GUIDELINES FOR THE MANAGEMENT OF ADULT LOWER RESPIRATORY TRACT INFECTIONS

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Publications

• Eur Respir J 2005; 26: 1138-1180

• Supplemental Information: Appendices 1-3
  www.ersnet.org/guidelines or www.escmid.org
  – Epidemiology, microbiology, risk factors
  – Antimicrobial pharmacodynamics/pharmacokinetics
  – Tables of evidence grading
Methods

- designed specific LRTI search filter
- systematic literature search 1966 – December 2002
- critically appraised publications
- Evidence graded
- Recommendations developed and graded according to standard criteria
GRADES OF RECOMMENDATIONS (RANGING FROM A1 TO C4)

A Consistent evidence -> Clear outcome
B Inconsistent evidence -> Unclear outcome
C Insufficient evidence -> Consensus

SUFFIX FOR RECOMMENDATION GRADES
FOR PREVENTIVE AND THERAPEUTIC
INTERVENTION STUDIES (INCL HARM)
1 Systematic Review (SR) or Meta-Analysis (MA) of RCTs
2 1 RCT, or >1 RCT but no SR or MA
3 1 cohort study, or >1 cohort study but no SR or MA
4 Other

FOR DIAGNOSTIC, PROGNOSTIC, AETIOLOGIC
AND OTHER TYPES OF STUDIES
1 SR or MA of cohort studies
2 1 cohort study, or >1 cohort study but no SR or MA
3 Other

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MANAGEMENT OUTSIDE HOSPITAL

DIAGNOSIS

WHEN SHOULD ASPIRATION PNEUMONIA BE CONSIDERED?
In patients with difficulties with swallowing who show signs of an acute LRTI. In these patients a chest X-ray should be performed. [C3]

WHEN SHOULD CARDIAC FAILURE BE CONSIDERED?
In patients above 65, with either orthopnoea, displaced apex beat and/or a history of myocardial infarction. [C3]

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DIAGNOSIS

WHEN SHOULD PULMONARY EMBOLISM BE CONSIDERED?
In patients with one of the following characteristics: a history of DVT or pulmonary embolism, immobilization in past 4 weeks, or malignant disease [C3]

WHEN SHOULD CHRONIC AIRWAY DISEASE BE CONSIDERED?
In patients with at least two of the following: wheezing, prolonged expiration, a smoking history, and symptoms of allergy, lung-function tests should be considered to assess the presence of chronic lung disease. [C3]
DIAGNOSIS

HOW TO DIFFERENTIATE BETWEEN PNEUMONIA AND OTHER RESPIRATORY TRACT INFECTIONS?
A patient should be suspected of having pneumonia when the following signs and symptoms are present:

an acute cough and one of the following:
new focal chest signs,
dyspnoea,
tachypnoea,
fever > 4days.

If pneumonia is suspected, a chest X-ray should be performed to confirm the diagnosis. [C1]
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DIAGNOSIS

SHOULD THE PRIMARY CARE PHYSICIAN TEST FOR A POSSIBLE MICROBIOLOGICAL AETIOLOGY OF LRTI?

Microbiological investigations are not usually recommended in primary care.[C1 – C3]
TREATMENT

SHOULD SYMPTOMATIC ACUTE COUGH BE TREATED?
Both dextromethorphan and codeine can be prescribed in patients with a dry and bothersome cough. [C1]

Expectorant, mucolytics, antihistamines and bronchodilators should not be prescribed in acute LRTI in primary care. [A1]
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TREATMENT

WHEN SHOULD ANTIBIOTIC TREATMENT BE CONSIDERED IN PATIENTS WITH LRTI?

- Suspected or definite pneumonia
- selected exacerbations of COPD
- age > 75 years and fever
- cardiac failure
- insulin-dependent diabetes mellitus
- a serious neurological disorder (stroke etc)
  [C2]

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WHAT ARE THE INDICATIONS FOR ANTIBIOTIC TREATMENT OF EXACERBATIONS OF CHRONIC OBSTRUCTIVE LUNG DISEASE (COPD)?

