New guidelines for the management of adult community-acquired pneumonia

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Purpose of review

Community-acquired pneumonia is a major cause of morbidity and mortality, and is the leading cause of death from an infectious disease. International societies have published and revised guidelines aiming to improve the management of adult community-acquired pneumonia, based on the best available evidence. The aim of this review is to compare the current guideline recommendations.

Recent findings

Aspects of guidelines differ based on local factors including resources and antimicrobial factors, as well as the differences in interpretation of existing evidence.

Summary

The lack of robust evidence behind aspects of guideline recommendations as well as the lack of adherence to published guidelines both need to be addressed if the management of community-acquired pneumonia is to be improved.

Keywords

adherence, antibiotics, community-acquired pneumonia, guidelines

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Abbreviations

ATS	American Thoracic Society
BTS	British Thoracic Society
CAP	community-acquired pneumonia
ERS	European Respiratory Society
ICU	intensive care unit
IDSA	Infectious Diseases Society of America
JRS	Japanese Respiratory Society

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Introduction

Community-acquired pneumonia (CAP) is a major cause of morbidity and mortality, and internationally is the leading cause of death from an infectious disease and the sixth leading cause of death overall. Over the past decade international societies have published and revised guidelines for the management of patients with CAP. The aim of this article is to review recent updates and highlight areas both of consensus and difference, as well as to evaluate the use of guidelines as a whole. A combined American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guideline is due to be published early in 2007, but at the time of writing the main national and international guidelines include the ATS (2001), IDSA (2003), British Thoracic Society (BTS) (2004; www.brit-thoracic.org.uk/guidelines) and European Respiratory Society (ERS) (2005). Their aim is to standardise care by providing management strategies based on best available evidence. The evidence may be the same; however, differences exist between guidelines not only in the scope of recommendations, but also due to regional differences in patient populations, causative agents, bacterial antibiotic resistance rates, drug licensing, healthcare structure and available resources. Recommendations made by one national organisation may therefore not be applicable to other countries.

Methodology

Whilst most societies have restricted their guidelines to CAP, the IDSA includes acute bronchitis and empyema within its guidelines [1], while the ERS addresses all aspects of care for respiratory tract infections both in the community and hospital settings [2••].

Diagnosis

The diagnosis of CAP is usually defined as the presence of signs or symptoms compatible with a respiratory tract infection in the presence of new consolidation on a chest radiograph. The chest radiograph is the gold standard; however, in primary care, given the frequency of attendances for respiratory tract infection it may not be cost-effective or practical for all patients with such symptoms to undergo chest radiography. The frequency of pneumonia is quoted as 5–10% among patients with symptoms of lower respiratory tract infection. The ATS recommend chest radiography if 'symptoms and physical examination suggest the possibility of pneumonia' [3]. The ERS similarly recommend that patients suspected of

having pneumonia (i.e. acute cough plus new focal chest signs, dyspnoea, tachypnoea or fever for more than 4 days) should undergo radiography [1]. The BTS include a definition of pneumonia in the community as the presence of focal clinical signs without any other explanation, without emphasis on radiology [4].

There is consensus that a chest radiograph should be performed on all patients admitted to hospital with suspected pneumonia [1,2••,3–9].

Microbial investigation

There is little evidence to suggest that microbial investigation affects mortality, but it can provide information to assist with antibiotic selection as well as epidemiological data. Controversy still exists over sputum examination. The ATS, BTS and ERS are all in agreement that due to the wide variability in sensitivity and specificity of sputum Gram staining, based not only on a patient's ability to expectorate, but also technical differences in slide preparation and interobserver variability, routine Gram staining should not be performed. It is suggested that sputum be sent for Gram stain only where good quality sputum is expectorated, as observed by qualified medical staff, and transported to the laboratory in a timely fashion. Thereafter, strict criteria should be used for both the quality assessment of the sputum sample and an agreed level of sensitivity adopted. Gram staining results should be considered when interpreting the significance of sputum cultures. Concordance suggests a definitive pathogen.

Between 5 and 38% cases of CAP are due to mixed organisms. The ERS and ATS recommend that Gram stain results are useful to expand the breadth of antimicrobial coverage based on the discovery of an unexpected organism, unlike the IDSA which not only recommends that Gram staining is conducted on all patients, but that positive results be used to narrow the therapeutic antimicrobial spectrum.

