

Management of Community Acquired Pneumonia (CAP) in Adults (ERS/ESCMID guidelines¹ adapted for Switzerland)

Appendix 1, Appendix 2, Appendix 3, Appendix References

(Appendices from ERS/ESCMID guidelines¹)

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Introduction

In May 2005, the European Respiratory Society (ERS) in collaboration with the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) published new guidelines for the management of adult lower respiratory tract infections (LRTI)¹. These guidelines are the result of an evidence-based review of more than 4'000 publications between 1966 and December 2002.

The impact of guidelines depends on their incorporation into the daily clinical practice and on the rapid clinical access at the bedside. In addition to the published and attached full-text guidelines a group of experts of the Swiss Society of Infectious Diseases presents a summary which focuses on the management of community-acquired pneumonia (CAP) outside and inside the hospital including tables and comments.

In the Swiss recommendations we considered our local prevalence of antibiotic resistance and – since the European guidelines only included publications up to December 2002 – discussed briefly new data available since 2003 addressing a shortening of the duration of antibiotic therapy.

1. Management outside hospital (see p. 1144 -1147 of *ref. 1*)

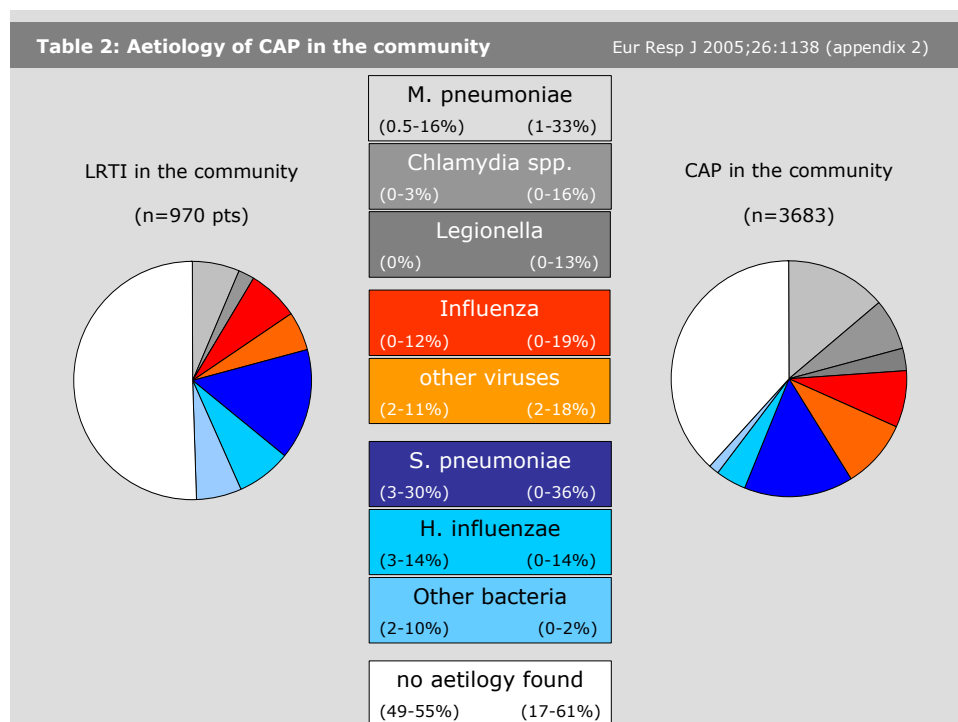
1.1 Diagnosis

- Pneumonia should be suspected, if a patient has an acute cough and one of the following signs:
 - new focal chest signs
 - dyspnoea
 - tachypnoea
 - fever lasting more than 4 days
- Chest-radiograph is recommended in this setting.
- See also *table 1 with definitions* of upper and lower respiratory tract infections.
- Aspiration pneumonia should be considered in patients with difficulties to swallow and who show signs of an acute LRTI. Chest radiograph is recommended in this setting.

