

---

Charles Darwin University

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

Chang, Anne; Marchant, Julie; Morris, Peter

*Published in:*  
Evidence-Based Child Health

*DOI:*  
[10.1002/ebch.1870](https://doi.org/10.1002/ebch.1870)

Published: 01/09/2012

*Document Version*  
Peer reviewed version

[Link to publication](#)

### *Citation for published version (APA):*

Chang, A., Marchant, J., & Morris, P. (2012). Commentary on 'Antibiotics for prolonged moist cough in children' with a response from the review authors. *Evidence-Based Child Health*, 7(5), 1716-1718.  
<https://doi.org/10.1002/ebch.1870>

### **General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

### **Take down policy**

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

This is the peer reviewed version of the following article: Rubin, B. K., Chang, A. B., Marchant, J. M. and Morris, P. S. (2012), Commentary on 'Antibiotics for prolonged moist cough in children' with a response from the review authors. *Evid.-Based Child Health*, 7: 1716-1718. doi:10.1002/ebch.1870 , which has been published in final form at <https://doi.org/10.1002/ebch.1870> . This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions.

## 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.

### 1 **Commentary by Bruce K. Rubin**

2  
3 Acute cough in children is most commonly due to a  
4 viral respiratory infection such as the common cold.  
5 There is clearly no benefit to using antibiotics to treat  
6 acute viral respiratory infections, and antibiotics do  
7 not decrease the severity or frequency of coughing.  
8 On the other hand, there is evidence supporting the  
9 use of antibiotic therapy in some young children with  
10 cough lasting for more than 3 weeks as it is postu-  
11 lated that many of these children will have bacteria  
12 and neutrophils in their airway signifying protracted  
13 bacterial bronchitis (1); protracted bacterial bronchitis  
14 is considered a form of ‘nonspecific’ cough; or cough  
15 that cannot be attributed to common conditions like  
16 postnasal drip, asthma, gastroesophageal reflux and  
17 bronchiectasis including cystic fibrosis. Nonetheless,  
18 the existence of protracted bacterial bronchitis as a  
19 clinical diagnosis remains controversial.

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

36 Critically, these recommendations are limited to  
37 children younger than 7 years who also have a ‘moist  
38 cough’ and have had this cough for at least 10 days.  
39 These limited data cannot be extrapolated to other  
40 patient groups. While there is no value in using  
41 antibiotics to treat an acute respiratory tract infection  
42 or a common cold, there is a risk that these data

43 may be misinterpreted to imply that moist cough in  
44 children should be treated using an antibiotic before  
45 an acute viral infection has been given the opportunity  
46 to spontaneously resolve.

47 The potential for overuse of antibiotics is a major  
48 problem and has led to the widespread develop-  
49 ment of bacterial resistance to commonly used antibi-  
50 otics. Antimicrobial stewardship has been an important  
51 focus of evidence-based therapy over the past decade.  
52 Thus, it is extremely important that antibiotics not be  
53 overused to treat a symptom that can be self-limiting.  
54 It is also important to balance the risk of antibiotic use  
55 which may be understated in this review. Allergy to  
56 penicillin is not uncommon in children and can be seri-  
57 ous. Less common, but life threatening, is the risk of  
58 severe unanticipated adverse effects such as Stevens-  
59 Johnson syndrome.

60 Our understanding of the role of bacteria and  
61 airway inflammation in producing chronic cough in  
62 children is evolving, and should lead to more rational  
63 selection of patient populations who would benefit  
64 from appropriate intervention with antibiotic therapy.  
65  
66  
67

### 68 **Declaration of interest**

69  
70  
71  
72  
73  
74  
75  
76  
77  
78  
79  
80  
81  
82  
83  
84

Bruce K. Rubin\*

Virginia Commonwealth University School of Medicine, Children's  
Hospital of Richmond at VCU, Richmond, VA, USA

Correspondence to: Bruce K. Rubin, Jessie Ball DuPont Distinguished  
Professor and Chair, Department of Pediatrics, Professor of  
Biomedical Engineering, Virginia Commonwealth University School  
of Medicine, Physician in Chief, Children's Hospital of Richmond at  
VCU, 1001 East Marshall St. PO Box 980 646, Richmond, VA  
23 298, USA

E-mail: BRubin@mcvh-vcu.edu

### **Keywords:**

## Reference

1. Marchant JM, Masters IB, Taylor SM, Cox NC, Seymour GJ, Chang AB. Evaluation and outcome of young children with chronic cough. *Chest* 2006; **129**: 1132–1141.

