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REVIEW

Management of community-acquired pneumonia: essential tips for the physician on call

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Abstract

Community-acquired pneumonia is a common clinical problem requiring admission to hospital, with a particularly high incidence in the elderly population and those with significant comorbidities. Diagnosis is made on the combination of a short history of respiratory symptoms and systemic ill-health with new examination and/or radiological features of consolidation. Multiple other infective and non-infective conditions can mimic community-acquired pneumonia, leading to misdiagnosis in 5–17% of cases. The CURB-65 score can identify patients with community-acquired pneumonia with a higher risk of mortality, but is insensitive at identifying patients requiring intensive care support and needs to be combined with clinical markers of potential severity. Both high admission levels of C-reactive protein and the failure of levels of C-reactive protein to decline by >50% by day 4 after admission are associated with higher risk of complications, need for ventilation or inotropic support, and mortality. Empirical antibiotic therapy for most patients admitted to hospital is combination of a ß-lactam and a macrolide. Short courses of antibiotics do not result in significantly different outcomes to longer courses unless the patient has developed complications such as a complex parapneumonic effusion. Implementation of a community-acquired pneumonia care bundle into clinical practice reduces mortality, and should be a high priority for all acute hospitals.

Key words: C-reactive protein; Care bundles; Community-acquired pneumonia; CURB-65; Resistant organisms

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Introduction and background on pneumonia

Pneumonia occurs when the alveoli become infected with microorganisms, causing a local and systemic inflammatory response that results in the alveoli filling with exudative fluid and inflammatory cells. It is this local alveolar inflammatory reaction to the infection which leads to consolidation, the clinical hallmark of pneumonia. Extensive consolidation compromises gas exchange and can lead to life-threatening hypoxia (Quinton et al, 2018).

Pneumonia is classified according to the patient's location when they acquired the infection. Community-acquired pneumonia occurs when infection is acquired outside the hospital and is by far the commonest type of pneumonia. It has an overall incidence estimated at between 1.5 and 14 cases per 1000 person-years depending on geographical location, the season (with a distinct increase in winter in the UK) and characteristics of the population (Prina et al, 2015). Hospital-acquired pneumonia is pneumonia acquired 48 hours after admission to hospital or within 14 days after discharge from hospital. Ventilator-acquired pneumonia is a subset of hospital-acquired pneumonia affecting patients 48 hours after endotracheal intubation (Jean et al, 2020). This classification allows clear communication between clinicians about the patient's condition, but importantly also ensures the correct empirical antibiotic therapy is chosen as the potential infecting microorganisms vary between the different types of pneumonia. Pneumonia developing in patients with a severe degree of immunosuppression such as chemotherapy-induced neutropenia, after organ transplantation, or in patients with advanced HIV infection is considered separately because of the extensive range of potential causative microorganisms (Di Pasquale et al, 2019).

Pneumonia is one of the most commonly encountered respiratory infections, accounting for approximately 230 000 deaths in Europe (29 000 in the UK) per year, and in the UK is responsible for more hospital admissions than any other lung disease (Chalmers et al, 2017; Marshall et al, 2018). Patients with community-acquired pneumonia who are admitted to hospital have a 30-day mortality rate of between 5% and 15% (Chalmers et al, 2017). The

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incidence of pneumonia is increasing over time, and at present Europe spends €5.7 billion per year on inpatient care and €500 million on outpatient care for patients with pneumonia (Chalmers et al, 2017). The incidence of community-acquired pneumonia and risk of death is related to age, sex and the presence of comorbidities (Prina et al, 2015; Luna et al, 2016). Community-acquired pneumonia is more common in older adults with approximately 45% of cases in the over 65-year-old age group (Cillóniz et al, 2018), and the incidence is also higher in men than in women (Prina et al, 2015). The exponential increase in the incidence of community-acquired pneumonia after 65 years of age is partially a result of the presence of associated comorbidities, but is also probably related to immunosenescence – the decreased efficacy of the adaptive and innate immune systems with increasing age (Cillóniz et al, 2018). The mortality of community-acquired pneumonia is also higher in patients with more than one comorbidity and some specific comorbidities, for example cardiac failure (20.5%) compared to patients with chronic obstructive pulmonary disease (8.1%) (Luna et al, 2016).

This article explores the diagnostic features of community-acquired pneumonia, some of the potential traps for misdiagnosis, the recognition of possible complications and patients with severe disease, and discusses some of the important issues when selecting appropriate antibiotic treatment.

