

The pulmonary physician in critical care • 3: Critical care management of community acquired pneumonia

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Severe community acquired pneumonia carries a high mortality. Early recognition of the severity of the illness, rapid and appropriate resuscitation, targeted antibiotic treatment, and the critical care support of multiple failing organ systems are all important in this group of patients. Only by improving all these aspects of care is it likely that survival will increase.

Community acquired pneumonia (CAP) is a common illness with an estimated incidence of 2–12 cases/1000 population per year.^{1,2} The majority of cases of CAP are successfully managed outside hospital, but approximately 20% require hospital admission. Out of this group about 10% develop severe CAP and need treatment in an intensive care unit (ICU). The mortality of these patients can exceed 50%, and the purpose of this article is to review the management of severe CAP. Excellent guidelines for the management of CAP have been produced by several organisations including the British Thoracic Society (BTS), the American Thoracic Society (ATS), European and Infectious Disease Working Groups.^{3–6} Revised BTS guidelines have recently been published⁴ and previous ATS recommendations are being revised. Any practitioner who is responsible for patients with CAP should consult one of these documents. This article will discuss both general approaches to CAP and also highlight specific areas of critical care management.

ASSESSMENT OF SEVERITY

For the purposes of epidemiological studies, the definition of severe CAP as “CAP needing ICU admission” is adequate. In practical management terms, however, a more detailed method of assessment is needed. Severe CAP is almost always a multiorgan disease and patients with severe CAP at presentation will either already have, or will be rapidly developing, multiple organ failure. It is important that respiratory and other “front line” physicians appreciate this aspect of the disease. Apparent stability on high flow oxygen can rapidly change to respiratory, circulatory, and renal failure. Progressive loss of tissue oxygenation needs to be anticipated, recognised quickly, and rapid action taken to prevent its progression to established organ failure.

The BTS guidelines define severe pneumonia (“rule 1”) as the presence of two or more of the following features on hospital admission⁴:

- Respiratory rate ≥ 30 /minute
- Diastolic blood pressure ≤ 60 mm Hg
- Urea > 7 mmol/l

The guidelines include three additional assessment recommendations. The presence of any one of these approximately doubles the rate of death:

- Altered mental status, confusion or an Abbreviated Mental Test score of $< 8/10$
- Hypoxaemia ($P_{O_2} < 8$ kPa or O_2 saturation $< 90\%$), with or without a raised F_{iO_2}
- Bilateral or multilobar (more than two lobes) shadowing on the chest radiograph

In a number of studies, use of BTS “rule 1” identifies a group of inpatients with a greater than 20% mortality from CAP.⁷

The ATS guidelines on CAP include minor and major criteria for severity assessment. Minor criteria on admission include:

- Respiratory rate > 30 /minute
- Severe respiratory failure ($P_{aO_2}/F_{iO_2} < 250$ mm Hg)
- Bilateral involvement on chest radiograph
- Multilobe involvement on chest radiograph
- Systolic blood pressure < 90 mm Hg
- Diastolic blood pressure < 60 mm Hg

Major criteria at or following admission include:

- Need for mechanical ventilation
- Increase in the size of radiographic infiltrates $\geq 50\%$ in the presence or absence of a clinical response or deterioration
- Need for vasopressor support for > 4 hours
- Worsening renal function as defined by a serum creatinine of ≥ 180 mmol/l

Using the need for ICU admission as the end point, various combinations of minor and major criteria give different combinations of specificity and sensitivity.¹ In the presence of at least one of the ATS criteria sensitivity was 98% but specificity only 32%. Positive predictive power was much improved using a combination of two of three major criteria and multilobar involvement. Sensitivity was 78% and specificity 94%.

