Pleural infection on the increase but with a better evidence base to inform clinical care

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Infection of the pleural space is an ancient disease, with the earliest recorded description more than 5000 years ago,1 and the first consistent description of its manifestations and treatment credited to the father of modern medicine, Hippocrates.2 Open thoracic drainage, with its associated high mortality, remained the standard treatment for pleural infection until the influenza pandemic of 1919, when closed tube drainage techniques described in the 19th century3 4 were used, and significantly reduced the associated mortality.5 The treatment principles described almost 100 years ago remain to this day in the treatment of pleural infection.6

For many years, pleural infection was considered to be a result of ‘pneumonia gone bad’ with fluid leaking out of the infected lung parenchyma resulting in an infected fluid collection which was poorly accessible to the immune system. The term ‘parapneumonic effusion’ exemplifies this possible aetiology. However, recent studies describing the microbiology associated with pleural infection suggest that this may be a too simplistic understanding of the pathological processes occurring. There are markedly different bacteriological patterns in pleural infection7 compared with pneumonia, suggesting microbiologically distinct diseases. Nonetheless, the more widespread use of early antibiotic therapy for pneumonia may be expected to result in decreasing rates of pleural infection, if all pleural infection is simply a complication of pneumonia not treated early enough.

Recent evidence suggests that this may not be the case, and it may be time to rethink our understanding of the development of pleural infection. The study by Grijalva et al8 in this issue of Thorax provides significant new data to a number of studies from the last 4 years9–11 demonstrating increasing incidence of pleural infection in both the adult and paediatric populations (see page 663). While a number of previous studies may be subject to selection bias, Grijalva et al employed a robust study design to minimise this, using a large national database of a wide range of hospital settings, an unbiased sampling strategy and wide diagnostic and procedural criteria. In addition, the authors stratified incidence changes by age (including paediatric and adult populations) and perhaps most interestingly by organism.

The authors report a significant (twofold) increase in the incidence of pleural infection—as expected, the incidence was highest in the oldest age strata (>65 years), but all age groups experienced a roughly twofold increase over the study period. Perhaps most interestingly, while rates of pneumococcal empyema appeared to remain stable in both adult and paediatric populations, the incidence of staphylococcal and especially streptococcal empyema showed a significant increase over the study period.

This study thus provides further evidence of the increasing burden of disease associated with pleural infection, and begins to pose intriguing questions as to the aetiology of this consistently reported increase. Within the paediatric sphere, there is continued debate as to the role of the heptavalent pneumococcal vaccine as a potential causative factor in this increase.12 13 While the Grijalva et al study suggests a changing microbiological pattern associated with increased incidence, perhaps favouring more resistant organisms that have been associated with a poorer prognosis in previous studies.7

The potentially changing microbiological face of pleural infection highlights the importance of swift and accurate microbiological diagnosis. The clinician treating pleural infection is at a particular disadvantage—previous studies demonstrate that around 40% of pleural infection will remain microbiologically obscure despite standard pleural fluid culture.7 Organisms resistant to standard pneumonia antibiotic regimens are common, and thus a significant proportion of patients will require empirical broad-spectrum antibiotics for the duration of their treatment,6 with the well-known attendant risks. Although several studies have assessed the use of bacterial genetic techniques to increase diagnostic yield,7 14–16 these techniques are far from proven in the clinical context and currently confined to research centres.

The study by Menzies et al (see page 658) provides the first comparative, prospective evidence of increased microbiological diagnostic yield in pleural infection using a widely available clinical test (the BACTEC blood culture bottle system, Becton, Dickinson U.K. Limited, Oxford, UK).17 Addition of blood culture bottle inoculated pleural fluid to standard pleural fluid culture increased microbiological diagnostic yield by 21%, and in a small proportion of cases (4%) where standard culture was positive, blood culture bottle inoculation suggested the presence of organisms which would alter antibiotic management. These findings are further supported by the lack of false positivity in control samples. Intriguingly, ‘standard’ culture was positive where the pleural fluid in blood culture bottle was negative in 29% of cases, suggesting potential organism preference for certain growth medium.

Complex bacterial genetic techniques merit further clinical investigation and may become an important diagnostic modality in the future. However, the study by Menzies et al17 demonstrates a significant increase in diagnostic yield using a widely available and relatively inexpensive technique, suggesting that inoculation of pleural fluid into blood culture bottles as an addition to standard pleural fluid culture should be added to standard practice today.

There is therefore compelling evidence that pleural infection is on the increase, and the suggestion that organisms associated with a poorer prognosis may be responsible. Although the precise reasons for this trend remain obscure, it is clear that pleural infection will continue to be an important clinical entity in everyday respiratory practice. Clinical studies, such as the two studies highlighted in this editorial, are vital in advancing our understanding of disease pattern and process, and improving delivery of care.

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Editorial
We would like to end this editorial with a tribute to Professor Robert J O Davies who unexpectedly died recently, and whose career was exemplified by such studies. He was well known around the world as a leading authority in pleural diseases and made significant contributions to the field, with a strong and lasting impact on the clinical care of patients with pleural disease. Professor Davies was instrumental in changing the image of pleural disease from a stagnant and ignored field to a vibrant subspecialty interest in the UK and beyond. He was passionate in promoting evidence-based care for pleural disease patients, and to this end set up a Respiratory Clinical Trials Unit at the Churchill Hospital in Oxford, from where he coordinated several landmark multicentre studies addressing key clinical questions in pleural infection, malignant pleural effusion and sleep medicine. His enthusiasm and drive generated a successful network of collaborating departments throughout the UK and he chaired the highly influential 2005 British Thoracic Society guidelines for the management of pleural disease, further contributing to his international reputation.

His contribution to pleural infection is perhaps best summed up by the most recent BTS Pleural Disease Guidelines, where his published original papers contributed to 5 of the 16 (31%) grade A or B recommendations in the pleural infection section. He will be greatly missed personally and professionally.

Acknowledgements We thank Professor John Stradling (Oxford, UK) for his help in writing the obituary.

Provenance and peer review Commissioned; not externally peer reviewed.

Published Online First 15 June 2011
doi:10.1136/thx.2011.161315

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