Diagnosis of community-acquired pneumonia and diagnostic pitfalls

To make a diagnosis of community-acquired pneumonia requires evidence of new lung consolidation (eg dyspnoea, pleuritic chest pain, signs of consolidation and/or air space shadowing on the chest radiograph) associated with evidence of a significant inflammatory response (eg a fever, tachycardia and raised C-reactive protein level or erythrocyte sedimentation rate) (Lim et al, 2009). However, these features also occur in many other less common conditions. Although pyrexia and raised levels of biomarkers such as C-reactive protein may suggest an infective aetiology, they are not specific for infectious causes of inflammation (Black, 2016) and are often abnormal in non-infective causes of lung inflammation. It is possible that 5–17% of patients admitted to hospital with a diagnosis of community-acquired pneumonia actually have non-infectious mimics of community-acquired pneumonia (Black, 2016), the correct diagnosis of which will enable the patient to receive appropriate treatment. An important clinical point is that community-acquired pneumonia will usually present with a short history of days rather than weeks – if a patient has a prolonged history of illness then other diagnoses need to be considered such as subacute lung infection (eg tuberculosis, actinomycosis) or non-infective causes of lung shadowing and inflammation (Figure 1).

A particularly cautious approach to making a diagnosis of community-acquired pneumonia is required when there is a background history of previous immunosuppression, lung diseases such as interstitial lung disease, bronchiectasis or allergic bronchopulmonary aspergillosis, and in patients who are taking certain drugs like amiodarone. These are all associated with non-community-acquired pneumonia lung infections (eg an infective exacerbation of bronchiectasis) and/or non-infective mimics of community-acquired pneumonia. Table 1 lists some common and less common conditions that are often misdiagnosed as community-acquired pneumonia and the clinical clues which can be used to differentiate them from community-acquired pneumonia. Often accurate interpretation of the chest radiograph suggests the cause of the patient's presentation is a diagnosis other than community-acquired pneumonia (Figure 1, Table 1).

Severity assessment and recognition of complications of community-acquired pneumonia

Community-acquired pneumonia can lead to several different serious complications, including severe physiological disturbance with acute respiratory failure as a result of extensive consolidation or the development of acute respiratory distress syndrome, and/or septic shock and organ dysfunction (Ferrer et al, 2018). Other complications reflect evolution

