

such a high cure and completion rate. Firstly, no outcome was reported in 18.1% (2364) of cases, and the demographics of the non-reported cases showed higher age and higher proportions of white ethnicity and pulmonary tuberculosis, all of which are more associated with adverse outcome. These individuals, if they had had reports, are likely to reduce the overall success figures as the authors themselves accept. Secondly, enhanced surveillance reports outcome if properly recorded but may miss important process errors, which would only be apparent as later relapse or drug resistance. The pilot for enhanced surveillance showed less than half were getting an appropriate four drug regimen, 11% were not on combination tablets and only 41% had minimum compliance monitoring,<sup>18</sup> all factors potentially leading to later relapse. Relapse is not recorded under enhanced surveillance but between 5% and 10% of notifications have a history of prior tuberculosis treatment, suggesting their current episode is a relapse. Relapse rates after treatment are seldom reported in the UK,<sup>29</sup> but would be expected to be between 0% and 3% from data from controlled clinical trials.<sup>3</sup>

Modification of the reporting criteria for the UK enhanced tuberculosis surveillance system seems appropriate from the analysis<sup>26</sup> but strenuous efforts need to be made to increase the level of outcome reporting above the current 82%, ideally to 100%. Short cross sectional audits may also be needed to confirm appropriate regimens, combination tablets and adequate adherence monitoring are being used.

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# Short course of antibiotic treatment in acute exacerbations of COPD

Robert Wilson

Antibiotics are commonly prescribed empirically for lower respiratory infections. Infections of the airway mucosa are

much more common than pneumonia and the illness they cause is less severe because the infection is superficial, most of the bacteria being found associated with mucus in the lumen. In many cases the infection will resolve spontaneously without antibiotic treatment. Most adult

patients are experiencing an exacerbation of chronic lung disease, particularly chronic obstructive pulmonary disease (COPD), when neutrophilic inflammation in response to bacterial infection leads to increased sputum volume and viscosity, and breathlessness due to airflow obstruction. In these circumstances, bacteria are cultured from sputum in about half of the cases which means that, in some of the others, accepting that sputum culture is not a sensitive investigation, antibiotics are given unnecessarily. Antibiotics are essential when a patient with severe COPD presents with purulent sputum and systemic symptoms of infection, but they are often given either to speed up recovery from a bacterial infection that

might be expected to resolve spontaneously following a successful host inflammatory response, or in a defensive manner to avoid the risk of airway infection progressing to pneumonia and causing deterioration in a more compromised patient whose host defences are more seriously impaired.

In recent years attention has rightly focused on trying to define which patients benefit from antibiotic treatment, and those in whom antibiotics can be avoided. The size of the likely benefit has to be taken into consideration when making a decision about antibiotic treatment because of the rise in antibiotic resistance among common respiratory pathogens,<sup>1</sup> which is directly related to the volume of antibiotic consumption in a community.<sup>2</sup> Sputum purulence has proved to be a reliable signal of bacterial infection<sup>3</sup> and, together with the symptoms of increased sputum volume and breathlessness, has been used in COPD guidelines for antibiotic use. These cardinal symptoms were used in the study performed by Anthonisen *et al.*<sup>4</sup> Antibiotics or placebo were given in a randomised, double-blind, crossover fashion for COPD exacerbations. Sputum cultures were not performed, so the outcome of the study cannot be related to microbiology. There was a significant benefit from antibiotics that was largely accounted for by patients who had all three symptoms (type 1 exacerbations), whereas there was no significant difference between antibiotic and placebo in patients with only one of the symptoms. However, in the type 1 exacerbations, 43% of patients recovered in the placebo group within 21 days. A recent Cochrane review<sup>5</sup> of antibiotics and COPD exacerbations showed that antibiotics reduce the risk of treatment failure (relative risk ratio 0.47) and the number of patients that needed to be treated to avoid a failure was three. Antibiotics influenced resolution of sputum purulence but did not influence recovery of peak flow or gas exchange.

