factors: recent parenteral antibiotic therapy (<3 months), severe COPD, bronchiectasis, tracheotomy (Grade B-1).
- It is recommended, in the absence of previously documented colonization with available antibiogram, to use cefepime or the piperacillin-tazobactam combination as first-line treatment. Aztreonam and ceftazidime exercise no intrinsic activity on the Grampositive pathogens (Streptococcus pneumoniae...) responsible for

CAP and must not be utilized as probabilistic antibiotic therapy for a patient with CAP (**Expert opinion**).

- In case of preliminarily documented colonization, it is recommended to take into account the most recent available antibiogram when choosing the beta-lactam to be utilized in the probabilistic treatment (Grade C-1).
- It is strongly recommended to conduct bacteriological documentation tests in case of probabilistic prescription of a beta-lactam acting on *P. aeruginosa*, the objective being to facilitate reevaluation of the antibiotic therapy and de-escalation when this bacterium is not isolated (Expert opinion).
- Probabilistic antibiotic therapy for severe CAP in a patient at risk of
   P. aeruginosa must also include a molecule acting on atypical bacteria
   (Grade B-1).

# 2.5. Indications for corticosteroids

# 2.5.1. The data from the literature

Two recent randomized trials on patients in critical care have recently been published.

The ESCAPe study tested the interest of delayed introduction (a median of 40 h after hospital admission) of 40 mg/d by continuous infusion of methylprednisolone, with progressive de-escalation over the following 21 days in a critical care population receiving invasive mechanical ventilation in 33 % of cases. Due to insufficient recruitment, the trial was prematurely discontinued before having reached its inclusion objective and without any benefit on mortality [56].

The CAPE-CODE trial evaluated the interest of early treatment consisting in 200 mg per day of hydrocortisone hemisuccinate (a median of 20 h after hospital admission) for severe CAP patients not in septic shock hospitalized in critical care (mechanical ventilation 44 %, high-flow nasal cannula oxygen therapy 41 %); those with myelosuppression, influenza or post-obstructive pneumonia were excluded. Following an initial period of full-dose treatment (four to seven days, according to clinical evolution), dosage decreased, with total treatment duration of 8 to 14 days. The trial was discontinued at an early stage (during the second interim analysis) due to a nearly 50 % reduction of mortality in the hydrocortisone arm, and to lessened intubation and vasopressor use [57].

# 2.5.2. The 2025 guidelines

- In non-severe (outpatient or hospitalized) CAP, the addition of corticosteroids is not recommended (Grade A-2).
- In severe (hospitalized in critical care) CAP, the addition of hydrocortisone hemisuccinate started during the first 24 h following the onset of severity signs is recommended, except in cases of myelosuppression, aspiration pneumonia, or influenza etiology. The initial dose is 200 mg per day, with reevaluation on the 4th day to determine dose tapering and a total duration ranging from 8 to 14 days (Grade A-1).

# 3. Biology

# 3.1. Biomarkers - C-reactive Protein (CRP)

# 3.1.1. Data from the recent literature

Several studies have assessed the interest of CRP dosing in pneumonia diagnosis and in differentiating the viral and bacterial etiologies of CAP [58-62].

Sensitivity and specificity of CRP levels in pneumonia diagnosis range from 40 to 90 % and vary considerably according to threshold [58–62]. No consensual threshold has been validated for positive CAP diagnosis or etiological diagnosis (bacterial *versus* viral).

From a prognostic standpoint, a high CRP level seems associated with a more severe prognosis [63–67]. That said, no study has

Infectious Diseases Now xxx (xxxx) xxx

Guidelines

conclusively proven that CRP dosage and/or follow-up leads to improved patient management and evolution.

During (outpatient or hospitalized) CAP cases, isolated use of CRP enables neither CAP diagnosis nor reliable differentiation of bacterial from viral infection. Lastly, no study has assessed the impact of CRP dosage on patient evolution and/or management.

# 3.1.2. The 2025 guidelines

In CAP patients (outpatient or hospitalized), CRP dosage is not systematically recommended for PAC diagnosis and/or follow-up (Grade C-1).

#### 3.2. Biomarkers - Procalcitonin (PCT)

#### 3.2.1. Data from the recent literature

Several trials and meta-analyses have demonstrated the interest of PCT dosing as a means of shortening the duration of antibiotic treatment of respiratory infections necessitating hospitalization, but this shortening never went below the recommended durations [68–70].

A blinded randomized trial showed no impact of PCT dosing on the reduction of antibiotic therapy duration for hospitalized lower respiratory tract infections, compared to high-quality care and/or care in accordance with recommendations based solely on clinical evaluation. [71].

In ambulatory medicine, a few studies (including a randomized trial) have shown that in suspected bacterial CAP/respiratory infections, PCT could help to reduce the number of antibiotic prescriptions [72]. However, uncertain accessibility and non-registration in the nomenclature of medical biology actions complicates its utilization in clinical practice.

#### 3.2.2. The 2025 guidelines

During cases of CAP necessitating outpatient or hospital-based care, systematic PCT dosing is not recommended for CAP diagnosis and/or follow-up (Grade C-1).

# 3.3. Indications for urinary antigen testing

# 3.3.1. *The data from the literature* The recent literature confirms:

- The low positivity rate of pneumococcal urinary antigen testing (4.2 %) associated with clinicians' disinclination to de-escalate antibiotic therapy following positive results limits the impact of this test on responsible use of antibiotics [73,74];
- While the positivity rate of urinary antigen testing for *Legionella* is low (1.6 %), positive results can nevertheless improve management of patients not admitted to critical care and in some cases not receiving probabilistic treatment for *Legionella* [74,75];
- Even though they are non-specific, criteria frequently associated with *Legionella* [74,75] help to target the patients most at risk and to enhance the profitability of urinary antigen testing.

# 3.3.2. The 2025 guidelines

- In cases of CAP necessitating outpatient care, it is not recommended to carry out *Legionella* or pneumococcal urinary antigen testing (Grade C-2).
- In cases of hospitalization for non-severe CAP, it is not recommended to carry out pneumococcal urinary antigen testing (Grade B-2). It is not recommended to carry out *Legionella* urinary antigen

- testing, except in the event of compelling arguments (cf. Table 2) (Grade B-2).
- In cases of hospitalization for severe CAP, it is recommended to carry out pneumococcal and *Legionella* urinary antigen testing<sup>2</sup> (Grade B-1).

# 3.4. Cytobacteriological examination of sputum (CBES) and other microbiological respiratory tract samples – Gram staining and culture

# 3.4.1. The data from the literature

The arguments in favor of trying to determine CAP etiology are the following: 1) A resistant pathogenic agent can be identified; 2) The antibiotherapy spectrum can be narrowed; 3) The detection of some pathogenic agents, one example being *Legionella*, has implications for public health; 4) Antibiotherapy can be adjusted when patients fail to respond to initial treatment; and 5) Constantly changing CAP epidemiology necessitates continuous evaluation.

There is a lack of high-level evidence demonstrating that CBES improves patients' individual prognosis. Indeed, the studies specifically evaluating the performances of direct testing after Gram staining of sputum and culture [76-79] or in combination with other microbiological tests [80-83] have not shown improved patient prognosis.

# 3.4.2. The 2025 guidelines

- In cases of CAP necessitating outpatient care, it is not recommended to carry out CBES (Grade C-2).
- In cases of hospitalization for non-severe CAP, it is recommended to carry out CBES in cases involving mucopurulent secretions (provided that the sputum sample is of good quality, and quickly delivered to a laboratory [84]), particularly in the following situations (Grade C-2):
- Patients probabilistically treated by non-conventional antibiotic therapy (other than amoxicillin, amoxicillin-clavulanic acid, macrolides or parenteral 3GC);
- Patients preliminarily identified as having MRSA respiratory infection or Pseudomonas aeruginosa;
- Hospitalized patients having received parenteral antibiotic therapy over the preceding three months;
- In the event of non-response to first-line antibiotic treatment and/or unfavorable evolution (72 h).
- In cases of hospitalization for severe CAP, particularly if the patient is intubated or ventilated, it is recommended to conduct direct microscopic examination after Gram staining and development of cultures based on deep respiratory samples (preferably obtained by means of tracheal suction, protected distal sampling and bronchoalveolar lavage) (Grade C-2).

# 3.5. Hemocultures

# 3.5.1. The data from the literature

In hospitalization due to CAP, the interest of hemocultures is low to moderate, and few data pertaining to high-risk populations are currently available. On the other hand, due to peculiar etiology and difficulties in diagnosis, hemocultures can be of interest for immunosuppressed patients. As regards sepsis and septic shock, the *Surviving Sepsis Campaign* recommends immediate hemoculture and antibiotic therapy prescription [85].

<sup>&</sup>lt;sup>2</sup> In the event of negative *Legionella* urinary antigen testing and clinical suspicion of severe *Legionella* CAP, it is recommended to carry out PCR (and culture) on lower respiratory tract specimens.

