

concept that individual diseases exhibit unique characteristics. Taking these characteristics into account should enable a more accurate assessment of disease severity. Numerous examples exist of disease-specific scores that outperform generic scores,<sup>13,14</sup> including the PSI in the context of patients hospitalised with CAP.<sup>15</sup> The study by Barlow *et al* extends this view to CURB65 in relation to SEWS and SIRS. However, the patient cohort in this study differs from other CAP cohorts in two substantial ways: (1) only 52% of the patients had chest radiographic confirmation of pneumonia and (2) the overall mortality of the cohort was high (19%) compared with other CAP studies such as the study by Man *et al*<sup>3</sup> in which the mortality rate was 8.6% (mean age of the cohorts was 74 years and 72 years, respectively). Confirmation of these findings in a separate cohort is therefore desirable.

Generic scores such as SIRS and SEWS have their roots in critical care and anaesthesia. These areas of medicine manage patients with diverse surgical and medical illnesses. The use of generic scores to triage and assess a wide case-mix of patients in a standardised manner is helpful. However, when managing an individual patient with a specific disease, they should be used alongside disease-specific severity scores that are likely to be more accurate, as is the case for CAP.

Where to from here? In the assessment of CAP we now have two validated tools that are reasonably good at stratifying patients according to mortality—the PSI and the CURB65 score. Each of these tools has advantages and disadvantages.<sup>16,17</sup> Centres should therefore adopt

the tool that best suits the local health-care setting. With regard to research, further validation of these tools in different patient cohorts, though desirable, should not detract from the pressing need to determine whether the use of severity assessment tools in the management of CAP ultimately leads to improved clinical outcomes.<sup>18</sup> Such intervention studies are needed if optimal management strategies for patients in different prognostic groups are to be defined.

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Cystic fibrosis/bronchiectasis exacerbations

## Pulmonary exacerbations in cystic fibrosis and bronchiectasis

J S Elborn, S C Bell

A series of papers reviewing pulmonary exacerbations in CF and bronchiectasis

In the current (*see page 360*) and forthcoming issues of *Thorax* we are publishing a series examining current practice and evidence of the epidemiology

and pathogenesis, prevention and treatment of pulmonary exacerbations in patients with cystic fibrosis (CF) and bronchiectasis.<sup>1–4</sup> This follows on from a

recent series examining aspects of exacerbations of chronic obstructive pulmonary disease and asthma. These reviews involved authors from Australia, USA and the UK, and each has considered the topics from both a paediatric and adult perspective. Several themes emerge in these reviews, including: (1) the challenges of diagnostic precision of definitions of respiratory exacerbations; (2) the need to develop new and/or novel endpoints for therapeutic trials for the treatment of exacerbations; and (3) the urgent need for multicentre studies to investigate both preventive and therapeutic interventions for patients with CF and bronchiectasis.

Goss and Burns highlight recent studies which have used definitions of

pulmonary exacerbations in patients with CF.<sup>1</sup> While many of the multicentre studies have used formal definitions of exacerbations, all have included components which are subjective and have had only limited validation.<sup>5–6</sup> Even the role of objective clinical measures in the definition of exacerbations, such as pulmonary function, has been questioned.<sup>1</sup> Two diagnostic scores have been recent useful additions for use in therapeutic trials, but further validation is required before they can be widely applied.<sup>1,7</sup> Chang and Bilton highlight the fact that very limited information is currently available on the definition of pulmonary exacerbations in patients with bronchiectasis.<sup>4</sup>

Until recently the change in forced expiratory volume in 1 s has been the primary endpoint for most CF therapeutic trials. Improved median survival<sup>8–9</sup> and reduction in the rate of decline of pulmonary function<sup>10–11</sup> suggest improvement in the outcome for patients with CF. Consequently, either larger study populations or longer clinical trials will be required to provide data to support the role of new treatments, if these classic trial endpoints are to continue to be used. As a result, new endpoints for trials have emerged, including changes in quality of life<sup>12</sup> and changes in the rates of and time to pulmonary exacerbation.<sup>13–14</sup> The inclusion of the latter two further highlights the need for more research on the validity of scoring systems to define respiratory exacerbations.

Evidence-based advances in the management of patients with CF have been seen in the past decade with the successful completion of numerous multicentre clinical trials. These studies have confirmed the role of mucolytics and hypertonic saline,<sup>6–15</sup> inhaled antibiotics (such as tobramycin),<sup>16</sup> anti-inflammatory therapies<sup>14–17</sup> and macrolides<sup>18–19</sup> in improving clinical outcomes, including in some cases the effects on exacerbation rates.<sup>6–15–16–19</sup> highlighted in the review by Bell and Robinson.<sup>2</sup> Furthermore, it is now clear that parenteral aminoglycosides (such as tobramycin) for the treatment of pulmonary exacerbations may be better administered by once daily dosing than by multiple daily doses.<sup>3</sup> Such evidence has led to major changes in practice for patients with CF. However, each of the reviews highlights significant gaps in the knowledge of many aspects of the treatment of patients with CF and bronchiectasis.<sup>1–4</sup>

While there are now some data supporting treatment choices for the most common bacterial pathogen in patients with CF (*Pseudomonas aeruginosa*), more study is required to extend the limited in vitro data to support antibiotic choices for

less common and often more resistant pathogens such as *Burkholderia cepacia* complex, *Stenotrophomonas maltophilia*, *Achromobacter xyloxidans* and methicillin-resistant *Staphylococcal aureus* in patients with CF. Such studies will require a collaborative and international approach to draw together sufficient patient numbers to provide study power and thus are likely to be extremely difficult to fund. Similarly, further study is required to examine treatment choices for very young children with CF which, to date, have received more limited attention in multicentre therapeutic studies.

There are also very few data currently available comparing the role of different treatments, both with each other and as complementary therapies. For example, we do not know whether rhDNase 1 is more effective than hypertonic saline or whether the effect of rhDNase 1 is enhanced by the administration of hypertonic saline to the same patient, or whether such combinations are counterproductive for some patients. Given that current clinical practice has often involved the addition of a new treatment modality to existing therapies, it is hoped that such comparisons could be performed in the future, particularly as many new treatments are expensive for our healthcare systems and/or are time-consuming for the patient.

Even more work remains to be performed to provide evidence to support treatment choices for patients with bronchiectasis. Most studies of preventive and treatment strategies of respiratory exacerbations in bronchiectasis have been undertaken at a single centre and have included small patient numbers where power calculations have not been reported and where the definitions of exacerbations have been limited. An important message of the study by O'Donnell *et al.*—who reported the results of a randomised controlled trial to assess the effect of rhDNase 1 in patients with idiopathic bronchiectasis—was that, while rhDNase 1 is an effective treatment in patients with CF, these benefits are not directly transferable to patients with bronchiectasis.<sup>16–20–21</sup> Studies addressing a specific treatment need to be performed in patients with bronchiectasis. The recent publication of the characteristics of a cohort of patients with bronchiectasis provides an opportunity to draw together clinicians and researchers with an interest in this understudied disease to allow the design, search for funding support and successful execution of multicentre studies.<sup>22–25</sup> However, funding bodies will need to take a far-reaching view and to look for improved patient outcomes by evidence-based treatment strategies, as is

starting to be realised for patients with CF.

Exacerbations of CF and bronchiectasis have a negative impact on patients' quality of life, require expensive treatment and are associated with poor outcomes. Finding ways to reduce the frequency of these events will improve the lives of people with chronic suppurative lung disease.

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