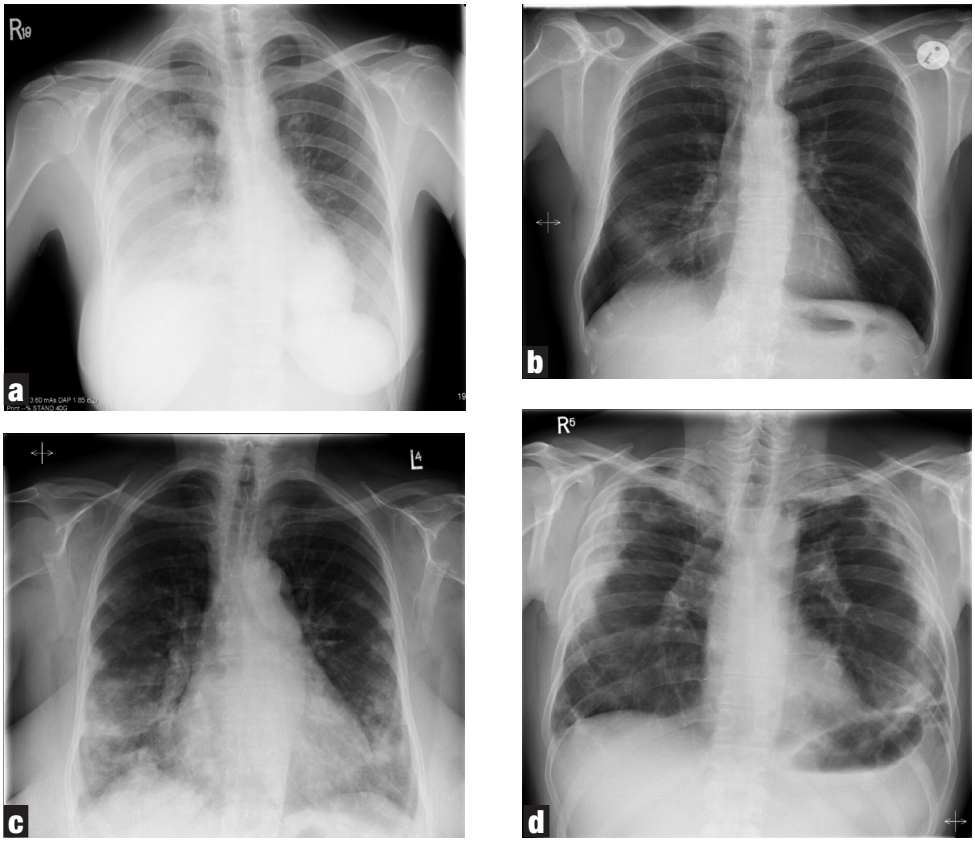

Figure 1. Chest radiographs of community-acquired pneumonia and clinical conditions that are often misdiagnosed as community-acquired pneumonia. a. Community-acquired pneumonia. The patient had 3 days' fever, cough, dyspnoea, and a C-reactive protein level of 278 mg/litre. The chest X-ray shows dense unilateral consolidation in lobar pattern. b. Subacute lung infection: actinomycosis. The patient had 3 months' fever, cough and poor response to amoxicillin. The chest X-ray shows right lower lobe consolidation. c. Organising pneumonia caused by amiodarone. The patient had 3 weeks' mild fever, cough, dyspnoea and a C-reactive protein level of 67 mg/litre, and is taking amiodarone for atrial fibrillation. The chest X-ray shows peripheral patchy basal consolidation. d. Pulmonary eosinophilia. The patient had 2 weeks' fever, cough, dyspnoea, and a C-reactive protein level of 222 mg/litre. The chest X-ray shows 'reverse bats wing' peripheral symmetrical subpleural consolidation.

of the infection such as infected parapneumonic effusions, empyema and lung abscess. These complications of community-acquired pneumonia will usually increase the length of stay in hospital, possibly require admission to intensive care for non-invasive (continuous positive airway pressure, optiflow) or invasive ventilatory support, or need interventions such as tube drainage or surgery. The development of a complication substantially increases mortality (Chalmers et al, 2009; Morgan and Glossop, 2016; Lee, 2017); for example, ventilated patients with community-acquired pneumonia have a 38% 30-day mortality (Ferrer et al, 2018). Early clinical recognition of patients with community-acquired pneumonia who are at risk of complications is essential to ensure rapid instigation of appropriate management that might avoid the development of complications or mitigate their impact.

The clinical prediction rule developed in the UK to classify severity for patients with community-acquired pneumonia is the CURB-65 score. With the CURB-65 score the patient is given a score of 0 (not met) or 1 (criteria met) for the following five factors:

1. Confusion (new onset confusion or abbreviated mental test score ≤8)
2. Urea >7 mmol/litre
3. Respiratory rate ≥30/minute
4. Blood pressure diastolic <60 mmHg or systolic <90 mmHg
5. Age ≥65 years (Lim et al, 2009; National Institute for Health and Care Excellence, 2019).

The mortality of patients with community-acquired pneumonia increases with the CURB-65 score, with a score of 0–1 having a <3% mortality, a score of 2 a 9% mortality,

Table 1. Conditions misdiagnosed as community-acquired pneumonia and clinical clues to the diagnosis

Condition		Clinical clues
Respiratory	Infective exacerbations of chronic obstructive pulmonary disease	No consolidation on chest radiograph, C-reactive protein level <40 mg/litre
	Influenza	High fever, rigour, coryzal or nasal symptoms, absence of lobar consolidation
	Bronchiectasis	Chronic daily sputum production or recurrent chest infections, normal or mildly raised C-reactive protein levels, ring shadows and tramlines on chest radiograph
	Acute respiratory distress syndrome	Rapid development of bilateral shadowing, severe hypoxia, PaO_2/FiO_2* ratios (mild <300 mmHg, moderate <200 mmHg, severe ≤100 mmHg)
	Allergic bronchopulmonary aspergillosis	Pre-existing asthma, central bronchiectasis, elevated total IgE, eosinophilia, expectorating sputum plugs, peribronchial shadowing
Cardiovascular	Pulmonary oedema	Bilateral fine crepitations, bilateral alveolar shadowing, small pleural effusions, history of cardiac impairment
	Pulmonary embolism	Pleuritic chest pain, peripheral deep vein thrombosis, risk factors for pulmonary embolism, wedge-shaped infarct on chest radiograph, C-reactive protein level <40 mg/litre
Neoplastic	Lung malignancy	Large intrapulmonary mass, bronchial obstruction leading to distal infection and/or collapse
	Lymphoma	Intrapulmonary masses in a non-lobar distribution
Immunological disorders	Organising pneumonia	Bilateral often subpleural patchy consolidation (non-lobar distribution)
	Eosinophilic pneumonia	Bilateral often subpleural patchy consolidation (reverse bats wing), bronchoalveolar lavage eosinophilia (systemic eosinophila not essential)
	Hypersensitivity pneumonitis	Ground-glass infiltrates mainly in upper zones, history of a risk occupation or hobby (eg owning pet birds)
	Granulomatosis with polyangiitis	Haemoptysis, renal impairment, upper respiratory tract symptoms, cavitation on chest imaging
	Diffuse alveolar haemorrhage	Haemoptysis, diffuse bilateral infiltrations or alveolar airspace shadowing, known vasculitis or autoimmune disease
Iatrogenic causes	Drug-induced toxicity	Drug history, subacute onset, bilateral crepitations and radiological infiltrates
	Radiation pneumonitis	Shadowing in the radiation field of recent radiotherapy treatment