Table 1: Definitions		Eur Resp J 2005;26:1138
Lower Respiratory tract infection (LRTI)	<input type="checkbox"/> acute illness (≤ 21 days) with cough as main symptom plus <input type="checkbox"/> ≥ 1 LRT-symptom: <input type="checkbox"/> sputum production <input type="checkbox"/> dyspnoea <input type="checkbox"/> wheezing <input type="checkbox"/> chest pain <input type="checkbox"/> no alternative explanation (e.g. sinusitis, asthma)	
Acute Bronchitis	<input type="checkbox"/> acute illness in a patient without chronic lung disease plus <input type="checkbox"/> symptoms of LRTI: <input type="checkbox"/> cough (productive / nonproductive) <input type="checkbox"/> dyspnoea <input type="checkbox"/> wheezing <input type="checkbox"/> chest pain <input type="checkbox"/> no signs & symptoms of pneumonia (s. below) <input type="checkbox"/> no alternative explanation (e.g. sinusitis, asthma)	
Influenza	<input type="checkbox"/> acute illness, usually with fever plus <input type="checkbox"/> ≥ 1 symptoms: <input type="checkbox"/> headache <input type="checkbox"/> myalgia <input type="checkbox"/> cough <input type="checkbox"/> sore throat <input type="checkbox"/> no signs & symptoms of pneumonia (s. below) <input type="checkbox"/> no alternative explanation (e.g. sinusitis, asthma)	
Community-acquired pneumonia (CAP)	<input type="checkbox"/> acute illness with cough plus ≥ 1 symptom: <input type="checkbox"/> new focal chest signs <input type="checkbox"/> fever > 4 days <input type="checkbox"/> dyspnoea / tachypnoae <input type="checkbox"/> no other obvious cause <input type="checkbox"/> definitive CAP, if supported by new infiltrate on chest-Xray	
Acute exacerbation of COPD	<input type="checkbox"/> worsening dyspnoea, cough and/or sputum sufficient to warrant a change in management in a patient with COPD	

1.2 Microbiological investigations

- Microbiological investigations are usually not recommended in primary care.
- Assessment of the microbiological aetiology may be useful only in certain subgroups with severe co-morbidity and a high probability of unusual microorganism or resistance problems or in immunocompromised patients.
- The most common causative organisms of LRTI and CAP in the community are summarized in table 2.



1.3 Treatment

- Symptomatic treatment:
 - A dry and bothersome acute cough can be treated with dextrometorphan or codein.
 - Expectorants, mucolytics, antihistamines and bronchodilators should not be prescribed in acute LRTI in primary care.

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- Antibiotic treatment in LRTI should be considered in the following situations:
 - Suspected or definite pneumonia (see table 1: definitions)
 - Additionally in selected patients with exacerbation of COPD:
 - All of three “Anthonisen” criteria: increased dyspnoea; increased sputum volume and increased sputum purulence
 - Patients with severe COPD (GOLD IV)
 - Age > 75 years and fever
 - Cardiac failure
 - Insulin-dependent diabetes mellitus
 - Serious neurological disorder (stroke etc)

GOLD* - classification of COPD

(*Global Initiative for Chronic Obstructive Lung Disease; <http://www.goldcopd.com>)

COPD: severity

Stadium	FEV1 (% predicted)	symptoms*	comment
0 (at risk)	≥ 80	+	normal lung function chronic cough with sputum
I (mild)	≥ 80	- / +	with/without chronic cough & sputum
II (moderate)	50-79	- / +	with/without chronic cough & sputum
III (severe)	30-49	- / ++	with/without chronic cough & sputum
IV (very severe)	<30 or <50 and	- / + or +++	pO ₂ < 8.0 kPa

* symptoms

-	no symptoms
- to +	variable
+	mild to moderate
++	limited to exertion
+++	with limitation of daily activities

- Recommended empiric antibiotic treatment in outpatients with CAP (s. table 3)
 - Empiric antibiotic treatment should be directed against the most common pathogens, *S. pneumoniae* and *H. influenzae* (see table 2).
Epidemiological factors, travel history and exposure (f.e. to animals) need to be taken into account.