Except for the Japanese Respiratory Society (JRS), all societies recommend that two sets of blood cultures be taken from all patients admitted to hospital with pneumonia, preferably before the administration of antibiotics [1,2••,3,4,6]. The JRS only recommend this in cases of severe pneumonia. Routine serological investigation and urinary antigen testing for *Legionella pneumophila* serogroup I and *Streptococcus pneumoniae* are only recommended for those with severe pneumonia by the BTS, ATS, IDS and ERS. The JRS advocates the use of urinary antigen testing for *S. pneumoniae* in all patients, and where appropriate *Legionella* and influenza A virus. Serological testing may be informative during outbreaks for epidemiological purposes, but due to the need for a convalescent sample it rarely impacts on clinical care.

Risk stratification

Evidence shows that clinicians may both overestimate the severity of pneumonia and yet still fail to recognise those at higher risk [10,11]. All guidelines recommend that clinical judgement be supplemented by objective severity scoring. Two main tools exist to risk stratify patients with pneumonia. The Pneumonia Severity Index classifies patients in terms of their mortality based on the presence of comorbidity, vital signs and laboratory abnormalities [10] (Table 1). These data have been extrapolated to provide data to determine who can safely be treated as outpatients. Classes I and II should not require hospital admission, class III may be suitable for outpatient care, and classes IV and V require admission. Classes IV and V are considered to have a high mortality and to be at greater risk of requiring admission to the intensive care unit (ICU). The Pneumonia Severity Index has been shown to reduce the admission of low-risk patients to hospital, although not by as much as would be thought, as over one-third of low-risk patients are admitted for other reasons including lack of social support or comorbidities [12]. This risk stratification is adopted by the IDSA and discussed in the ATS guidelines.

The CURB-65 score recommended by the BTS provides a complementary guide for identification of the more severely ill [4,5,13] (Fig. 1). It is simple and easily calculated based on only five variables. It too has been

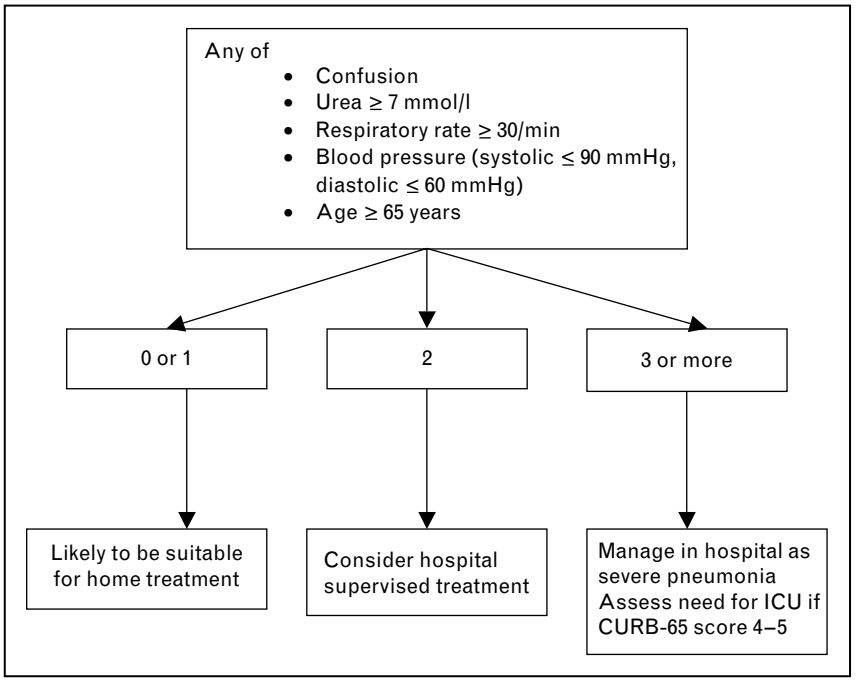
Table 1 Pneumonia Severity Index [10]

Criteria	
Age	
Male	age (years) − 0
Female	age (years) − 10
Nursing home resident	10
Comorbidity	
Neoplastic	30
Liver	20
Congestive heart failure	10
Cerebrovascular disease	10
Renal disease	10
Vital signs abnormality	
Mental confusion	20
Respiratory rate >30/min	20
Systolic blood pressure <90 mmHg	20
Temperature <35 or >40°C	15
Tachycardia >125 b.p.m	10
Laboratory abnormalities	
Blood urea nitrogen >11 mmol/l	20
Sodium <130 mmol/l	20
Glucose >250 mg/dl	10
Haematocrit <30%	10
Radiographic abnormalities	
Pleural effusion	10
Oxygenation parameters	
Arterial pH < 7.35	30
PaO_2 < 60 mmHg	10
SaO_2 < 90%	10

Risk class 1: age <50 year no comorbidity, no vital signs abnormality; risk class II: <70 points; risk class III: 71–90 points; risk class IV: 91–130 points; risk class V: >130 points. Copyright 1997 Massachusetts Medical Society.