*From Black (2016), Lee (2017), Quinton et al (2018). *ratio of arterial oxygen partial pressure (PaO_2 in mmHg) to fractional inspired oxygen (FiO_2)*

a score of 3 a 15% mortality, and scores of 4 or 5 a 40+% mortality (Lim et al, 2009; National Institute for Health and Care Excellence, 2019). The score is also used to assess patient placement (0–1 = treat at home, 2+ = admit to hospital, 3+ = consider referral to intensive care), and dictates which antibiotic regimen should be used. The CURB-65 is a very useful management tool for patients with community-acquired pneumonia, and does identify patients at high risk of death. However, the CURB-65 and other more complex pneumonia severity scores like the Pneumonia Severity Index are insensitive for predicting which of these patients are at risk of developing complications or will need treatment in intensive care (Chalmers et al, 2009; Liu et al, 2016). For example, Ilg et al (2019) found that 16% of patients admitted with community-acquired pneumonia with a CURB-65 score of 0–1 will require admission to intensive care; conversely Charles et al (2008) found that a CURB-65 score of 3+ only identified 39% of patients needing admission to intensive care.

This gap in the utility of the CURB-65 score has led to several attempts to develop new clinical scoring systems that are able to accurately identify patients with community-

acquired pneumonia who are at risk of complications or who might need intensive care treatment (Charles et al, 2008; Chalmers et al, 2009; Liu et al, 2016). These scoring systems tend to have increased sensitivity and specificity for identifying severe cases of community-acquired pneumonia. However, they are more complex than the CURB-65 score, making them much less easy to use, and they still fail to identify a substantial minority of patients with community-acquired pneumonia who develop severe disease. Several of the criteria identified by these severity scoring systems (Table 2) are physiological markers for patients who are unwell, for example a significant alveolar/arterial oxygen gradient or thrombocytopenia (Morgan and Glossop, 2016; Ferrer et al, 2018). As such, they are readily identified by the clinician. Overall these data suggest that combining recognition of these markers of physiological disturbance with the CURB-65 score will help ensure patients at risk of developing severe community-acquired pneumonia are better recognised.

One biomarker that can also help with assessment of severity is measurement of serum levels of the acute phase protein C-reactive protein. C-reactive protein is released by the liver in response to raised interleukin-6 levels and has a very large dynamic range, from a normal level of <5 mg/litre to levels that can reach 500+ mg/litre in acute severe infections such as community-acquired pneumonia (Chalmers et al, 2008). An admission C-reactive protein level >250 mg/litre is an independent marker for raised mortality, associated with a 15% higher mortality in patients with a CURB-65 score of 3+ (Chalmers et al, 2008). If the admission C-reactive protein level is >100 mg/litre then there is a 16-fold increase in the risk of complications for patients with community-acquired pneumonia, and a specific increased risk of developing a complex parapneumonic effusion (the commonest infective complication) (Chalmers et al, 2008, 2009). C-reactive protein levels can be used to provide information to aid diagnosis, and serial measurements can ascertain whether there has been a response to treatment (Chalmers et al, 2008, 2009; Lim et al, 2009). Table 3 summarises the usefulness of C-reactive protein measurements in the management of patients with community-acquired pneumonia.