Guidelines Infectious Diseases Now xxx (xxxx) xxx

#### 3.5.2. The 2025 guidelines

- In cases of CAP necessitating outpatient care, it is not recommended to carry out hemoculture (expert opinion).
- In cases of hospitalization for non-severe CAP, it is recommended to carry out hemoculture only in the following situations (expert opinion):
- · Diagnostic uncertainty;
- Immunodepression;
- In patients probabilistically treated by means of non-conventional antibiotic therapy (other than amoxicillin, amoxicillin-clavulanic acid or parenteral 3GC);
- In patients with history of MRSA respiratory infection or Pseudomonas aeruginosa;
- In hospitalized patients having received parenteral antibiotic therapy over the preceding three months;
- In the event of non-response to first-line antibiotic treatment and/or unfavorable evolution at 72 h.
- In cases of hospitalization for severe CAP, it is recommended to carry out hemoculture (Grade B-1).

# 3.6. Molecular biology tests

Real-time PCR (Polymerase chain reaction) is the main currently applied technique; it has become the gold standard for the detection of respiratory viruses and atypical bacteria. This method is extremely sensitive and specific and enables acquisition of rapid results (less than one to four hours, depending on working platforms and/or available equipment).

The PCRs utilized differ particularly in terms of the number of sought-after pathogens ("monoplex" = one pathogen, "biplex" = two pathogens...).

In a context characterized by co-circulation of several viruses (influenza A and B, RSV, SARS-CoV-2...), RT-PCR tests searching for a single pathogen are no longer currently recommended. Triplex and quadruplex real-time RT-PCR searches for three or four viruses (influenza A and B, SARS-CoV-2 and RSV), and differs from broad-range or broad-panel PCR ("syndromic") testing.

Available only over the last few years, syndromic panels present an appreciable advantage: Starting with a single sample, it is now possible to amplify several different genomic sequences, thereby highlighting most of the viruses responsible for respiratory pathologies, and simultaneously screening for certain bacterial pathogens (the composition of the panels varies according to the manufacturers).

Different "syndromic panels" exist:

- "High" respiratory panels: Based mainly on nasopharyngeal swab, and also on oropharyngeal swab, saliva sample and expectoration, this type of panel can (according to the different kits) highlight 10 to 15 viruses and a number of atypical bacteria:  $Mycoplasma\ pneumoniae$ ,  $Chlamydophila\ pneumoniae\ \pm\ Bordetella\ pertussis\ and\ parapertussis\ \pm\ Legionella\ pneumophila$ .
- "Low" respiratory panels: Based mainly on lower respiratory tract sampling (bronchial and tracheal aspiration, protected distal sampling, bronchoalveolar lavage) in cases of pneumonia, these panels have also been validated for analysis of expectorations. The main currently available panel can highlight 18 bacteria, 15 of which are "cultivatable" (S. pneumoniae, S. aureus, E. coli, H. influenzae, P. aeruginosa, K. oxytoca...) with semi-quantification (ML estimation of DNA copy number) and the three atypical ones (M. pneumoniae, C. pneumoniae, L. pneumophila) with qualitative detection, as well as nine viruses and seven determinants of antibiotic resistance (mecA, BLSE type CTX-M ESBL, de types KPC, NDM, VIM, IMP and OXA-48-like carbapenemases).

Due to poor performances with nasopharyngeal samples, syndromic

PCR in search for *L. pneumophila* can be considered only with regard to expectoration or other deep respiratory sample [86–90].

# 3.6.1. The data from the literature

The impact of molecular biology tests on patient management is hard to assess, especially insofar as it depends on the testing site (medical biology laboratory or delocalized care service: emergency ward, medicine department, critical care...), on the type of panel used (simplex or quadruplex RT-PCR, "high" or "low" PCR syndromic panel), and on the sample taking site (nasopharyngeal swab *versus* deep airways).

As concerns care pathways, several studies have pointed to a positive impact of quadruplex RT-PCR and "high" syndromic panels on nasopharyngeal sample following detection of respiratory viruses; waiting periods in emergency wards and duration of hospitalization can be shortened; test results are promptly delivered, and persons with respiratory viruses can be rapidly isolated [91–101].

From a therapeutic standpoint, detection of SARS-CoV-2 or the influenza virus by PCR facilitates the introduction of earlier and more frequent antiviral treatment [102]. Of note, few specific antiviral therapies other than those addressing influenza and SARS-CoV-2 infection are currently carried out, a factor limiting the therapeutic interest of the detection of more diversified respiratory viruses.

That much said, a multicenter randomized trial conducted in an emergency unit for patients presenting with CAP [103] and a meta-analysis [104] have shown that the "high" syndromic PCR panels performed on nasopharyngeal sample have little or no impact on antibiotic consumption. This is probably due to the fact that RT-PCRs are mainly designed to search for viruses, and that the exclusive highlighting of a respiratory virus in a nasopharyngeal sample from a patient with a CAP diagnosis does not necessarily rule out an associated bacterial coinfection or superinfection of the lungs, and therefore does not allow for the cessation of antibiotic treatment. It bears mentioning that in this type of situation, the discontinuation of antibiotic treatment has got to be associated with a set of (clinical, biological, imagery-based) arguments, as well as the PCR result.

However, some "high" syndromic PCR panel conclusions obtained through nasopharyngeal sampling allow detection of *M. pneumoniae* and consequently have a positive impact on the introduction or modification of antibiotic treatment.

Lastly, and notwithstanding the substantial cost of the "high" and "low" syndromic panels, as of now we have no reliable cost-effectiveness data.

# 3.6.2. The 2025 guidelines

- In cases of CAP necessitating outpatient care: Searching for respiratory viruses and utilization of multiplex PCR (syndromic testing) are not recommended (Expert opinion).
- In cases of hospitalization for non-severe CAP:
  - It is recommended, taking into account the epidemic context, to carry out quadruplex RT-CPR in search of influenza viruses A / B, RSV, and/or SARS-CoV-2.
  - "High" syndromic RT-PCR panel or extended search (depending
    on the local equipment available) including *M. pneumoniae*through nasopharyngeal sampling can be proposed immediately
    or as a second-line approach if quadruplex RT-PCR yields negative
    results (Grade C- 2):
    - 1- When a search for atypical bacteria, particularly *M. pneumoniae*, is under consideration (depending on clinical presentation and/or epidemiology), and if specific PCR is not available:
    - 2- If the highlighting of a virus other than RSV/Influenza A and B/SARS-CoV-2 can have a pronounced impact on patient management (antibiotic de-escalation or discontinuation, isolation).
- In cases of hospitalization for severe CAP:

Infectious Diseases Now xxx (xxxx) xxx

Guidelines

- It is recommended, taking into account the economic context, to carry out quadruplex RT-CPR in search of influenza viruses A/B, RSV and SARS-CoV-2. (**Grade C- 2**).
- "High" syndromic RT-PCR panel or extended search (depending
  on the local equipment available) including M. pneumoniae)
  through nasopharyngeal sampling can be proposed immediately
  or as a second-line approach if quadruplex RT-PCT yields negative
  results (Grade C- 2):
  - 1- When a search for atypical bacteria, particularly *M. pneumoniae*, is under consideration (depending on clinical presentation and/or epidemiology), and if specific PCR is not available;
  - 2- If the highlighting of a virus other than RSV/Influenza A and B/SARS-CoV-2 can have a pronounced impact on patient management (antibiotic de-escalation or discontinuation, isolation).

"Low" syndromic RT-PCR panel through the deep airways (tracheal aspiration, protected distal sample, bronchoalveolar lavage or, by default satisfactory expectoration) can be proposed (Grade C- 2):

- 1- When non-conventional antibiotic therapy, different from the 3GC+Macrolide association, is used in probabilistic treatment;
- 2- When a search for atypical bacteria, especially Legionella,<sup>3</sup> is being considered (according to presentation and epidemiology, and if PCR specific to Legionella is not available).

#### 4. Imagery

# 4.1. Thoracic ultrasound – Indication to confirm or rule out the CAP diagnosis

# 4.1.1. The data from the literature

All in all, the studies having evaluated the diagnostic performances of clinical thoracic ultrasound in CAP diagnosis report satisfactory performance. For example the meta-analysis by Orso *et al.* [105] reported on the results of 17 prospective studies including 5108 patients admitted to emergency units for suspected CAP (41 % of confirmed cases). Pooled analysis of the results showed AUC at 0.97, sensitivity of 92 % [86–95] and specificity of 93 % [86–97]. Among these 17 studies, 11 presented sensitivity > 90 %, while six presented specificity > 90 %.

A recent review of the literature by Strøm *et al.* [106] evaluated the performances of ultrasound in CAP diagnosis; it was limited to 17 studies (2170 patients) in which the operator was neither a radiologist nor a sonographer. Sensitivity ranged from 68 to 100 % (sensitivity > 91 % for 14/17 studies) and specificity from 57 à 100 % (specificity > 80 % for 9/13 studies). The experience reported by the different operators was pronouncedly variable [107–109]. While these differences had relatively little impact on sensitivity, they reduced specificity in some studies. Lastly, when testing duration was mentioned, it was invariably lower than 10 min.