Figure 1 CURB-65 index [13]

The CURB-65 score recommended by the British Thoracic Society provides a complementary guide for identification of the more severely ill. ICU, intensive care unit.



validated, although with fewer patients than the Pneumonia Severity Index. The CURB-65 scoring system is also recommended by the Japanese and Swedish Guidelines [7,9]. The ERS guidelines offer both severity scores as options. All societies acknowledge that severity indicators should be used only as an adjunct to clinical judgement when deciding which patients require hospital admission.

The ATS has modified the criteria used to define severe CAP requiring admission to the ICU. Previous strategies were over sensitive and lacked specificity as they defined 65–68% of all patients admitted to hospital as having severe pneumonia [6]. Revised guidelines define severe CAP as the presence of either one major criteria (need for mechanical ventilation or septic shock) or two of the three minor criteria (systolic blood pressure below 90 mmHg, multilobular disease, PaO_2/FiO_2 ratio below 250) [3]. The BTS defines severe CAP as a CURB-65 score of 3 or more and a score of 4 or 5 requires assessment for ICU admission, although it has not been formally tested to define the need for ICU [5]. A difficulty with the endpoint of ICU admission is that admission criteria vary from hospital to hospital.

Microbiology and antibiotics

Early administration of antibiotics after diagnosis of pneumonia has been shown to be associated with a decrease in mortality. The evidence for the exact timing of administration is somewhat inconclusive, however, as a subsequent trial found patients who received antibiotics within 2 h actually had worse outcomes [14,15]. The ATS and BTS advocate administration within 8 h of admission to hospital. The IDSA advocate timely administration rather than recommending specific time periods [16].

Recommended antibiotic therapy differs between the various guidelines and this is probably due to different perceptions of the importance of infections caused by atypical organisms, differences in antibiotic resistance, differences in the interpretation of the clinical relevance of antibiotic resistance as well as antibiotic licensing. Penicillin resistance among *S. pneumoniae* varies with levels as high as 9.2% in Spain and 15.9% in the US [17]. Resistance in the UK and Holland is much lower (quoted at 1.5 and 0.5%, respectively [18]), and these guidelines support the use of more traditional β-lactam antibiotics as first-line therapy. In Japan, the rate of *S. pneumoniae* resistance to macrolides is over 50% and although penicillin resistance is increasing, their use is still recommended for treatment of outpatient presumed bacterial pneumonia. The clinical significance of in-vitro resistance remains controversial.

All guidelines aim to rationalise antibiotic selection based on the prevalence of different causative organisms as well as disease severity. The ATS makes further subclassification based on modifying factors such as the likelihood of drug-resistant *S. pneumoniae*, Gram-negative organisms and *Pseudomonas aeruginosa* amongst select

Table 2 Modifying factors that increase the risk of infection with specific pathogens (American Thoracic Society guidelines) [3]

Penicillin-resistant and drug-resistant pneumococci	age >65 years β-lactam therapy in past 3 months alcoholism immune-suppressive illness (including steroids) multiple medical comorbidities exposure to child in day care centre
Enteric Gram-negatives	residence in nursing home underlying cardiopulmonary disease multiple medical comorbidities recent antibiotic therapy
Pseudomonas aeruginosa	structural lung disease corticosteroid therapy (>10 mg day) broad spectrum antibiotics of >7 days in past month malnutrition

groups (Table 2). The IDSA follows similar recommendations and categorises patients in terms of comorbidities and the use of antibiotics in the preceding 3 months to identify those at greater risk of drug-resistant *S. pneumoniae* and Gram-negative organisms. The ERS gives criteria when *P. aeruginosa* might be suspected. Both the ATS and IDSA now class nursing home-acquired pneumonia as a form of hospital-acquired pneumonia.