An antibiotic should be given in exacerbations of COPD in patients with all three of the following symptoms: increased dyspnoea, sputum volume and sputum purulence.

In addition antibiotics should be considered for exacerbations in patients with severe COPD. [C1]
TREATMENT

WHICH ANTIBIOTICS SHOULD BE USED IN PATIENTS WITH LRTI?

Tetracycline and amoxicillin are antibiotics of first choice.

In case of hypersensitivity a newer macrolide like azithromycin, roxithromycin or clarithromycin is a good alternative in countries with low pneumococcal macrolide resistance.

National/Local resistance rates should be considered when choosing a particular antibiotic. When there are clinically relevant bacterial resistance rates against all first choice agents, treatment with levofloxacin or moxifloxacin may be considered. [C4]
TREATMENT

IS ANTIVIRAL TREATMENT USEFUL IN PATIENTS WITH LRTI?

The empirical use of antiviral treatment in patients suspected of having influenza is usually not recommended [B1].

Only in high risk patients who have typical influenza symptoms (fever, muscle ache, general malaise and respiratory tract infection), for less than two days, and during a known influenza epidemic can antiviral treatment be considered. [C1]
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TREATMENT

HOW SHOULD PATIENTS WITH LRTI BE MONITORED?
A patient should be advised to return if the symptoms take longer than three weeks to disappear.

Clinical effect of antibiotic treatment should be expected within three days and patients should be instructed to contact their doctor if this effect is not noticeable. Seriously ill patients, i.e. having at least two of the following symptoms/characteristics:
• High fever
• Tachypnoea
• Dyspnoea
• Relevant comorbidity
• Age over 65 years

All patients or persons in their environment should be advised to contact their doctor again if fever exceeds 4 days, dyspnoea gets worse, patients stop drinking or consciousness is decreasing. [C3]
COMMUNITY-ACQUIRED PNEUMONIA

WHO SHOULD BE ADMITTED TO HOSPITAL?

The decision to hospitalise remains a clinical decision.

However, this decision should be validated against at least one objective tool of risk assessment. Both the Pneumonia Severity Index (PSI) and the CURB index are valid tools in this regard. In patients meeting a PSI of IV and V and/or a CURB of two or more, hospitalisation should be seriously considered. [A3]

Additional requirements of patient management as well as social factors not related to pneumonia severity must be considered as well.
COMMUNITY-ACQUIRED PNEUMONIA

WHO SHOULD BE CONSIDERED FOR ICU ADMISSION?

Criteria of acute respiratory failure, severe sepsis or septic shock and radiographic extension of infiltrates should prompt consideration of the admission to the ICU or an intermediate care unit.

The presence of at least two of systolic blood pressure < 90 mmHg, severe respiratory failure (PaO2/FIO2 < 250), Involvement of > 2 lobes on chest radiograph (multilobar involvement)

or one of requirement for mechanical ventilation or requirement of vasopressors > 4 hours (septic shock)

indicates severe CAP and can be used to guide ICU referral. [A3]
COMMUNITY-ACQUIRED PNEUMONIA

WHAT LABORATORY STUDIES SHOULD BE PERFORMED?

The amount of laboratory and microbiological work-up should be determined by the severity of pneumonia. [A3]

WHAT IS THE VALUE OF BLOOD CULTURES IN THE DIAGNOSIS?

Blood cultures should be performed in all patients with CAP who require hospitalization. [A3]
COMMUNITY-ACQUIRED PNEUMONIA

WHAT OTHER INVASIVE TECHNIQUES FOR NORMALLY STERILE SPECIMENS CAN BE USEFUL IN THE LABORATORY DIAGNOSIS OF PNEUMONIA?

a) Diagnostic thoracentesis should be performed when a significant pleural effusion is present. [A3]

b) Because of the inherent potential adverse effects, Trans Thoracic Needle Aspiration can be considered ONLY on an individual basis for some severely ill patients, with a focal infiltrate in whom less invasive measures have been non diagnostic.[A3]

c) Bronchoscopic Protected Specimen Brush (PSB) and Bronchoalveolar Lavage (BAL): BAL may be the preferred technique in non-resolving pneumonia. [A3] Bronchoscopic sampling of the lower respiratory tract can be considered in intubated patients and selected non-intubated patients, where gas exchange status allows. [A3]
MANAGEMENT INSIDE HOSPITAL

COMMUNITY-ACQUIRED PNEUMONIA

WHAT IS THE VALUE OF SPUTUM EXAMINATION?