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Table 3: CAP: empirical therapy		adapted for Switzerland from Eur Resp J 2005;26:1138	
Assessment	First Choice	Alternative Therapy	
Mild (ambulatory)	AmoxiClav 3x625 mg p.os <i>or</i> Doxycycline* 2x100 mg p.os	Macrolide [§] Respiratory Quinolone [¥]	
Moderate (hospital ward) (combination only in high-risk patients)	AmoxiClav 3x1.2 g i.v. +/- Clarithro 2x500 mg p.os	Respiratory Quinolone [¥]	
	Ceftriaxone 1x2 g i.v. +/- Clarithro 2x500 mg p.os		
Severe (ICU-admission)	Ceftriaxone 1x2 g i.v. <u>plus</u> Clarithromycine 2x500 mg p.os	Levofloxacin 2x500 mg i.v.	
Severe and risk of <i>P. aeruginosa</i>	Pip/Taz 3x4.5 g i.v. <u>plus</u> Ciprofloxacin 2x750 mg p.os	Carbapenem [‡] <u>plus</u> Ciprofloxacin 2x750 mg p.os	
	Cefepime 3x2 g i.v. <u>plus</u> Ciprofloxacin 2x750 mg p.os		

* covers also „atypical“ pathogens like *Mycoplasma pneumoniae* and *Chlamydia* spp.
[§] Clarithromycine 2x500 mg p.os *or* Azithromycine 1x500 mg p.os AmoxiClav = Amoxicilline/Clavulanate
[¥] Levofloxacin 1(-2)x500 mg p.os / i.v. *or* Moxifloxacin 1x400 mg p.os Clarithro = Clarithromycine
[‡] Meropenem 3x2 g i.v. *or* Imipenem 4x500 mg i.v. Pip/Taz = Piperacilline/Tazobactam

