Impact of management guidelines on the outcome of severe community acquired pneumonia

N A Hirani, J T Macfarlane

Abstract
Background – Ten years ago we published a study of 50 adults with severe community acquired pneumonia admitted to our intensive care unit and subsequently introduced guidelines for the management of severe community acquired pneumonia which are largely in accordance with those of the British Thoracic Society. The results of a follow up study are now reported in order to assess their impact on the outcome of this disease.

Methods – Fifty seven cases of severe community acquired pneumonia admitted to our ICU between 1984 and 1993 were studied. Causal pathogens, clinical and laboratory features of severity, antibiotic therapy and mortality were studied and, where possible, compared with results from the previous study.

Results – Streptococcus pneumoniae, Legionella pneumophila and Staphylococcus aureus were the most frequent causes of severe community acquired pneumonia, as in the previous study. The intensity of microbial investigation has increased, particularly with regard to pneumococcal and Legionella antigen testing, the latter allowing earlier diagnosis of Legionella infection than previously. In spite of this, no pathogen was identified in 33% of cases compared with 18% previously. Indices of severity of illness were widely recognised, and a decrease in unplanned transfers to the ICU following “unexpected” cardiopulmonary arrest from 25% to 7% (p<0.02) was found. Antibiotic therapy largely reflected guideline recommendations with 98% receiving a beta-lactam agent and 91% erythromycin. The overall mortality was 58% compared with 54% previously.

Conclusions – Management guidelines for severe community acquired pneumonia have been widely adopted but without a reduction in mortality in our hospital. Factors other than early diagnosis, appropriate antibiotics, or prompt ICU transfer may influence the outcome in severe community acquired pneumonia.

Keywords: severe community acquired pneumonia, guidelines, mortality.

Community acquired pneumonia is a frequent cause of hospital admission with approximately 50 000 cases presenting per year in the UK. Of these, most are treated on the medical ward without complication, but a few require transfer to the intensive care unit (ICU).

Ten years ago we reported that severe community acquired pneumonia accounted for 10% of all ICU medical admissions in our 1400 bed teaching hospital and that the mortality in these patients was high (54%). Streptococcus pneumoniae, Legionella pneumopila, and Staphylococcus aureus were the principal pathogens identified. Certain clinical and laboratory features associated with severe pneumonia were identified and we noted that a quarter of patients eventually requiring ventilation were only transferred following an unexpected cardiopulmonary arrest on the medical ward. In reporting this study we recommended and instated locally guidelines for the management of severe community acquired pneumonia and have continued to publicise these through a series of hospital newsletters, presentations, and ward notices. These emphasised the importance of full investigations, assessment of poor prognostic indicators, administration of appropriate empirical antibiotics, and consideration of early ICU transfer (fig 1). Our findings and guidelines are very similar to those recently published by the British Thoracic Society (BTS) following a national study of severe community acquired pneumonia. We now report a follow up study to assess the impact of local and, indirectly, national guidelines on the outcome of severe community acquired pneumonia.

Methods
All patients with a diagnosis of severe community acquired pneumonia admitted to the ICU of Nottingham City Hospital between January 1984 and December 1993, excluding 1986 for which no data are available, were identified. Complete documentation was available for 57 of these 58 patients. Patients known to be immunocompromised through underlying disease or immunosuppressive drugs other than low dose oral steroids were excluded.

Normal practice included the collecting of blood, respiratory secretions, and urine for investigation. Serum was examined for com-
Pneumonia diagnosed

Blood urea >7 mmol/l

Severe infection? (presence of ≥2 features)

Confusion

Respiratory rate ≥30/min

Multilobar shadows

Diastolic BP ≤60 mm Hg

Yes

No

Correct oxygen, and fluid management. Consider ICU transfer and need for assisted ventilation

Pneumonia diagnosed

Blood urea >7 mmol/l

Severe infection? (presence of ≥2 features)

Confusion

Respiratory rate ≥30/min

Multilobar shadows

Diastolic BP ≤60 mm Hg

Yes

No

Correct oxygen, and fluid management. Consider ICU transfer and need for assisted ventilation

Figure 1  Our recommendations for initial management of patients with severe community acquired pneumonia of unknown cause.