Antibiotic selection

Patients with community-acquired pneumonia are initially given antibiotics empirically as a microbiological diagnosis is usually not available for over 24 hours, and in fact is not achieved in the majority of patients outside of research studies (Prina et al, 2015; Bianchini et al, 2019). Treatment is commenced as recommended by the British Thoracic Society (Lim et al, 2009) and National Institute for Health and Care Excellence (2019) guidelines, and involves a broad-spectrum ß-lactam and a macrolide (Table 4). This combination covers the main bacterial pathogens *Streptococcus pneumoniae* (up to 50% of cases) (Cillóniz

Table 2. Clinical parameters associated with severe community-acquired pneumonia (%=proportion of severe community-acquired pneumonia patients with that parameter)

White cell count $<4 \times 10^9$/litre	7%
PaO_2/FiO_2* ratio ≤250 mmHg	59%
Urea ≥7.14 mmol/litre	54%
Respiratory rate ≥30 breaths per minute	56%
Confusion/disorientation	48%
Thrombocytopenia $<100 \times 10^9$/litre	4%
Multilobar infiltrates	45%
Hypothermia (<36 °C)	11%
Hypotension	15%

*From Morgan and Glossop (2016), Ferrer et al (2018). *ratio of arterial oxygen partial pressure (PaO_2 in mmHg) to fractional inspired oxygen (FiO_2)*

et al, 2018), and the atypical bacteria *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* (10–15% of cases) (National Institute for Health and Care Excellence, 2019). In addition, the empirical regimen for community-acquired pneumonia usually has good activity against the less common causative bacterial pathogens such as *Haemophilus influenzae*, *Staphylococcus aureus* and *Klebsiella pneumoniae*. However, this empirical regimen is only appropriate for cases of community-acquired pneumonia; a much higher proportion of cases of hospital-acquired pneumonia is caused by Gram-negative bacteria that are potentially antimicrobial resistant (Jean et al, 2020), and pneumonia in the immunosuppressed can also be caused by fungi and viruses (Di Pasquale et al, 2019). Hence it is important to ensure the patient presenting with pneumonia has not recently been in hospital, and does not have significant immunosuppression such as undiagnosed HIV infection with a low CD4 cell count.

The risk that community-acquired pneumonia is caused by an antimicrobial-resistant organism such as *Pseudomonas aeruginosa* (a frequent pneumonia pathogen in cases of hospital-acquired pneumonia and in immunocompromised patients) (Di Pasquale et al, 2019; Jean et al, 2020) remains low in the UK, but is probably rising because of the increasing age and presence of comorbidities in patients presenting with community-acquired pneumonia (Shindo et al, 2013). Ensuring infection with resistant organism is not missed is important as (perhaps not surprisingly) antibiotic treatment with lack of activity against the microbial cause of community-acquired pneumonia is associated with treatment failure. Risk factors for infection with a resistant organism are listed in Table 5, and are largely related to a poor overall health status of the patient; in the absence of any risk factors 3.7% of patients have infection with a resistant organism (Shindo et al, 2013).

An additional potential risk factor for infection with a resistant organism is a recent travel history, as high levels of macrolide and penicillin resistance are common among *S. pneumoniae* isolates in some parts of the world (Schroeder and Stephens, 2016). Travel is also a risk factor for infection with contagious respiratory viruses such as Middle Eastern respiratory syndrome or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; the virus which causes COVID-19), and a history of travel to affected areas means a patient with community-acquired pneumonia should be isolated until a coronavirus infection has been excluded.

Studies on the duration of antibiotics for community-acquired pneumonia have shown that a short course (≤7 days) of antibiotics does not result in significantly poorer outcomes to a long course (>7 days) (Li et al, 2007). Reduction in exposure to antibiotics will reduce cost and antibiotic resistance, and improve patient adherence (Li et al, 2007). A 5-day course

Table 3. Utility of C-reactive protein when managing patients with community-acquired pneumonia

Admission level of C-reactive protein and rate of complications	<100 mg/litre 4% rate of complications and reduced 30-day mortality (odds ratio 0.18)
	>400 mg/litre 71% rate of complications
	>250 mg/litre 15% increase in mortality in patients with a CURB-65 score of 3+
	>200 mg/litre associated with slower radiographic resolution
Failure of admission C-reactive protein to fall by >50% at day 4 is associated with	Higher risk of mortality (odds ratio 24.5)
	Empyema or complicated parapneumonic effusion (odds ratio 15.4)
	Requirement for invasive ventilation and/or inotropic support (odds ratio 7.1)

From Chalmers et al (2008), Lim et al (2009)

