Who gives pertussis to infants? Source of infection for laboratory confirmed cases less than 12 months of age during an epidemic, Sydney, 2009

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Abstract

An important approach to protecting infants against pertussis is to provide a booster vaccination to close contacts, however this strategy requires a good understanding of infection sources to be effective. The objective of this study was to identify the most important sources of transmission of pertussis infection to infants, regardless of hospitalisation status. Standardised interviews were conducted during routine follow-up calls with the parent or guardian of laboratory confirmed pertussis cases less than 12 months of age notified to 3 Sydney metropolitan public health units during a pertussis outbreak from January to May 2009. All contacts with a coughing illness or laboratory confirmed pertussis during the 3 weeks prior to onset of illness in the index case, were recorded. A source of infection could not be identified for 29 infants (31%) and a total of 86 known or suspected sources were identified for the other 66 infants. The most frequently identified sources were siblings (36%) and parents (24%), followed by other family members (21%), friends (13%), and settings outside the home such as medical centres (6%). Of 20 siblings aged 3 or 4 years, 16 (80%) were sources of infection, compared with 14 of the 44 (32%) other siblings less than 18 years of age. During this epidemic siblings were more important sources of infant infection than parents. Siblings aged 3 and 4 years of age were particularly important transmitters of pertussis infection to infants. Minimising pertussis infection in 3 and 4 year olds may be an important measure to prevent infant infection. *Commun Dis Intell* 2010;34(2):116–121.

Keywords: whooping cough, *Bordetella pertussis*, infants, source of infection, immunisation strategy

Introduction

A resurgence of reported pertussis over the last 2 decades has been documented in countries with established pertussis immunisation programs with high levels of coverage, including Australia.[1,2] Infection rates have primarily increased in those over 10 years of age, due to waning immunity, and in infants less than 5 months of age.[2,3] The current Australian immunisation schedule for pertussis consists of 3 primary doses of diphtheria-tetanus-acellular pertussis vaccine (DTPa) at 2, 4 and 6 months, followed by a booster at 4 years and a 2nd booster of adolescent formulation dTpa between 12 and 17 years of age.[4] Thus infants are not fully protected against pertussis infection for the first few months of life, during which the burden of morbidity and mortality is greatest.[5]

Parents are the most commonly identified source of transmission of pertussis to young infants, accounting for approximately half the identified sources across a range of studies in different countries, with siblings accounting for about another quarter (Table 1). To our knowledge only one of these studies[6] was not limited to only severe index infant pertussis cases that required hospitalisation or resulted in death.

The recent pertussis epidemic in Australia, and New South Wales in particular,[15] presented an opportunity to collect detailed information regarding the source of pertussis infection during a period of high community transmission. Given the importance of accurately determining the source of infection and the lack of reliable existing data sources in New South Wales, the current study was developed to systematically identify and record all possible sources of infection for laboratory confirmed cases less than 1 year of age and attribute a level of evidence to each potential source. It is also the first Australian study to include pertussis cases of varying severity, not just those requiring hospital admission. Mild cases also have an important role in sustaining high levels of transmission and we hypothesised that a careful assessment of all notified cases, regardless of hospitalisation status, may identify sources other than mothers as playing an important role in the transmission of pertussis to infants.

Methods

For the purpose of this study we included only pertussis cases less than 12 months of age confirmed by polymerase chain reaction (PCR) laboratory test. Under New South Wales protocols, source of

Table 1: Summary of studies investigating source of infant pertussis infection

Country	Year	Study population	n*	Parents† (%)	Siblings† (%)	Reference
England	1998–2000	Hospitalisations <5 months of age	33	42	27	7
Multinational‡	2003–2004	Hospitalisations <6 months of age	44	55	16	8
United States	1999–2002	Notifications <12 months of age	264	47	19	6
Australia	2001	Hospitalisations <12 months of age identified through APSU	72	53	23	9
Australia	1997–2006	Hospitalisations <12 months of age	26	52	45	10
Multinational§	2001–2004	Hospitalisations <12 months of age	24	50	17	11
United States	1990–1999	Deaths <12 months of age	46	52	41	12
Canada	1991–1997	Hospitalisations <24 months of age	431	20	53	13
France	1996–2006	Hospitalisations <6 months of age	892	55	25	14

* Number of index cases for which a source could be identified.