Gram stain is recommended when a purulent sputum sample can be obtained from patients with CAP and is processed timely. [A3]

A culture from a purulent sputum specimen of a bacterial species compatible with the morphotype observed in the Gram stain, that is processed correctly is worthwhile for confirmation of the species identification and antibiotic susceptibility testing. [B3]

WHAT CAN ANTIGEN TESTS OFFER IN THE DIAGNOSIS OF CAP?

*L pneumophila* serogroup 1 antigen detection in urine is recommended for patients with severe CAP and in other patients where this infection is clinically or epidemiologically suspected. [A3].

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COMMUNITY-ACQUIRED PNEUMONIA

WHAT CAN SEROLOGIC TESTS OFFER IN THE DIAGNOSIS OF PNEUMONIA?
Serologic tests for the management of the individual patient with LRTI are not recommended. [A3]
Serology for infections caused by *M. pneumoniam*, *C. pneumoniae* and Legionella is more useful in epidemiologic studies than in the routine management of the individual patient. [A3]

ARE AMPLIFICATION TESTS USEFUL FOR THE DIAGNOSIS OF LRTI?
Application of molecular tests for the detection of influenza and RSV may be considered during the winter season and for the detection of atypical pathogens provided the tests are validated and the results can be obtained sufficiently rapidly to be therapeutically relevant. [A3]
COMMUNITY-ACQUIRED PNEUMONIA

WHAT CLASSIFICATION SHOULD BE USED FOR TREATMENT?
Antimicrobial treatment has to be empiric and should follow an approach according to the individual risk of mortality. The assessment of severity according to mild, moderate and severe pneumonia implies a decision about the most appropriate treatment setting (ambulatory, hospital ward, ICU). [A4]

Antimicrobial treatment should be initiated as soon as possible. [A3]

The guidance of empiric initial antimicrobial treatment should follow: general patterns of expected pathogens according to pneumonia severity and additional risk factors, regional and local patterns of microbial resistance and considerations of tolerability and toxicity of antimicrobial agents in the individual patient.
## MANAGEMENT INSIDE HOSPITAL

### TREATMENT OPTIONS FOR HOSPITALIZED PATIENTS WITH MODERATE COMMUNITY-ACQUIRED PNEUMONIA (IN NO SPECIAL ORDER) [C4]

<table>
<thead>
<tr>
<th>PREFERRED (IN REGIONS WITH LOW PNEUMOCOCCAL RESISTANCE RATES)</th>
<th>ALTERNATIVE (IN REGIONS WITH INCREASED PNEUMOCOCCAL RESISTANCE RATES OR MAJOR? INTOLERANCE TO PREFERRED DRUGS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G ± macrolide</td>
<td>Levofloxacin #</td>
</tr>
<tr>
<td>Aminopenicillin ± macrolide *#</td>
<td>Moxifloxacin §§</td>
</tr>
<tr>
<td>Aminopenicillin / β-lactamase inhibitor #</td>
<td></td>
</tr>
<tr>
<td>± macrolide *</td>
<td></td>
</tr>
<tr>
<td>Non-antipseudomonal cephalosporin II or III ± macrolide *</td>
<td></td>
</tr>
</tbody>
</table>

# Can be applied as sequential treatment using the same drug
* new macrolides preferred to erythromycin
§ within the fluoroquinolones, moxifloxacin has the highest antipneumococcal activity
Experience with ketolides is limited but they may offer an alternative when oral treatment is adequate
For recommended dosages see main document Appendix A3.