Nonsevere community-acquired pneumonia

The ATS, IDSA and Canadian Thoracic Society rely on the use of advanced generation macrolides and respiratory quinolones. The ERS and BTS advocate the continued use of β-lactams as first-line therapy with the addition if required of simple macrolides (Table 3). This is in part related to resistance levels, but may also be related to the more limited experience with the newer antibiotics due to their period of licence. Resistance to the respiratory quinolones is increasingly reported which may well increase as their use becomes more widespread [19]. The JRS only advocates the use of respiratory fluoroquinolones in select groups (older, comorbidity, recent antibiotics use and in severe pneumonia) as resistance rates in Japan, particularly in those over 65 years, are above 15%. Other issues regarding their use relates to greater costs and the recent association with *Clostridium difficile* diarrhoea [20].

Severe community-acquired pneumonia

The BTS and ERS guide antibiotic therapy based on the severity of disease. The ATS, IDSA and Canadian Thoracic Society define different management strategies based on the site of treatment and the presence of comorbidities or modifying factors and the likelihood of *Pseudomonas* infection (Table 4). This aims to identify groups with a higher prevalence of resistant pathogens. The American societies also distinguish between patients in the community and those in nursing homes. The ATS and IDSA both consider nursing home-acquired pneumonia as a form of hospital-acquired pneumonia as specified in the 2005 hospital-acquired pneumonia guidelines [21]. This is in contrast to the BTS, whose antibiotic strategy in this group is based on evidence that the prevalence of pathogens follows the same distribution as patients in the community.

Guideline impact

Guidelines will only be useful if they are adopted and shown to alter outcome. Several articles have focused on the effect of adherence to guidelines on the quality of care delivered. Menendez *et al.* [22] concluded that nonadherence to published guidelines when selecting empirical antibiotic therapy, particularly amongst patients classified as having severe pneumonia, was associated with a higher mortality. Another study concluded that the adoption of moderate and high-intensity guideline implementation reduced the number of low-risk patients admitted to hospital. They also found that moderate intensity guideline use increased the number of high-risk patients managed inappropriately in the community, thus supporting the adoption of high-intensity strategies. Even within this group they found that over 25% of patients were treated with inappropriate antibiotic therapy [23]. As well as varying between hospitals and the training status of physicians, nonadherence to guidelines has been found to be greater amongst nonrespiratory physicians. The adherence rate amongst intensive care units is quoted as low as 67% [24].

One factor in encouraging adherence to guidelines must be their effectiveness at delivering the information. The ATS guideline is a long document with complicated antibiotic strategies summarised on no less than five tables, but clear algorithms help to transmit the message. The IDSA does incorporate tabled information, but again it is a document that requires time to digest. The BTS guidelines offer a brief summary statement and simple presentation and management strategies, while the ERS adopts a question and answer format.

With the assumption that adherence to national guidelines is associated with better outcomes, the Community Acquired Pneumonia Organisation evaluated the actual care delivered to patients hospitalised with a diagnosis of community acquired pneumonia. Performance indicators were calculated for all aspects of management including diagnosis, hospitalisation, respiratory isolation, microbiological investigation, empirical antibiotic selection and discharge. They concluded practice was frequently not in accordance with recommended guidelines and it is the role of international organisations to help to improve compliance [25]. These findings are supported by Maxwell *et al.* [26] in the CAPTION (Community-Acquired Pneumonia: Towards Improving Outcomes Nationally) study. They evaluated the management of

Table 3 Antibiotic therapy in nonsevere community-acquired pneumonia

	American Thoracic Society	Infectious Diseases Society of America	Canadian Thoracic Society	European Respiratory Society	British Thoracic Society
Outpatient: no cardiopulmonary disease or modifying factors (Group 1)	advanced macrolide or doxycycline	Macrolide or doxycycline respiratory fluoroquinolone[b] advanced macrolide + amoxycillin[b] advanced macrolide + augmentin	macrolide or doxycycline	amoxicillin or tetracycline	amoxicillin or erythromycin/ clarithromycin[a]
Outpatient: cardiopulmonary disease ± modifying factors (Group 2)	β-lactam + macrolide or doxycycline or respiratory fluoroquinolone alone	advanced macrolide or respiratory fluoroquinolone respiratory fluoroquinolone[b] advanced macrolide + β-lactam	advanced macrolide or respiratory fluoroquinolone or amoxicillin/clavulanate + macrolide	as above	as above
Inpatient: cardiopulmonary disease ± modifying factors (Group 3a)	intravenous β-lactam + intravenous/ *per os* macrolide or doxycycline or respiratory fluoroquinolone alone	respiratory fluoroquinolone advanced macrolide + β-lactam advanced macrolide + respiratory fluoroquinolone[b]	respiratory fluoroquinolone, or second-, third- or fourth-generation cephalosporin + macrolide	penicillin G or aminopenicillin or coamoxiclav or second/third-generation cephalosporin ± macrolide or respiratory fluoroquinolone	(a) as home treated (b) amoxicillin + macrolide or respiratory fluoroquinolone
Inpatient: no cardiopulmonary disease ± modifying factors (Group 3b)	intravenous azithromycin alone (doxycycline + β-lactam[a]) or respiratory fluoroquinolone alone	as above	as above	as above	as above