▪ Anti-viral treatment

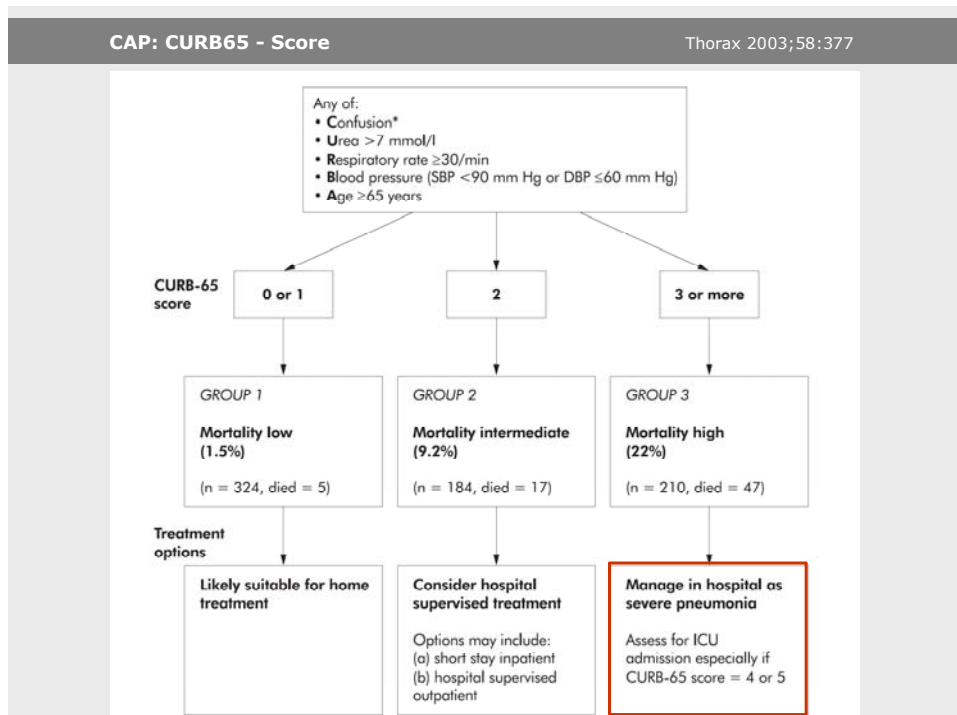
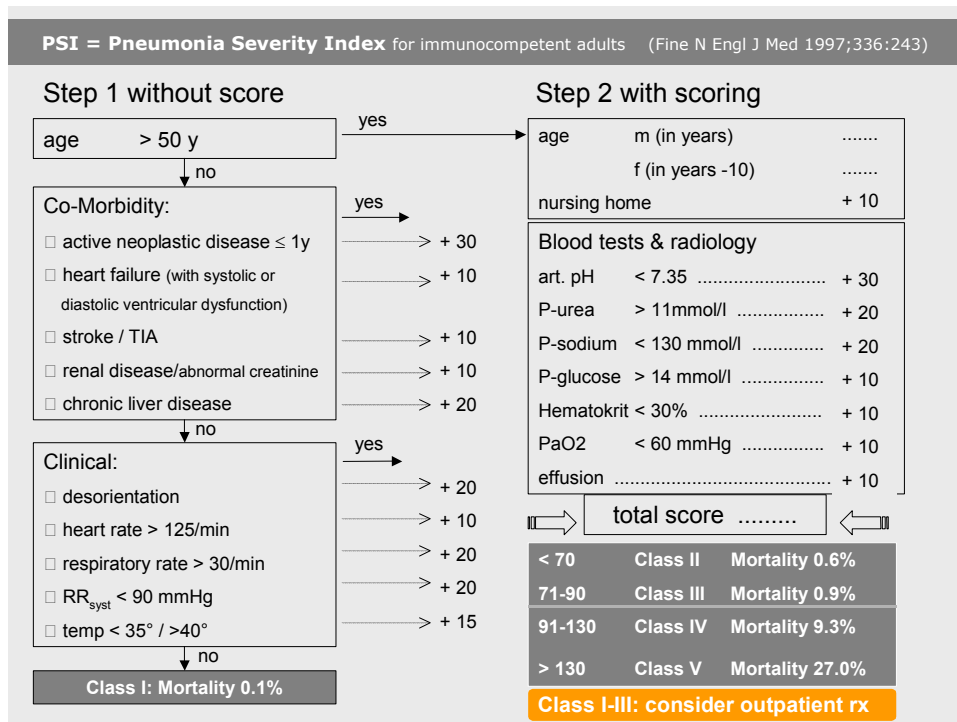
- The empirical use of anti-viral treatment in patients suspected of suffering from influenza is usually not recommended. Anti-viral therapy (f.e. Oseltamivir 2x75 mg x 5 days) can be considered in the influenza season in high-risk patients (f.e. patients after transplantations) with influenza symptoms (see [table 1: definitions](#)) for < 2 days. Keep in mind that Oseltamivir has not been assessed sufficiently in immunocompromised hosts.

1.4 Monitoring

- There are no studies assessing what would be the best follow up procedure in the primary care setting
- Recommendations:
 - Advise patients to return if fever exceeds 4 days, dyspnoea gets worse, patients stop drinking or consciousness decreases.
 - Plan a second visit in advance 2 days after the first visit in more seriously ill patients with 2 of the following characteristics: high fever; tachypnoea; dyspnoea; relevant co-morbidity; age > 65 years.
 - In case of antibiotic treatment: Advise patients to return if clinical signs do not improve within 3 days.
 - Advise patients to return if symptoms take >3 weeks to disappear.

