Moderate and Severe CAP: Diagnosis and Management

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Pneumonia is a common clinical disorder with an estimated incidence of 12 cases per 1000 population per year. In healthy individuals, many microorganisms colonise the nasopharynx and oropharynx. Microaspiration of contaminated secretions can cause infections in the lower airways. The glottal refl exes, the presence of complement proteins and immunoglobulins, the secretion of peptides with antimicrobial activities, and the inhibition of bacteria binding all protect the lower airways.36 The healthy microbiota of the upper airway also exert protection eff ects by competing with pathogens for nutritional resources and interacting with cellular receptors. The use of broad-spectrum antibiotics can modify the microbiota and predispose to infection.[1]

Microbiological evaluations (figure 1) are recommended for higher-risk patients such as those with severe community-acquired pneumonia, special disorders (eg, asplenia, immunosuppression, HIV infection, and alcohol abuse), severe sepsis or septic shock, a risk of resistant pathogens, and failure of the initial empirical treatment.

	Outpatient	Inpatient, low severity	Inpatient, no ICU, moderate severity	Inpatient, ICU, high severity
Sputum culture	None routinely	Yes	Yes	Yes
Blood culture	None routinely	None routinely	Yes	Yes
Legionella urinary antigen	None routinely	None routinely	Yes	Yes
Pneumococcal urinary antigen	None routinely	None routinely	Yes	Yes
Invasive respiratory tract sample culture	None routinely	None routinely	None routinely	Yes
Others	None routinely	None routinely	None routinely	Yes*

Figure 1: **Microbiological investigations**
ICU=intensive care unit. *Others indicates fungal, tuberculosis cultures, PCR, specific serology, lung biopsy.

Imaging Thoracic images are essential for several aspects of pneumonia management. Chest radiograph has diagnostic accuracies of 75% for alveolar consolidation and 47% for pleural eff usion, considering CT as the gold standard technique.[2]

Acute management Site of care Early in the evaluation of patients with communityacquired pneumonia, two questions need to be answered: does the patient need to be admitted in the hospital and should they be treated in intensive care? These decisions need to be made early because it has been widely shown that late admission into intensive care is associated with increased mortality.60 By contrast, the admission of patients who can be treated outside the hospital is associated with increased costs and risk of the development of nosocomial infections.61 Clinical judgment is the main determinant of the site-ofcare decision.6 Oxygen saturation (SpO_2) and arterial gas analysis can give important information about severity (eg, SpO_2 <92% can be considered a safer cutoff than can SpO_2 <90% for hospital admission).62 Furthermore, scores and biomarkers can assist the clinical judgment.[3]

Assessment of pneumonia severity

Assessing the severity of pneumonia is important for deciding upon the advisability of hospitalizationandforassessment of prognosis.Several scales are used for this purpose. The simplest one is CURB65. Its shorter version,CRB65,is suitablefor the initial assessment in the emergency department (Table 1). Patients with CURB 65 score 0 or 1 may be treated at home. Patients with score2+ should be hospitalized and score 3+ is an indicator of severe pneumonia.54 CRB65 is based totally on clinical indicators.Patients with score1+ should be treated in hospital.[4]

Table 1. CURB65 scale (adapted from Lim et al. 2003)

	Points	Mortality rate (%)
	0	0.7
Confusion	1	3.2
Urea >7 mmol/l	2	13
Respiratory rate 30+	3	17
Blood pressure < 90/60	4	41.5
Age 65+ years	5	58

A more comprehensive scale for severity assessment is the Pneumonia Severity Index, or PSI (Table 2). Patients from classes I and II may be treated at home. The assessment scales are useful, but clinical judgement is important. The other indicators for hospitalization are need for parenteral antibiotic treatment, drug or alcohol abuse and the inability of a patient to care for him or herself.

