Note

Review of 17 Cases of Pneumonia Caused by *Streptococcus pyogenes*

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**Abstract** *Streptococcus pyogenes* is an uncommon cause of community-acquired pneumonia and there have been few recent specific accounts of the condition. To describe the current nature of this disease in the UK, data was gathered on patients with clinical pneumonia from whom *Streptococcus pyogenes* was cultured principally from blood or other relevant normally sterile sites. In the Harrogate and Northallerton districts of North Yorkshire, pneumonia accounted for nine (20%) cases and a quarter of all deaths in a complete sequence of 45 patients with *Streptococcus pyogenes* bacteraemia detected during the 16-year-period 1981–1996. An analysis is presented of those cases together with eight recent cases from counties York, Durham and Isle of Wight during 1995–1997. Of the total 17 cases, nine occurred in women and eight in men; the age range was 30–92 years. The organism was isolated from blood culture in 15 (88%) patients. Eight (47%) patients died, five within 1 day of hospitalisation. Fourteen (82%) cases occurred in the winter months October to March, including all the fatal cases and all eight in which a clinical ‘viral’ prodrome was observed. Predisposing medical or surgical conditions were present in 65% of the patients. Major complications included septicaemia, pleural reaction, shock, pulmonary cavitation, osteomyelitis and metastatic abscesses. Seven serotypes of *Streptococcus pyogenes* were encountered, with M-type 1 predominating (the cause in 60% of cases). All infections were community acquired; two small clusters of fatal pneumonia were seen.

**Introduction**

*Streptococcus pyogenes* is an uncommon cause of acute pneumonia [1] that sometimes occurs as a secondary infection following acute viral infections such as measles and influenza [2–5]. In the earlier years of this century, it was estimated to account for 2–5% of cases of lobar/lobular pneumonia [6]. At that time outbreaks were reported in military camps, particularly when streptococcal upper respiratory tract infection or scarlet fever was also prevalent [4, 5]. In these youthful populations, the rate of bacteraemia was low; case fatality rates also fell to low levels after the advent of antibiotics [5]. According to recent accounts, pneumonia has occurred in outbreaks in homes for the elderly and as sporadic infection in adults in the community, often in patients with medical risk factors such as diabetes or immunosuppression [7, 8]. A heightened mortality rate for this infection has been noted in older patients and in those with bacteraemia [6]. With the resurgence of serious forms of *Streptococcus pyogenes* infection in many parts of the world during the last 15 years, several authors have noted an increased occurrence of previously rare forms of this infection, including pneumonia and necrotising fasciitis [7, 9]; streptococcal toxic shock syndrome has also occurred in some patients with these diseases [8, 10, 11].

*Streptococcus pyogenes* pneumonia often features a rapid onset of dyspnoea and fever with a predominant symptom of chest pain, and there is a high rate of pleural effusion and empyema [5, 6]; other complications include bacteraemia and necrotising pneumonia [3] leading to abscess and extending infection.
Mortality rates in bacteraemic case series [7, 9, 12] amount to 30–60%. We report the details of 17 patients with severe *Streptococcus pyogenes* pneumonia seen during the period 1981–1997.

### Materials and Methods

In the Harrogate and Northallerton districts of North Yorkshire (population 260,000), clinical and laboratory details of all patients (*n*=45) in whom serious *Streptococcus pyogenes* infection, including bacteraemia and infection of normally sterile sites, was detected in the 16-year period 1981–1996 were compiled from records made at the time and from a review of case notes. Cases of pneumonia were analysed as shown below, together with eight further cases of serious forms of *Streptococcus pyogenes* infection detected in the diagnostic laboratories in York, County Durham and the Isle of Wight in the period 1995–1997. The diagnosis of pneumonia was based on the typical clinical features of this disease and was established from the patient’s history, the physical examination, and the radiological, pathological and (in 4 cases) autopsy findings. Sputum was often not available before antimicrobial therapy was commenced in these seriously ill patients. In view of the likely contamination of expectorated sputum with streptococci from the throat, no systematic analysis or review was made of patients yielding *Streptococcus pyogenes* from this specimen during the period of the study. Organisms were typed at the Streptococcus Reference Unit, Respiratory and Systemic Infection Laboratory, Central Public Health Laboratory, Colindale, London. This included standard M, T and opacity factor typing on all isolates, together with R28 protein typing when indicated (the latter antigen is similar to, but more reliably detected than, the M-protein on the surface of type 28 strains).

#### Results and Discussion

In the Harrogate and Northallerton study, nine of 45 (20%) patients in whom *Streptococcus pyogenes* bacteraemia was detected had pneumonia, giving an annual incidence of 2.2 detected cases per 1 million population. In our previously reported series [13], pneumonia accounted for a quarter of all deaths in patients with *Streptococcus pyogenes* bacteraemia.

