Author's response to reviews

Title: Children with pertussis inform the investigation of other pertussis cases among contacts

Authors:

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Author's response to reviews:

Dear Reviewers
re: Children with pertussis inform the investigation of other pertussis cases among contacts

We have revised the article as suggested and rewritten some paragraphs. The list of comments and changes are below. Please do not hesitate to contact us should you require any additional information.

Yours sincerely

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Corrections suggested by the editor:

We recommend that you ask a native English speaking colleague to help you copyedit the paper.

Reply from the authors
The manuscript has been revised by one of the authors Dr Laura Rodrigues from U.K. Some paragraphs and phrases were rewritten to be better understood.

We ask that you consider re-phrasing your title to make it clearer.

Reply from the authors
We have modified the title
Now is: Children with pertussis inform the investigation of other pertussis cases among contacts.

Competing interests
Reply from the authors
We have added after the "Conclusions":
This research received grants from the Pan-American Health Organization/World Health Organization

Authors’ contributions
Reply from the authors
We have added between the "Competing interests" and "Acknowledgements"

P.N. Baptista and V. Magalhaes conceived the study and supervised all aspects of its implementation. L. C. Rodrigues synthesized analyses and led the writing.

Acknowledgements
Reply from the authors
We have added after the "Authors' contributions":
The authors are grateful to the Pertussis Laboratory Program - Center for Disease Control and Prevention, Atlanta - USA, that have contributed materials for the isolation of the Bordetella pertussis. The authors are
also grateful to Professor Marcelo Magalhaes and Nadila Ferreira who have done the procedures to isolate the Bordetella pertussis.

Reviewer: Daniel Floret

1. As PCR or serology are apparently not available in this hospital, the criteria used by the authors for definition have low sensibility. So, it seems important to try to better evaluate the number of cases who may have been missed?
   Reply from the authors
   In the study, B. pertussis was isolated in 52 of the 416 individuals that had nasopharyngeal swabs collected. PCR can increase almost fivefold the number of confirmed pertussis cases when compared with culture*. So 52 x 5 = 260
   Furthermore, each positive culture allowed identifying 2 new cases by epidemiological linkage. So 260 x 2 = 520. We have identified 158 pertussis cases and we could have identified 520 cases, so (520-158=362). Therefore 362 cases of pertussis may have been missed.
   * Fry NK, Tzivra O, Li YT et als. Laboratory diagnosis of pertussis infections: the role of PCR and serology. Journal of Medical Microbiology 2004;53:519-525

2. How many contacts do not attend though eligible?
   Reply from the authors
   Results
   Paragraph - 3
   Line - 9
   Twenty-two contacts were excluded because information about them was insufficient to classify them into cases or not cases. Two parents report relatives with cough who did not attend to the hospital.

3. This study can not identify asymptomatic carrier who may be involved in the spread of the disease?
   Reply from the authors
   Material and Methods
   Paragraph - 2
   Line - 7
   Although asymptomatic carrier state exist, they are not a factor in transmission.

4. Who contaminated who - source of infection?
   Reply from the authors
   Paragraph 2
   line 3
   The primary case- the source of infection to the household - was older than 11 and a half years for 79% (66/84) of all secondary cases and for 76%(19/25) of the secondary cases under 6 months of age.

5. Why 11 and half years?
   Reply from the authors
   Until 2004 in Brazil, the last dose of DwPT (fourth dose) was applied at 15 months of age. Children at 111/2 years old had received the last dose of DwPT 10 years before. Studies have found that 10 years after the last dose of DwPT, children have low or no protection from pertussis.

6. How pertussis is surveyed in Brazil?
   Reply from the authors
   Pertussis is a nationally notifiable disease in Brazil. Reporting is mandated (by state legislation). Health care professionals should report the case to the state health department. There are sentinel hospitals where the notification is daily. The hospital where the study was done is a sentinel hospital and has a service of pediatric infectious diseases.

7. 25.8% of index cases was vaccinated, that is rather high, comments, how older were they?
   Reply from the authors
   Brazil has a high vaccine coverage. All children older than 6 months of age and younger than 5 years of aged had received at least 3 doses of pertussis vaccine.
All index cases were under 111/2 years of age, 92.2% (10/51) were under 5 years and 72.5% (37/51) were under 6 months of age.