The meta-analysis performed by El Moussaoui *et al.*<sup>6</sup> published in this issue of *Thorax* (see page 415) has addressed an important aspect of antibiotic treatment. Some COPD guidelines have recommended a choice of antibiotic to use during exacerbations, but none has addressed the length of the course of treatment. The authors list the benefits of a shorter course: better patient compliance, fewer side effects and, most importantly, reduced risk of antibiotic resistance development. The result is clear: short-course treatment—which

usually means 5 days—is equally efficacious as longer courses (7–10 days). Eradication of bacteria from sputum was also equivalent. This is a very important message for clinicians. The result was the same in trials in which short and longer courses of the same antibiotic were included and when antibiotics were grouped by class. The authors rightly restrict their conclusions to mild to moderate cases. COPD is a very heterogeneous condition and patients enrolled into clinical trials do not usually have life-threatening disease, and protocols exclude sicker patients that are more likely to fail. Trials have usually had a primary end point soon after the end of treatment and so may have missed early relapse due to inadequate treatment.

In the above-mentioned Cochrane review<sup>5</sup> a significant benefit for antibiotics versus placebo was found for mortality (relative risk ratio 0.23), but this result was heavily influenced by a single study in patients with severe exacerbations requiring ventilator support.<sup>7</sup> Several COPD studies have sought to identify risk factors for poor outcome of an exacerbation.<sup>8</sup> Frequent exacerbations, low forced expiratory volume in 1 s, comorbid diseases (especially cardiovascular and diabetes), low body mass index, current smoking habit, alcohol consumption, duration of COPD and older age have all been identified as risk factors in different studies.<sup>8</sup> In these patients, clinical response—particularly sputum colour and, in a hospitalised patient, return of inflammatory markers to baseline—should determine length of treatment. Some patients with COPD who may have regular sputum production and be particularly prone to infective exacerbations have underlying bronchiectasis.<sup>9</sup> This is another group in which the course of treatment might need to be longer, although it could be argued that these patients are particularly prone to resistance development because of the larger concentration of bacteria in the airway lumen. Short-course treatment would therefore still be desirable if it was proved to be effective.

A rapid specific biomarker to identify bacterial lower respiratory tract infections would provide a major advance in the antibiotic management of patients with COPD, particularly if it could also be used to judge response to treatment. While procalcitonin has shown some promise in this regard,<sup>10</sup> more work is needed to explore its application. For the time being, clinical judgement will

determine which patients receive an antibiotic and the length of time for which treatment should be given. Present guidelines are not consistent, but purulent sputum as a marker of bacterial infection, together with increased sputum volume and/or increased breathlessness indicated by the study of Anthonisen *et al.*,<sup>4</sup> are recommended to judge the need for antibiotic. The meta-analysis by El Moussaoui *et al.* has shown that, in patients without risk factors for poor outcome, a 5-day course of antibiotic should be used. Further studies are needed in at-risk groups because short courses might still be effective for some antibiotics that penetrate well into the respiratory mucosa, and are active against resistant strains that are more common in at-risk patients who have received antibiotics previously. A weakness of the meta-analysis is that most studies include a new antibiotic seeking registration in the short-term arm and not older agents such as amoxicillin, tetracycline and erythromycin. However, at the present time, few studies have shown superiority of one antibiotic over another in this patient group.<sup>8</sup> Future studies should involve follow-up for several weeks after the end of treatment to ensure early relapse does not occur because of bacterial persistence, and should include tools such as patient reported outcome questionnaires to determine speed and extent of recovery rather than the traditional end point of a judgement by the clinician as to whether or not the patient requires more antibiotic.

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# Celebrating 25 years of the BTS: the Silver Jubilee Meeting

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The BTS took over the entire Queen Elizabeth II Conference Centre in London again this year to host its Silver Jubilee year Winter Meeting. This, the biggest and most comprehensive meeting so far, was also the first to accommodate an additional day for allied health professionals, held in conjunction with the Association of Chartered Physiotherapists in Respiratory Care (ACPRC).

## PRESIDENT'S ADDRESS AND RECEPTION

In his Presidential address, “Beyond the prescription”, Professor Martyn Partridge focused on the way health care delivery might change in the future with more consultations being delivered in community-based clinics at times which would be more convenient to our patients.