† Percentage of all identified sources (some index cases had more than one potential source identified in some studies whereas others only identified a 'most likely source' for each case).

‡ France, Germany, United States and Canada.

§ Brazil, Costa Rica, Germany, Singapore, Spain, Taiwan and Uruguay.

APSU Australian Paediatric Surveillance Unit

infection information is routinely collected from the parent or guardian of each case under 2 years of age. Unfortunately however, options for completing this field in the electronic Notifiable Diseases Database (NDD) are inconsistent with those provided on the paper data collection form, making data entry, extraction, and interpretation difficult.

An enhanced data collection form was developed to ensure systematic and careful collection of detailed source of infection information by public health unit (PHU) staff during routine pertussis follow-up calls to the infant's parent or guardian. A known or suspected source was defined as any person who came into contact with the case infant for greater than 1 hour in the 3 weeks prior to the onset of illness and who had a clinically consistent coughing illness (a coughing illness lasting two or more weeks; severe fits or bouts of coughing; vomiting after coughing or; 'whooping' sound during coughing) or laboratory evidence of pertussis infection. All potential sources of infection were recorded for each infant and age, sex, relationship to infant, and level of evidence of the source individual's infection (clinical symptoms, doctor diagnosed, laboratory confirmed) was collected. Further risk factors such as overseas travel or exposure through a health care worker were also ascertained.

PHUs within three of the 4 Area Health Services covering metropolitan Sydney participated in the study: Sydney South West (SSW); Sydney West (SW); and the Hornsby Office of Northern Sydney and Central Coast (NSCC). De-identified completed paper forms from participating PHUs were returned in weekly batches by secure fax to SSW, where they were assigned a study identification number and entered into an Epi Info database (Version 3.4.3, US Centers for Disease Control and Prevention, Atlanta, GA, USA). Data collection began in the last week of January 2009 and ceased in the first week of May. Data completeness for this case series was determined at the end of the study by extracting the total number of pertussis cases that met the study inclusion criteria from NDD and comparing this with the number for which the enhanced data collection form had been administered.

Results

Enhanced source of infection data was collected for a total of 95 laboratory confirmed cases notified to participating PHUs during the study period; 44 from SW, 41 from SSW, and 10 from NSCC. A total of 111 cases that met the study inclusion criteria were extracted from NDD at the conclusion of the study, therefore overall data completeness was 88%.

The median age of the cases was 3 months, with 47 males and 47 females (sex was not recorded for 1 case). The median household size, including the infant, was 5 persons (range 3–11). Twenty-four infants were too young to be vaccinated, 14 were not fully vaccinated for age, and immunisation status was unknown for a further two. Of the 56 infants who were reported to be fully immunised for age, 32 were between 2 and 5 months of age and would not have received the full 3 dose primary vaccine series. Thirty-five cases were hospitalised as a result of the

pertussis infection, all except two of which were less than 5 months of age, and hospitalisation status was recorded as unknown for a further 9 infants. The percentage of cases for which a source was identified and the percentage with siblings was similar between hospitalised and non-hospitalised cases (Table 2).

A source of infection could not be identified for 29 infants (31%) and a total of 86 known or suspected sources were identified for the other 66 infants. The most frequently identified sources were those who lived in the same household as the infant with siblings representing over double the proportion of infection sources (36%) compared with mothers (15%). Other family members (e.g. aunts, uncles, grandparents) (21%), and friends (13%) were also significant sources of infection. While a specific source individual could not be identified for 5 infants, two were potentially exposed in childcare, one attended a medical centre in which people were coughing, one was exposed in a hospital emergency department, and 1 infant most likely acquired the infection overseas. Only ¼ of the suspected source individuals were laboratory confirmed, with the majority (61%) being implicated on the basis of clinically consistent pertussis symptoms (Table 3).

Overall, 53 household sources of infection were identified (62%), and source of infection varied with age as shown in Figure 1. No clear pattern was evident, with household and non-household sources relatively evenly distributed by age. For infants that had siblings, they were the most common source, followed by infection sources that were unable to be identified. In non-sibling households, parents and other family members were most frequently identified, each contributing ⅓ of the infection sources (Table 4).