GUIDELINES FOR THE MANAGEMENT OF ADULT LOWER RESPIRATORY TRACT INFECTIONS, ERJ 2005
**MANAGEMENT INSIDE HOSPITAL**

**TREATMENT OPTIONS FOR PATIENTS WITH SEVERE COMMUNITY-ACQUIRED PNEUMONIA [C4]**

<table>
<thead>
<tr>
<th>NO RISK FACTORS FOR <em>P. aeruginosa</em></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(see main document Section 2, Table 2.1.7.)</td>
<td></td>
</tr>
<tr>
<td>Non-antipseudomonal cephalosporin III + macrolide *</td>
<td></td>
</tr>
<tr>
<td>or</td>
<td></td>
</tr>
<tr>
<td>Non-antipseudomonal cephalosporin III + (moxifloxacin or levofloxacin)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>RISK FACTORS FOR <em>P. aeruginosa</em></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(see main document Section 2, Table 2.1.7.)</td>
<td></td>
</tr>
<tr>
<td>Antipseudomonal cephalosporin ** or acylureidopenicillin / β-lactamaseinhibitor or carbapenem + ciprofloxacin</td>
<td></td>
</tr>
</tbody>
</table>

* new macrolides preferred to erythromycin
** Cefepime, not ceftazidime
For recommended dosages see main document Appendix A3.

**GUIDELINES FOR THE MANAGEMENT OF ADULT LOWER RESPIRATORY TRACT INFECTIONS, ERJ 2005**
WHAT SHOULD BE THE DURATION OF TREATMENT?

The appropriate duration of antimicrobial treatment has not been settled. In comparative studies, the usual duration of treatment is around seven to ten days. Intracellular pathogens such as Legionella spp. should be treated for at least 14 days [C4].
COMMUNITY-ACQUIRED PNEUMONIA

WHEN SHOULD IV BE USED AND WHEN SHOULD THE SWITCH TO ORAL OCCUR?

In mild pneumonia, treatment can be applied orally from the beginning. [A3] In patients with moderate pneumonia, sequential treatment should be considered in all patients except the most severely ill.

The optimal time to switch to oral treatment is also unknown; it seems reasonable to target this decision according to the resolution of the most prominent clinical features at admission.[A3]
Low molecular heparin is indicated in patients with acute respiratory failure. [A3].

The use of noninvasive ventilation is not yet standard of care but may be considered particularly in patients with COPD [B3].

The treatment of severe sepsis and septic shock is confined to supportive measures [A3].

Steroids have no place in the treatment of pneumonia unless septic shock is present [A3].
Response to treatment should be monitored by simple clinical criteria including body temperature, respiratory and haemodynamic parameters. The same parameters should be applied to judge the ability of hospital discharge [A3].

Complete response including radiographic resolution requires longer time periods. Discharge decisions should be based on robust markers of clinical stabilization [A3].
COMMUNITY-ACQUIRED PNEUMONIA

HOW SHOULD THE NONRESPONDING PATIENT BE ASSESSED?

Two types of treatment failures, nonresponding pneumonia and slowly resolving pneumonia should be differentiated [A3].

The evaluation of nonresponding pneumonia depends on the clinical condition; in unstable patients, full reinvestigation followed by a second empiric antimicrobial treatment regimen is recommended. The latter may be withheld in stable patients.

Slowly resolving pneumonia should be reinvestigated according to clinical needs according to the condition of the patient and his individual risk factors [C3].
SHOULD INFLUENZA VACCINE BE USED TO PREVENT LRTI?

For influenza vaccination the following are recommended:

Influenza vaccine should be given yearly to persons at increased risk for complications due to influenza [A1]. Vaccination is recommended for immunocompetent adults belonging to one, or more, of the following categories; age $\geq 65$ years, institutionalisation, chronic cardiac diseases, chronic pulmonary diseases, diabetes mellitus, chronic renal diseases, hemoglobinopathies, and women who will be in the second or third trimester of pregnancy during the influenza season.

Repeated vaccinations are safe and do not lead to a decreased immune response [B1]. In adults inactivated, rather than live attenuated, vaccine is recommended [A1].