Contrarily to chest X-ray, thoracic ultrasound is difficult to reinterpret by another practitioner. Inter-operator reproducibility was only rarely assessed.

# 4.1.2. The 2025 guidelines

In cases of suspected CAP (severe and non-severe) necessitating outpatient or hospital-based care, thoracic ultrasound is a reliable tool for the diagnosis of pneumonia and can be proposed as a first-line method and as an alternative to chest X-ray, provided that the practitioner has received validated preliminary training.

It is particularly indicated for patients suffering from acute

respiratory failure, as this condition hinders the acquisition high-quality chest X-ray (**Grade B-2**).

4.2. Thoracic imaging (Chest X-ray or thoracic ultrasound) – Indication to confirm or rule out the CAP diagnosis

#### 4.2.1. The data from the literature

To our knowledge, there is currently no randomized trial comparing a clinical-biological diagnosis strategy to a conventional chest X-ray (CXR) strategy for CAP diagnosis in terms of antibiotic consumption and adverse effects. In the absence of a highly suggestive clinical picture characterized by a unilateral crackling sound, it seems reasonable to confirm the CAP diagnosis by means of thoracic imagery [110].

# 4.2.2. The 2025 guidelines

- In cases of CAP necessitating outpatient care, chest imaging (high-quality CXR or thoracic ultrasound) is recommended for diagnosis of pneumonia, and should be obtained promptly (< 3 days) (Grade B-2).
- In the event of strong presumption in favor of bacterial CAP, its acquisition must not delay the initiation of antibiotic therapy. When the chest imaging interpreted by a trained professional appears normal, the CAP diagnosis and the indication for antibiotic therapy are imperatively to be reconsidered.
- If not initially performed, chest imaging should be obtained in case of unfavorable evolution at 72 h of antibiotic therapy (the indication for follow-up imaging is considered in a dedicated chapter) (Grade Expert opinion).
- In cases of non-severe and severe CAP necessitating hospitalbased care, chest imaging (CXR or thoracic ultrasound, or even CT-scan) is recommended (Grade B-2).

# 4.3. Chest CT-scan - Indications to confirm or rule out the CAP diagnosis

#### 4.3.1. The data from the literature

Several clinical studies have evaluated the diagnostic performances of chest CT-scan, more particularly low-dose scan, in patients with suspected CAP diagnosis.

Regardless of the CXR result, a chest CT-scan helps refine the diagnosis of CAP. In a study including 58 patients admitted to an emergency unit due to suspected CAP and receiving CXR in a recumbent position, systematic chest CT-scan enabled revision of the diagnosis, whatever the (positive or negative) CXR result, and ensured a correct diagnosis, even when CXR had not done so [111]. A recent study demonstrated that chest CT-scan more reliably detects CAP (12 % vs. 6 %) in patients presenting with few if any respiratory signs (Blinded Trial ancillary study). Two studies employing similar methodology showed that a chest CT-scan carried out within four hours after admission to an emergency unit or within 72 h after admission to a geriatric ward modified CAP diagnosis based on clinical criteria in 59 % and 45 % of cases respectively. This diagnostic reclassification was congruent with the findings of an adjudication committee having taken into account the elements contributing to a diagnosis at one month [112,113].

Chest CT-scan permits more pertinent diagnostic precision in certain categories of patients; it seems to be of particular interest when a clinician is uncertain about the diagnosis [114]. Bedridden patients with suspected CAP are more often diagnosed using thoracic CT-scan when the parenchymal pathology reaches the lower lobes [111]. Two scores have been proposed to guide the indication for thoracic CT-scan in patients with suspected CAP [115,116]. They include clinical and radiological scores (presence/absence of infiltrate), as well as biological data (CRP, PCR result); given these, more than half of the concerned patients are in a zone of uncertainty and should undergo a CT scan, or even 69 % if the PCR result is not taken into account when calculating the score [115].

<sup>&</sup>lt;sup>3</sup> If negativity of *Legionella Sg1* antigen testing.

Guidelines Infectious Diseases Now xxx (xxxx) xxx

Chest CT-scan modifies medical decisions, particularly regarding antibiotic therapy. Following chest CT-scan, management strategies for orientation and treatment are modified [112], and the most interesting impact is on antibiotic therapy. While antibiotic treatment starts after CXR in 65 % of patients, subsequent to chest CT-scan it is suspended, started or modified in nearly one out of two patients. All in all, the choice of antibiotic after chest CT-scan is more congruent with best practice guidelines [117].

In addition, even when radiologic semiology of the scan is non-specific, it can in some cases orient the etiological diagnosis (particularly in immunosuppressed patients), thereby modifying the choice of probabilistic antibiotic therapy [118–120].

These benefits are counterbalanced by several unresolved questions. The impact of radiation on patient health is a constant source of preoccupation. While low-dose chest CT-scan limits exposure, the latter remains greater than exposure entailed by standard CXR [121]. In fact, there is no evidence of improved vital or functional prognosis for patients; the literature reports no modification regarding mortality, admission to critical care, hospitalization duration [112,122] or quality of life at one month [123] according to whether the CAP diagnosis has been rendered by chest CT-scan or CXR. What is more, there is no evidence of reduced medical resources consumption. That said, data on this aspect remain limited; while quality of care is improved, the literature provides no evidence of lessened resource usage [112] and to conclude, there is no medico-economic assessment convincingly demonstrating that the cost of scanning device would be offset by a reduction of the overall costs of care in CAP cases.

Insofar as scanographic pictures of CAP are markedly diverse, interpretation of chest CT-scan remains highly specific and complex [120].

# 4.3.2. The 2025 guidelines

- In cases of CAP necessitating outpatient care, it is not recommended to utilize chest CT-scan for first-line CAP diagnosis (Grade C-1).
- In cases of hospitalization for (severe and non-severe) CAP, it is recommended to use low-dose chest CT-scan for patients with diagnostic uncertainty after an initial evaluation based on a combination of clinical signs and the results of either a chest X-ray or thoracic ultrasound (Grade B-1).

# 4.4. Follow-up chest imaging - Indications for systematic imaging

# 4.4.1. The data from the literature

The interest of follow-up imaging in cases of CAP initially consists in detection of lung cancer having gone unnoticed during the initial CAP diagnosis. In a study involving 232 patients with lung cancer, 15 % of the cancers were revealed on the occasion of an infectious episode [124]. In addition, given the non-resolution of abnormalities on chest X-ray, other significant non-tumoral pathologies such as mycobacterial or fungal infections can be revealed [125].

Several studies with diverse methodology and in heterogeneous populations have dealt with the frequency of lung cancer diagnosis on the occasion or in the aftermath of a CAP episode; the percentage ranges from 0.7 to 9.2 %, depending on populations and follow-up duration [124–130].

To sum up, and in accordance with the existing guidelines, it does not seem necessary to systematically obtain follow-up chest imaging in case of favorable clinical evolution and in the absence of risk factors for lung cancer. Conversely, chest CT-scan seems justified in the event of persistent symptoms and/or risk factors for cancer: age  $\geq$  50 years combined with active smoking or cessation within the past 15 years ( $\geq$  20 pack-years).

#### 4.4.2. The 2025 guidelines

- In cases of (severe and non-severe) CAP necessitating outpatient or hospital-based care, it is not recommended to systematically obtain follow-up imaging in the event of favorable clinical evolution and in the absence of risk factor for lung cancer (Grade C-2).
- In cases of (severe and non-severe) CAP necessitating outpatient or hospital-based care, it is recommended to perform a chest CTscan in the event of:
- Non-improvement or worsening of respiratory signs at H72 despite well-conducted first-line treatment (Expert advice).
- Risk factor for cancer (screening): age ≥ 50 years associated with smoking (≥ 20 pack-years, either active or discontinued for fewer than 15 years), following a waiting period of at least two months (Grade C-2), and after having informed the patient within a shared decision-making framework.