## 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


Anne B. Chang,\* Julie M. Marchant, Peter S. Morris  
Qld Children’s Respiratory Centre, Qld Children’s Medical research Institute, Royal Children’s Hospital, Brisbane, Australia

Correspondence to: Anne B. Chang, Qld Children’s Respiratory Centre, Qld Children’s Medical research Institute, Royal Children’s Hospital, Brisbane; Division of Child health, Menzies School of Health Research, Charles Darwin University, Darwin, Australia  
E-mail: Anne.Chang@menzies.edu.au




## Keywords:

## References

1. Marchant JM, Masters IB, Taylor SM, *et al.* Utility of signs and symptoms of chronic cough in predicting specific cause in children. *Thorax* 2006; **61**: 694–698.
2. Chang AB. State of the art: cough, cough receptors, and asthma in children. *Pediatric Pulmonology* 1999; **28**: 59–70.
3. Marchant JM, Masters IB, Taylor SM, *et al.* Evaluation and outcome of young children with chronic cough. *Chest* 2006; **129**: 1132–1141.
4. Everard M. New respect for old conditions. *Pediatric Pulmonology* 2007; **42**: 400–402.
5. Schaefer OP, Irwin RS. Unsuspected bacterial suppurative disease of the airways presenting as chronic cough. *American Journal of Medicine* 2003; **114**: 602–606.
6. Wilson R, Dowling RB, Jackson AD. The biology of bacterial colonization and invasion of the respiratory mucosa. *European Respiratory Journal* 1996; **9**: 1523–1530.

- 1 7. Slauson DO, Hahn FF. Criteria for development of animal models  
2 of diseases of the respiratory system: the comparative approach  
3 in respiratory disease model development. *American Journal of*  
4 *Pathology* 1980; **101**: S103–S122.
- 5 8. McNeil C, Macgregor AR, Alexander WA. Studies of pneumonia  
6 in childhood: IV. Bronchiectasis and fibrosis of the lung. *Archives*  
7 *of Disease in Childhood* 1929; **4**: 170–189.
- 8 9. Finke W. Prospects for prevention of chronic bronchitis  
9 and bronchiectasis; rational management of bronchopulmonary  
10 infections by penicillin aerosol therapy. *Journal of Pediatrics* 1948;  
11 **33**: 29–42.
- 12 10. Field CE. Bronchiectasis in childhood; III. Prophylaxis, treatment  
13 and progress with a follow-up study of 202 cases of established  
14 bronchiectasis. *Pediatrics* 1949; **4**: 355–372.
- 15 11. Croxatto OC, Lanari A. Pathogenesis of bronchiectasis; experi-  
16 mental study and anatomic findings. *Journal of Thoracic Surgery*  
17 1954; **27**: 514–528.
- 18 12. Donnelly DE, Critchlow A, Everard ML. Outcomes in children  
19 treated for persistent bacterial bronchitis. *Thorax* 2007; **62**: 80–84.
- 20 13. Goldsobel AB, Chipps BE. Cough in the pediatric population.  
21 *Journal of Pediatrics* 2010; **156**: 352–358.
- 22 14. Kompore M, Weinberger M. Protracted bacterial bronchitis in  
23 young children: association with airway malacia. *Journal of*  
24 *Pediatrics* 2012; **160**: 88–92.
- 25 15. Zgherea D, Mendiratta M, Marcus MG, *et al.* Bronchoscopic  
26 findings in children with chronic wet cough. *Pediatrics* 2012;  
27 (Epub ahead of print), DOI: 10.1542/peds.2011-805.
- 28 16. Shields MD, Bush A, Everard ML, *et al.* British Thoracic Society  
29 Guidelines Recommendations for the assessment and management  
30 of cough in children. *Thorax* 2008; **63**(Suppl. 3): iii1–iii15.
- 31 17. Corbelli R, Guinand S, Barazzone AC. Childrens' chronic cough  
32 revisited. *Revue Médicale Suisse* 2009; **5**: 409–404.
- 33 18. Chang AB, Landau LI, van Asperen PP, *et al.* The Thoracic  
34 Society of Australia and New Zealand. Position statement. Cough  
35 in children: definitions and clinical evaluation. *Medical Journal of*  
36 *Australia* 2006; **184**: 398–403.
- 37 19. Gibson PG, Chang AB, Glasgow NJ, *et al.* CICADA: cough in  
38 children and adults: diagnosis and assessment. Australian Cough  
39 Guidelines summary statement. *Medical Journal of Australia* 2010;  
40 **192**: 265–271.
- 41 20. Marchant JM, Gibson PG, Grissell TV, *et al.* Prospective assess-  
42 ment of protracted bacterial bronchitis: airway inflammation and  
43 innate immune activation. *Pediatric Pulmonology* 2008; **43**:  
44 1092–1099.
- 45 21. Chang AB, Yerkovich ST, Gibson PG, *et al.* Pulmonary innate  
46 immunity in children with protracted bacterial bronchitis. *Journal*  
47 *of Pediatrics* 2012; (in press) (Accepted 25 January 2012).
- 48 22. Douros K, Alexopoulou E, Nicopoulou A, *et al.* Bronchoscopic  
49 and high resolution CT findings in children with chronic wet  
50 cough. *Chest* 2011; **140**: 317–323.
- 51 23. Marchant JM, Morris P, Gaffney J, *et al.* Antibiotics for prolonged  
52 moist cough in children. *Cochrane Database of Systematic Reviews*  
53 2005. 
- 54 24. Darelid J, Lofgren S, Malmvall BE. Erythromycin treatment is  
55 beneficial for longstanding *Moraxella catarrhalis* associated cough  
56 in children. *Scandinavian Journal of Infectious Diseases* 1993; **25**:  
57 323–329.
- 58 25. Gottfarb P, Brauner A. Children with persistent cough – outcome  
59 with treatment and role of *Moraxella catarrhalis*? *Scandinavian*  
60 *Journal of Infectious Diseases* 1994; **26**: 545–551.
- 61 26. Chang AB, Robertson CF, van Asperen PP, *et al.* A multi-centre  
62 study on chronic cough in children: burden and etiologies based  
63 on a standardized management pathway. *Chest* 2012; (Epub ahead  
64 March 29).
- 65 27. Marchant JM, Masters IB, Champion A, *et al.* Randomised  
66 controlled trial of amoxicillin-clavulanate in children with chronic  
67 wet cough. *Thorax* 2012; (Epub ahead March 24).
- 68 28. Chang AB, Redding GJ, Everard ML. State of the Art – chronic  
69 wet cough: protracted bronchitis, chronic suppurative lung disease  
70 and bronchiectasis. *Pediatric Pulmonology* 2008; **43**: 519–531.

