

Dr Cochrane

Chronic cough: a natural (and parental) disaster

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The second in this series of Dr Cochrane clinical vignettes is based upon an overview of Cochrane Reviews that was published in the previous issue of *Evidence-Based Child Health*: Russell K, Chang AB, Foisy M, Thomson D and Williams K: ***The Cochrane Library and the Treatment of Chronic Cough in Children: An Overview of Reviews***. *Evid.-Based Child Health* 2010, **5**: 1196–1205.

Dr Cochrane is a unique self-learning experience – the integration of Cochrane evidence with a quirky fictional story and multiple-choice questions provides readers with the opportunity to explore and understand the applicability of a Cochrane Review or Overview in a new way.

In this series of fictional clinical vignettes, Dr Cochrane travels across time from the past century to the present day, to solve clinical problems using evidence from Cochrane Reviews. Read the associated article and/or listen to the Evidence-Based Child-Health podcast available online at www.cochrane.org/podcasts/ and then test your knowledge with six multiple choice questions. You can find the answers to the questions in this issue on page 2007.

In the next issue of *Evidence-based Child Health*, Dr Cochrane explores the evidence for croup, based upon the Cochrane Overview available in this issue (Bjornson C, Russell K, Foisy M and Johnson DW: ***The Cochrane Library and the Treatment of Croup in Children: An Overview of Reviews***. *Evid.-Based Child Health* 2010, **5**, 1555–1565).

On 6 April 2009 an earthquake measuring more than 6 on the Richter scale struck central Italy, killing 308 people. Twenty of the victims were children. Between 3,000 and 11,000 buildings in the medieval city of L'Aquila, the epicenter, were damaged. Around 65,000 people were made homeless. The name of this Baroque city means 'The Eagle'.

Nine months later, in November 2009, Dr Cochrane was directed early in the morning to the medical care centre. He was one of the volunteers from all over Europe joining the medical teams to provide help for those still living in the tent camp that provided temporary shelter. The immense tent sprawl was shaken by the icy mountain wind. An 80-year-old woman, or maybe older, sitting outside a tent looked him over cautiously then started to pray again. Or was it a lament?

Dr Cochrane was assigned to pediatric clients and families. A pediatric nurse – Giuseppe Bastianelli – assisted him with the task of caring for young patients and supporting Archie's not-all-that-fluent Italian. Luckily, medical problems in the camp

were rarely acute. The majority of patients and families needed moral support and prescriptions for a few drugs, often the continuation of previous treatment for chronic illnesses.

Among the children, the illness which emerged most was chronic cough. Parents were often concerned about their child's health. Furthermore, although transmission of infection by a cough across tents was implausible, you can easily hear a cough through canvas walls in a tent camp so others in the camp also complained.

Question 1 (More than one answer may be correct)

Which of the following statements about chronic cough in children are true?

1. Chronic cough is most frequent in industrialized countries where it has a higher prevalence (15%) than in non-industrialized countries (10%).
2. In the medical literature, cough is often defined as chronic after persistence for about four weeks.

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3. In non-specific cough, secretions are very limited or non-existent. This cough is classified as 'dry'.
4. Chronic cough is very common and should generally be treated by the children's care-giver using over-the-counter medications.
5. Asthma and non-specific cough are rarely related.

The first children standing in line were familiar to Dr Cochrane. Claudio (seven years old), and his twin younger sisters Teresa and Irene (five years old), were housed with their parents in a big tent near Dr Cochrane's temporary home. Claudio had typical pneumonia a few months before, as reported in his medical record and had been admitted to a nearby hospital for a short time. The pneumonia cleared up but a sequel of that episode was a chronic cough that had bothered Claudio over the last few months. Several times, field doctors had to reassure Claudio's mother about the real course of the chronic cough and its probable spontaneous resolution. Nevertheless, the twice-weekly visits to check Claudio's symptoms and review his health after the pneumonia may have created some worries throughout his large family.

Question 2 (One correct answer)

Cochrane systematic reviews often use statistical measures of association to describe the relationship between two quantities. In this overview Relative Risk (RR) is used. Which of the following statements best defines RR?

1. RR describes the odds of the event in the treatment group compared to the odds in the control group and is interpreted as statistically significant if the 95% CI does not cross one.
2. RR describes the probability of the event in the treatment group compared to the probability in the control group and is interpreted as statistically significant if the 95% CI does not cross one.
3. RR describes the probability of the event in the treatment group compared to the probability in the control group and is interpreted as statistically significant if the 95% CI does not cross zero.
4. RR is used frequently in the statistical analysis of continuous outcomes where the outcome of interest has relatively low probability.
5. If the RR is more than 75% the degree of statistical heterogeneity among the studies is considerable and meta-analysis should be avoided.

At the latest visit, the cough was reported to be dry but now it had seemed slightly different. Dr Cochrane checked the chest sounds. Bubbly noises ...

Question 3 (More than one answer may be correct)

Among children with chronic cough with 'wet' sounds, what did the overview show regarding antibiotics compared to placebo?