Table 2. Pneumonia severity index (PSI) (adapted from Fine et al. 1997)

Parameter			Point
Age			1 for each year
Gender			Women – 10
Nursing home resident			+10
History of cancer			+30
History of liver disease			+20
History of heart failure			+10
History of cerebrovascular failure			+10
History of chronic renal disease			+10
Altered mental status			+20
Breathing rate > 30			+20
Systolic BP < 90 mmHg			+20
Temperature > 40°C, or < 35°C			+15
Heart rate > 125			+10
Arterial pH < 7.35			+30
PaO_2 < 60 mmHg (< 90% O_2Sat)			+10
Na < 130 mmol/l			+30
Urea > 11 mmol/l			+20
Glycaemia > 14 mmol/l			+10
Haematocrit < 30%			+10
Pleural effusion			+10
Class	**Number**	**Mortality rate**	**Risk**
1		0.1%	Low
2	<70	0.6%	Low
3	71–90	2.8%	Low
4	91–130	8.2%	Moderate
5	>130	29.2%	High

Patients should be admitted to intensive care when they require mechanical ventilation or vasopressors (both of which are major criteria for severe pneumonia in the American Thoracic Society and Infectious Diseases Society of America guidelines). In addition to the major criteria, nine minor criteria are included to predict admission into intensive care.[5]

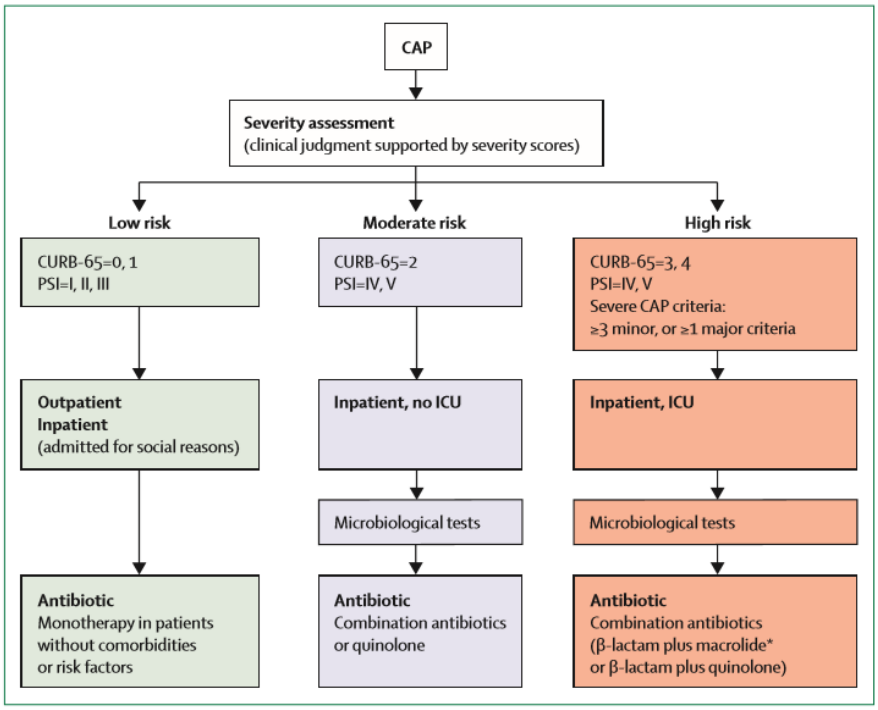

Figure 2: **Acute management of the community-acquired pneumonia**
CAP=community-acquired pneumonia. CURB-65=Confusion Urea Respiratory rate Blood pressure and age ≥65 year old score. PSI=Pneumonia Severity Index. ICU=intensive care unit. *Combination with macrolide is preferred.

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When microbiological tests become available, it is important to re-evaluate antibiotic treatment. Antibiotics should be adapted according to antibiogram results, narrowed according to the identifi ed pathogen, and discontinued when a diagnosis of pneumonia is unlikely Stewardship is fundamental to avoid the continuation of unnecessary treatment, increasing the selective pressure for resistance, and reducing the risks of unnecessary complications. Selection of antibiotics Antibiotic treatment is typically chosen empirically because of the absence of microbiological results upon diagnosis. The choice of the empirical antibiotic depends on the most likely pathogen, individual risk factors, comorbidities, allergies, and cost-eff ectiveness (appendix). Figure 2 and the table describe the management and antibiotic treatment proposed by community-acquired pneumonia guidelines. Several studies have shown reductions in mortality when these guidelines are followed. Guidelines suggest the coverage of S pneumoniae and atypical pathogens (eg, combination of a β-lactam plus macrolide or respiratory flouroquinolone). For severe community-acquired pneumonia, coverage of typical and atypical pathogens seems to be protective of mortality and is recommended by major guidelines.3–5 Macrolides seem to have additional benefi ts due to their immuno modulatory eff ects in severe community-acquired pneumonia.[6,7]