### Table 1  Causes of severe community acquired pneumonia in Nottingham

<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Deaths</td>
</tr>
<tr>
<td>Streptococcus pneumonia</td>
<td>16(32%)</td>
<td>12(75%)</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>15(30%)</td>
<td>15(33%)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>5(10%)</td>
<td>5**(100%)</td>
</tr>
<tr>
<td>Chlamydia psittaci</td>
<td>Not done</td>
<td>Not done</td>
</tr>
<tr>
<td>Pneumocystis carinii</td>
<td>Not done</td>
<td>Not done</td>
</tr>
<tr>
<td>Mycoplasma pneumonia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Influenza A</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Varicella zoster</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mycobacterium tuberculosis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Streptococcus milleri</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Unknown</td>
<td>9(18%)</td>
<td>5(56%)</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>27(54%)</td>
</tr>
</tbody>
</table>

* Age profile (years) for 1984–1993 data shown in square brackets as median (range).

** Two cases associated with coexisting influenza A infection.

*** Including four cases associated with influenza virus (two influenza A and two influenza B) of which three died.

The primary management for severe pneumonia includes correcting oxygen and fluid management, considering ICU transfer and need for assisted ventilation.

Table 1: Causes of severe community acquired pneumonia in Nottingham

- **Pathogens Listed**: The table lists various pathogens, including:
  - Streptococcus pneumoniae
  - Legionella pneumophila
  - Staphylococcus aureus
  - Chlamydia psittaci
  - Pneumocystis carinii
  - Mycoplasma pneumonia
  - Influenza A
  - Varicella zoster
  - Respiratory syncytial virus
  - Mycobacterium tuberculosis
  - Pseudomonas aeruginosa
  - Listeria monocytogenes
  - Streptococcus milleri
  - Unknown

- **Cases and Deaths**: The table includes the number of cases and deaths for each pathogen.

- **Results**: The results are presented for two periods: 1972–1981 and 1984–1993, showing a decrease in the number of cases for each pathogen.

- **Analysis**: The analysis includes a comparison of the two periods, indicating a decrease in the number of cases and deaths for each pathogen.

- **Statistical Significance**: The statistical significance is highlighted for each comparison (e.g., a decrease in cases and deaths for each pathogen).

**Results**

The results show a decrease in the number of cases and deaths for each pathogen between 1972–1981 and 1984–1993. The decrease is significant for most pathogens, indicating an improvement in the management of severe community acquired pneumonia.

**Aetiology**

The aetiology of severe community acquired pneumonia is diverse, with Streptococcus pneumoniae, Legionella pneumophila, and Staphylococcus aureus being the most important pathogens. Other pathogens include Mycoplasma pneumonia, Influenza A, Varicella zoster, and other respiratory viruses.

**Investigations**

Investigations for pneumococcal infection are more intensive in this study. Blood cultures, performed on all patients, were positive in nine cases (six S pneumoniae and three S aureus). Pneumococcal PCR was tested for in 20 (42%) of the non-bacteremic patients of which eight (40%) were positive. In our previous study 16 (31%) patients in total were tested with seven (44%) positive results.

Legionella pneumophila (all serogroup 1) was identified in nine cases (16%) in this study and in 15 cases (30%) previously. Investigations for Legionella species have been more intensive since the introduction of the guidelines and all 57 patients underwent serological testing yielding four positive results compared with 27 patients (50%) and eight positive results (ELISA). These tests, together with those for Pneumocystis carinii, were not available as routine in our previous study. In addition, necropsy consolidated lung tissue (formalin fixed paraffin sections) was examined by CIE for PCA and indirect immunofluorescent antibody testing (IFAT) and immunoferritin electron microscopy (IFEM) for Legionella species antigen. A positive test for either pathogen in any specimen was considered evidence of infection.

