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Pertussis in young infants: apnoea and intra-familial infection

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ABSTRACT

This study investigated 41 infants, aged <4 months, who were hospitalised with symptoms compatible with pertussis. Of these, 16 had *Bordetella pertussis* infection confirmed by real-time PCR. For four of these 16 patients, the initial sample was PCR-negative, but samples collected 5–7 days after the onset of infection were PCR-positive. PCR was also positive with samples from 15/16 families and 20/41 household contacts. Nine of the 20 positive household contacts were asymptomatic. Among the 16 infants with proven pertussis, apnoea was more frequent than in a control group for whom PCR was negative with both children and household contacts (69% vs. 28%). It was concluded that real-time PCR performed with samples from household contacts facilitates the diagnosis of infants suspected clinically of having pertussis, thereby enabling earlier treatment.

Keywords Apnoea, *Bordetella pertussis*, household contacts, infants, pertussis, real-time PCR

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INTRODUCTION

Pertussis is under-diagnosed in adults vaccinated during infancy in countries where a high vaccine coverage of infants and children has been achieved [1,2]. In France, children are first vaccinated at an age of 2 or 3 months, according to the vaccination recommendations [3]. A previous study conducted in the Paris area, which is a region with a vaccination coverage of >90% in infancy, showed that 30% of adult patients with a cough lasting >8 days and without an evident diagnosis had biological signs of *Bordetella pertussis* infection [4]. Atypical pertussis in adults contributes to the spread of the disease among non-immunised infants. The French National Pertussis network demonstrated that pertussis is diagnosed mainly in children aged <1 year (80% of cases), which is the age at which the disease can be most serious and life-threatening in conjunction with apnoea [2,5–7]. In France, pertussis is the most frequent cause of mortality associated with community-acquired bacterial infection in children aged <2 months [8].

The present study used a *Bordetella*-specific PCR to systematically screen the household contacts of young infants hospitalised with apnoea or paroxysmal or vomiting cough during the winter of 2004–2005, which was a season with known reported cases of pertussis in Paris. The aim of the study was to investigate the utility of such a systematic screen of household contacts in diagnosing the disease in children.

PATIENTS AND METHODS

A *B. pertussis*-specific real-time PCR (see below) was performed systematically on nasopharyngeal aspirates from all infants aged <4 months who were hospitalised with apnoea, with or without a cough, or for a paroxysmal or a vomiting cough, between 15 October 2004 and 15 March 2005. Apnoea occurred just before admission, while the onset of cough was 2–5 days previously. Samples from infants were collected upon admission, and were also collected systematically from household contacts, i.e., parents, siblings and grandparents, if they lived in the same dwelling. Household contacts were questioned concerning the presence, duration and nature of any cough (particularly during nocturnal sleep). Two groups of infants were then investigated: (i) infants with a positive diagnosis of pertussis (a positive PCR sample from the infant or from one household contact); and (ii) infants with a negative diagnosis of pertussis (PCR-negative samples from both

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children and household contacts). The children were hospitalised in the general paediatric ward of Saint-Vincent de Paul Hospital, which is a teaching hospital situated in the centre of Paris. When the *Bordetella*-specific PCR was negative or uninterpretable with samples from an infant, but positive with samples from a household contact, the PCR was repeated after 5–7 days with samples from the infant.

Nasopharyngeal aspirates were obtained from young children, while a nasopharyngeal sample was collected with a Dacron swab from adults. Nucleic acids were extracted from clinical specimens with a QiaAmp DNA blood minikit (Qiagen, Hilden, Germany). All samples (200 μL) were extracted according to the manufacturer's instructions. Real-time PCR was performed as described previously using Hotstar *Taq* Master Mix (Qiagen) [9] and primers specific for a 181-bp region of IS*481* (accession no. L26973). The PCR profile comprised 10 min at 95°C, followed by 50 cycles of 10 s at 95°C, 10 s at 55°C and 20 s at 72°C. Amplification, detection and data analysis were performed with a Light Cycler 2.0 (Roche Diagnostics, Meylan, France). Negative controls with no template were included in each PCR run and after every ten samples.

All infants were also screened systematically for respiratory syncytial virus (RSV), influenza virus, parainfluenza virus and adenovirus using standard virological diagnostic procedures.

RESULTS

Bordetella-specific PCR was performed with samples from 41 infants aged <4 months and with samples from 80 household contacts. The diagnosis of pertussis was confirmed by PCR (group 1) for 16 infants (three patients aged <1 month, five aged 1–2 months, and eight aged 2–4 months). For 12 infants, the first PCR was positive; for four other infants, the initial PCR was negative, but was positive for one of the household contacts. A second PCR, performed with samples collected after 5–7 days, was positive for three of these four patients. The remaining patient, a boy aged 3 months, yielded a negative second PCR result, but had typical whooping cough with paroxysms, and the mother's PCR result was positive. Overall, for four of the 16 patients, a positive *Bordetella*-specific PCR with samples from the parents helped to confirm the diagnosis of pertussis infection in the infants.

Of these 16 infants, 11 had apnoea, alone in three cases and associated with cough in eight cases. Five other infants had a paroxysmal cough with vomiting, with three being hospitalised for RSV bronchiolitis. Among the 11 infants with apnoea, eight were admitted to the paediatric intensive care unit (PICU). Overall, six of 16 infants were co-infected with RSV. No other viral infections were detected.

In 15 of 16 families of the positive infants, at least one household contact had a positive *Bordetella*-specific PCR result. In one family, only the mother was tested and she was negative. Overall, 20 (48.8%) household contacts yielded a positive *Bordetella*-specific PCR result. The positive household contacts comprised nine (56.2%) of 16 mothers, four of ten fathers (six were not tested), five (45.4%) of 11 siblings, and one of four grandparents. In seven of the 16 cases, the infant was the first child and was living with his parents only. Of the 20 household contacts positive for *B. pertussis*, only ten had a cough lasting for >5 days, with waking during nocturnal sleep in four cases. Among the other household contacts, four did not cough, and five had a mild cough lasting <5 days, which was considered to be common during the winter season (Table 1).

All the parents and siblings living with the infants had received a whole-cell pertussis vaccine during childhood. This information was not available for the four grandparents living in the household. No sibling aged <6 years was PCR-positive, and two brothers (aged 7 and 8 years) who were PCR-positive did not have a cough.

Patients and household contacts positive for *B. pertussis* received treatment with macrolides (clarythromycin or azithromycin). In the infants, apnoeas eased within 2–4 days of commencing treatment, but the cough took longer to disappear. Two of these 16 infants had received a single dose of acellular pertussis vaccine. The others had not received any vaccine.

During the same period, 26 other infants aged <4 months were hospitalised with symptoms resembling pertussis, i.e., apnoea in seven (28%) cases (alone in two cases and apnoea with cough in five cases), or vomiting cough (18 cases), with four of these 18 cases having a cough with paroxysms on the day of admission. All of these infants were negative when tested using the *Bordetella*-specific real-time PCR (group 2). The real-time PCR was also performed with specimens from 39 household contacts, including 23 mothers and 16 fathers, but was negative on every occasion. The apnoea and/or cough were probably related in most cases to gastro-oesophageal reflux or viral infection; indeed, 13 infants were infected with RSV. Five of these 26 infants were admitted to the PICU. The four infants who had paroxysmal cough were all