Review of the evidence for the use of erythromycin in the management of persons exposed to pertussis

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Authors' objectives
To assess the evidence for the use of erythromycin for the prevention of secondary transmission of pertussis (whooping cough).

Searching
MEDLINE was searched from 1980 to 1996 using the following keywords: 'whooping cough', 'Bordetella pertussis', 'treatment', 'prophylaxis', 'erythromycin', 'controlled trials', 'case-control' and 'cohort studies'. The bibliographies of key review articles on prophylaxis against pertussis, and one author's 20-year collection of papers on pertussis were also handsearched. Several international experts were contacted to help identify studies currently in progress. The search was limited to articles written in the English language.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), retrospective cohort studies, case-control studies, and uncontrolled case series and clinical reports, were included. The randomised trials were placebo-controlled.

Specific interventions included in the review
Erythromycin given as treatment for primary cases of pertussis, in order to prevent its spread, and/or as a prophylaxis in secondary contacts. The drug doses and regimens were not described.

Participants included in the review
People with primary pertussis, and close contacts of pertussis sufferers, were included.

Outcomes assessed in the review
Attack rates, as confirmed by bacteriological culture, serological response, or clinical assessment. Adverse effects were also assessed.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The included studies were classified according to a hierarchy of evidence scheme, which was adapted from Stevens and Raftery (see Other Publications of Related Interest). However, the methodological quality of the individual studies was not assessed.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined by a narrative summary, and some were presented in a tabular format.
How were differences between studies investigated?
There were no formal tests of heterogeneity. The studies were grouped according to design within the narrative summary.

Results of the review
Overall, 14 papers met the inclusion criteria: 3 RCTs, 3 retrospective cohort studies, 1 case-control study, and 7 uncontrolled case series or case reports. It was not possible to calculate the exact number of the included participants from the information given; at least 2,660 individuals participated.

Findings from 2 RCTs suggested that erythromycin was not effective as a prophylaxis. However, both trials had methodological problems, including small sample size. Results from a larger trial showed a statistically-significant difference for the proportion of cases with positive bacteriological cultures (erythromycin 6.6% versus placebo 20.3%; relative rate difference 67.5%, 95% confidence intervals: 7.6, 88.7). However, there was no significant difference in the serological response between the groups. The erythromycin group had significantly more adverse advents than the placebo group (34.3% versus 15.9%, p=0.0003), which were mainly diarrhoea and nausea. The results from the retrospective cohort studies, case-control studies, and uncontrolled case series and case reports generally favoured the use of erythromycin as a prophylaxis for close contacts. Two cohort studies reported gastrointestinal adverse effects with erythromycin use.

Authors’ conclusions
There was only weak evidence to support the use of erythromycin prophylaxis. The overall quality of this evidence was judged to be II-2, i.e. evidence obtained from well-designed cohort or case-controlled analytical studies, preferably from more than one centre or research group). The effect was at best modest when compared with the protection conferred by an effective whole-cell vaccine. There was no evidence of any benefit to contacts other than household-type contacts.

CRD commentary
Adequate details were given of the review objectives and search strategy. It is possible that further material may have been identified had other sources been accessed and language restrictions applied. A discussion about the possible impact of publication bias would have been useful. Some of the selection criteria for the primary studies were unclear, particularly in connection with the outcomes. Some details of the primary material were given in the text and tables. However, the studies were only classified according to design, with no systematic assessment of the methodological quality of the individual evaluations, thus the narrative synthesis was sometimes difficult to interpret. The narrative method of summary was appropriate given the likely heterogeneity between the studies. There were no details about the review process, i.e. how many reviewers were involved, how decisions were made, how the data were extracted, and how disagreements were resolved. The authors’ conclusions appear to follow-on from the evidence presented in the review.

Implications of the review for practice and research
Reviewer's statement: Further research in this area may be useful.

Bibliographic details
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Other publications of related interest

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**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.