If you would like to make a comment on the above article, you are invited to submit a letter to the Editor by email (child@ualberta.ca). Selected letters may be edited and published in future issues of the journal.

1	<hr/>	61
2	<b>QUERIES TO BE ANSWERED BY AUTHOR</b>	62
3		63
4	<b>IMPORTANT NOTE: Please mark your corrections and answers to these queries directly onto the proof</b>	64
5	<b>at the relevant place. Do NOT mark your corrections on this query sheet.</b>	65
6	<hr/>	66
7	<b>Queries from the Copyeditor:</b>	67
8	AQ1 Please provide “Declaration of Interest” for this commentar 	68
9	AQ2 Please provide keywords not more than six for this commentary.	69
10	AQ3 We have expanded “NNT” as number needed to treat. Please confirm  rrect.	70
11	AQ4 Please provide “Declaration of Interest” for this commentary.	71
12	AQ5 Please provide keywords not more than six for this commentary.	72
13	AQ6 The style of this journal demands that ‘ <i>et al</i> ’ follows the names of at least six authors. Only three names	73
14	have been provided for all “ <i>et al.</i> ” references. Please provide three more names for the same.	74
15	AQ7 Please provide the volume and page range for references “15, 21, 23, 26, an  .	75
16		76
17	<hr/>	77
18		78
19		79
20		80
21		81
22		82
23		83
24		84
25		85
26		86
27		87
28		88
29		89
30		90
31		91
32		92
33		93
34		94
35		95
36		96
37		97
38		98
39		99
40		100
41		101
42		102
43		103
44		104
45		105
46		106
47		107
48		108
49		109
50		110
51		111
52		112
53		113
54		114
55		115
56		116
57		117
58		118
59		119
60		120

Uncorrected Proofs