An analysis of those nine cases together with eight from the catchment areas of the co-authors (total 17 cases, see Table 1) gave the following results. There were nine women and eight men with an age range of 30–92 years (mean age, 57 years). The organism was isolated from blood culture in 15 (88%) patients, from sputum/bronchial aspirates in five (in 1 case the aspirate was the only site of isolation), from pleural aspirates in two and from postmortem lung tissue in two. Eight (47%) patients (mean age, 55 years) died, five within 1 day of hospitalisation. Eight (47%) patients were known to have experienced a respiratory ‘viral’ prodrome, which was confirmed as influenza A in one. Fourteen (82%) cases occurred in the winter months October to March, including all fatalities and all cases in which viral prodromes occurred. Medical and surgical conditions likely to predispose to serious infection were present in 65% of patients. Complications included the following: signs of septicaemia (i.e. a

### Table 1 Details of 17 patients with *Streptococcus pyogenes* pneumonia diagnosed in 1981–1997 in the UK

| Month/year | Sex/Age (yr) | Streptococcal type | Leucocytosis (×10^9 cells) | Lymphopenia (×10^9 cells) | Additional features | Predisposing factors | Outcome |
|------------|--------------|------------------|----------------------------|--------------------------|-------------------|---------------------|---------|
| 12/95      | M/30 M1      | –                | +                          |                          | lung necrosis, cavitation TSS, DIC, convulsions | smoker, alcoholic, NSAIDs | died    |
| 1/87       | F/31 M1      | + n/a            |                            |                          | empyema, desquamation surgical decocrtation | smoker, influenza A | survived |
| 10/95      | M/31 M1      | + n/a            |                            |                          | pneumothorax, TSS, anaemia | none | survived |
| 1/96       | F/32 M1      | n/a              |                            |                          | pharyngitis, viral prodrome | none | died |
| 1/97       | M/35 n/t     | +                |                            |                          | viral prokrome, septicaemia, cyanosis, empyema, 10 kg weight loss | none | survived |
| 2/95       | F/48 n/t     | +                |                            |                          | viral prokrome | none | survived |
| 12/96      | F/50 M1      | + b              |                            |                          | hypotension, DIC | alcoholic | died |
| 6/89       | M/52 M75     | n/a              |                            |                          | none | multiple myeloma, steroids | survived |
| 12/96      | M/52 M1      | - leucopoeia     |                            |                          | haemoptysis, viral prodrome | smoker | died |
| 2/81       | F/55 T13M    | n/a              |                            |                          | septicaemia, hypotension | paraplegia, kyphosclerosis | died |
| 12/95      | M/62 M1      | –                |                            |                          | diarrhoea, vomiting, viral prokrome | none | died |
| 9/97       | F/63 M58     | +                |                            |                          | cellulitis foot, osteomyelitis multiple abscesses | osteoarthritis, NSAIDs | survived |
| 2/87       | M/78 M9      | – n/a            |                            |                          | septicaemia, anaemia | lung cancer, debility | died |
| 12/95      | F/79 M1      | leucopoeia       |                            |                          | septicaemia, viral prokrome | none | died |
| 3/88       | F/81 M6      | +                |                            |                          | pleural effusion, anaemia | arthritis | survived |
| 10/89      | M/91 R28     | +                |                            |                          | viral prokrome, septicaemia, anaemia | prostate cancer, NSAIDs | survived |
| 2/81       | F/92 M1      | – n/a            |                            |                          | debility, anaemia | dementia | survived |

*12 g/dl haemoglobin

Streptococcal toxic shock syndrome; DIC, disseminated intravascular coagulation; NSAIDs, nonsteroidal anti-inflammatory drugs; n/a, data not available; n/t, organism not saved for typing

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^1 General physical frailty

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severe generalised illness associated with positive blood culture but without signs of extrathoracic localisation of infection) in nine patients, pleural reaction in five, streptococcal toxic shock syndrome in two, hypotension in two further patients (i.e. a total of 4 of 17 [24%] patients had documented hypotension), desquamating rash in two, disseminated intravascular coagulation in two, pneumothorax in one, osteomyelitis of the clavicle with multiple soft tissue abscesses in one, and necrotising pneumonia with cavitation and convulsions in one. Of the 14 patients tested, blood analysis showed anaemia in 43%, elevated total leucocyte count in 57% and depressed total leucocyte count in 21%. Ten patients were tested for lymphopenia, nine of whom were lymphopenic. Table 1 shows the nonavailability of data. Typing of 15 patient isolates showed nine of M-type 1 (i.e. 60% of the infections) and one each of M-types 6, 9, 58, 75, and R-type 28. Six of nine (67%) patients infected with M-type 1 isolates died, as compared with two of six (33%) infected with other types.

All infections were community acquired. A likely source of infection was known in only three cases, one in which pharyngitis had occurred previously, and two in which the patients were exposed to nursing-home staff with superficial infections of the skin and eye featuring the same M-types of *Streptococcus pyogenes*. Apparent clustering of M-type 1 *Streptococcus pyogenes* pneumonia associated with influenza-like prodromes included two fatal cases (4 days apart) in a family and two fatal cases in a small town within 1 week.