2. Decision outpatient versus inpatient treatment (see page 1147-1148 of *ref. 1*; see also *table 1: definitions*)

The decision to hospitalise remains a clinical decision. However, the decision should be validated against at least one objective tool of risk assessment (*Pneumonia severity index = PSI* or *CURB65- score*). In patients with a PSI of IV and V or a CURB-score ≥ 2 , hospitalisation should be seriously considered.

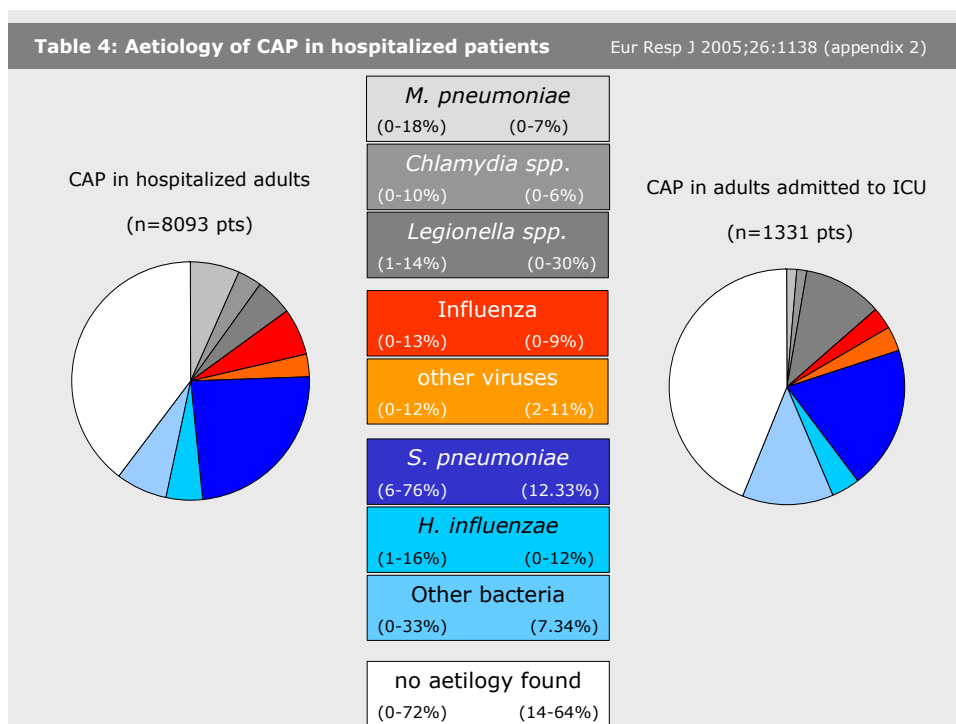


3. Management inside hospital (see p. 1147-1158 of [ref.1](#))

3.1 Diagnosis

- Pneumonia should be suspected, if a patient has an acute cough and one of the following signs:
 - new focal chest signs
 - dyspnoea
 - tachypnoea
 - fever lasting more than 4 days
- Chest-radiograph is recommended in this setting.

3.2 Laboratory Studies recommended for patients with CAP who require hospitalisation (see [table 4](#) for causative organisms).



- Arterial blood gas or pulse oximetry determination and basic blood tests (red & differential white blood cell count, creatinine, urea nitrogen, aminotransferases, sodium, potassium, C-reactive protein)
- Blood cultures in all patients who require hospitalisation
- Sputum gram stain and culture, if a high quality sputum (≤ 10 squamous epithelial cells and ≥ 25 PMN / low power (100x) field) can be obtained.
- Urine-antigen-testing for *L. pneumophila* serogroup 1 in patients with severe CAP or if this infection is clinically or epidemiologically suspected.