Table 4. Preferred antibiotic treatment for community-acquired pneumonia

Mild (CURB-65: 0–1)	Amoxicillin 500 mg three times per day or clarithromycin 500 mg twice daily
Moderate (CURB-65: 2)	Amoxicillin 500 mg three times per day and clarithromycin 500 mg twice daily
Severe (CURB-65: 3+)	Co-amoxiclav 1.2 g three times per day and clarithromycin 500 mg twice daily

CURB-65 = confusion, urea, respiratory rate, blood pressure, age ≥65 years. From Lim et al (2009)

of antibiotics should suffice in most cases of low-severity community-acquired pneumonia except if there are infective complications such as lung abscess or complex parapneumonic effusion, or infection with microorganisms such as Gram-negative pathogens that are thought to require more prolonged therapy (Lim et al, 2009; Prina et al, 2015; National Institute for Health and Care Excellence, 2019).

Improving outcomes

Is there any evidence that the high risk of morbidity and mortality associated with community-acquired pneumonia can be improved? The answer to this question is yes. Administration of the pneumococcal and the annual influenza vaccination to the elderly population is an important preventative approach, and pneumococcal vaccination of children has also resulted in significant herd immunity protection of adults (Cillóniz et al, 2018). The British Thoracic Society has developed a community-acquired pneumonia care bundle (Table 6), implementation of which in 16 UK hospital trusts was associated with improvements in oxygen assessment, early antibiotic administration (odds ratio 1.26 and 1.52 respectively), and most importantly in 30-day mortality (8.8% vs 13.6%, odds ratio 0.59). Wider implementation of the care bundle on a regional scale using pay for performance as an incentive reduced 30-day community-acquired pneumonia mortality by 1.9% (Sutton et al, 2012).

Bianchini et al (2019) reported that using an innovative pharmacist-directed pneumonia diagnostic care bundle also improved management, increasing antimicrobial de-escalation by twofold as well as reducing antimicrobial adverse drug events, *Clostridium difficile* infection and 30-day readmission. These data show that implementation of focused attempts to improve community-acquired pneumonia management can be successful and lead to significant improvements in patient care.

Table 5. Risk factors for resistant organisms (univariate analysis)

Risk factor	Odds ratio
Home intravenous therapy	1.17
Chronic lung disease	1.23
Nursing home resident	2.58
Immunosuppression	2.68
Use of gastric acid suppressive agents	2.78
Non-ambulant patients	2.89
Home wound care in previous 90 days	2.95
Use of antibiotics in the previous 90 days	3.6
Hospitalisation for ≥2 days in the preceding 90 days	4.63
Feeding tube present	6.15
Meticillin-resistant *Staphylococcus aureus* infection in the previous 90 days	6.3

From Shindo et al (2013)

Table 6. Care bundle

Chest X-ray within 4 hours of hospital admission
Oxygen assessment and prescription
Severity assessment (using CURB-65 as part of the assessment)
Antibiotic administration within 4 hours

From Lim et al (2016)

Key points

- Accurate interpretation of the chest radiograph is key to identifying potential differential diagnoses and complications of community-acquired pneumonia.
- The CURB-65 scoring system is an essential management tool for patients with community-acquired pneumonia but is insensitive at identifying severe cases requiring intensive care treatment, and needs to be combined with a clinical assessment of physiological markers of severity.
- Failure of the C-reactive protein level on admission to fall by >50% at day 4 is associated with higher risk of mortality, complications and invasive ventilation/inotrope use.
- The outcomes of short- or long-course antibiotic treatments for patients with community-acquired pneumonia are similar.
- The mortality of community-acquired pneumonia can be reduced by establishing appropriate systems to ensure care bundles are adhered to.

Conclusions

In the UK, community-acquired pneumonia is the commonest serious infectious disease and is increasing in incidence. The clinical syndrome of community-acquired pneumonia usually presents with a relatively short duration of symptoms over days rather than weeks, and a combination of new consolidation and evidence of systemic inflammation. Many rarer inflammatory lung conditions mimic community-acquired pneumonia although these often have a longer disease course measured in weeks rather than days and distinctive radiological features; accurate interpretation of the chest X-ray is key to making the correct diagnosis. The CURB-65 score is an essential management tool for patients with community-acquired pneumonia, but needs to be used in conjunction with other clinical markers of severity to identify patients at high risk of developing complications or requiring intensive care treatment. Establishing appropriate systems of care that can ensure delivery of care bundles improves outcomes of patients with community-acquired pneumonia, and should be a high priority for all acute hospitals.

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Conflicts of interest

The authors declare no conflicts of interest.

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