*Streptococcus pyogenes* is a rare cause of community-acquired pneumonia. Apart from occasional case reports, there have been few recent publications describing the condition. In the 16-year study in North Yorkshire, pneumonia was the major clinical feature in 20% of cases of *Streptococcus pyogenes* bacteraemia detected; other such series in recent years have recorded pneumonia in a similar range of 10–24% [7–9, 12].

Investigators have noted the occurrence of *Streptococcus pyogenes* pneumonia following measles and acute viral respiratory tract infections [3, 4], perhaps as a result of virus-induced epithelial damage in the tract together with transient immune suppression. A synergistic interplay involving influenza virus activation has also been noted as a result of the direct and indirect effects of streptococcal protease and streptokinase [14]. However, during influenza epidemics *Streptococcus pyogenes* has remained a relatively rare cause of secondary bacterial pneumonia [2]. The marked seasonal variation in occurrence of the disease noted in this and other reports is consistent with the concept that infection is often secondary to viral infections featuring a winter peak. It was notable that 11 of 15 (73%) of our typed strains were of the lower M-number types of *Streptococcus pyogenes*; such strains have been associated more frequently with respiratory infections than those affecting the skin [15], the latter often having complex T-typing patterns and, because they were detected later in the historical study of streptococci, generally having been allocated higher numbers in the numerical sequence of M-types.

We found a high rate of *Streptococcus pyogenes* bacteraemia (88%), but our study was retrospective and based partly on a review of the records of blood culture and culture of other normally sterile yet infected sites, an approach that would naturally emphasise the most serious cases. Case ascertainment was further influenced by the decision not to make a systematic review of patients yielding *Streptococcus pyogenes* from sputum. If bacteraemia is infrequent in this disease, as was thought to be the case earlier in this century [4, 5], our ascertainment is likely to underestimate the occurrence of *Streptococcus pyogenes*-associated pneumonia, particularly in its less severe forms, and it would be difficult to extrapolate accurate incidence/prevalence figures from the data.

The overall mortality rate in our study was high (47%), and a fatal outcome was seen in a high proportion of those infected with the currently prevailing M-type 1 streptococcal strains, including several younger patients with few, if any, predisposing medical conditions. Fatal infection with such strains in previously healthy young adults has been noted by others in recent years [10]. All three patients in our study with documented leucopenia at admission died of the infection, adding weight to the suggestion of others [12] that this could be an adverse prognostic sign. As described recently by other authors [3, 8, 11], we encountered two patients in whom *Streptococcus pyogenes* pneumonia was accompanied by toxic shock syndrome. In one, toxic shock syndrome occurred in association with radiologically demonstrated bilateral basal pneumonia and pneumothorax, and in the other, who had necrotising pneumonia with cavitation, the organism was isolated from blood and sputum cultures (both patients were infected with M-type 1 isolates). In the former patient and in a second with radiologically proven lower lobe pneumonia yielding the organism from bronchial aspirate and postmortem lung tissue, the clinical course was complicated by the development of adult respiratory distress syndrome (ARDS). Bacterial pneumonia and adult respiratory distress syndrome can co-exist, as we believe occurred in these cases. In the other cases in this report, a diagnosis of pneumonia apparently was readily established based on the clinical and investigational findings. Streptococcal exotoxins, in addition to their perceived role in toxic shock syndrome, might be responsible for endothelial activation and pooling of lymphocytes leading to lymphopenia [7], a condition found in nine of the ten patients tested in our study.
As noted in much earlier studies [5, 6] troublesome pleural effusions and empyema occur frequently in streptococcal pneumonia. In our series pleuritic chest pain was a predominant feature in seven patients at presentation to hospital. In one 30-year-old male patient who died 1 day after admission, chest drains were required for pleural effusion, and a shaggy fibrous exudate was noted on the pleura at autopsy. In four of nine (44%) survivors (2 yielding Streptococcus pyogenes from aspirated fluid) early pleural effusion and empyema persisted in at least two cases for up to 3 months, requiring repeated drainage of up to 1200 ml of fluid and, in one case, surgical decortication. The antimicrobial and supportive management of the patients described in this study varied from case to case and centre to centre and no useful detailed conclusions could be drawn on optimal procedures. One patient died at home and seven others within 4 days of hospitalisation (mode 1 day); five (31%) hospitalised patients were managed in an intensive care unit, and antibiotic courses were often of 2–3 weeks’ duration.

Streptococcus pyogenes strains of M-type 1 and M-type 3 (which was not seen in our study) have been isolated most frequently in the recent resurgence of severe streptococcal infection in many countries of the world. The data suggest that a significant proportion of the infections described here were caused by virulent resurgent strains.

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