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- Urine-antigen-testing for *S. pneumoniae* in high-risk patients, if a sputum sample is not conclusive or not available² (ERS/ESCMID-guidelines do not recommend urine-antigen-testing for *S. pneumoniae* unless more studies are available).
- Serological tests are not recommended for an individual patient and are more useful for epidemiological studies (e.g. *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and *Legionella* spp.).
- Amplification tests for the detection of influenza and respiratory syncytial virus during the winter season and for atypical pathogens in severe cases (*Legionella* spp., *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*) may be considered, if results can be obtained sufficiently rapid to be therapeutically relevant.
- Diagnostic puncture (see table 5) in case of a significant pleural effusion (> 10 mm depth in ultrasonography)
- Bronchoalveolar lavage (BAL) or bronchoscopic protected specimen brush in nonresolving pneumonia
- Bronchoscopic sampling in intubated patients

Table 5: Interpretation of pleural effusion:

N Engl J Med 2002;346:1971

aspect	straw-yellow (transudate > exsudate), yellow-green (collagenosis), dark-green (billooma), brown (hematoma, amebic abscess (odorless)), bloody (tumor, asbestosis, post-cardiotomy, lung-infarction), whitish (chylothorax), purulent odor (empyema, anaerobic bacteria),
Light-criteria: Transudate vs. Exsudate	exsudate propable, if 1.) protein ratio pleura/serum >0.5 or 2.) LDH ratio pleura/serum > 0.6 or 3.) LDH pleura > 2/3 upper normal limit serum
Total protein (TP)	<30 g/l: most likely transudate (f.e. cardiac failure, liver-cirrhosis, pulmonary embolus) „pseudoexsudat“: albumin-gradient serum-pleura >12 g/l under diuretic therapy >30 g/l: exsudat (in case of TB often >40 g/l) (pneumonia, tumor, pulmonary embolus) >70 g/l: M. Waldenström / multiple myeloma
LDH	>1000 U/l: Empyema, collagenosis, malignoma (level correlates with the extend of the inflammation)
pH normal: pH 7.60	pH <7.2: bacterial infection (rarely in case of malignoma); Drainage if pH <7.0 cave: check venous pH in case of striking pleural pH
Glucose	<3.3 mmol/l: Empyema, collagenosis, malignoma, tuberculosis
Differential cell count	>50 x10 ⁹ /l: suspect empyema >10 x10 ⁹ /l: parapneumonic effusion <5 x10 ⁹ /l: tuberculosis, malignoma >50% PMN acute inflammatory (pneumonia, pulmonary embolism, pancreatitis) Lymphocytosis: tuberculosis; malignoma (eventually Dresslers-syndrom) Eosinophilia >10% most often blood or air in pleural space; rarely drugs, asbest, Churg-Strauss, TB Malignant cells in 60-70% of malignomas, depending on amount of fluid investigated
specials	Amylase pleura/serum >1: pancreatitis, malignoma, esophageal perforation elevated lipid level: chylothorax.

3.3 Antimicrobial treatment

- Empiric antimicrobial treatment should be initiated as soon as possible.
- A severity assessment according to the individual risk of mortality should be performed. The assessment to mild (ambulant), moderate (hospital ward) and severe pneumonia (intensive care unit) implies a decision regarding the most appropriate treatment setting.
- The empiric therapy should also consider general and local patterns of resistance of the leading pathogens and considerations of tolerability and toxicity in the individual patient.
- Additional risk factors (epidemiological factors, travel history and exposure) need to be taken into account (ref 1 p.1155; table 12).
- Empiric treatment options are shown in table 3.
- Recommended treatment options for specific pathogens are shown in table 6.