Of the 81 persons identified as potential sources of infection, 49 were children under 18 years of age. Exact age was recorded for 45 of these children of which almost half (22) were aged 3 or 4 years. Figure 2 shows the age distribution for the 30 source children who were siblings, combined with the age

Table 2: Hospitalisation status of infant pertussis cases, by age, whether a source was identified, and if the case had siblings

Infant age	Hospitalised		Not hospitalised		Unknown	
	n	%	n	%	n	%
< 2 months	15	43	4	8	5	50
2–3 months	13	37	9	19	3	30
4–5 months	6	17	7	14	0	–
6–11 months	1	3	29	59	2	20
Source identified						
Yes	25	69	34	69	7	70
No	11	31	15	31	3	30
Siblings						
Yes	31	86	36	73	9	90
No	5	14	13	27	1	10

Table 3: Known or suspected sources of infection, by method of diagnosis

Source	Method of diagnosis				Total	Per cent
	Clinical symptoms	Doctor diagnosed	Laboratory confirmed	Not applicable*		
Mother	7	2	4	0	13	15
Father	7	0	1	0	8	9
Sibling	24	1	6	0	31	36
Other family	9	3	6	0	18	21
Friend	8	0	3	0	11	13
Other	0	0	0	5	5	6
Total	55	6	20	5	86	100

* Source location rather than specific individual identified, therefore the method of diagnosis of source is not applicable.

Table 4: Known or suspected sources of infection, by number of siblings in index case household

Source	No siblings		1 sibling		More than 1 sibling	
	n	%	n	%	n	%
Mother	6	20.0	2	6.5	5	9.3
Father	4	13.3	1	3.2	3	5.6
Sibling	N/A	N/A	10	32.3	21	38.9
Other family	10	33.3	5	16.1	3	5.6
Friend	3	10.0	3	9.7	5	9.3
Other setting	3	10.0	2	6.5	0	–
Source unknown	4	13.3	8	25.8	17	31.5

distribution of the other siblings in the household of the index cases who were not sources of infection (34 out of 35 for which age was recorded). While the infants in the study were more likely to have older siblings around 3 or 4 years of age, 16 of 20 (80%) siblings aged 3 or 4 years were sources of infection compared with 14 of the 44 (32%) other siblings aged less than 18 years.

Figure 1: Known or suspected sources of infection, by age of index infant case

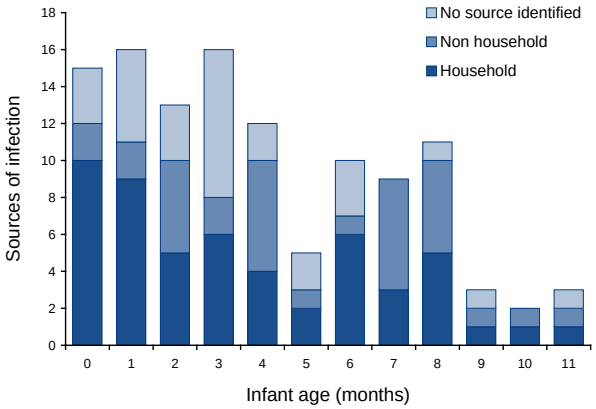
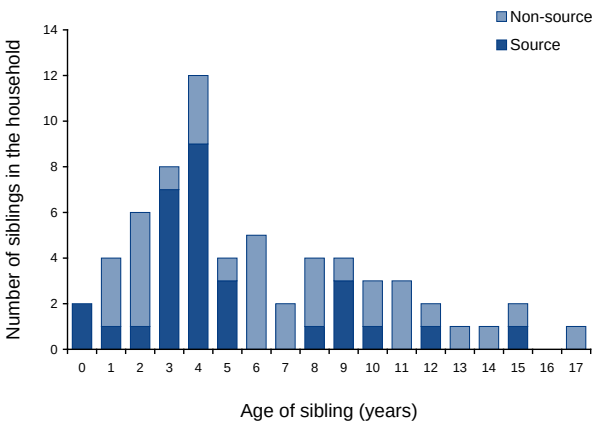


Figure 2: Age distribution of siblings less than 18 years of age resident in the index cases households



