Community-acquired pneumonia

Russell Allan

Abstract

Community-acquired pneumonia (CAP) is a common inflammatory process contained within the lung tissue in response to infection with non-hospital pathogens. Full resolution usually occurs with appropriate antimicrobial therapy. A significant proportion of patients develop severe CAP where there is failure to contain the local immune response and these patients may require admission to the intensive care unit (ICU). The CURB-65 severity score is a rapid, objective way of predicting mortality and can be used to guide site of care decisions in conjunction with clinical assessment. Microbiological investigations permit pathogen-specific antibiotic therapy and provide epidemiological data. Appropriate and timely administration of antibiotics is the mainstay of treatment. Complications include empyema, treatment failure, sepsis, respiratory failure and death.

Keywords Antimicrobial therapy; community-acquired pneumonia; intensive care; microbiological investigation; severity scores; treatment failure

Royal College of Anaesthetists CPD Matrix: 2A12, 2C01, 2C03, 3C00

Learning objectives

After reading this article, you should be able to:

- identify clinical markers in patients with severe community acquired pneumonia (CAP) requiring ICU admission
- list appropriate investigations
- describe specific treatment regimes
- describe complications of CAP

Community-acquired pneumonia (CAP) is an acute infection of the lung parenchyma. It should be differentiated for acute lung diseases that affect the airways including infections such as bronchitis. It is managed as an outpatient in greater than 50% of cases. The incidence of hospitalization is approximately 1–1.4 per 1000 population. The proportion of admitted patients who require ICU management for CAP is approximately 6% but increasing. In the UK, mortality in the community is less than 1%, while the mortality of patients admitted to ICU is over 30%.[1]

CAP is usually caused by bacteria and less commonly by viruses. Occasionally a primary viral infection may precede a more significant bacterial pneumonia. The presentation and treatment of CAP in immunosuppressed patients (cystic fibrosis, HIV and malignancy) differs and will not be considered here.

The defining features of CAP in hospital patients are:

- presentation with cough and new focal chest signs on examination
- at least one systemic feature of sweating, shivers, malaise and/or temperature of 38°C or more
- new shadowing on chest X-ray for which there is no other explanation (i.e. pulmonary oedema or infarction)
- patient presents with the above as the primary reason for attendance and is managed as pneumonia.[1]

Russell Allan *MBChB FFICM is a Consultant in Critical Care at the Queen Elizabeth University Hospital, Glasgow, UK. Conflicts of interest: none declared.*

Aetiology

The frequency with which different organisms cause CAP in hospitalized and in ICU patients are shown in Figure 1. 'Atypical' pathogens are classically *Legionella pneumophiliae*, *Mycoplasma pneumoniae* and *Chlamydia pneumonia*. Less common pathogens are *Haemophilus influenzae*, Gram-negative enteric bacilli, *Chlamydophila psittaci* and *Coxiella burnetii*. The term atypical is un-helpful and should be abandoned as it incorrectly implies that there is a characteristic clinical presentation for patients with these organisms.

Clinical features

In the majority of cases CAP presents as an acute illness with cough, purulent sputum and fever together with physical signs or radiological changes consistent with lung consolidation. Patients can rapidly deteriorate from respiratory failure and/or sepsis. This may not be recognized in younger patients due to their ability to compensate for pending organ failure. Although certain symptoms and sign are more common with specific organisms none allow accurate diagnosis. Importantly, legionella can occur in outbreaks and mycoplasma in epidemics separated by 4 years.

Risk factors

Pre-existing comorbidity is an important contributor as it is present in 63% of patients developing CAP who require hospitalization. This is most commonly in the form of chronic obstructive pulmonary disease (32%), asthma (13%) and cardiac problems (15%). Other conditions which predispose include diabetes, chronic liver disease, chronic kidney disease, alcohol dependency, increasing age and immunosuppression. These factors also influence mortality.

Scoring systems

Several scoring systems have been developed to predict mortality. The CURB65 severity score is the simplest and has been validated (Table 1). British Thoracic Society (BTS) guidelines recommend referral to ICU in patients presenting with a score of 4–5.[1]

The SMART-COP scoring system was developed in Australia to predict the need for invasive ventilation. This acronym represents systolic blood pressure below 90 mmHg, multilobar infiltrates, albumin less than 35 g/litre, raised respiratory rate (>25 for those age <50 years, and >30 for those age >50 years),