Table 6: treatment for specific pathogens in CAP modified from Eur Resp J 2005;26:1138

Pathogen	Comment	Recommended Therapy
<i>S. pneumoniae</i>	susceptible (MIC* < 0.1 mg/dl)	Penicilline, Amoxicilline; Cefuroxime (in case of penicillind skin allergy); resp. Quinolone (in case of severe penicilline allergy)
	intermediate resistant (0.1 < MIC* ≤ 1 mg/dl)	High-dose Amoxicilline, 3° Cephalosporine, resp. Quinolone, Telithromycin
	highly resistant (MIC* ≥ 2 mg/dl)	resp. Quinolone, Vancomycine, Teicoplanin, Linezolid
<i>S. aureus</i>	MSSA	Flucloxacilline, 1° Cephalosporine, Clindamycine
	MRSA	Vancomycin, Teicoplanin +/- Rifampicine, Linezolid
<i>H. influenza</i>	ampicillin resistant	Amoxicilline/Clavulanate, resp. Quinolone
<i>M. pneumoniae</i>		Doxycycline, Macrolide, resp. Quinolone, Telithromycin
<i>Chl. pneumoniae</i>		Doxycycline, Macrolide, resp. Quinolone, Telithromycin
<i>Legionella</i> spp.		Macrolide, resp. Quinolone
<i>Coxiella burnetii</i>		Macrolide, resp. Quinolone

* MIC for penicilline

3.4 Intensive care unit (ICU) admission

- ICU admission should be considered in patients with severe CAP and/or:
 - Respiratory failure: Acute or severe (PaO₂/FiO₂ <250; oxygen saturation <90% with 6 l/min O₂)
 - Requirement for mechanical ventilation or vasopressors > 4h
 - Severe sepsis or septic shock
 - Radiographic extension of infiltrates (i.e. multilobar involvement)

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Chest 1992;101:1644	
SIRS (=systemic inflammatory response syndrome) if ≥ 2 of:	
<input type="checkbox"/> Heart rate	$>90/\text{min.}$ exception: patient with neg. chronotropic medication or pacemaker-rhythm
<input type="checkbox"/> Core temperature	$\geq 38.0^\circ\text{C}$ or $\leq 36.0^\circ\text{C}$
<input type="checkbox"/> Respiratory rate	$>20/\text{min.}$ or $\text{pCO}_2 < 4.25\text{ kPa}$ or mechanical ventilation
<input type="checkbox"/> White cell count	$\geq 12'000/\mu\text{l}$ or $\leq 4000/\mu\text{l}$ or $>10\%$ immature neutrophils
Sepsis	
<input type="checkbox"/> SIRS plus	known or suspected infection (cave: bacteremia is not essential)
Severe Sepsis (in-hospital-mortality 30%)	
<input type="checkbox"/> Sepsis plus	hypotension or organ dysfunction
<input type="checkbox"/> hypotension:	BP (mmHg): ≤ 90 or MAP ≤ 70 or decrease >40 from baseline for at least 1 hour despite adequate volume resuscitation
<input type="checkbox"/> organ dysfunction	<input type="checkbox"/> urine output $<0.5\text{ml/kg}$ for $\geq 1\text{h}$ or acute renal failure <input type="checkbox"/> $\text{PaO}_2/\text{FiO}_2 \leq 250$ (or ≤ 200 if lung is the only dysfunctional organ) <input type="checkbox"/> hepatic dysfunction (hyperbilirubinemia, transaminitis) <input type="checkbox"/> acute alteration in mental status (delirium) <input type="checkbox"/> $\text{pH} \leq 7.30$ or base deficit $>5\text{ mmol/l}$ and P-Lactate $\geq 1.5 \times$ upper limit of normal
Septic shock (in-hospital-mortality 50%)	
<input type="checkbox"/> Severe Sepsis	with persistent hypoperfusion or hypotension despite adequate fluid resuscitation

3.5 Duration of treatment

- The appropriate duration of antimicrobial treatment has not been settled.
- The usual duration is 7-10 days, intracellular pathogens (i.e. *Legionella* spp.) should be treated for at least 14 days.
- The trend is to shorten the duration of antibiotic therapy. Generally we recommend antibiotic treatment until the patient is afebrile for 3-5 days.
- Since 2003, several studies addressing shorter courses of therapy in selected patients were published (five days levofloxacin 750 mg/d in mild-to severe CAP³; three day regimen in mild-to-moderate CAP with substantially improvement after three days of intravenous amoxicillin therapy⁴). Shorter courses are not discussed in the ERS / ESCMID guidelines.

