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Commentary on 'Antibiotics for prolonged moist cough in children' with a response from the review authors

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Commentary

Commentaries on 'Antibiotics for prolonged moist cough in children' with a response from the review authors

These are commentaries on a Cochrane review, published in the issue of EBCH, first published as: Marchant JM, Morris PS, Gaffney J, Chang AB. Antibiotics for prolonged moist cough in children. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD004822. DOI: 10.1002/14651858.CD004822.pub2.

Further information for this Cochrane review is available in this issue of EBCH in the accompanying Summary article.

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Commentary by Bruce K. Rubin

Acute cough in children is most commonly due to a viral respiratory infection such as the common cold. There is clearly no benefit to using antibiotics to treat acute viral respiratory infections, and antibiotics do not decrease the severity or frequency of coughing. On the other hand, there is evidence supporting the use of antibiotic therapy in some young children with cough lasting for more than 3 weeks as it is postulated that many of these children will have bacteria and neutrophils in their airway signifying protracted bacterial bronchitis (1); protracted bacterial bronchitis is considered a form of 'nonspecific' cough; or cough that cannot be attributed to common conditions like postnasal drip, asthma, gastroesophageal reflux and bronchiectasis including cystic fibrosis. Nonetheless, the existence of protracted bacterial bronchitis as a clinical diagnosis remains controversial.

This review examines the results of two studies evaluating the use of antibiotics compared with either placebo or no therapy in children younger than 7 years who have prolonged moist cough of duration more than 10 days. This is distinct from both acute cough and chronic dry cough. The evidence suggests that administration of antibiotics will decrease the severity and duration of coughing in some of these children. However, the studies used for this analysis contain heterogeneous populations and methodological flaws, which make these recommendations less than robust. Furthermore, almost all children with prolonged moist cough eventually have spontaneous resolution of their symptoms and there is no clear evidence that withholding antibiotics from children with prolonged moist cough will lead to long-term adverse outcomes.

Critically, these recommendations are limited to children younger than 7 years who also have a 'moist cough' and have had this cough for at least 10 days. These limited data cannot be extrapolated to other patient groups. While there is no value in using antibiotics to treat an acute respiratory tract infection or a common cold, there is a risk that these data may be misinterpreted to imply that moist cough in children should be treated using an antibiotic before an acute viral infection has been given the opportunity to spontaneously resolve.

The potential for overuse of antibiotics is a major problem and has led to the widespread development of bacterial resistance to commonly used antibiotics. Antimicrobial stewardship has been an important focus of evidence-based therapy over the past decade. Thus, it is extremely important that antibiotics not be overused to treat a symptom that can be self-limiting. It is also important to balance the risk of antibiotic use which may be understated in this review. Allergy to penicillin is not uncommon in children and can be serious. Less common, but life threatening, is the risk of severe unanticipated adverse effects such as Stevens-Johnson syndrome.

Our understanding of the role of bacteria and airway inflammation in producing chronic cough in children is evolving, and should lead to more rational selection of patient populations who would benefit from appropriate intervention with antibiotic therapy.

Declaration of interest

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Reference

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Response by author

We thank Professor Rubin for his interest in the subject and his commentary. We however, respectfully disagree with many of his points. Firstly, protracted bacterial bronchitis (PBB) is not considered a form of 'nonspecific' cough (1). Nonspecific cough, as described about 13 years ago refers to 'dry cough in the absence of identifiable respiratory illness' (2).

Secondly, although we were the first group to label PBB as a clinical entity (so as to improve recognition and thus appropriate treatment) (3), the concept of cough resulting from endobronchial infection and inflammation in the airways is far from new, as outlined by Everard (4). Indeed, this association has also been described in adults (5), and in papers from previous decades. Pathobiological studies (6–8) and clinical observations suggest many patients with chronic, wet cough have bronchitis initially that, if persistent and left untreated, may evolve into bronchiectasis (9,10). Animal studies have shown that infection is a necessary condition for the development of bronchiectasis, as experimentally imposed bronchial stenosis in the absence of infection does not lead to bronchiectasis distal to the obstruction (11).

Thirdly, in our current era, PBB is internationally accepted (12,13), increasingly recognized (14,15) and has been incorporated into paediatric guidelines in many countries (16–19). Increasingly, pathobiological studies relating to PBB and wet cough in general are published (20–22).

Fourthly, the statement that 'almost all children with prolonged moist cough eventually have spontaneous resolution of their symptoms' is not referenced. Clearly, resolution with placebo treatment does occur (substantial improvement at follow up was seen in 36% and 21% in the two trials included in our review). However, this is much more likely in children who receive antibiotics as reflected in the number needed to treat for benefit of 3 (95%CI = ~~4–5~~) (23). In support of this, the progression of illness, as defined by requirement for further antibiotics in both papers (24,25), was significantly lower in the treatment group (pooled OR = 0.10; 95%CI = ~~0.03–0.34~~). The number needed to treat to avoid progression of disease was 4 (95%CI = ~~3–5~~) (23). Before antibiotics were discovered and widely available, not every exposed individual succumbed to infection and the clinical symptoms of the same type of infection varied among patients. Clearly, host response factors play a key role in determining clinical presentation and subsequent course of infection.

We do agree that the studies in the Cochrane review contain methodological flaws (as stated in our Cochrane review) (23). The two randomized controlled trials (24,25) in the Cochrane review were studies published in the early 1990s and the methodology issues must be interpreted in the context of that era. The post-CONSORT era started in 1998. However, there are very few randomized controlled trials on prolonged cough in children; the authors (24,25) of these randomized controlled trials are commended on their foresight. The conclusions of our Cochrane review (and earlier studies) are now further strengthened by recent studies. Our recent multi-centre national study involving 346 children (26), as well as a double-blind placebo-controlled randomized controlled trial (supported by bronchoalveolar data) (27) lend further substantial support: for the clinical entity of PBB; that use of appropriate antibiotics is efficacious and; that treatment significantly improves cough and parental-proxy cough-specific (PC-QOL) and generic (PedsQL) quality of life. We agree with Professor Rubin that antibiotics are not without side effects. Parents should be informed of both the likely benefits and harms when considering this treatment option. Finally, it is important that clinicians are cognizant that although most chronic wet cough in the absence of other symptoms and signs is PBB, not all wet cough is PBB (28), and that the management of acute cough differs from that for chronic cough.

Declaration of interest

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