In health care personnel we recommend yearly vaccination, especially in settings where elderly persons or other high risk groups are treated [B2].
SHOULD PNEUMOCOCCAL VACCINE BE USED TO PREVENT LRTI?

For pneumococcal vaccination the following are recommended
The evidence for vaccination with the 23-valent polysaccharide pneumococcal vaccine is less strong than that for influenza vaccination, but we recommend the vaccine to be given to all adult persons at risk for pneumococcal disease [B4].

Risk factors for pneumococcal disease are age ≥ 65 years, institutionalisation, dementia, seizure disorders, congestive heart failure, cerebrovascular disease, chronic obstructive pulmonary disease, history of a previous pneumonia, chronic liver disease, diabetes mellitus, functional or anatomic asplenia, and chronic cerebrospinal fluid leakage [B3]. Although smoking seems to be a significant risk factor in otherwise healthy younger adults measures aimed at reducing smoking and exposure to environmental tobacco smoke should be preferred in this group.

Revaccination, once, can be considered in the elderly, 5-10 years after primary vaccination [B3]
PREVENTION BY VACCINATION

WHAT IS THE BEST WAY TO IMPLEMENT INFLUENZA AND PNEUMOCOCCAL VACCINATION POLICIES?

Active interventions to enhance vaccination with either, or both vaccines is effective and needed to achieve an adequate vaccination coverage of the targeted population [B1]
<table>
<thead>
<tr>
<th>SETTING</th>
<th>LRTI TYPE</th>
<th>SEVERITY/SUB-GROUP</th>
<th>PREFERRED</th>
<th>ALTERNATIVE*</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMMUNITY</td>
<td>LRTI@</td>
<td>ALL</td>
<td>AMOXICILLIN or TETRACYCLINE**</td>
<td>CO-AMOXICLAV MACROLIDE*** LEVOFLOXACIN MOXIFLOXACIN</td>
</tr>
<tr>
<td>HOSPITAL</td>
<td>COPD@</td>
<td>MILD</td>
<td>AMOXICILLIN or TETRACYCLINE**</td>
<td>CO-AMOXICLAV MACROLIDE*** LEVOFLOXACIN MOXIFLOXACIN</td>
</tr>
<tr>
<td>COPD</td>
<td>MODERATE / SEVERE</td>
<td>CO-AMOXICLAV</td>
<td>LEVOFLOXACIN MOXIFLOXACIN</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>+ RISK FACTORS FOR <em>Ps aeruginosa</em></td>
<td>CIPROFLOXACIN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAP</td>
<td>NON-SEVERE</td>
<td>PENICILLIN G ± MACROLIDE*** •AMINOPENICILLIN ± MACROLIDE*** •CO-AMOXICLAV ± MACROLIDE*** •2nd OR 3rd CEPHALOSPORIN ± MACROLIDE***</td>
<td>LEVOFLOXACIN MOXIFLOXACIN</td>
<td></td>
</tr>
<tr>
<td>CAP</td>
<td>SEVERE</td>
<td>3rd CEPHALOSPORIN + MACROLIDE***</td>
<td>3rd CEPHALOSPORIN + (LEVOFLOXACIN OR MOXIFLOXACIN)</td>
<td></td>
</tr>
<tr>
<td>CAP</td>
<td>SEVERE + RISK FACTORS FOR <em>Ps aeruginosa</em></td>
<td>ANTI-PSUEDOMONAL CEPHALOSPORIN + CIPROFLOXACIN</td>
<td>ACYLUREIDOPENICILLIN/β-LACTAMASE INHIBITOR + CIPROFLOXACIN or CARBAPENEM + CIPROFLOXACIN</td>
<td></td>
</tr>
<tr>
<td>BRONCHIECT ASIS</td>
<td>NO RISK ACTORS FOR <em>Ps aeruginosa</em></td>
<td>AMOXICILLIN CLAVULANATE MOXIFLOXACIN LEVOFLOXACIN</td>
<td></td>
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