#### Reviewers

Pr François-Xavier BLANC (Pneumologie, CHU Nantes), Pr Philippe BONNIAUD (Pneumologie, CHU Dijon), Pr Jacques CADRANEL (Pneumologie, AP-HP Tenon), Pr Clémence MARTIN (Pneumologie, AP-HP Cochin), Pr Camille TAILLE (Pneumologie, AP-HP Bichat), Pr David MONTANI (Pneumologie, AP-HP Kremlin Bicêtre), Dr Eric Bonnet (CRATB Occitanie, Toulouse), Dr Yousra Kherabi (Maladies Infectieuses, AP-HP Bichat), Pr Jean-Paul Stahl (Maladies Infectieuses, CHU Grenoble), Dr Josette Raymond (Bactériologie, AP-HP Cochin), Dr Sylvain Diamantis (Maladies Infectieuses, CH Melun), Pr Muriel Fartoukh (Médecine intensive réanimation, AP-HP Tenon), Pr Charles Edouard Luyt (Médecine intensive réanimation, AP-HP Pitié Salpétrière), Dr Eric Farfour (Microbiologie, CH Foch, Suresnes), Pr Sabine Pereyre (Microbiologie, CHU Bordeaux), Pr Marie Kempf (Microbiologie, CHU Angers), Pr Jérôme Le Goff (Virologie, CHU Saint Louis, Paris), Pr Sonia Burrel (Virologie, CHU Bordeaux), Pr Lucie Cassagnes (Radiologie, CHU Clermont Ferrand), Dr Marie Pierre Debray (Radiologie, AP-HP Bichat), Pr Gilbert Ferretti (Radiologie, CHU Grenoble), Pr Pierrick Le Borgne (Service d'accueil des urgences, CHRU Strasbourg), Dr Jean-Baptiste Bouillon (Service d'accueil des urgences, CHU Clermont Ferrand), Dr Geoffroy Rousseau (Service d'accueil des urgences SMUR, CHU Angers), Dr Delphine Douillet (Service d'accueil des urgences SMUR, CHU Angers), Dr Jeremy Guenezan (Service d'accueil des urgences, CHU Poitiers), Dr Josselin Le Bel (Médecine générale, Paris), Pr Serge Gilberg (Médecine générale, Paris), Dr Alexandre Malmartel (Médecine générale, Morsang sur Orge), Pr Rémy Boussageon (Médecine Générale, Lyon), Pr Henri Partouche (Médecine générale, Saint Ouen).

# Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### References

- [1] Agence Française de Sécurité Sanitaire des Produits de San (AFSSAPS), Société de Pathologie Infectieuse de Langue Française (SPILF), Société Française de Pneumologie (SPLF). Antibiothérapie par voie générale dans les infections respiratoires basses de l'adulte. 2010.
- [2] Guz D, Bracha M, Steinberg Y, Kozlovsky D, Gafter-Gvili A, Avni T. Ceftriaxone versus ampicillin for the treatment of community-acquired pneumonia. A propensity matched cohort study. Clin Microbiol Infect 2023;29:70–6. https://doi. org/10.1016/j.cmi.2022.07.022.
- [3] Batard E, Javaudin F, Kervagoret E, Caruana E, Le Bastard Q, Chapelet G, et al. Are third-generation cephalosporins associated with a better prognosis than amoxicillin-clavulanate in patients hospitalized in the medical ward for community-onset pneumonia? Clin Microbiol Infect 2018;24:1171–6. https:// doi.org/10.1016/j.cmi.2018.06.021.
- [4] Gorgulho A, Cunha F, Alves Branco E, Azevedo A, Almeida F, Duro R, et al. Appropriateness of empirical prescriptions of ceftriaxone and identification of opportunities for stewardship interventions: a single-centre cross-sectional study. Antibiotics (Basel) 2023;12:288. https://doi.org/10.3390/antibiotics12020288.

Infectious Diseases Now xxx (xxxx) xxx

#### Guidelines

- [5] Carrim M, Wolter N, Benitez AJ, Tempia S, Du Plessis M, Walaza S, et al. Epidemiology and Molecular Identification and Characterization of *Mycoplasma pneumoniae*, South Africa, 2012–2015. Emerg Infect Dis 2018;24:506–13. https://doi.org/10.3201/eid2403.162052.
- [6] Chen K, Jia R, Li L, Yang C, Shi Y. The aetiology of community associated pneumonia in children in Nanjing, China and aetiological patterns associated with age and season. BMC Public Health 2015;15:113. https://doi.org/10.1186/ s12889-015-1422-1.
- [7] Meyer Sauteur PM, Beeton ML. European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Mycoplasma and Chlamydia Infections (ESGMAC), and the ESGMAC Mycoplasma pneumoniae Surveillance (MAPS) study group. Mycoplasma pneumoniae: delayed re-emergence after COVID-19 pandemic restrictions. Lancet. Microbe 2023;82666–5247(23):00344. https://doi.org/10.1016/82666-5247(23)00344-0.
- [8] Beeton ML, Zhang X-S, Uldum SA, Bébéar C, Dumke R, Gullsby K, et al. Myco-plasma pneumoniae infections, 11 countries in Europe and Israel, 2011 to 2016. Eurosurveillance 2020;25:1900112. https://doi.org/10.2807/1560-7917. ES.2020.25.2.1900112.
- [9] Sharma L, Losier A, Tolbert T, Dela Cruz CS, Marion CR. Atypical Pneumonia: Updates on Legionella, Chlamydophila, and Mycoplasma Pneumonia. Clin Chest Med 2017;38:45–58. https://doi.org/10.1016/j.ccm.2016.11.011.
- [10] Pereyre S, Goret J, Bébéar C. Mycoplasma pneumoniae: Current Knowledge on Macrolide Resistance and Treatment. Front Microbiol 2016;7:974. https://doi. org/10.3389/fmicb.2016.00974.
- [11] Waites KB, Xiao L, Liu Y, Balish MF, Atkinson TP. Mycoplasma pneumoniae from the Respiratory Tract and Beyond. Clin Microbiol Rev 2017;30:747–809. https://doi.org/10.1128/CMR.00114-16.
- [12] Ishimaru N, Suzuki S, Shimokawa T, Akashi Y, Takeuchi Y, Ueda A, et al. Predicting Mycoplasma pneumoniae and Chlamydophila pneumoniae in community-acquired pneumonia (CAP) pneumonia: epidemiological study of respiratory tract infection using multiplex PCR assays. Intern Emerg Med 2021;16:2129–37. https://doi.org/10.1007/s11739-021-02744-6.
- [13] Kohlhoff SA, Hammerschlag MR. Treatment of chlamydial infections: 2014 update. Expert Opin Pharmacother 2015;16:205–12. https://doi.org/10.1517/14556566.2015.999041
- [14] Infections respiratoires à Mycoplasma pneumoniae: la HAS publie des réponses rapides. Haute Autorité de Santé n.d. https://www.has-sante.fr/jcms/p\_ 3482986/fr/infections-respiratoires-a-mycoplasma-pneumoniae-la-has-publiedes-reponses-rapides (accessed February 8, 2024).
- [15] Burdet C, Lepeule R, Duval X, Caseris M, Rioux C, Lucet J-C, et al. Quinolones versus macrolides in the treatment of legionellosis: a systematic review and metaanalysis. J Antimicrob Chemother 2014;69:2354–60. https://doi.org/10.1093/ iac/dku159.
- [16] Jasper AS, Musuuza JS, Tischendorf JS, Stevens VW, Gamage SD, Osman F, et al. Are Fluoroquinolones or Macrolides Better for Treating Legionella Pneumonia? A Systematic Review and Meta-analysis. Clin Infect Dis 2021;72:1979–89. https://doi.org/10.1093/cid/ciaa441.
- [17] Ruiz-Spinelli A, Rello J. Legionella pneumonia in hospitalized adults with respiratory failure: Quinolones or macrolides? Eur J Intern Med 2024;120:62–8. https://doi.org/10.1016/j.eiim.2023.09.013.
- [18] Cecchini J, Tuffet S, Sonneville R, Fartoukh M, Mayaux J, Roux D, et al. Antimicrobial strategy for severe community-acquired legionnaires' disease: a multicentre retrospective observational study. J Antimicrob Chemother 2017;72: 1502–9. https://doi.org/10.1093/jac/dkx007.
- [19] Gershengorn HB, Keene A, Dzierba AL, Wunsch H. The Association of Antibiotic Treatment Regimen and Hospital Mortality in Patients Hospitalized With Legionella Pneumonia. Clin Infect Dis 2015;60:e66–79. https://doi.org/10.1093/ cid/civ157
- [20] Trémolières F, Mayaud C, Mouton Y, Weber P, Dellatolas F, Caulin E. Efficacy and safety of pristinamycin vs amoxicillin in community acquired pneumonia in adults. Pathol Biol (Paris) 2005;53:503–10. https://doi.org/10.1016/j. pathio.2005.07.010.
- [21] Poirier R. Pristinamycin in the treatment of acute communicable pneumopathies in adults. Presse Med 1999;28(Suppl 1):13–5.
- [22] Self WH, Wunderink RG, Williams DJ, Zhu Y, Anderson EJ, Balk RA, et al. Staphylococcus aureus Community-acquired Pneumonia: Prevalence, Clinical Characteristics, and Outcomes. Clin Infect Dis 2016;63:300–9. https://doi.org/ 10.1093/cid/ciw300.
- [23] Cilloniz C, Dominedò C, Gabarrús A, Garcia-Vidal C, Becerril J, Tovar D, et al. Methicillin-susceptible staphylococcus aureus in community-acquired pneumonia: Risk factors and outcomes. J Infect 2021;82:76–83. https://doi.org/10.1016/i.iinf.2020.10.032.
- [24] Kim T, Huh JW, Hong S-B, Jung J, Kim MJ, Chong YP, et al. Epidemiology and Characteristics of Respiratory Syncytial Virus Pneumonia in Critically Ill Adults. Open Forum Infect Dis 2023;10:ofad131. https://doi.org/10.1093/ofid/ofad131.
- [25] Li JZ, Winston LG, Moore DH, Bent S. Efficacy of short-course antibiotic regimens for community-acquired pneumonia: a meta-analysis. Am J Med 2007;120: 783–90.
- [26] Tansarli GS, Mylonakis E. Systematic review and meta-analysis of the efficacy of short-course antibiotic treatments for community-acquired pneumonia in adults. Antimicrob Agents Chemother 2018;62:e00635–718. https://doi.org/10.1128/ AAC.00635-18.
- [27] Dimopoulos G, Matthaiou DK, Karageorgopoulos DE, Grammatikos AP, Athanassa Z, Falagas ME. Short- versus Long-Course Antibacterial Therapy for Community-Acquired Pneumonia. Drugs 2008;68:1841–54. https://doi.org/ 10.2165/00003495-200868130-00004.