Treatment

Antibiotic treatment must be started as soon as possible, because a delay in treatment is associated with a worse prognosis.56 In one study the mortality rate of HAP where treatment was delayed was 91%, versus 30% in patients whose treatment started early. Antibiotic treatment should ideally be started within 4 h after the first visit of a doctor. Timing of antibiotic treatment the first dose of antibiotics should be given as soon as possible after diagnosis of community-acquired pneumonia. The antibiotics should be started preferably within the fi rst 4–8 h of hospital arrival and a shorter time to the first dose of antibiotic can be a marker of quality of care.95 However, a meta-analysis of stable patients with community-acquired pneumonia revealed that administration within 4 h was not associated with lower mortality (OR 0·95, 95% CI 0·73–1·23) and the pressure for rapid antibiotic administration was associated with an increased risk of misdiagnosis and an increased risk of adverse eff ects.97 In unstable patients with severe sepsis or septic shock, the time to the first dose is strongly associated with a reduction in mortality, and administration in the

first hour after diagnosis is recommended. Recommended antibiotics differ between areas, depending on local patterns of infective agents and their likely drug sensitivity and resistance.

	American (IDSA/ATS)[3]		British (NICE/BTS)[4,6]		European[5]	
	Preferred	Alternative	Preferred	Alternative	Preferred	Alternative
Outpatient without comorbidities; low severity	Macrolide	Doxycycline	Amoxicillin	Macrolide or tetracycline	Amoxicillin or tetracycline	Macrolide
Outpatient with comorbidities or high rate bacterial resistance	β-lactam plus macrolide	Respiratory fluoroquinolone			Respiratory fluoroquinolone	
Inpatient not in ICU; moderate severity	β-lactam* plus macrolide	Respiratory fluoroquinolone	Amoxicillin plus macrolide	Respiratory fluoroquinolone†	Aminopenicillin with or without macrolide	Respiratory fluoroquinolone
Inpatient in ICU; high severity	β-lactam‡ plus macrolide	β-lactam‡ plus respiratory fluoroquinolone	β-lactamase stable β-lactams¶ plus macrolide	Respiratory fluoroquinolone†	Third-generation cephalosporin§ plus macrolide	Respiratory fluoroquinolone with or without a third-generation cephalosporin§

Local or adapted guidelines should be used to adapt for different epidemiology. IDS=Infectious Diseases Society of America. ATS=American Thoracic Society. NICE=National Institute for Health and Care Excellence. BTS=British Thoracic Society. ICU=intensive care unit. *Preferred β-lactam drugs include cefotaxime, ceftriaxone, and ampicillin. †Respiratory fluoroquinolone limited to situations in which other options cannot be prescribed or are ineffective (eg, hepatotoxicity, skin reactions, cardiac arrhythmias, and tendon rupture). ‡Preferred β-lactam drugs include cefotaxime, ceftriaxone, or ampicillin-sulbactam. ¶β-lactamase-stable β-lactams include co-amoxiclav, cefotaxime, ceftaroline fosamil, ceftriaxone, cefuroxime, and piperacillin-tazobactam. §Third-generation cephalosporin (eg, cefotaxime, ceftriaxone).

