

Children With Chronic Cough

When Is Watchful Waiting Appropriate? Development of Likelihood Ratios for Assessing Children With Chronic Cough

Anne B. Chang, PhD; Peter P. Van Asperen, MD; Nicholas Glasgow, MD; Colin F. Robertson, MD; Craig M. Mellis, MD; I. Brent Masters, PhD; Louis I. Landau, MD; Laurel Teoh, MD; Irene Tjhung, MD; Helen L. Petsky, PhD; and Peter S. Morris, PhD

BACKGROUND: Chronic cough is associated with poor quality of life and may signify a serious underlying disease. Differentiating nonspecific cough (when watchful waiting can be safely undertaken) from specific cough (treatment and further investigations are beneficial) would be clinically useful. In 326 children, we aimed to (1) determine how well cough pointers (used in guidelines) differentiate specific from nonspecific cough and (2) describe the clinical profile of children whose cough resolved without medications (spontaneous resolution).

METHODS: A dataset from a multicenter study involving children newly referred for chronic cough (median duration, 3-4 months) was used to determine the sensitivity, specificity, predictive values, and likelihood ratios (LRs) of cough pointers (symptoms, signs, and simple investigations [chest radiography, spirometry]) recommended in guidelines.

RESULTS: The pretest probability of specific cough was 88%. The absence of false-positive results meant that most pointers had strongly positive LRs. The most sensitive pointer (wet cough) had a positive LR of 26.2 (95% CI, 3.8-181.5). Although the absence of other individual pointers did not change the pretest probability much (negative LR close to 1), the absence of all pointers had a strongly negative LR of 0 (95% CI, 0-0.03). Children in the resolved spontaneously group were significantly more likely to be older, to be non-Indigenous, and to have a dry cough and a normal chest radiograph.

CONCLUSIONS: Children with chronic dry cough without any cough pointers can be safely managed using the watchful waiting approach. The high pretest probability and high positive LRs of cough pointers support the use of individual cough pointers to identify high risk of specific cough in pediatric chronic cough guidelines.

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ABBREVIATIONS: LR = likelihood ratio; PBB = protracted bacterial bronchitis; QoL = quality of life

AFFILIATIONS: From the Child Health Division (Drs Chang, Teoh, Tjhung, and Morris), Menzies School of Health Research, Charles Darwin University, Darwin, NT; Queensland Children's Respiratory Centre (Drs Chang, Masters, and Petsky), Queensland Children's Medical Research Institute, Royal Children's Hospital, Brisbane, QLD; Discipline of Paediatrics and Child Health (Dr Van Asperen), Sydney Medical School, and Central Clinical School (Dr Mellis), University of Sydney, Sydney, NSW; Department of Respiratory Medicine (Dr Van Asperen), The Children's Hospital at Westmead, Sydney Children's Hospital Network,

Westmead, NSW; Medical School (Dr Glasgow), Australian National University, Canberra, ACT; Department of Respiratory Medicine (Dr Robertson), Murdoch Children's Research Institute, Royal Children's Hospital, Melbourne, VIC; Medical Workforce (Dr Landau), Health Department of Western Australia and The University of Western Australia, Perth, WA; The Canberra Hospital (Dr Teoh), Canberra, ACT; and Thursday Island Primary Health Care Centre (Dr Tjhung), Thursday Island, QLD, Australia.

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Chronic cough is a common reason why parents seek a consultation in pediatric practice. In the management of chronic cough in children, identification of the underlying cause (ie, obtaining the correct diagnosis), as opposed to empirical treatment, is considered important.¹⁻³ Several factors underpin the importance of obtaining the correct diagnosis with consequent cough resolution upon appropriate treatment. First, chronic cough may signify the presence of a serious underlying airways disease.^{4,5} Early diagnosis of these conditions (eg, bronchiectasis, aspiration lung disease) would lead to earlier treatment and prevent further ongoing lung injury.^{5,6} Second, parents of children with chronic cough have substantial stress and impaired quality of life (QoL) that improves when the cough abates.^{4,7,8} Third, many parents seek repeated consultations for their child's cough until the cough resolves. Our single-center⁷ and multicenter studies⁴ showed that 75% to 80% of children had more than five consultations prior to presentation to a respiratory specialist for cough. Earlier resolution of cough through identification and treatment of the etiology would reduce the economic burden associated with recurrent consultations. Finally, obtaining a correct diagnosis potentially reduces use of unnecessary investigations and medications with consequent severe adverse events.^{9,10}