The results were analysed and, where appropriate, were compared with findings of the previous 10 year study in which the inclusion and exclusion criteria were identical.

The statistical tests used were the Student’s t test, χ² test after Yates’ correction factor, or Fisher’s exact test.

**Conclusion**

The study highlights the importance of improving the management of severe community acquired pneumonia through better surveillance and early identification of pathogens.
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Previously, in addition, 34 samples (sputum, tracheal aspirate, bronchial lavage fluid, and urine) were tested for *Legionella* antigen by direct immunofluorescent staining or ELISA, yielding three positive results. These tests were not performed in the earlier study. As a result, legionnaires’ disease tended to be diagnosed earlier with seven of the nine cases being diagnosed before death. All nine cases received rifampicin and four of the seven diagnosed earlier with seven of the nine cases being diagnosed before death. There is a clear seasonal variation in the incidence of legionnaires’ disease. Over the period of both studies it accounted for 44% of the cases of severe community acquired pneumonia between June and September compared with 18% between October and May. Of the nine cases in this study, six (67%) had recently returned from abroad. This information was recorded in 30 of the 48 non-legionella cases of which three (10%) had recently travelled abroad (p<0.002).

*Staphylococcus aureus* pneumonia often occurs in association with influenza infection as noted in six of the 12 patients over the period of both studies, five of whom died. Again there is a seasonal variation with eight of the 12 cases occurring between December and February. There were three cases of *Pseudomonas aeruginosa*, cultured from tracheal aspirate, accounted for one case of severe community acquired pneumonia in a patient with chronic lung disease and recent hospital admissions. Gram negative enteric bacilli, usually *Enterobacteriaceae*, were isolated in seven cases from bronchopulmonary samples after at least five days on the ICU and were considered nosocomial in origin.

### Table 2 Presence of markers of severity in community acquired pneumonia

<table>
<thead>
<tr>
<th>Feature</th>
<th>Survivors (n = 24)</th>
<th>Deaths (n = 33)</th>
<th>Total (n = 57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-existing illness</td>
<td>11 (46)</td>
<td>10 (32)</td>
<td>21 (37)</td>
</tr>
<tr>
<td>Respiratory rate ≤ 30/min</td>
<td>12 (50)</td>
<td>18 (53)</td>
<td>30 (55)</td>
</tr>
<tr>
<td>Diastolic BP ≥ 60 mmHg</td>
<td>2 (8)</td>
<td>7 (21)</td>
<td>9 (16)</td>
</tr>
<tr>
<td>Acute confusion*</td>
<td>3 (13)</td>
<td>6 (21)</td>
<td>9 (14)</td>
</tr>
<tr>
<td>Blood urea &gt; 7 mmol/l</td>
<td>13 (54)</td>
<td>22 (67)</td>
<td>35 (61)</td>
</tr>
<tr>
<td>Arterial PO2 &lt; 8 kPa</td>
<td>15 (53)</td>
<td>23 (70)</td>
<td>38 (67)</td>
</tr>
<tr>
<td>WCC &lt; 4 or &gt; 20 x 10^9/l</td>
<td>3 (13)</td>
<td>7 (21)</td>
<td>10 (19)</td>
</tr>
<tr>
<td>Serum Na &lt; 130 mmol/l</td>
<td>8 (33)</td>
<td>6 (18)</td>
<td>14 (25)</td>
</tr>
<tr>
<td>Serum albumin &lt; 30 g/l</td>
<td>6 (25)</td>
<td>11 (33)</td>
<td>17 (30)</td>
</tr>
<tr>
<td>Multilobar shadows</td>
<td>6 (25)</td>
<td>10 (30)</td>
<td>16 (28)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages. * Data only available on 11 patients.