More than a decade ago the BTS performed a ground breaking study on severe CAP.⁸ In their series 60 patients from 25 hospitals required ICU care in a 12 month period. One of the more striking findings was that eight patients were admitted to the ICU only after suffering cardiorespiratory arrest on general medical wards. In retrospect, six of these eight could have been identified using the BTS “rule 1” severity guide. In a related study CAP related deaths over 3 years

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in patients aged <65 years in the Nottingham area of the UK were retrospectively audited.⁹ They found evidence of suboptimal care in a number of cases, including a lack of appreciation of disease severity, lack of input from senior doctors, and lack of suitable investigations including arterial blood gas measurements. These and other studies provided evidence of suboptimal management of patients with severe CAP in the late 1980s and early 1990s. They also produced clear and simple assessment tools and guidelines to improve practice. Unfortunately, recent reports suggest that these important lessons have not been learnt. McQuillan and coworkers recently performed a confidential inquiry into the quality of care before admission to the ICU¹⁰ which covered a wide range of both medical and surgical admissions including patients with severe CAP. The study found that suboptimal care had been given to 54% and, importantly, that hospital mortality in this group was significantly higher than in those managed well (56% *v* 35%). Errors in the management of the airway, breathing, circulation, monitoring, and oxygen therapy were common.

Correct management of severe CAP before admission to the ICU is therefore essential. Recognition of the severity of illness is the first vital step, in which application of the BTS severity rules and screening pulse oximetry are useful tools. Repeated regular assessment by the same observer in the initial stages of the illness is necessary and rapid review by a critical care practitioner should be arranged for any patient who meets the BTS or similar severity criteria or who is deteriorating. The need for increasing F_{IO_2} , altered mental state (confusion, aggression), and the onset of either respiratory or metabolic acidosis are all signs of disease progression and the need for further intervention.

In the UK the recent publication of the Department of Health document “*Comprehensive Critical Care*”¹¹ suggests expanding high dependency or—in the new terminology—level 2 care. This would provide a suitable environment for the initial treatment of patients with severe CAP who do not need immediate mechanical ventilation. These patients are likely to benefit from more intensive monitoring (arterial line, central venous line, urinary catheter) and treatment (rapid correction of hypovolaemia, inotropic support, continuous positive airway pressure (CPAP), non-invasive ventilation (NIV)). Level 2 care also allows the rapid initiation of invasive mechanical ventilation when needed.

CO-MORBIDITY

The original BTS study on severe CAP pointed to the importance of pre-existing co-morbidity⁸: 63% of this group had serious pre-morbid conditions including chronic obstructive pulmonary disease (COPD, 32%), asthma (13%), and cardiac problems (15%). Other significant conditions included diabetes, chronic liver disease, chronic renal failure, and alcohol dependency. Immunosuppression was also a risk factor for severe CAP. The incidence of severe CAP increases with age and increasing age probably adversely affects outcome; analysis of 11 studies of CAP in the elderly¹² showed that more than 90% of pneumonia deaths occurred in patients over the age of 70.

MICROBIOLOGY

In the last decade a number of important facts have been established about the microbiology of CAP¹²: (1) a relatively small number of pathogens account for the majority of infections; (2) *Streptococcus pneumoniae* has been consistently shown to be the commonest pathogen in Europe and North America; and (3) in at least one third of cases no definite causative pathogen can be isolated. However, the relative importance of pathogens varies considerably worldwide. For example, in a report from Singapore, *Burkholderia pseudomallei* was the most common cause of severe CAP.¹³

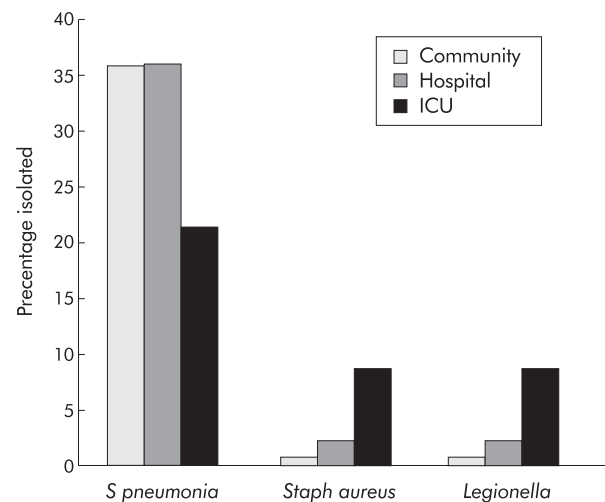


Figure 1 Percentage isolation of *S pneumoniae*, *Staph aureus*, and *Legionella* species from patients with CAP treated in the community, general medical wards, and intensive care units. *S pneumoniae* remains the commonest pathogen isolated in the critically ill but the frequency of *Staph aureus* and *Legionella* infections significantly increases in this group. Data adapted from the BTS guidelines.⁴