Table: **Empirical antibiotics suggested for community-acquired pneumonia**

When a high probability of multi-resistant pathogens is expected, treatment could be an antipseudomonal cephalosporin (e.g. ceftazidime) or antipseudomonal carbapenem (e.g. imipenem), or a beta-lactamate antibiotic potentiated by a beta-lactamase inhibitor (e.g. piperacilin-tazobactam) plus an anti pseudomonal fluoroquinolone (e.g.ciprofloxacin),or aminoglycoside (e.g. tobramycin) plus vancomycin or linezolid.28 Some authors advise that ciprofloxacin, ceftazidime and imipenem should not be used in monotherapy due to the risk of resistance, but others are of the opinion that monotherapy, which is cheaper, should be used. A synergic effect of antibiotics in combination is not proven and use of unnecessary antibiotics increases the risk of resistance developing. The advantage of an antibiotic combination is better probability of empiric treatment effectiveness. When combined therapy including aminoglycoside has been effective, it is possible to stop the aminoglycoside after 5–7 days. Atypical pneumonia caused by Mycoplasma or Chlamydia requires treatment with antibiotics that are active intracellularly (e.g. tetracycline, macrolides, fluoroquinolones) for 10–14 days.[8,9]

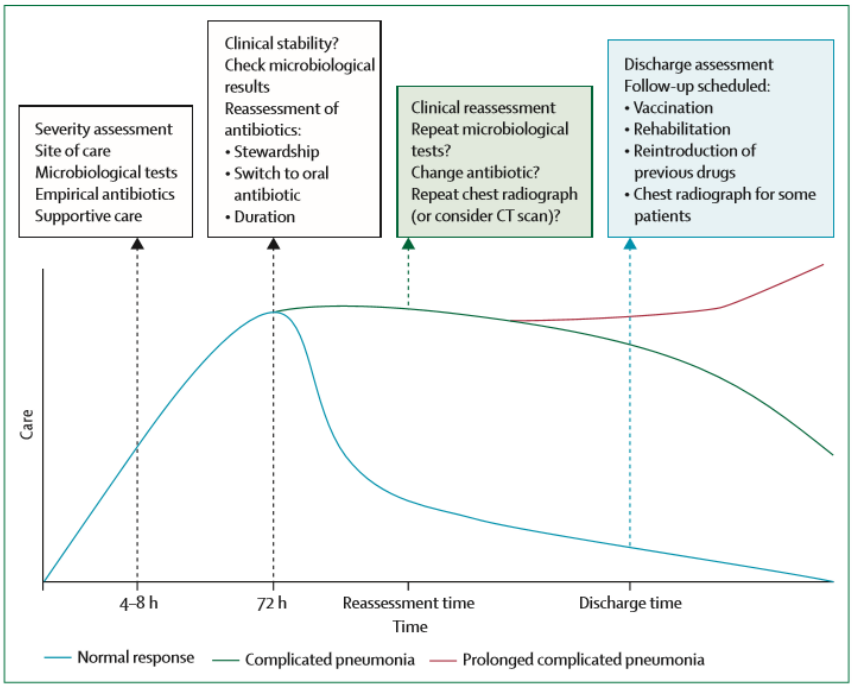

Figure 3: **Acute and long-term assessment of community-acquired pneumonia**

Duration of therapy 5 days of treatment should be given for low-severity pneumonia with clinical stability after 3 days of treatment, and 7 days should be given for severe pneumonia, which should be adapted depending on the improvements in symptoms and stability.[10] Biomarkers can be used to guide antibiotic duration. One-time PCT values lower than 0·25 μg/mL or a decrease from the peak by 80–90% are a strong indication that antibiotics should be discontinued. After the initial management of community-acquired pneumonia, the subsequent days are fundamental for good outcomes and high-quality management needs a multidimensional approach (figure 3). The evaluation of clinical stability (appendix) is a fundamental aspect of community-acquired pneumonia care. Stability criteria offer information about antibiotic treatment (eg, the appropriateness of such treatment, switching to oral medication, and short antibiotic treatment durations) and indications for hospital discharge that reduce hospital length-of-stay.

The development of severe sepsis is the primary reason for failure. Outpatients also need an early follow-up (after 72 h) to detect development of failure. Non-responding pneumonia is a different disorder that comprises the persistence of pulmonary infiltrates 1 month after symptom onset and can be due to many causes, such as the presence of lung cancer or an underlying lung disease.[11]

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