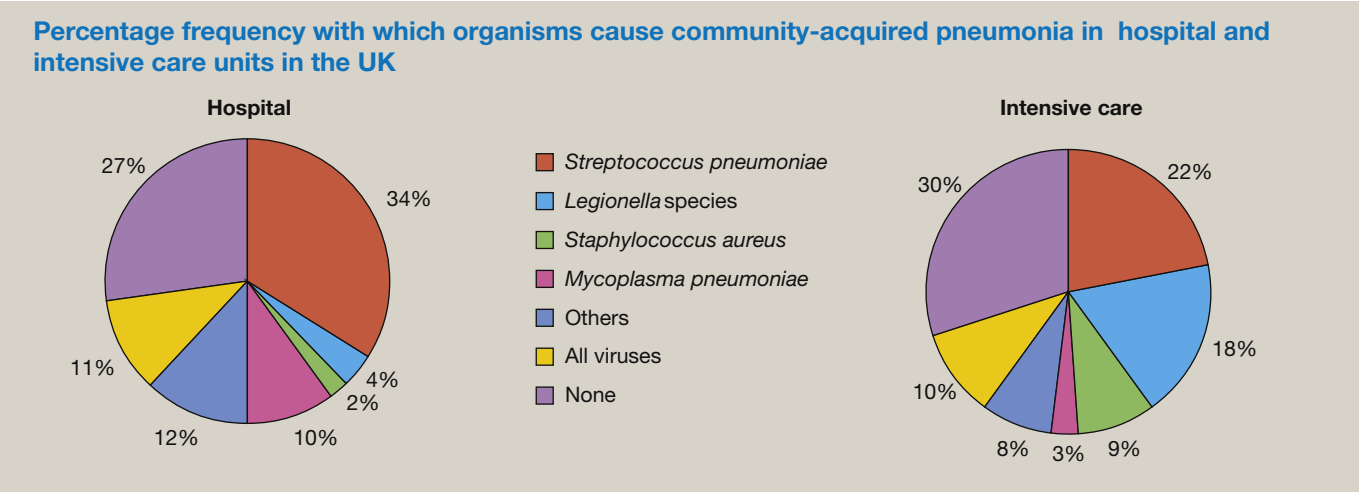

Figure 1

tachycardia (>125/minute), confusion, low oxygen (<9 kPa if age <50 or <8 kPa if age >50), and arterial pH <7.35. The abnormalities in systolic blood pressure, oxygenation and arterial pH each received two points, while the five other criteria received one point each. With three or more points, the need for invasive ventilation was predicted with a sensitivity of 92% and specificity of 62%. The CURB65 was less sensitive (39%) but more specific (74%) at predicting the need for invasive ventilation.[2]

The PIRO score (Predisposition, Insult, Response Organ dysfunction) is used to assess severity of illness in ICU patients. There are eight variables: comorbidities (chronic obstructive pulmonary disease, immunocompromise); age >70 years; multilobar opacities in chest radiograph; shock; severe hypoxaemia; acute renal failure; bacteraemia; and acute respiratory distress syndrome (ARDS). One point is given for each variable. Very high scores (5–8) predict 28 mortality better than APACHE II.[3]

CURB65 severity score and predicted mortality

One point for each feature presenting:

- **C**onfusion
- **U**rea >7 mmol/litre
- **R**espiratory rate ≥30/minute
- **B**lood pressure (SBP <90 or DBP ≤60 mmHg)
- **A**ge >65

CURB65 score	Severity	Risk of death (%)
0–1	Low	<3
2	Moderate	9
3–5	High	15–40

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table 1

General investigations

Full blood count in bacterial CAP may show neutrophilia or neutropenia. Patients may have raised urea. Hyponatraemia can occur due to inappropriate antidiuretic hormone secretion mediated by lung inflammation. A falling C-reactive protein or procalcitonin (PCT) indicates response to treatment. An ECG and troponin level is necessary because acute coronary syndrome (ACS) occurs concurrently in 5% of patients. Chest X-ray can show consolidation, which can either be patchy or lobar. It can also show air bronchograms or interstitial shadowing which can be confused with interstitial oedema from heart failure. It is not possible to accurately predict the aetiology from radiological features.

Microbiological investigations

Findings of clinical assessment and general investigations are not specific enough to confidently diagnose a specific organism and as such an empirical approach to antimicrobial treatment should be adopted based on local sensitivities and incidence of specific pathogens. This should however be supported by a strong culture of antimicrobial stewardship which includes making best attempts to isolate specific pathogen and adjusting antimicrobial cover based on this.