Reviewer: Alberto E Tozzi

1. The authors state that index cases were recruited during a surveillance activity. It would be useful to describe which clinical symptoms are considered as suspected pertussis and who is considered eligible for microbiological examination. It would also be useful to give more details about the hospital setting in which the study was performed. How many patients are admitted in one year? Is the hospital serving a rural or metropolitan area? Etc.

Clinical symptoms of suspected pertussis
Reply from the authors
Material and Methods
Paragraph - 1
Line - 3
Children were considered a suspected case of pertussis if they had a cough illness lasting at least 7 days, with either paroxysms of coughing, inspiratory "whoop", post-tussive vomiting or cyanosis during the paroxysms of coughing without other apparent cause.
Line - 9
every contacts of a confirmed case of pertussis with recent history of cough.
Who was eligible for microbiological examination?
Reply from the authors
Material and Methods
Paragraph - 2
Line - 1
Nasopharyngeal swabs were collected from every index cases and every contacts of the index cases that had cough within the last 21 days and had attended to the Hospital.
Hospital setting in which the study was performed?
Reply from the authors
The study was performed in the pediatric infectious disease service of the School Hospital Oswaldo Cruz, in the emergency service, outpatients service and in the infirmary.
How many patients are admitted in one year? Rural? Metropolitan?
Reply from the authors
Material and Methods
Paragraph - 1
Line - 1
In 2003, in the Oswaldo Cruz School Hospital (a metropolitan sentinel surveillance hospital for infectious diseases).
In the Pediatric Infectious Diseases Service, near one thousand patients are admitted at the inpatient department each year.

2. Were frequent contacts with relatives and neighbors precisely defined (number of hour together in a day)?
Reply from the authors
Results
Paragraph - 5
Line - 1
All the contact cases identified by the index cases were relatives (flow chart). Among the contacts, 56% (60/107) of the pertussis cases were women and 44% (47/107) were men. chi2 3.68 P=0.05. Many relative were living in the same household, the same street or the same neighborhood. The ones that were living in different neighborhoods used to spend the week-end together in the same household.

3. It seems from the text that suspected cases among the household and contacts were defined as simple cough. Was a specific definitions applied? Paroxysm whooping?
Reply from the authors
Material and Methods
Paragraph - 1
Line - 3
Children were considered a suspected case of pertussis if they had a cough illness lasting at least 7 days, with either paroxysms of coughing, inspiratory "whoop", post-tussive vomiting or cyanosis during the paroxysms of coughing without other apparent cause.
Line - 9
every contacts of a confirmed case of pertussis with recent history of cough.

4. More information should be given about the personal characteristics of backtraced cases. In particular the reader would be interested in understanding more precisely the dynamic of transmission in the household. From Table 1 it seems that a certain number of index cases are defined as secondary cases. Which definitions are used for defining primary, co-primary, and secondary cases? Is it possible to give more information on who was identified as the source of infection? What about age group and other characteristics of cases found with the investigation? How many parents and how many adolescents were discovered by the investigation? A flow chart would also help.

Which definitions are used for defining primary, co-primary, and secondary cases?
Reply from the authors
Material and Methods
Paragraph - 2
Line - 1
Index cases - the case that was first reported to the hospital.
Primary cases - first individual that presented cough and had pertussis diagnosis confirmed.
Co-primary cases - had symptoms onset within 6 days after the onset in the primary case.
Secondary cases - had symptoms onset 7 or more days after onset in the primary case.
Not a case of pertussis - contacts without pertussis symptom.
In particular the reader would be interested in understanding more precisely the dynamic of transmission in the household. Who was the source of infection?
Reply from the authors
Discussion
Paragraph - 2
Line - 3
The primary case - the source of infection to the household members - was older than 11 and a half years for 79% (66/84) of all secondary cases and in 76% (19/25) if the secondary case was under 6 months of age. What about age group and other characteristics of cases found with the investigation? How many parents and how many adolescents were discovered by the investigation? A flow chart would also help.
Reply from the authors
All index cases were under 111/2 years of age, 92.2% (10/51) were under 5 years and 72.5% (37/51) were under 6 months of age. Among the contacts of the index cases that were identified as a pertussis case, 40.2% (43/107) were between 6 months and 111/2 years of age and 59.8% (64/107) were older than 111/2 years of age.
How many parents and how many adolescents were discovered? A flow chart would also help.
Reply from the authors
Results
after paragraph 4
We have done a flow chart.