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

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might be expected to resolve sponta-
neously following a successful host 
inflammatory response, or in a defensive 
manner to avoid the risk of airway 
fection progressing to pneumonia and 
causing deterioration in a more compro-
mised 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,1 
which is directly related to the volume of 
antibiotic consumption in a community.2 
Sputum purulence has proved to be a 
reliable signal of bacterial infection3 and, 
together with the symptoms of increased 
sputum volume and breathlessness, has 
been used in COPD guidelines for anti-
biotic use. These cardinal symptoms were 
used in the study performed by Anthonisen et al.4 Antibiotics or placebo 
were given in a randomised, double-blind, 
crossover fashion for COPD exacerba-
tions. Sputum cultures were not per-
formed, 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 exacerba-
tions), whereas there was no significant difference between antibiotic 
and placebo in patients with only one of 
the symptoms. However, in the type 1 
exacerbations, 45% of patients recovered 
in the placebo group within 21 days. A 
recent Cochrane review5 of antibiotics and 
COPD exacerbations showed that anti-
biotics 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 al6 in this issue of 
Thorax (see page 415) has addressed an 
important aspect of antibiotic treatment. 
Some COPD guidelines have recom-
manded a choice of antibiotic to use 
during exacerbations, but none has 
defined the length of the course of 
treatment. The authors list the benefits of 
a shorter course: better patient compli-
ance, fewer side effects and, most impor-
tantly, reduced risk of antibiotic 
resistance development. The result is 
clear: short-course treatment—which 
usually means 5 days—is equally effica-
cious 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 
incorporated and when antibiotics were 
grouped by class. The authors rightly 
restriced their conclusions to mild to 
moderate cases. COPD is a very hetero-
genous condition and patients en-
rolled into clinical trials do not usually 
have life-threatening disease, and pro-
tocols 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 
review6 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.7 Several 
COPD studies have sought to identify 
isk factors for poor outcome of an 
exacerbation.8 Frequent exacerbations, 
low forced expiratory volume in 1 s, co-
morbid diseases (especially cardiovascular 
and diabetes), low body mass index, 
original smoking habit, alcohol consump-
tion, duration of COPD and older age 
have all been identified as risk factors in 
different studies.8 In these patients, clin-
ical 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 parti-
cularly prone to infective exacerbations 
have underlying bronchiectasis.9 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 resis-
tance development because of the larger 
concentration of bacteria in the airway 
lumen. Short-course treatment would 
therefore still be desirable if it was proved 
be effective. 

A rapid specific biomarker to identify 
bacterial lower respiratory tract infec-
tions 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,10 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 puru-
ulent sputum as a marker of bacterial 
fection, together with increased sputu-
num volume and/or increased breath-
lessness indicated by the study of 
Anthonisen et al.4 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 anti-
biotic 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 weak-
ness of the meta-analysis is that most 
udies include a new antibiotic seeking 
registration in the short-term arm and 
not older agents such as amoxicillin, 
tetracycline and erythromycin. How-
ever, at the present time, few studies 
have shown superiority of one antibiotic 
over another in this patient group.6 Future studies should involve follow-up 
for several weeks after the end of 
treatment to ensure early relapse does 
ot occur because of bacterial persist-
ence, and should include tools such as 
patient reported outcome questionnaires 
to determine speed and extent of recov-
ery 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 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 neo-vascularisation by airway smooth muscle in asthma.1 The BALR prize went to Dr Yang for his studies on altered gene regulation in familial pulmonary hypertension2 and the BLF prize winner was Dr Kevin for his work on a novel cytokine found to induce eosinophilic airway inflammation.3

Other abstracts submitted for prizes covered a wide range of topics such as statin treatment in hypoxic pulmonary hypertension,4 the search for molecules to block polymerisation of Z α1-antitrypsin5 and the role of vascular endothelial growth factor on the cell cycle of alveolar cells.6

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 short-course cognitive behavioural therapy targeted at “re-activating” patient 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-morbidities7 and systemic pathologies8 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,9 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.10

Ironically, the discussions on novel therapies for COPD were centred around old medicines such as the mucolytic edroterone11–14 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.15 A review from Leicester of a multidisciplinary emergency meeting for lung volume reduction surgery demonstrated an impressive throughput of patients which might advocate a more widespread use in other centres.16

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

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 SCPO 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.19 Evidence from two groups20 21 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.22

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 control23 to