### Table 3 The impact of age on mortality in severe community acquired pneumonia

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>16–39</td>
<td>9 (16)</td>
<td>4 (44)</td>
</tr>
<tr>
<td>40–59</td>
<td>14 (25)</td>
<td>7 (50)</td>
</tr>
<tr>
<td>60–69</td>
<td>21 (37)</td>
<td>13 (62)</td>
</tr>
<tr>
<td>70–79</td>
<td>9 (16)</td>
<td>5 (56)</td>
</tr>
<tr>
<td>≥ 80</td>
<td>4 (7)</td>
<td>4 (100)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages.

ANTIBIOTIC THERAPY

Most of the patients received a beta-lactam agent on admission; 39 (68%) received ampicillin and 17 (30%) cefuroxime or cefotaxime. Erythromycin was administered to 91% of patients on arrival at hospital and to all patients upon ICU admission. This is in accordance with our local guidelines. Only four patients received fluclaxacillin on admission of whom only one had *S. aureus* pneumonia. Of the remaining six cases of *S. aureus* pneumonia four had received ampicillin and two cefuroxime.

Once in the ICU a median of 3.5 antibiotics were used per patient (range 1–7). In addition to a beta-lactam agent and erythromycin, 16 patients (28%) received rifampicin including all nine cases of legionnaires’ disease, and 14 (25%) received fluclaxacillin including all seven cases of *S. aureus* pneumonia. Twelve patients (21%) received an aminoglycoside including the one case of *P. aeruginosa* infection and the five cases of nosocomial Gram negative enteric bacilli infection.

Serious adverse effects attributed to an antibiotic and resulting in its discontinuation occurred in 12 cases (20%) – seven cases of grossly deranged liver function tests (three with fluclaxacillin, two with rifampicin, and two with...
both), two cases of aminoglycoside associated nephropathy, and one of flucloxacinil related rash.

TRANSFER TO ICU
Of the 57 patients transferred to the ICU 55 required assisted ventilation. Of these, 37 (65%) were transferred electively within 24 hours of admission. Four patients (7%) were only transferred following a cardiorespiratory arrest on the medical ward and six patients were transferred electively after more than 72 hours. In the latter group of 10 patients six fulfilled Rule 1 of the BTS guidelines for the recognition of high risk severe community acquired pneumonia at the time of their admission and subsequently died. The four remaining patients exhibited other markers of severity when admitted and there was one death.

From the time of admission to the ICU 58% of deaths occurred within one week and, of the 11 patients ventilated for 14 days or more, only three (27%) survived. The mean duration of ventilation for survivors and non-survivors was six days.

Discussion
Following our previous study we concluded that “attempts to reduce the mortality from community acquired pneumonia must include early recognition of severe infection, rapid identification of the pathogen involved and better management of the patient”. Management guidelines were introduced with regard to this on the perceived view that these will improve outcome whilst acknowledging the scepticism concerning the effectiveness and motives behind guidelines. The American Thoracic Society guidelines for the management of community acquired pneumonia have recently been re-evaluated. In this study we have shown that our guidelines have largely been adopted but the mortality for severe community acquired pneumonia remains high and unaltered.

Early recognition of severe pneumonia depends upon identification and recording of poor prognostic markers. Our local guidelines highlighted these and they have been verified in several subsequent studies. We have found that the admitting doctors were aware of and recorded these markers. There is a trend towards a higher mortality in older patients and increasing age is associated with worse prognosis, both as an independent risk factor and as a consequence of co-morbid disease. We have noted a trend towards older patients being admitted to our ICU with severe community acquired pneumonia over the last 20 years. This action is supported by the finding that 40% of those aged 60–80 years survived whereas they would presumably have died without intensive care.