BTS guidelines suggest the need for different microbiological investigations based on CAP severity.[1] Patients with lowest disease severity (i.e. CURB65 0–1) do not require any routine microbiological investigations. They may however be clinical or epidemiological reasons that investigations may be necessary and appropriate. In contrast, those with higher severity CAP should all have the complete microbiological panel as described:

- **Blood culture** – positive in 4–18% of pneumonia with higher sensitivity where taken prior to antibiotic treatment.[1]
- **Sputum culture** – significant issue with false positives due to upper respiratory tract commensals. This is further exacerbated if sampling is delayed after antibiotic course has begun.

- **Pneumococcal urinary antigen** – has a greater sensitivity than cultures and remains positive in 80–90% of patients after 7 days of antibiotic treatment. Its presence is also a marker of increased severity.
- ***Legionella* urinary antigen** – sensitivity 80%; specificity 95% for *L. pneumophila* serotype 1 (accounts for the vast majority of cases of Legionnaires' disease although incidence of alternative legionella species or serogroups increases in hospital acquired legionella infections making this test less reliable as a 'rule out' in nosocomial infections).
- ***Legionella* respiratory secretion culture** – laboratories usually do not routinely perform this test on respiratory sample and therefore it should be specifically requested. This is the only available method of confirming a non-*L. pneumophila* serotype 1 organism. It is also important for epidemiological purposes.
- **Polymerase chain reaction (PCR)** – this has become increasingly accessible over the last decade and is a significant advancement in the accurate diagnosis of respiratory viruses and atypical organism (including *M. pneumonia*, *Chlamydia* spp, *Pneumocystis jirovecii*, respiratory syncytial virus, influenza A + B, parainfluenza 1–3, adenovirus)

Potential additional tests

- **Pleural fluid analysis** – when present and accessible should be sent for pneumococcal Ag, culture and microscopy.
- **Tuberculosis analysis** – cultures can take weeks to months to become positive; early presumptive diagnosis may make use of Ziehl-Neelson staining, clinical and radiological features.
- **Bronchoalveolar lavage (BAL)** – most useful in immunocompromised patients and when pneumonia is failing to respond.

Treatment

Basic care

Oxygen therapy should be used to achieve saturation targets appropriate for the individual. Patients are also often dehydrated or hypovolaemic with compromised organ perfusion. They may therefore require intravenous fluid therapy. Analgesia is often required to target pleuritic pain and may help with expectoration. Thromboprophylaxis should be considered where a period of immobility is likely.

Antimicrobial therapy

Empirical antibiotic therapy within 4 hours is advised[1] and this should be reduced to within 1 hour when severe sepsis accompanies CAP. Figure 2 shows the antibiotic regime for severe CAP recommended by the British Thoracic Society.[1] Alternations to this guidance may be considered in the following circumstances:

- Recent viral illness – addition of flucloxicillin to cover for possible *Staphylococcus aureus* superimposed on influenza infection.
- Cavitation in intravenous drug users – vancomycin or linezolid especially if MRSA colonized.
- Recent travel – penicillin resistant pneumococcus common in certain European countries including Spain, Hungry and Greece and therefore may preferably choose a quinolone.
- Immunocompromise – if *P. jirovecii* a possible cause co-trimoxazole may be added.

Optimal duration of antibiotic use remains uncertain and is likely to vary depending on precise diagnosis and response. BTS guidelines have suggested a 7–10 day course in severe CAP; however, they acknowledge that this may need to be extended up to 21 days in particular circumstances including *S. aureus* or Gram- negative infections. In less severe CAP there is reason to believe that a 5-day antibiotic course is optimal.[4]

The use of procalcitonin (PCT) to guide safe and timely cessation of antibiotics has been well studied but remains controversial. There is reasonable agreement that the use of specific PCT algorithms does not decrease mortality or morbidity and the most recent randomized controlled trial has shown no significant reduction in antibiotic duration using PCT guidance in contrast to previous evidence.[5,6] It is possible that trending PCT levels may be helpful by indicating initial treatment failure or prognostication yet this remains unproven. Regardless of whether PCT is used, all areas caring for CAP patients should have an antibiotic stewardship programme in place.

Anti-inflammatory therapy

The use of steroids and the dosing regimen remains controversial, and further studies are in progress including the Extended Steroid in CAP(e) (ESCAPe) study which is looking specifically at the ICU population. A meta-analysis preformed in 2015 demonstrated a trend towards reduction in mortality with steroid use which became significant in the more severe subgroup.[7] Furthermore, there is evidence to support a beneficial