In addition to *S pneumoniae*, other important pathogens in CAP include *Haemophilus influenzae*, *Legionella* species, *Staphylococcus aureus*, Gram negative organisms, *Mycoplasma*, *Coxiella* species, and respiratory viruses. European and North American studies have found similar incidences of specific pathogens. In a survey of 16 studies of severe CAP the following pathogens were isolated: *S pneumoniae* 12–38%; *Legionella* spp 0–30%; *Staph aureus* 1–18%; and Gram negative enteric bacilli 2–34%.¹ There is an important change in the frequency of these pathogens depending on the severity of the illness (fig 1). In the UK there is a high relative frequency of *Legionella* and *Staph aureus* in severe CAP compared with cases cared for in the community or the general wards. The relative frequency of *S pneumoniae* is reduced in severe CAP, but it remains the most frequent pathogen isolated.

MICROBIOLOGICAL INVESTIGATION AND DIAGNOSIS

At least three strategies have been used in the microbiological diagnosis of severe CAP. These can be summarised as (1) the syndrome approach; (2) the laboratory based approach; and (3) the empirical approach.¹ The strengths or weaknesses of each of these strategies will be reviewed in the following sections.

The syndrome approach

This is based on the assumption that different pathogens cause distinct and non-overlapping clinical syndromes. The terms “typical” and “atypical” pneumonia were adopted to describe these syndromes. Typical pneumonia was caused by the pneumococcus and was said to present with pyrexia of greater than 39°C, pleuritic chest pain, a lobar distribution of consolidation, and an increase in immature granulocytes. Features of atypical pneumonia included a more gradual onset and a diffuse interstitial or alveolar pattern on the plain chest radiograph.

Numerous studies, however, have shown that clinical overlap between the different pathogens is great and that no single or combination of symptoms and plain chest radiology will reliably differentiate between the different pathogens.¹ In severe CAP the situation is even more difficult; case series of severe pneumococcal, staphylococcal, and legionella pneumonia show no reliable distinguishing features. In a recent series

Box 1 BTS guidelines for routine investigations in hospital for all patients with severe CAP

- Blood cultures
- Sputum or lower respiratory tract sample for Gram stain, routine culture, and sensitivity tests
- Pleural fluid analysis, if present
- Pneumococcal antigen test on sputum, blood, or urine
- Investigations for legionella pneumonia including (a) urine for legionella antigen, (b) sputum or lower respiratory tract samples for legionella culture and direct immunofluorescence, and (c) initial and follow up legionella serology
- Respiratory samples for direct immunofluorescence to respiratory viruses, *Chlamydia* species, and possibly *Pneumocystis*
- Initial and follow up serology for atypical pathogens

of 84 patients requiring ICU admission for severe legionella pneumonia, 39% had only unilateral radiographic changes at presentation.¹⁴ Hyponatraemia is often quoted as a sign of legionella pneumonia but in this series¹⁴ hyponatraemia was strongly associated with poor outcome, suggesting that it is a marker of disease severity rather than disease type.