The BTS medal was jointly presented to Professor Peter Barnes and Dr Alistair Brewis for their outstanding contributions to respiratory medicine and, at the lively reception, Professor Sue Hill, Chief Scientific Officer at the Department of Health, presented the BTS Silver Jubilee Awards. These covered seven categories celebrating innovation and excellence in respiratory medicine care and service delivery and were a showcase of achievement through teamwork. Also at the reception, the BTS Young Investigator Prize was awarded to Dr David Simcock for his work on airway neovascularisation by airway smooth muscle in asthma.<sup>1</sup> The BALR prize went to Dr Yang for his studies on altered gene regulation in familial pulmonary hypertension<sup>2</sup> and the BLF prize winner was Dr Kewin for his work on a novel cytokine found to induce eosinophilic airway inflammation.<sup>3</sup>

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Other abstracts submitted for prizes covered a wide range of topics such as statin treatment in hypoxic pulmonary hypertension,<sup>4</sup> the search for molecules to block polymerisation of Z  $\alpha_1$ -antitrypsin<sup>5</sup> and the role of vascular endothelial growth factor on the cell cycle of alveolar cells.<sup>6</sup>

## CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

In recognition of the increasing interest and research in COPD, a large proportion of the programme was devoted to this topic. At the symposium “COPD – more than tobacco, not just the lung”, Professor John Ayres gave a valuable global perspective of the disease, reminding us of the growing impact of biomass and vehicular pollution in the developing world. We also heard about how short-course cognitive behavioural therapy targeted at “revolving door” patients and delivered by a respiratory nurse specialist reduced acute health care utilisation in Newcastle. Along similar lines, Dr Sarah Booth raised awareness of some non-pharmacological tools such as cold facial stimulation that can be used to tackle breathlessness in COPD.

Continuing interest in co-morbidities<sup>7</sup> and systemic pathologies<sup>8,9</sup> associated with COPD were well covered. Particularly interesting was a pilot study from Edinburgh showing abnormal endothelial function in patients with COPD. Here invasive studies of forearm blood flow demonstrated impaired acetylcholine-mediated vasomotor response compared with controls,<sup>10</sup> providing evidence for a mechanism of increased cardiovascular morbidity in COPD. The same group presented data on an association between the severity of emphysema and increased arterial stiffness, a marker of cardiovascular risk.<sup>11</sup>

Ironically, the discussions on novel therapies for COPD were centred around old medicines such as the mucolytic erdoxime<sup>12–14</sup> and the macrolide antibiotic erythromycin. In the 1-year double-blind placebo-controlled ELECT study, the

long-term use of erythromycin was associated with fewer exacerbations, but the mechanism was unclear with no observable effect on either airway or systemic inflammation.<sup>15</sup> A review from Leicester of a multidisciplinary emphysema meeting for lung volume reduction surgery demonstrated an impressive throughput of patients which might advocate a more widespread use in other centres.<sup>16</sup>

Posters included a review of the successful establishment of the BTS home oxygen database,<sup>17</sup> and several on exacerbation characteristics including a study on first exacerbations requiring hospital admission showing worrying deficiencies in diagnosis and treatment.<sup>18</sup>

## NON-INVASIVE VENTILATION (NIV)

The delivery and experience of NIV continues to expand, but much clinical practice lacks trial evidence. Dr Mark Elliott presented valuable randomised controlled data from the 3CPO trial showing that, in acute cardiogenic pulmonary oedema, NIV induced a faster improvement in respiratory distress and metabolic disturbance than standard therapy alone, and that continuous positive airway pressure and non-invasive positive pressure ventilation appear to be equally efficacious.<sup>19</sup> Evidence from two groups<sup>20,21</sup> was also presented for the usefulness of a protocol to reduce weaning time in patients on NIV in both respiratory and medical wards. There was an excellent medical student presentation from the Lane Fox Unit at St Thomas' Hospital which looked at the number of patients initiated on home mechanical ventilation (HMV) over a 2-year period; increasing numbers of patients were reported, mainly due to an expansion of the obstructive sleep apnoea/obesity group despite a decrease in HMV for neuromuscular disease.<sup>22</sup>

## ASTHMA

The title of Professor Sebastian Johnson's lunchtime lecture perhaps most appropriately summarised the consensus of delegates at the asthma sessions: “80 years of asthma research: a lot done, still more to do”. It was evident, though, that a great deal was being done, particularly on clinical aspects. These ranged from the investigation of the effects of mechanical heat recovery ventilation on asthma control<sup>23</sup> to