- [28] el Moussaoui R, de Borgie CAJM, van den Broek P, Hustinx WN, Bresser P, van den Berk GEL, et al. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study. BMJ 2006;332:1355.
- [29] Dinh A, Ropers J, Duran C, Davido B, Deconinck L, Matt M, et al. Discontinuing β-lactam treatment after 3 days for patients with community-acquired pneumonia in non-critical care wards (PTC): a double-blind, randomised, placebo-controlled, non-inferiority trial. Lancet 2021;397:1195–203. https://doi.org/10.1016/ S0140-6736(21)00313-5.
- [30] Eliakim-Raz N, Robenshtok E, Shefet D, Gafter-Gvili A, Vidal L, Paul M, et al. Empiric antibiotic coverage of atypical pathogens for community-acquired pneumonia in hospitalized adults. Cochrane Database Syst Rev 2012;2012: CD004418. Doi: 10.1002/14651858.CD004418.pub4.
- [31] Lee JS, Giesler DL, Gellad WF, Fine MJ. Antibiotic therapy for adults hospitalized with community-acquired pneumonia: A systematic review. JAMA 2016;315: 593–602. https://doi.org/10.1001/jama.2016.0115.
- [32] Nie W, Li B, Xiu Q. β-Lactam/macrolide dual therapy versus β-lactam monotherapy for the treatment of community-acquired pneumonia in adults: a systematic review and meta-analysis. J Antimicrob Chemother 2014;69:1441–6. https://doi.org/10.1093/jac/dku033.
- [33] Horita N, Otsuka T, Haranaga S, Namkoong H, Miki M, Miyashita N, et al. Beta-lactam plus macrolides or beta-lactam alone for community-acquired pneumonia: A systematic review and meta-analysis. Respirology (Carlton, Vic) 2016;21: 1193–200. https://doi.org/10.1111/resp.12835.
- [34] Giamarellos-Bourboulis EJ, Siampanos A, Bolanou A, Doulou S, Kakavoulis N, Tsiakos K, et al. Clarithromycin for early anti-inflammatory responses in community-acquired pneumonia in Greece (ACCESS): a randomised, double-blind, placebo-controlled trial. The Lancet Respir Med 2024. https://doi.org/10.1016/\$2213-2600(23)00412-5. S2213260023004125.
- [35] Sicot N, Khanafer N, Meyssonnier V, Dumitrescu O, Tristan A, Bes M, et al. Methicillin resistance is not a predictor of severity in community-acquired Staphylococcus aureus necrotizing pneumonia-results of a prospective observational study. Clin Microbiol Infect 2013;19:E142–8. https://doi.org/10.1111/ 1469-0691.12022.
- [36] Prina E, Ranzani OT, Polverino E, Cillóniz C, Ferrer M, Fernandez L, et al. Risk factors associated with potentially antibiotic-resistant pathogens in communityacquired pneumonia. Ann Am Thorac Soc 2015;12:153–60. https://doi.org/ 10.1513/AnnalsATS.201407-3050C.
- [37] Gross AE, Van Schooneveld TC, Olsen KM, Rupp ME, Bui TH, Forsung E, et al. Epidemiology and Predictors of Multidrug-Resistant Community-Acquired and Health Care-Associated Pneumonia. Antimicrob Agents Chemother 2014;58: 5262–8. https://doi.org/10.1128/AAC.02582-14.
- [38] Webb BJ, Dascomb K, Stenehjem E, Vikram HR, Agrwal N, Sakata K, et al. Derivation and Multicenter Validation of the Drug Resistance in Pneumonia Clinical Prediction Score. Antimicrob Agents Chemother 2016;60:2652–63. https://doi.org/10.1128/AAC.03071-15.
- [39] Barreto JV, Dias CC, Cardoso T. Risk factors for community-onset pneumonia caused by drug-resistant pathogens: A prospective cohort study. Eur J Intern Med 2022;96:66–73. https://doi.org/10.1016/j.eiim.2021.10.005
- 2022;96:66–73. https://doi.org/10.1016/j.ejim.2021.10.005.

  [40] Cillóniz C, Gabarrús A, Ferrer M, Puig de la Bellacasa J, Rinaudo M, Mensa J, et al. Community-Acquired Pneumonia Due to Multidrug- and Non-Multidrug-Resistant Pseudomonas aeruginosa. Chest 2016;150:415–25. https://doi.org/10.1016/j.chest.2016.03.042
- [41] Chang K-Y, Wu P-C, Lee C-H, Lee Y-C, Chen H-C, Huang W-C, et al. Clinical Features and Antimicrobial Susceptibility of Pseudomonas aeruginosa and Acinetobacter baumannii Complex Isolates in Intensive Care Patients with Chronic Obstructive Pulmonary Disease and Community-Acquired Pneumonia in Taiwan. Int J Chron Obstruct Pulmon Dis 2021;16:1801–11. https://doi.org/10.2147/ COPD.S311714.
- [42] Rodrigo-Troyano A, Suarez-Cuartin G, Peiró M, Barril S, Castillo D, Sanchez-Reus F, et al. *Pseudomonas aeruginosa* resistance patterns and clinical outcomes in hospitalized exacerbations of COPD: Sensitive Pseudomonas aeruginosa in COPD. Respirology 2016;21:1235–42. https://doi.org/10.1111/resp.12825.
- [43] Smith D, Gill A, Hall L, Prevalence TAM. Pattern, Risks Factors and Consequences of Antibiotic Resistance in COPD: A Systematic Review. COPD: J Chron Obstruct Pulmon Dis 2021;18:672–82. https://doi.org/10.1080/15412555.2021.2000957.
- [44] Ward RA, Cadigan FC. The development of erythrocytic stages of Plasmodium falciparum in the gibbon. Hylobates lar Mil Med 1966;131(Suppl):944–51.
- [45] Mendoza SA, Jones KL. Ask the expert. Pediatr Nephrol 1990;4:497. https://doi. org/10.1007/BF00869829
- [46] Vallés J, Martin-Loeches I, Torres A, Diaz E, Seijas I, López MJ, et al. Epidemiology, antibiotic therapy and clinical outcomes of healthcare-associated pneumonia in critically ill patients: a Spanish cohort study. Intensive Care Med 2014; 40:572–81. https://doi.org/10.1007/s00134-014-3239-2.
- [47] Di Pasquale MF, Sotgiu G, Gramegna A, Radovanovic D, Terraneo S, Reyes LF, et al. Prevalence and Etiology of Community-acquired Pneumonia in Immuno-compromised Patients. Clin Infect Dis 2019;68:1482–93. https://doi.org/10.1003/rid/civ/793
- [48] Sishta SK, Troupe A, Marszalek KS, Kremer LM. Huntington's chorea: an electroencephalographic and psychometric study. Electroencephalogr Clin Neurophysiol 1974;36:387–93. https://doi.org/10.1016/0013-4694(74)90188-6.
- [49] Song J-U, Park HK, Kang HK, Lee J. Proposed risk factors for infection with multidrug-resistant pathogens in hemodialysis patients hospitalized with pneumonia. BMC Infect Dis 2017;17:681. https://doi.org/10.1186/s12879-017-2788-8.