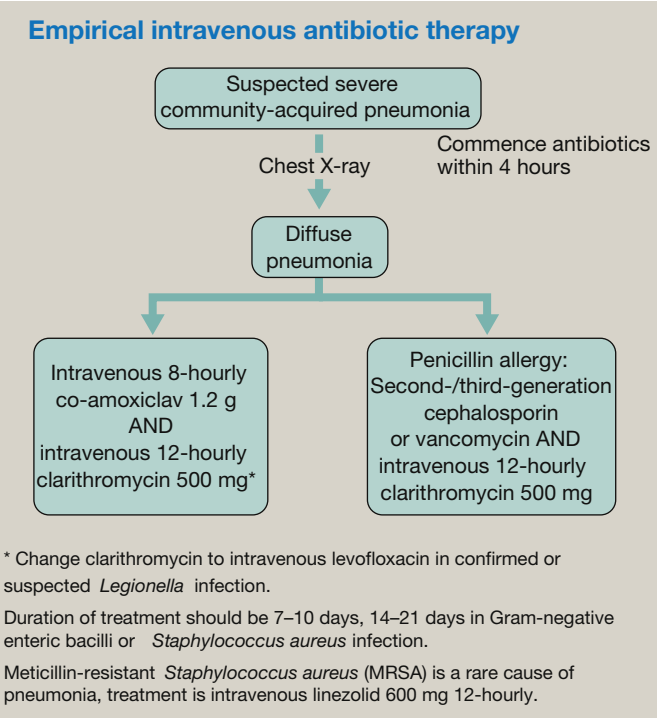

Figure 2

Treatment failure

Possible causes	Considerations/actions[a]
Resistant or unusual organisms	Review history (e.g. travel, hospitalization, immunosuppression), review microbiology results and perform further samples[b]
	Bronchial alveolar lavage (BAL)
Lack or delayed host response to appropriate treatment	Consider all alternative causes of treatment failure
Empyema	Thoracocentesis and drainage if confirmed
	Surgical involvement may be required
Abscess	CT chest; change antibiotics and prolonged course required
	Surgical involvement may be required
Incorrect initial diagnosis (malignancy, ILD, PTE)	Review history. Bronchoscopy
	CT chest; biopsy
Superimposed nosocomial infection (pulmonary and nonpulmonary)	Further samples;[b] BAL
Superimposed non-infective problem (pulmonary oedema, PTE, drug fever)	Thorough repeat history and examination
	Repeat chest X-ray
	CT chest
Post-obstructive pneumonia (e.g. malignancy, foreign body, etc.)	Review history; CT chest
	Bronchoscopy; biopsy

[a] In all cases consider respiratory specialist review.
[b] Interpret with caution any sputum sample from patients who have received prior days of antibiotic therapy as they are likely to have upper airway colonization (particularly *Staphylococcus aureus* and Gram-negative bacilli). BAL may be more helpful in this setting.

Table 2

morbidity effect with demonstration of less treatment failure, less ARDS, a reduction in duration of instability and of ventilation. Other than hyperglycaemia, adverse events were no more common in the intervention group. Despite this the British Thoracic Society guidelines have not recommended routine use even in severe CAP.[1]

Complications

Respiratory failure

Various degrees of respiratory failure are seen in patients with pneumonia, including in those with or without primary ARDS as classified by the Berlin criteria. Often it is the oxygen requirement that results in the eventual transfer to critical care.

Non-invasive ventilation should normally be avoided for patients with CAP, particularly where secretions are problematic. Although a Cochrane review demonstrated a possible reduction in invasive ventilation rates, hospital mortality rate was unaltered versus standard oxygen therapy.[8] Any decision to try non-invasive ventilation in the context of CAP should be made by a senior clinician and if used it should be early in the hospital admission, for a short period and there should be a low threshold for converting to invasive ventilation.

Nasal high-flow devices have been shown to be beneficial at reducing mortality and duration of ventilation when compared to non-invasive ventilation and standard oxygen therapy. Post hoc evaluation has also suggested that, in the more severely hypoxic subgroup, rates of intubation are also reduced.[9]

Hypoxaemia despite adequate non-invasive approaches should be managed by invasive ventilation. Excessive tidal volumes (>6–8 ml/kg) may be harmful and should be avoided when possible particularly, but not exclusively, when ARDS criteria is met.[10]

Sepsis

Often this infection originating in the lung parenchyma will enter the blood stream and cause a dysregulated host response resulting in organ dysfunction. This defines sepsis and results in a significant increase in mortality. Treatment should follow the surviving sepsis campaign guidance with particular focus on early antibiotics to reduce mortality.

Treatment failure

Treatment failure is defined as a lack of improvement in clinical signs. It can be early (<72 hours) or late (>72 hours). It occurs in up to 15% of hospitalized CAP and this is likely to be significantly higher in the more severe CAP managed in ICU. Subsequent management can be complex (Table 2). ◆

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