The laboratory based approach

There are a number of reasons for attempting to identify precisely the pathogen in severe CAP: to confirm the diagnosis, to guide antibiotic choice, to define antibiotic sensitivities, and to provide epidemiological information. All current guidelines recommend intensive microbiological investigation. The BTS recommendations for routine investigations in severe CAP are summarised in box 1.⁴ While it is difficult to disagree with this thorough approach to diagnosis, a number of practical problems require discussion. Firstly, there is no good evidence that this strategy alters the outcome of severe CAP and retrospective studies disagree about the impact of laboratory based microbiological testing on outcome.^{15–16} In at least 30% of cases no pathogen can be isolated and this group has as good a prognosis. Outcome in severe CAP is also strongly related to secondary factors including the number of failed organs and co-morbidities. For these reasons the precise identification of the respiratory pathogen may have little impact on recovery. Secondly, current diagnostic tests are neither sensitive nor specific in severe CAP.¹⁷ One difficulty is that isolation of a pathogen in severe CAP does not necessarily indicate causation unless the pathogen is never isolated from healthy individuals—for example, *Mycobacterium tuberculosis*. Respiratory tract specimens containing few squamous epithelial cells, numerous neutrophils, and large numbers of Gram positive, lancet-shaped diplococci are highly specific for pneumococcal pneumonia. However, sensitivity is much lower. Poorly obtained or processed specimens and lack of observer experience can dramatically alter the yield. Sputum culture suffers from similar problems of low sensitivity and specificity, with the quality of the sample and prior antibiotic treatment having a major impact on yield. Blood cultures are positive in only 4–18% of hospitalised patients with CAP.¹⁷ Pneumococcus is the most common pathogen isolated but prior antibiotic treatment significantly reduces yield.

Pneumococcal polysaccharide antigen can be detected in respiratory or other fluids by a variety of methods. It has the advantage of being less strongly influenced by prior antibiotics, but sensitivity and specificity are very variable between studies. Urinary antigen testing for legionella serogroup 1 is more than 95% specific for infection, but sensitivity is low and the test does not detect other *Legionella* species. There is current interest in the detection of specific microbiological nucleic acids by amplification techniques such as reverse transcriptase polymerase chain reaction (RT-PCR). These

techniques are likely to suffer from similar sensitivity and specificity problems that affect conventional tests.

Most patients with severe CAP require endotracheal intubation and mechanical ventilatory support. In these circumstances, fiberoptic bronchoscopy becomes relatively straightforward and safe. Should all intubated patients with severe but microbiologically undiagnosed CAP be bronchoscoped? An evidence based approach cannot be taken as randomised controlled trials have not been performed. The advantages are that other pathology such as endobronchial obstruction may be discovered and that a targeted sample of lower respiratory tract secretions may be obtained. However, samples obtained using standard techniques are always contaminated by upper airway flora and are probably no better than standard sputum samples. Protected specimen brush (PSB) and bronchoalveolar lavage (BAL) are techniques which attempt to overcome some of these obstacles. PSB techniques use a telescoped plugged catheter that is passed through the bronchoscope. It contains a brush protected by a plug which is used to obtain the sample and then placed in culture medium. Quantification of the subsequent culture is usually performed to improve diagnosis. Studies on non-intubated patients with CAP report potential pathogens in 54–85% of cases. However, the yield in three series of intubated patients with severe CAP already receiving antibiotics was reduced to 13–48%.^{18–20} BAL samples a larger lung volume than PSB and the yield appears to be comparable to PSB, although the evidence is very limited. In patients with CAP who fail to respond to initial treatment, BAL identifies pathogens in 12–30%.^{21–22} Hence, while the yield in severe CAP is relatively low, it is recommended that bronchoscopy is performed where the diagnosis is not established or where treatment is failing.

Empirical approach to microbiological treatment

All major guidelines take the view that clinical syndromes are non-specific and that diagnostic tests are either too slow or insufficiently reliable to help in the initial choice of treatment. An empirical approach relies on a good knowledge of the range of likely local pathogens and the fact that a small number of antibiotics (or a single agent) will usually be effective. It has the added advantage of preventing long delays in treatment while the results of laboratory tests are awaited. The performance of diagnostic tests is encouraged as a guide to modify antibiotic treatment if a pathogen is identified.