Guidelines Infectious Diseases Now xxx (xxxxx) xxx

- [50] Willis J, Schiffman R, Rosman NP, Kwan ES, Ehrenberg BL, Rice JC. Asymmetries of Sleep Spindles and Beta Activity in Pediatric EEG. Clin Electroencephalogr 1990;21:48–50. https://doi.org/10.1177/155005949002100115.
- [51] Liu VX, Fielding-Singh V, Greene JD, Baker JM, Iwashyna TJ, Bhattacharya J, et al. The timing of early antibiotics and hospital mortality in sepsis. Am J Respir Crit Care Med 2017;196:856–63. https://doi.org/10.1164/rccm.201609-1848OC.
- [52] Seymour CW, Gesten F, Prescott HC, Friedrich ME, Iwashyna TJ, Phillips GS, et al. Time to Treatment and Mortality during Mandated Emergency Care for Sepsis. N Engl J Med 2017;376:2235–44. https://doi.org/10.1056/NEJMoa1703058.
- [53] Rhee C, Kadri SS, Dekker JP, Danner RL, Chen H-C, Fram D, et al. Prevalence of antibiotic-resistant pathogens in culture-proven sepsis and outcomes associated with inadequate and broad-spectrum empiric antibiotic use. JAMA Netw Open 2020;3:e202899. https://doi.org/10.1001/jamanetworkopen.2020.2899.
- [54] Sibila O, Laserna E, Maselli DJ, Fernandez JF, Mortensen EM, Anzueto A, et al. Risk factors and antibiotic therapy in P. aeruginosa community-acquired pneumonia. Respirology 2015;20:660-6. https://doi.org/10.1111/resp.12506.
- [55] Nair GB, Niederman MS. Updates on community acquired pneumonia management in the ICU. Pharmacol Ther 2021;217:107663. https://doi.org/10.1016/j.pharmthera 2020 107663
- [56] Meduri GU, Shih M-C, Bridges L, Martin TJ, El-Solh A, Seam N, et al. Low-dose methylprednisolone treatment in critically ill patients with severe communityacquired pneumonia. Intensive Care Med 2022;48:1009–23. https://doi.org/ 10.1007/s00134-022-06684-3.
- [57] Dequin P-F, Meziani F, Quenot J-P, Kamel T, Ricard J-D, Badie J, et al. Hydrocortisone in Severe Community-Acquired Pneumonia. N Engl J Med 2023;388: 1931–41. https://doi.org/10.1056/NEJMoa2215145.
- [58] Flanders SA, Stein J, Shochat G, Sellers K, Holland M, Maselli J, et al. Performance of a bedside C-reactive protein test in the diagnosis of community-acquired pneumonia in adults with acute cough. Am J Med 2004;116:529–35. https://doi.org/10.1016/j.amjmed.2003.11.023.
- [59] Holm A, Nexoe J, Bistrup LA, Pedersen SS, Obel N, Nielsen LP, et al. Aetiology and prediction of pneumonia in lower respiratory tract infection in primary care. Br J Gen Pract 2007;57:547–54.
- [60] Almirall J, Bolíbar I, Toran P, Pera G, Boquet X, Balanzó X, et al. Contribution of C-reactive protein to the diagnosis and assessment of severity of communityacquired pneumonia. Chest 2004;125:1335–42. https://doi.org/10.1378/ chest.125.4.1335.
- [61] Ruiz-González A, Utrillo L, Bielsa S, Falguera M, Porcel JM. The Diagnostic Value of Serum C-Reactive Protein for Identifying Pneumonia in Hospitalized Patients with Acute Respiratory Symptoms. J Biomark 2016;2016:2198745. https://doi. org/10.1155/2016/2198745.
- [62] van Vugt SF, Broekhuizen BDL, Lammens C, Zuithoff NPA, de Jong PA, Coenen S, et al. Use of serum C reactive protein and procalcitonin concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough: diagnostic study. BMJ 2013;346:f2450. https://doi.org/10.1136/bmi.f2450.
- [63] Park JH, Wee JH, Choi SP, Oh SH. The value of procalcitonin level in communityacquired pneumonia in the ED. Am J Emerg Med 2012;30:1248–54. https://doi. org/10.1016/j.ajem.2011.08.009.
- [64] Kim MW, Lim JY, Oh SH. Mortality prediction using serum biomarkers and various clinical risk scales in community-acquired pneumonia. Scand J Clin Lab Invest 2017;77:486–92. https://doi.org/10.1080/00365513.2017.1344298.
- [65] Kruger S, Ewig S, Marre R, Papassotiriou J, Richter K, Von Baum H, et al. Procalcitonin predicts patients at low risk of death from community-acquired pneumonia across all CRB-65 classes. Eur Respir J 2008;31:349–55. https://doi. org/10.1183/09031936.00054507.
- [66] Que Y-A, Virgini V, Lozeron ED, Paratte G, Prod'hom G, Revelly J-P, et al. Low C-reactive protein values at admission predict mortality in patients with severe community-acquired pneumonia caused by Streptococcus pneumoniae that require intensive care management. Infection 2015;43:193–9. https://doi.org/10.1007/s15010-015-0755-0.
- [67] Haugen J, Chandyo RK, Brokstad KA, Mathisen M, Ulak M, Basnet S, et al. Cytokine Concentrations in Plasma from Children with Severe and Non-Severe Community Acquired Pneumonia. PLoS One 2015;10:e0138978. https://doi.org/ 10.1371/journal.pone.0138978.
- [68] Christ-Crain M, Jaccard-Stolz D, Bingisser R, Gencay MM, Huber PR, Tamm M, et al. Effect of procalcitonin-guided treatment on antibiotic use and outcome in lower respiratory tract infections: cluster-randomised, single-blinded intervention trial. Lancet 2004;363:600–7. https://doi.org/10.1016/S0140-6736(04)15591-8.
- [69] Schuetz P, Christ-Crain M, Thomann R, Falconnier C, Wolbers M, Widmer I, et al. Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: the ProHOSP randomized controlled trial. JAMA 2009;302:1059-66.
- [70] Schuetz P, Müller B, Christ-Crain M, Stolz D, Tamm M, Bouadma L, et al. Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. Cochrane Database Systematic Rev 2012. https://doi.org/10.1002/ 14651858\_cd007488\_pub2.
- [71] Huang DT, Yealy DM, Filbin MR, Brown AM, Chang C-C-H, Doi Y, et al. Procalcitonin-guided use of antibiotics for lower respiratory tract infection. N Engl J Med 2018;379:236–49. https://doi.org/10.1056/NEJMoa1802670.
- [72] Lhopitallier L, Kronenberg A, Meuwly J-Y, Locatelli I, Mueller Y, Senn N, et al. Procalcitonin and lung ultrasonography point-of-care testing to determine antibiotic prescription in patients with lower respiratory tract infection in primary care: pragmatic cluster randomised trial. BMJ 2021:n2132. Doi: 10.1136/bmj. n2132.