Advanced-generation macrolide: azithromycin or clarythromycin. β-Lactam: oral cefpodoxime, cefuroxime, high-dose amoxicillin, amoxicillin/clavulanate or intravenous ceftriaxone then oral cefpodoxime. Respiratory fluoroquinolone: levofloxacin, moxifloxacin.

[a] Penicillin allergic/intolerant. Admitted for nonclinical reasons or previously untreated in community.

[b] Recent antibiotic therapy.

Table 4 Antibiotic therapy in severe community-acquired pneumonia

	American Thoracic Society	Infectious Diseases Society of America	Canadian Thoracic Society	European Respiratory Society	British Thoracic Society
ICU: risk of *Pseudomonas*	antipseudomonal β-lactam + antipseudomonal quinolonone or antipseudomonal β-lactam + aminoglycoside + macrolide or nonpseudomonal fluoroquinolone	antipseudomonal agent + ciprolfloxacin or antipseudomonal agent + aminoglycoside + either respiratory fluoroquinolone or macrolide	antipseudomonal fluoroquinolone + antipseudomonal β-lactam or aminoglycoside or antipseudomonal β-lactam + aminoglycoside + macrolide	antipseudomonal cephalosporin + ciprofloxacin carbapenem or acylureidopenpenicillin/ β-lactamase inhibitor + ciprofloxacin	coamoxiclav or second/third-generation cephalosporin + macrolide ± rifampicin or respiratory fluoroquinolone + benzylpenicillin
ICU: no risk of *Pseudomonas*	β-lactam + either macrolide or fluoroquinolone	β-lactam + either advanced macrolide or respiratory fluoroquinolone respiratory fluoroquinolone ± clindamycin (penicillin allergic)	respiratory fluoroquinolone + third-generation cephalosporin or amoxicillin/clavulanate or macrolide + third-generation cephalosporin or amoxicillin/clavulanate	third-generation cephalosporin + macrolide or third-generation cephalosporin + respiratory fluoroquinolone	
Nursing home	as Group 3a	respiratory fluoroquinolone advanced macrolide + amoxicillin/clavulantate	outpatient as Group 2; inpatient as Group 3	respiratory fluoroquinolone or amoxicillin/clavulantate + macrolide or second-generation cephalosporin + macrolide (o/p)	same treatment as per severity

ICU, intensive care unit. Antipseudomonal β -lactam: cefepime, imipenem, meropenem, piperacillin/tazobactam. Second-generation cephalosporin: cefuroxime. Thrid-generation cephalosporin: cefotaxime, ceftriaxone. Respiratory fluoroquinolone: levofloxacin, moxifloxacin (moxifloxacin not licensed in the UK for severe community-acquired pneumonia).

CAP in Australian emergency departments as compared to national guidelines. They concluded that overall concordance was very low, with only 18% of antibiotics prescribed in accordance with recommended guidelines and severity assessment documented in only 5% of presentations. Maxwell *et al.* [26] also acknowledge that despite low compliance with guidelines in Australian emergency departments, this had no effect on patient mortality or length of stay.

Performance indicators act as standards, based on evidence or consensus opinion, with which quality of medical care can be measured. The IDSA guidelines are the only guidelines to recommend specific performance indicators. There is, however, a surprising lack of quality evidence behind the majority of the guideline recommendations. As Woodhead [27] addresses in a recent Editorial, only 6.5% of ATS guidelines, 9.6% of Canadian guidelines, 15% of BTS guidelines and 21% of IDSA guidelines are based on 'best-level' evidence. A final word would emphasise the need for further randomised controlled trials to provide more evidence in this field.

Conclusion

Guidelines are here to stay and provide standards by which to guide and judge care. CAP is a diverse illness and its management has been dealt with by many guidelines. In some areas there is concurrence, in others there is not. Where guidelines differ it is often for lack of robust evidence. The highlighting of such evidence gaps should act as a spur to researchers and those funding research for the future.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 221).

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