ANTIMICROBIAL TREATMENT

Detailed reviews of candidate antibiotics for the treatment of severe CAP are available in recently published articles.^{23–24} If the specific pathogen has been isolated, then the choice is relatively straightforward. The optimal choice of antibiotics for the empirical treatment of severe CAP is less clear. This will be determined by local surveillance data but in Europe and North America must include effective treatment for *S pneumoniae*, *Legionella* spp, *Haemophilus* spp and *Staphylococcus* spp. Gram negative bacilli are a rare cause of severe CAP in most series, although they may be found in patients with pre-existing lung disease or on steroid therapy.

Antibiotic resistance is becoming an increasing problem with a number of reports of penicillin resistant *S pneumoniae*. In the UK, however, clinically relevant *S pneumoniae* resistance is rare and the BTS guidelines continue to recommend amoxicillin alone for non-severe home based CAP treatment.

The severely ill patient with CAP requires a broader antibiotic coverage that must include the pathogens most commonly causing severe CAP. The BTS guidelines⁴ recommend the combination of amoxicillin/clavulanate with clarithromycin and the optional addition of rifampicin. The

amoxicillin/clavulanate combination will cover both the pneumococcus and beta-lactamase producing pathogens such as *H influenzae*. Clarithromycin is a macrolide antibiotic that is effective against “atypical” organisms including *Legionella* spp and against *S pneumoniae*. Rifampicin is effective against *Legionella* spp and provides antistaphylococcal cover. Other antibiotic regimens have been suggested for the empirical treatment of severe CAP but there is little objective evidence to support one approach over another. Alternatives for patients intolerant of the preferred combination include:

- Substitution of cefuroxime, cefotaxime, or ceftriaxone for amoxicillin/clavulanate; clarithromycin and rifampicin remain
- Use of a single fluoroquinolone with Gram positive cover (e.g. levofloxacin)

INTENSIVE CARE TREATMENT

Published case series of severe CAP emphasise that the ICU treatment of this group of patients involves the support of multiple failing organ systems. Most patients die of the complications of multiorgan failure rather than from respiratory failure alone. In the BTS severe CAP study 32% developed acute renal failure and 55% septic shock; 25% developed central nervous system problems including vascular events and convulsions.⁸

Patients with severe CAP have sepsis from a respiratory source and are optimally managed by a team with experience of the complications of sepsis. These patients often require haemofiltration for renal replacement therapy, invasive circulatory monitoring, and the use of vasopressors and inotropes. Survivors of severe CAP tend to have prolonged ICU admissions and complications are frequent. In the BTS study 12 of the 18 patients who still required ventilatory support at 14 days ultimately survived. Most patients who need prolonged ventilatory support will require a tracheostomy to wean from ventilation.

RESPIRATORY MANAGEMENT

All patients with severe CAP require high flow oxygen therapy. In all except those with a background of chronic respiratory failure, F_{iO_2} can be rapidly titrated against non-invasive S_{aO_2} measurements with regular arterial blood gas analysis used to check calibration. Hypercapnia is a sign of ventilatory failure and indicates the need for more intensive support (usually intubation and mechanical ventilation). Increasing metabolic acidosis indicates the development of circulatory shock and the requirement for fluid resuscitation and inotropic support.

CPAP can improve oxygenation in diffuse lung disease by recruiting and stabilising collapsed alveolar units. It is a standard treatment in severe pneumocystis pneumonia and a few case reports describe its successful use in severe CAP.²⁵ However, a recent randomised controlled trial of CPAP in patients at high risk of developing acute respiratory distress syndrome (ARDS) was negative.²⁶ In the study 123 consecutive adult patients with marked impairment of gas exchange ($P_{aO_2}/F_{iO_2} < 300$ mm Hg) were randomised to either standard treatment or standard treatment and facial CPAP. The group was heterogeneous but 52 patients had pneumonia. There was no significant difference in intubation rates (34% v 39% in the standard group) or hospital mortality. Of concern was the occurrence of four cardiorespiratory arrests in the CPAP group, probably due to delayed endotracheal intubation.