The initial step in obtaining a diagnosis requires differentiating those who require treatment (ie, specific cough) from those whose cough is likely to resolve without treatment. In the latter group, a watchful waiting approach has been suggested.^{1,3} To differentiate these groups, identification of cough pointers (symptoms, signs, and simple investigations [e-Table 1]) is used in

many chronic cough guidelines (eg, Australian,¹ British,² United States³). However, published evidence is scarce on how well cough pointers differentiate specific from nonspecific cough and on the profile of children whose chronic cough is likely to resolve without treatment. Obtaining evidence for the utility of these clinical findings and investigations will increase the robustness of these guidelines necessary in current standards of evidence-based medicine.¹¹ Additionally, when evaluating children with chronic cough, development of category-orientated likelihood ratios (LRs)¹² for cough pointers (e-Table 1) would help clinicians to differentiate children for whom watchful waiting can be safely undertaken from those who would benefit from treatment and further investigations.

In this study involving 326 children newly referred for chronic cough,⁴ we evaluated data relating cough pointers to specific cough and the three most common etiologies from our recent multicenter study. In the field of chronic cough, our multicenter study^{4,13} had unique features of research rigor,¹⁴ including the following: (1) Rules for assigning etiology of cough were defined a priori; (2) the diagnoses, particularly those of protracted bacterial bronchitis (PBB) and asthma, were temporally related to treatment within a strict time frame; (3) validated cough outcome measures were used; and (4) the children were followed for 6 months to ensure that misdiagnosis had not occurred. We hypothesized that cough pointers are clinically valid (have high positive LR) and can be used to differentiate specific cough from cough that resolves without treatment (spontaneous resolution).

Materials and Methods

Data collected from our multicenter cohort study⁴ formed the dataset of this article. Briefly, 346 children aged < 18 years newly referred for chronic cough (duration, > 4 weeks) to any of the participating sites were enrolled. These sites were clinics at five major hospitals (Brisbane, Sydney, Melbourne, Canberra, Darwin) and three regional-remote clinics in Orange, New South Wales; Anangu-Pitjantjatjara Lands, Central Australia; and Thursday Island, Queensland. We excluded children with a known chronic respiratory illness previously diagnosed by a respiratory physician or those who have had diagnosed conditions confirmed by objective tests (eg, asthma, cystic fibrosis, bronchiectasis) prior to

referral. Children with asthma diagnosed by a nonrespiratory physician were not excluded because asthma is commonly misdiagnosed in our setting. Written informed consent was obtained from parents, and the study was approved by the ethics committees of all participating sites.

Enrolled children were managed in accordance with a standardized evidence-based cough algorithm¹³ until the study's end point, which was defined as either a primary diagnosis established with cough resolved or the presence of exit criteria (hospitalization related to etiology of the cough or 12 months postenrollment, whichever occurred earliest). The ascribed etiology was defined a priori and based on a temporal and prompt response to the treatment as defined by a validated cough score (verbal categorical descriptive score).¹⁵ Chest radiograph and spirometry findings were interpreted by the attending respiratory physician as a dichotomous variable (normal/abnormal).

Statistics

Because the data had a skewed distribution, medians and interquartile ranges were used for continuous measures. The χ^2 test was used for categorical data. Kruskal-Wallis analysis was used for group comparisons. SPSS software (IBM Corporation) was used, and a two-tailed $P \leq .05$ was considered significant. For calculation of the OR and 95% CI, where

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CORRESPONDENCE TO: Anne B. Chang, PhD, Queensland Children's Respiratory Centre, Royal Children's Hospital, Herston, QLD 4029, Australia; e-mail: annechang@ausdoctors.net

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