- [73] Schimmel JJ, Haessler S, Imrey P, Lindenauer PK, Richter SS, Yu P-C, et al. Pneumococcal urinary antigen testing in united states hospitals: a missed opportunity for antimicrobial stewardship. Clin Infect Dis 2020;71:1427–34. https://doi.org/10.1093/cid/ciz983.
- [74] Bellew S, Grijalva CG, Williams DJ, Anderson EJ, Wunderink RG, Zhu Y, et al. Pneumococcal and Legionella Urinary Antigen Tests in Community-acquired Pneumonia: Prospective Evaluation of Indications for Testing. Clin Infect Dis 2019;68:2026–33. https://doi.org/10.1093/cid/ciy826.
- [75] Allgaier J, Lagu T, Haessler S, Imrey PB, Deshpande A, Guo N, et al. Risk factors, management, and outcomes of legionella pneumonia in a large, nationally representative sample. Chest 2021;159:1782–92. https://doi.org/10.1016/j. chest.2020.12.013.
- [76] Sato T, Aoshima M, Ohmagari N, Tada H, Chohnabayashi N. Usefulness of sputum Gram staining in community-acquired pneumonia. Nihon Kokyuki Gakkai Zasshi 2002;40:558–63.
- [77] Shariatzadeh MR, Marrie TJ. Does sputum culture affect the management and/or outcome of community-acquired pneumonia? East Mediterr Health J 2009;15: 792–9
- [78] Signori LGH, Ferreira MW, Vieira LCHR, Müller KR, de Mattos WLLD. Sputum examination in the clinical management of community-acquired pneumonia. J Bras Pneumol 2008;34:152–8. https://doi.org/10.1590/s1806-3213200800230005
- [79] Uematsu H, Hashimoto H, Iwamoto T, Horiguchi H, Yasunaga H. Impact of guideline-concordant microbiological testing on outcomes of pneumonia. Int J Qual Health Care 2014;26:100–7. https://doi.org/10.1093/intqhc/mzt078.
- [80] Lidman C, Burman LG, Lagergren A, Ortqvist A. Limited value of routine microbiological diagnostics in patients hospitalized for community-acquired pneumonia. Scand J Infect Dis 2002;34:873–9. https://doi.org/10.1080/ 0036554021000026967.
- [81] Sanyal S, Smith PR, Saha AC, Gupta S, Berkowitz L, Homel P. Initial microbiologic studies did not affect outcome in adults hospitalized with community-acquired pneumonia. Am J Respir Crit Care Med 1999;160:346–8. https://doi.org/ 10.1164/airccm.160.1.9806048.
- [82] van der Eerden MM, Vlaspolder F, de Graaff CS, Groot T, Bronsveld W, Jansen HM, et al. Comparison between pathogen directed antibiotic treatment and empirical broad spectrum antibiotic treatment in patients with community acquired pneumonia: a prospective randomised study. Thorax 2005;60:672–8. https://doi.org/10.1136/thx.2004.030411.
- [83] Ewig S, Torres A, Angeles Marcos M, Angrill J, Rañó A, de Roux A, et al. Factors associated with unknown aetiology in patients with community-acquired pneumonia. Eur Respir J 2002;20:1254–62. https://doi.org/10.1183/ 09031936.02.01942001.
- [84] Société Française de Microbiologie (SFM), Société Française de Mycologie Médicale (SFMM), Société Française de Parasitologie. Référentiel en microbiologie Médicale (REMIC). 2022.
- [85] Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med 2021;47:1181–247. https://doi.org/ 10.1007/s00134-021-06506-v.
- [86] Robert S, Lhommet C, Le Brun C, Garot D, Legras A, Mankikian J, et al. Diagnostic performance of multiplex PCR on pulmonary samples versus nasopharyngeal aspirates in community-acquired severe lower respiratory tract infections. J Clin Virol 2018;108:1–5. https://doi.org/10.1016/j.jcv.2018.08.001.
- [87] Lee D-H, Choi Y-J, Kim J, Han E, Bae M-H. Pre-Pandemic Distribution of Bacterial Species in Nasopharyngeal Swab Specimens from Pediatric and Adult Patients Detected via RT-PCR Using the Allplex Respiratory Panel. Life (Basel) 2023;13: 1840. https://doi.org/10.3390/life13091840.
- [88] Maze MJ, Slow S, Cumins A-M, Boon K, Goulter P, Podmore RG, et al. Enhanced detection of Legionnaires' disease by PCR testing of induced sputum and throat swabs. Eur Respir J 2014;43:644–6. https://doi.org/10.1183/ 09031936.00191913.
- [89] Cho M-C, Kim H, An D, Lee M, Noh S-A, Kim M-N, et al. Comparison of sputum and nasopharyngeal swab specimens for molecular diagnosis of Mycoplasma pneumoniae, Chlamydophila pneumoniae, and Legionella pneumophila. Ann Lab Med 2012;32:133–8. https://doi.org/10.3343/alm.2012.32.2.133.
- [90] Diederen BMW, Van Der Eerden MM, Vlaspolder F, Boersma WG, Kluytmans JAJW, Peeters MF. Detection of respiratory viruses and Legionella spp. by real-time polymerase chain reaction in patients with community acquired pneumonia. Scand J Infect Dis 2009;41:45–50. https://doi.org/10.1080/ 00365540802448799.
- [91] Rogers BB, Shankar P, Jerris RC, Kotzbauer D, Anderson EJ, Watson JR, et al. Impact of a Rapid Respiratory Panel Test on Patient Outcomes. Arch Pathol Lab Med 2014;139:636–41. https://doi.org/10.5858/arpa.2014-0257-OA.
- [92] Gadsby NJ, Russell CD, McHugh MP, Mark H, Conway Morris A, Laurenson IF, et al. Comprehensive Molecular Testing for Respiratory Pathogens in Community-Acquired Pneumonia. Clin Infect Dis 2016;62:817–23. https://doi.org/10.1093/ cid/civ1214.
- [93] Wabe N, Li L, Lindeman R, Yimsung R, Dahm MR, McLennan S, et al. Impact of rapid molecular diagnostic testing of respiratory viruses on outcomes of adults hospitalized with respiratory illness: a multicenter quasi-experimental study. J Clin Microbiol 2019;57. https://doi.org/10.1128/JCM.01727-18. e01727-18.
- [94] Andrews D, Chetty Y, Cooper BS, Virk M, Glass SK, Letters A, et al. Multiplex PCR point of care testing versus routine, laboratory-based testing in the treatment of adults with respiratory tract infections: a quasi-randomised study assessing impact on length of stay and antimicrobial use. BMC Infect Dis 2017;17:671. https://doi.org/10.1186/s12879-017-2784-z.

Guidelines Infectious Diseases Now xxxx (xxxxx) xxx

- [95] Brendish NJ, Malachira AK, Armstrong L, Houghton R, Aitken S, Nyimbili E, et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. Lancet Respir Med 2017;5:401–11. https://doi.org/ 10.1016/S2213-2600(17)30120-0.
- [96] Shengchen D, Gu X, Fan G, Sun R, Wang Y, Yu D, et al. Evaluation of a molecular point-of-care testing for viral and atypical pathogens on intravenous antibiotic duration in hospitalized adults with lower respiratory tract infection: a randomized clinical trial. Clin Microbiol Infect 2019;25:1415–21. https://doi.org/ 10.1016/j.cmi.2019.06.012.
- [97] Buchan DW, Windham S, Balada-Llasat J-M, Leber A, Harrington A, Relich R, et al. Practical Comparison of the BioFire FilmArray Pneumonia Panel to Routine Diagnostic Methods and Potential Impact on Antimicrobial Stewardship in Adult Hospitalized Patients with Lower Respiratory Tract Infections. J Clin Microbiol 2020;58:e00135–220. https://doi.org/10.1128/JCM.00135-20.
- [98] Monard C, Pehlivan J, Auger G, Alviset S, Tran Dinh A, Duquaire P, et al. Multicenter evaluation of a syndromic rapid multiplex PCR test for early adaptation of antimicrobial therapy in adult patients with pneumonia. Crit Care 2020; 24:434. https://doi.org/10.1186/s13054-020-03114-v.
- [99] Clark TW, Beard KR, Brendish NJ, Malachira AK, Mills S, Chan C, et al. Clinical impact of a routine, molecular, point-of-care, test-and-treat strategy for influenza in adults admitted to hospital (FluPOC): a multicentre, open-label, randomised controlled trial. Lancet Respir Med 2021;9:419–29. https://doi.org/10.1016/ S2213-2600(20)30469-0.
- [100] Trabattoni E, Le V, Pilmis B, Pean de Ponfilly G, Caisso C, Couzigou C, et al. Implementation of Alere i Influenza A & B point of care test for the diagnosis of influenza in an ED. Am J Emerg Med 2018;36:916–21. Doi: 10.1016/j. ajem.2017.10.046.
- [101] Rappo U, Schuetz AN, Jenkins SG, Calfee DP, Walsh TJ, Wells MT, et al. Impact of Early Detection of Respiratory Viruses by Multiplex PCR Assay on Clinical Outcomes in Adult Patients. J Clin Microbiol 2016;54:2096–103. https://doi.org/ 10.1128/JCM.00549-16.
- [102] Stamm BD, Tamerius J, Reddy S, Barlow S, Hamer C, Kempken A, et al. The influence of rapid influenza diagnostic testing on clinician decision-making for patients with acute respiratory infection in urgent care. Clin Infect Dis 2023;76: 1942–8. https://doi.org/10.1093/cid/ciad038.
- [103] Cartuliares MB, Rosenvinge FS, Mogensen CB, Skovsted TA, Andersen SL, Østergaard C, et al. Evaluation of point-of-care multiplex polymerase chain reaction in guiding antibiotic treatment of patients acutely admitted with suspected community-acquired pneumonia in Denmark: A multicentre randomised controlled trial. PLoS Med 2023;20:e1004314. https://doi.org/10.1371/journal. pmed.1004314.
- [104] Clark TW, Lindsley K, Wigmosta TB, Bhagat A, Hemmert RB, Uyei J, et al. Rapid multiplex PCR for respiratory viruses reduces time to result and improves clinical care: Results of a systematic review and meta-analysis. J Infect 2023;86:462–75. https://doi.org/10.1016/j.iinf.2023.03.005.
- [105] Orso D, Guglielmo N, Copetti R. Lung ultrasound in diagnosing pneumonia in the emergency department: a systematic review and meta-analysis. Eur J Emerg Med 2018;25:312–21. https://doi.org/10.1097/MEJ.0000000000000517.
- [106] Strøm JJ, Haugen PS, Hansen MP, Graumann O, Jensen MBB, Aakjær AC. Accuracy of lung ultrasonography in the hands of non-imaging specialists to diagnose and assess the severity of community-acquired pneumonia in adults: a systematic review. BMJ Open 2020;10:e036067. https://doi.org/10.1136/bmjopen-2019-036067.
- [107] Amatya Y, Rupp J, Russell FM, Saunders J, Bales B, House DR. Diagnostic use of lung ultrasound compared to chest radiograph for suspected pneumonia in a resource-limited setting. Int J Emerg Med 2018;11:8. https://doi.org/10.1186/ s12245-018-0170-2.
- [108] Corradi F, Brusasco C, Garlaschi A, Paparo F, Ball L, Santori G, et al. Quantitative analysis of lung ultrasonography for the detection of community-acquired pneumonia: A pilot study. Biomed Res Int 2015;2015:1–8. https://doi.org/ 10.1155/2015/868707
- [109] Parlamento S, Copetti R, Di Bartolomeo S. Evaluation of lung ultrasound for the diagnosis of pneumonia in the ED. Am J Emerg Med 2009;27:379–84. https://doi. org/10.1016/j.ajem.2008.03.009.
- [110] Gupta AB, Flanders SA, Petty LA, Gandhi TN, Pulia MS, Horowitz JK, et al. Inappropriate Diagnosis of Pneumonia Among Hospitalized Adults. JAMA Intern Med 2024;184:548. https://doi.org/10.1001/jamainternmed.2024.0077.
- [111] Esayag Y, Nikitin I, Bar-Ziv J, Cytter R, Hadas-Halpern I, Zalut T, et al. Diagnostic value of chest radiographs in bedridden patients suspected of having pneumonia. Am J Med 2010;123(88):e1–5. https://doi.org/10.1016/j.amjmed.2009.09.012.
- [112] Claessens Y-E, Debray M-P, Tubach F, Brun A-L, Rammaert B, Hausfater P, et al. Early Chest Computed Tomography Scan to Assist Diagnosis and Guide Treatment Decision for Suspected Community-acquired Pneumonia. Am J Respir Crit Care Med 2015;192:974–82. https://doi.org/10.1164/rccm.201501-0017OC.
- [113] Prendki V, Scheffler M, Huttner B, Garin N, Herrmann F, Janssens J-P, et al. Low-dose computed tomography for the diagnosis of pneumonia in elderly patients: a prospective, interventional cohort study. Eur Respir J 2018;51:1702375. https://doi.org/10.1183/13993003.02375-2017.
- [114] Pandharipande PV, Reisner AT, Binder WD, Zaheer A, Gunn ML, Linnau KF, et al. CT in the emergency department: a real-time study of changes in physician decision making. Radiology 2016;278:812–21. https://doi.org/10.1148/ radiol.2015.15.0473
- [115] Loubet P, Tubiana S, Claessens YE, Epelboin L, Ficko C, Le Bel J, et al. Community-acquired pneumonia in the emergency department: an algorithm to facilitate