3.6 Switch from intravenous to oral treatment

- In patients with moderate to severe CAP, treatment should be started intravenously.
- The optimal time to switch to oral treatment is unknown. The ERS / ESCMID guidelines suggest to target this decision according to the resolution of the most prominent clinical features upon admission (i.e. resolution of fever).

3.7 Additional therapies

- Low molecular weight heparin in patients with acute respiratory failure.
- In patients with severe sepsis and septic shock, aggressive volume therapy (“*early goal-directed therapy*”), maintenance of glycemic control and low-dose steroids in patients with relative adrenal insufficiency (f.e. hydrocortone 3x100 mg i.v. after Synacthen®-test) are recommended.

3.8 Monitoring of CAP

- Response to therapy should be monitored by clinical criteria (temperature, respiratory and hemodynamic parameters). The same parameters should be applied to judge the possibility of hospital discharge.
- Complete response, including radiographic resolution, requires longer time periods.

3.9 Non-responding patients

- Treatment failures should be differentiated in non-responding pneumonia and slow resolving pneumonia.
- In case of non-responding pneumonia in an unstable patient, full reinvestigation (including BAL) followed by a second empiric antimicrobial treatment regimen is recommended.
- Slowly resolving pneumonia should be reinvestigated according to clinical needs (empyema?, abscess?) in relation to the condition and individual risk factors of the patient.

4. Prevention (see page 1164-1169 of ref.1)

4.1 Vaccination against influenza and *S. pneumoniae*

(see annually updated Swiss recommendations)

- In brief, annual influenza vaccination (inactivated vaccine) is recommended for all adults with ≥ 1 of the following:
 - age ≥ 65 y; institutionalisation; chronic cardiac, pulmonary or renal disease, diabetes, hemoglobinopathies; patients with immunosuppression; health care workers; females who will be in the 2° or 3° trimester of pregnancy during the influenza season.

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- The 23-valent polysaccharide pneumococcal vaccine is recommended for all adults at risk for pneumococcal disease:
 - age \geq 65y; institutionalisation; chronic cardiac, pulmonary, renal or liver disease; diabetes; functional or anatomic asplenia; HIV positive patients; dementia; seizures; chronic cerebrospinal fluid leakage
 - Consider revaccination after 5-10 years.

4.2 Preventive measures in unusual situations

- Prevention of influenza with anti-virals is only recommended for very high risk patients (e.g. lung transplant), i.e. if vaccination could not be given and can be considered in unusual situations like outbreaks within closed communities.
- Not recommended preventive measures are:
 - Oral immunisation with bacterial extracts or H. influenza oral vaccine
 - Prophylactic use of antibiotics or inhaled steroids or long-acting β 2-agonists to prevent LRTI in patients with chronic bronchitis or COPD
 - Treatment of upper respiratory tract infection with antibiotics will not prevent LRTI.
 - Regular use of oral mucolytics in patients with chronic bronchitis or COPD to prevent LRTI .

5. Literature

1. Woodhead M, Blasi F, Ewig S, et al. Guidelines for the management of adult lower respiratory tract infections. *Eur Respir J* 2005;26:1138-1180.
2. Roson B, Fernandez-Sabe N, Carratala J, et al. Contribution of a urinary antigen assay (Binax NOW) to the early diagnosis of pneumococcal pneumonia. *Clin Infect Dis* 2004;38:222-226.
3. Dunbar LM, Wunderink RG, Habib MP, et al. High-dose, short-course levofloxacin for community-acquired pneumonia: a new treatment paradigm. *Clin Infect Dis* 2003;37:752-760.
4. El Moussaoui R, De Borgie CA, Van den Broek P, 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;332:1355-1361.