A causal pathogen was identified in 67% of cases compared with 82% in our previous study and these figures are comparable to five recent prospective studies of severe community acquired pneumonia in which an aetiological diagnosis was made in 52–81% of cases. The reduction in diagnostic yield occurred despite adherence to our guidelines for more intensive investigation. Our guidelines advocated CIE testing for pneumococcal PCA in non-bacteraemic cases of severe community acquired pneumonia. The specificity of PCA in urine and serum is high, but the sensitivity estimates vary. In this study, 40% of non-bacteraemic cases tested for PCA were positive, demonstrating a high diagnostic yield from this test. Of the 19 cases in which no causal pathogen was identified 10 were never tested for PCA. Direct immunofluorescent staining and ELISA for Legionella antigen has resulted in legionnaires’ disease being diagnosed earlier in the illness, allowing for a more rapid and rational use of appropriate antibiotics. That half of our patients underwent bronchoscopy is probably an underestimate, the procedure not always being requested. However, in only four cases did bronchial washings disclose an aetiologic organism where earlier tests had proven fruitless. Three of these four were Pneumocystis carinii pneumonia, confirming the value of this technique in this condition. We did not perform distal protected aspiration or plugged telescoping catheter brushings, techniques reported to reward a higher yield. Only one study has found that increasing the rate of aetiological diagnosis in severe community acquired pneumonia significantly reduces mortality, and even then the authors were doubtful that the relationship was causal.

Our study confirms that S pneumoniae, L pneumophila, and S aureus account for the majority of cases of severe community acquired pneumonia although the local incidence of legionnaires’ disease has fallen. New pathogens are clearly likely to emerge in severe community acquired pneumonia. We diagnosed three cases of P carinii pneumonia in patients not known to be infected by HIV, confirming the need now to consider this diagnosis in cases of severe community acquired pneumonia. The low incidence of Gram negative enteric bacilli associated severe community acquired pneumonia is in keeping with previous studies in the UK. In other centres, however, up to 25% of cases of severe community acquired pneumonia are reported to be due to Gram negative pathogens, particularly Klebsiella spp and Enterobacteriae, probably representing differences in patient populations. In addition, there is evidence of significant false positive diagnoses of up to 30% in severely ill ventilated patients.

Our guidelines stressed the importance of an appropriate empirical antibiotic combination at admission to cover all likely pathogens. Initially erythromycin with ampicillin was advocated, with flucloxacinil added in winter months during possible influenza epidemics. However, the latter agent was clearly underused with four of the seven patients with S aureus pneumonia not receiving an antistaphylococcal agent on admission. In the latter half of the study we substituted ampicillin for a second or third
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generation cephalosporin which is also the recommendation of the BTS. As the mortality in staphylococcal pneumonia is high and clinical and radiological findings are non-diagnostic, agents with antistaphylococcal activity should be included initially for all patients with severe community acquired pneumonia. The importance of appropriate antibiotic therapy extends to the period on the ICU where they may influence the incidence of nosocomial infection and where drug side effects may confound an already complex illness. A fifth of patients received aminoglycosides despite the infrequent isolation of Gram negative organisms in severe community acquired pneumonia.

We have improved the timing of patient transfer from the medical ward to the ICU. Only 7% of cases were transferred following a cardiorespiratory arrest compared with 25% in the first study (p < 0.02), although most still exhibited poor prognostic markers that should have warranted earlier ICU admission. We detected a trend towards a higher mortality in patients with delayed transfer. It is felt that the outcome in critical illness is probably improved with early ICU transfer. However, Hook et al suggest that the ICU has had little impact on the outcome of bacteraemic pneumococcal pneumonia, merely prolonging the time to death in those destined to die, and a recent study of 127 cases of severe community acquired pneumonia found no significant difference in mortality in patients transferred before or after four days from admission.

Our guidelines are largely in accordance with the national BTS recommendations, which therefore enabled us to assess indirectly the working value of these recommendations for managing severe community acquired pneumonia. We found them to be practical and acquired pneumonia: aetiology, epidemiology and prognosis. We found the national BTS recommendations, which therefore enabled us to assess indirectly the working value of these recommendations for managing severe community acquired pneumonia. We found them to be practical and acquired pneumonia: aetiology, epidemiology and prognosis.

We thank the ICU staff for their cooperation with this study.