- diagnosis and guide chest CT scan indication. Clin Microbiol Infect 2020;26:382. e1–7. https://doi.org/10.1016/j.cmi.2019.06.026.
- [116] Garin N, Marti C, Carballo S, Darbellay Farhoumand P, Montet X, Roux X, et al. Rational Use of CT-Scan for the Diagnosis of Pneumonia: Comparative Accuracy of Different Strategies. J Clin Med 2019;8:514. https://doi.org/10.3390/ icm8040514
- [117] Tubiana S, Epelboin L, Casalino E, Naccache J-M, Feydy A, Khalil A, et al. Effect of diagnosis level of certainty on adherence to antibiotics' guidelines in ED patients with pneumonia: a post-hoc analysis of an interventional trial. Eur J Emerg Med 2023;30:102–9. Doi: 10.1097/MEJ.00000000000954.
- [118] Franquet T. Imaging of pneumonia: trends and algorithms. Eur Respir J 2001;18: 196–208. https://doi.org/10.1183/09031936.01.00213501.
- [119] Franquet T. Imaging of Community-acquired Pneumonia. J Thorac Imaging 2018; 33:282-94. https://doi.org/10.1097/RTI.000000000000347.
- [120] Debray MP, Carette MF, Loubet P, Pasquet B, Houhou Fidouh N, Benjoar M, et al. CT features of community-acquired pneumonia at the emergency department. Respir Med Res 2022;81:100892. https://doi.org/10.1016/j. resmer.2022.100892.
- [121] Ludes C, Schaal M, Labani A, Jeung M-Y, Roy C, Ohana M. Ultra-low dose chest CT: The end of chest radiograph? Presse Med 2016;45:291–301. https://doi.org/ 10.1016/j.lpm.2015.12.003.
- [122] Upchurch CP, Grijalva CG, Wunderink RG, Williams DJ, Waterer GW, Anderson EJ, et al. Community-Acquired Pneumonia Visualized on CT Scans but Not Chest Radiographs: Pathogens, Severity, and Clinical Outcomes. Chest 2018; 153:601–10. https://doi.org/10.1016/j.chest.2017.07.035.
- [123] van den Berk IAH, Kanglie MMNP, van Engelen TSR, Altenburg J, Annema JT, Beenen LFM, et al. Ultra-low-dose CT versus chest X-ray for patients suspected of pulmonary disease at the emergency department: a multicentre randomised clinical trial. Thorax 2023;78:515–22. https://doi.org/10.1136/thoraxjnl-2021-218337.
- [124] Holmberg H, Kragsbjerg P. Association of pneumonia and lung cancer: the value of convalescent chest radiography and follow-up. Scand J Infect Dis 1993;25: 93-100
- [125] Little BP, Gilman MD, Humphrey KL, Alkasab TK, Gibbons FK, Shepard J-A-O, et al. Outcome of recommendations for radiographic follow-up of pneumonia on outpatient chest radiography. AJR Am J Roentgenol 2014;202:54–9. https://doi.org/10.2214/AJR.13.10888.
- [126] Macdonald C, Jayathissa S, Leadbetter M. Is post-pneumonia chest X -ray for lung malignancy useful? Results of an audit of current practice. Intern Med J 2015;45: 329–34. https://doi.org/10.1111/imj.12699.
- [127] Tang KL. Incidence, correlates, and chest radiographic yield of new lung cancer diagnosis in 3398 patients with pneumonia. Arch Intern Med 2011;171:1193. https://doi.org/10.1001/archinternmed.2011.155.
- [128] Mortensen EM, Copeland LA, Pugh MJ, Fine MJ, Nakashima B, Restrepo MI, et al. Diagnosis of pulmonary malignancy after hospitalization for pneumonia. Am J Med 2010;123:66–71. https://doi.org/10.1016/j.amjmed.2009.08.009.
- [129] Marrie TJ. Pneumonia and carcinoma of the lung. J Infect 1994;29:45–52. https://doi.org/10.1016/S0163-4453(94)95060-1.
- [130] Søyseth V, Benth JŠ, Stavem K. The association between hospitalisation for pneumonia and the diagnosis of lung cancer. Lung Cancer 2007;57:152–8. https://doi.org/10.1016/j.lungcan.2007.02.022.

Aurélien Dinh<sup>a,\*</sup>, François Barbier<sup>b</sup>, Jean-Pierre Bedos<sup>c</sup>, Mathieu Blot<sup>d</sup>, Vincent Cattoir<sup>e</sup>, Yann-Erick Claessens<sup>f</sup>, Xavier Duval<sup>g</sup>, Pierre Fillâtre<sup>h</sup>, Maxime Gautier<sup>i</sup>, Yann Guegan<sup>j</sup>, Sophie Jarraud<sup>k</sup>, Alban Le Monnier<sup>l</sup>, David Lebeaux<sup>m</sup>, Paul Loubet<sup>n</sup>, Constance de Margerie<sup>o</sup>, Philippe Serayet<sup>p</sup>, Yacine Tandjaoui-Lambotte<sup>q,r</sup>, Emmanuelle Varon<sup>s</sup>,

Yves Welker<sup>t</sup>, Damien Basille<sup>r,t,u,v</sup>

<sup>a</sup> Maladies infectieuses AP-HP Raymond-Poincaré-Ambroise-Paré Boulogne-Billancourt France

<sup>b</sup> Médecine intensive réanimation CHU Orléans France <sup>c</sup> Médecine intensive réanimation CH André Mignot-Versailles Le Chesnay France

d Maladies infectieuses CHU Dijon France

<sup>e</sup> Microbiologie CHU Rennes France

<sup>f</sup> Médecine d'urgence CH Princesse Grace-Monaco Monaco

<sup>g</sup> Maladies infectieuses AP-HP Bichat Paris France

<sup>h</sup> Médecine intensive réanimation CH Saint Brieuc France

<sup>i</sup> Médecine d'urgence CH Simone Veil-Eaubonne France

<sup>j</sup> Médecine générale Lanrivoare France

k Microbiologie HCL Lyon France

<sup>1</sup> Microbiologie Hôpital St Joseph-Paris Marie Lannelongue Paris France <sup>m</sup> Maladies infectieuses AP-HP St Louis-Lariboisière Paris France <sup>n</sup> Maladies infectieuses CHU Nîmes France

o Radiologie AP-HP Saint Louis Paris France

<sup>p</sup> Médecine générale Remoulins France

<sup>q</sup> Pneumologie-Maladies infectieuses CH Saint Denis France

# ARTICLE IN PRESS

Guidelines Infectious Diseases Now xxx (xxxxx) xxx

<sup>r</sup> GREPI groupe de recherche et d'enseignement en pneumo-infectiologie — Société de Pneumologie de Langue Française Paris France <sup>s</sup> Microbiologie Centre Hospitalier Inter Communal-Créteil France <sup>t</sup> Maladies infectieuses CH Poissy France <sup>u</sup> Pneumologie CHU Amiens-Picardie France v G-ECHO groupe échographie thoracique du pneumologue - Société de Pneumologie de Langue Française Paris France

\* Corresponding author. *E-mail address:* aurelien.dinh@aphp.fr (A. Dinh).