NIV is a further treatment option in severe CAP. Its use in exacerbations of COPD is supported by a number of randomised clinical trials.²⁷ A recent randomised trial of NIV in severe CAP has also been reported.²⁸ Fifty eight consecutive patients with severe CAP were randomised to either conventional treatment or conventional treatment and NIV. Both the intubation rate (50% v 21%) and length of stay in the ICU (6 v

1.8 days) were significantly reduced by NIV. However, subgroup analysis shows that the benefit only occurred in patients with COPD. Of concern was the trend to higher mortality in the NIV treated patients without COPD. Similarly, a small randomised study of NIV given in the emergency room for pneumonia had a higher mortality in the NIV group.²⁹ One explanation for the higher mortality in NIV treated patients is delay in intubation which was demonstrated in the emergency room study. The message is clear. Non-invasive respiratory support (CPAP or NIV) should only be given to patients with severe CAP in designated and properly staffed critical care areas. In addition, enthusiasm for non-invasive support should not delay intubation, particularly in patients without COPD.

Most patients with severe CAP (88% in the BTS study) will require intubation and mechanical ventilation. A number of these will develop diffuse lung injury and should be managed in a manner identical to others with ARDS (see article later in this series by Cordingley and Keogh). In occasional cases with focal pneumonia massive shunt across the diseased lobe is the cause of severe hypoxaemia. The use of positioning and differential lung ventilation has been described in this situation.^{30–32} Placing the “good lung down” may increase P_{aO_2} by 1.5–2.0 kPa as blood flow increases to the well ventilated lung. Differential lung ventilation requires the placement of a double lumen tube. The correct placement of such tubes can be difficult in the stable patient and requires great expertise in the severely ill. Following placement, each lung can be separately ventilated and the effects of different ventilatory strategies assessed.

The optimal ventilatory strategy for most patients with severe CAP has not been established. Both volume controlled and pressure controlled modes are used with varying levels of positive end expiratory pressure (PEEP). The recent multicentre ARDS study on ventilation suggests that a volume limited strategy should be adopted to reduce ventilator associated lung injury.³³ Although the approach of limiting tidal volume and airway pressure and allowing a controlled degree of hypercapnia is appealing, this strategy has not been examined in patients with severe CAP without ARDS.

FAILURE TO IMPROVE

Lack of clinical response at 48–72 hours is usually taken as an indication of probable treatment failure, although improvement in the elderly may take longer. The diagnosis should be reviewed and conditions such as cardiac failure and pulmonary infarction excluded. Culture results will be available by this stage and may necessitate a change in antibiotics. Pulmonary and extrapulmonary complications of infection should be investigated and treated. These include lung abscess and necrosis, empyema, meningitis, endocarditis, and nosocomial infections (including pneumonia and line infections). A recent multicentre study on the management of ventilator associated pneumonia suggested that bronchoscopy and lavage may be useful at this stage.³⁴ The possibility of immunosuppression should be considered and a history of recent foreign travel excluded. Pathogens that are very unusual in the UK are common causes of CAP in some countries¹⁵ and tuberculosis still occasionally presents as overwhelming pneumonia.

OUTCOME AND PROGNOSIS

The mortality of patients with CAP needing ICU admission is high. A meta-analysis found a mortality of 36.5% in ICU admissions with a range of 21.7–57.3%.³⁵ In the early 1970s Knaus and coworkers developed a predictive model of ICU outcome known as the APACHE (acute physiology and chronic health evaluation) scoring system.³⁶ This model has been refined and alternative models produced. All these systems indicate that outcome in ICU is related to the initial severity of

illness (as measured by abnormal physiology on admission), the type of illness, and the pre-admission health status of the patient. Increasing age also has a negative impact on outcome. A number of studies have confirmed that these variables are important determinates of outcome in severe CAP.¹ The independent impact of individual pathogens on survival is more difficult to determine. *S pneumoniae*, *Staph aureus*, *Legionella* spp, and Gram negative bacilli have all been reported in different studies to be independently associated with death.

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