1. Children receiving antibiotics were significantly less likely to require additional medical treatment (RR:0.15; 95% CI 0.05 to 0.49).
2. Inhaled corticosteroids are a potentially useful treatment for specific cough although their role has not been fully elucidated in this overview.
3. Children treated with amoxicillin and erythromycin experienced more adverse events than those given a placebo.
4. For every three children treated with antibiotics, one child was cured (95% CI 2.00 to 4.00).
5. Children taking antibiotics were significantly more likely than those given placebo to be cured or substantially improved at follow-up (RR 2.42; 95% CI 1.65 to 3.53).

Claudio did not present with any other symptoms (e.g. fever). The physical examination did not show crepitations, wheeze, asymmetry of breath sounds or cervical and supraclavicular lymphadenopathy. After having received close attention, the little patient was dismissed. Dr Cochrane was thinking how to explain the idea of antibiotic therapy to Claudio's mother without arousing additional concern. A delicate task, especially considering the language barrier. His thinking was interrupted by Irene who took her brother's place on the examination couch. Irene started to cough so as to get to Archie to examine her. The cough was slightly different from Claudio's. Dr Cochrane murmured, 'Dry'. Bastianelli smiled to him, beckoning.

Question 4 (One correct answer)

Among children with chronic 'dry' cough, what did the overview show regarding the effectiveness of drugs compared to placebo?

1. Anti-histamines are effective.
2. β_2 agonists are effective.
3. Low-dose inhaled corticosteroids are effective.
4. Leukotriene receptor antagonists are effective.
5. Very high-dose inhaled corticosteroids are effective but not recommended.

The records showed that at previous visits, Irene was also seen with Claudio. Both had always had the same kind of cough up to this time. Their mother was convinced that an epidemic was raging in the family and blamed everything on the camp: the tent, the damp, the cold, the food, and even the doctors,

especially when they insisted that everything was under control.

Dr Cochrane started to auscult Irene's chest, breaking off from time to time to speak with the children and their mother.

Dr Cochrane asked Irene: 'Do you feel pain somewhere?'

'No, I'm grown-up and I do not feel pain and I do not cry'.

Dr Cochrane smiled 'It seems that Irene is really growing up. She mimics most of the things adults do. Am I guessing right?'

Mother: 'She's just a parrot, an annoying parrot. For some months now she's been repeating things, everything. When she repeats, she wants me to watch her and compliment her on her performance. Teresa and Claudio are much more independent'. Mother then continued: 'The Ruggeri family's son had cough and asthma. He is taking a spray with corticosteroids and he is better now. Dr Cochrane, do you think Claudio and Irene need that spray too?'

Question 5 (One correct answer)

Among children with 'dry' cough, what did the overview show about low-dose inhaled corticosteroids compared to placebo?

1. There was a significant decrease in the frequency of cough, but only after one week of treatment (RR 0.78; 95% CI 0.66 to 0.91).
2. There was a significant decrease in frequency of cough, both at three to four days (RR 0.89; 95% CI 0.75 to 1.03) and at one week (RR 0.78; 95% CI 0.66 to 0.91).
3. There was a significant decrease in the frequency of cough, but only after one week of treatment (MD -27.00; 95% CI -36.00 to -18.00).
4. There was no significant decrease in the frequency of cough (MD -27.00; 95% CI -83.07 to 29.07).
5. They are effective but only when parents keep a symptom score.

Dr Cochrane: 'Madame, I'm going to prescribe a drug but not a corticosteroid as only a high dose would work and the risk of side effects is greater

than the benefit for cough. Claudio, I shall prescribe you an antibiotic. This pill will hopefully reduce the frequency of your cough'. Claudio was listening. 'In two weeks, you have to come back to this clinic and tell me, or another doctor, how your cough is doing. You must come back to see me if in the next few days you have nausea, headache or if your skin changes color or appearance'.

Teresa: 'Fabulous! Will those pills make him green like a lizard?'

Dr Cochrane: 'Not exactly, I would say red or strawberry color'.

Irene: 'WOW! He might become strawberry-colored'.

Mom: 'Don't talk a load of nonsense! Listen to the doctor'.

Question 6 (More than one answer may be correct)

In children with non-specific cough, high-dose inhaled corticosteroids may relieve cough symptoms. What did the overview highlight regarding high-dose inhaled corticosteroids?

1. High-dose inhaled corticosteroids benefit patients in one or two weeks.
2. The dose used in the studies included was very high: up to 2 mg/day.
3. High-dose inhaled corticosteroids benefit patients in a time span of two weeks.
4. Very high-dose inhaled corticosteroids may expose children to the risk of adrenal insufficiency.
5. The dose used in the studies included was very high: up to 25 mg/day.

Irene then started to whine: 'What about me? Can I have a pill to change color too? Please...'

Dr Cochrane looked straight at Irene: 'Irene, you are grown up and it seems to me you are strong enough not to need a pill. Your lungs are big and strong. But if you want I can make something for you. Do you want me to paint your face as a fancy mask?'

Irene and the other brothers: 'Oh yes!'

Dr Cochrane: 'I need a couple of surgical skin markers. Mr Bastianelli, please can you find out where they are and prepare me a spot of iodine-povidone in a gauze?'