Discussion

Only 2 previous studies have investigated the source of infant pertussis infection in Australia. The first utilised the Australian Paediatric Surveillance Unit to identify 140 infants aged less than 12 months who were hospitalised for pertussis in 2001.[9] Contact with a person with a coughing illness compatible with pertussis was identified in 51% of cases. In the 72 cases where a source of infection was identified, a parent was identified as the source in 38 (53%) (mother 30, father 8) cases less than 24 weeks of age, but no parents were the source of infection for infants aged over 24 weeks. Siblings accounted for another 16 (22%) coughing contacts, with the remainder made up of grandparents, other relatives or non-family contacts. The second Australian study was a retrospective case series of 55 infants less than 12 months of age hospitalised at a tertiary paediatric hospital in Brisbane between 1997 and 2006 identified through hospital discharge coding and laboratory database.[10] A total of 31 potential sources were identified for 26 cases, of which 16 (52%) were parents and 14 (45%) were siblings. Of the 15 index cases where at least 1 parent was identified as the source of infection, 13 were under 3 months of age and all were aged under 4 months.

The present study is the first to investigate the source of infection among notified, PCR confirmed pertussis cases in Australia, including those not admitted to hospital. Importantly, interviews with parents or guardians were conducted shortly after notification and at the same time as public health investigation and follow-up to maximise the opportunity to recall coughing household members or visitors. Siblings were the most commonly identified source of infection for infants less than 12 months of age (36%

of all identified sources of infection). Parents were less frequently identified as the source of infection compared with the majority of previous studies (Table 1), with mothers representing a likely source of infection in only 15% of infants, compared with 42% and 26% in the two previous Australian studies.[9,10] Other non-household members and settings also made up a substantial proportion of infection sources, and even in households where the infant did not have siblings, only 1/3 of the infection sources were parents. The reason for the divergence observed in the present study is not entirely clear, but may reflect different transmission dynamics during the recent epidemic period, compared with studies that were conducted during periods of lower transmission. Based on the above findings, the cocoon strategy to selectively vaccinate household contacts of newborns would help to prevent some, but clearly not all, transmission to infants.

The finding that a high proportion of siblings aged 3 or 4 years were sources of infection identifies this group as an important reservoir for transmitting pertussis to infants during the outbreak. This could be a result of increased exposure to other children around this age, for example in child care settings. However, it may also be an indication that many children are not receiving the 4th dose of DTPa at 4 years of age on time. Furthermore, a dose of DTPa was previously recommended at 18 months of age, but was ceased in September 2003 due to the propensity for adverse reactions to result from this dose and it was thought the primary series provided sufficiently prolonged immunity until the booster dose at 4 years of age.[4] Elimination of the dose at 18 months may have resulted in waning immunity and an increased susceptibility to infection prior to receiving the 4th dose in the current schedule. It is of course not possible to determine this directly based on the results of the current study, but a review of the timing of the 4th dose may be required.

Infection risk also appeared to increase with household size and the number of older siblings present. The median household size in which the cases resided in this study was 5 persons. Data regarding the size and age structure limited to households with children are not reported in Australia, however the average size of households of OECD countries that do report such data are 2.7 and 3.9 for single parents and couples with children, respectively.[16] Therefore this study provides some evidence to support the particular importance that members of large households with newborn infants receive booster vaccinations.

This study was limited by the fact we were unable to identify a source of infection for 31% of the index cases. These cases may reflect a true unknown exposure, or have resulted from incomplete parental recall. However, as mentioned previously, this is a common issue in previous studies and in comparison the overall percentage of infants for which a source was identified was relatively high in the present study. This study was subject to recall bias as some parents may not have accurately remembered their infant's history of exposure to persons with a coughing illness, however, this would most likely have been minimal as interviews were conducted shortly after the infection was notified. Furthermore, only a minority of individuals suspected as sources of infection were laboratory confirmed, and the reliance on clinical symptoms to identify source cases may have missed subclinical cases or misclassified those with a coughing illness due to a pathogen other than *B. pertussis*.

The enhanced source of infection data collection form was not administered to all cases that met the criteria for inclusion in the study. However, the data completeness of 87.5% was greater than the 80% reported in the previous investigation into source of infection of notified cases in the United States of America.[6] Regardless, the review of the routinely collected data from SSW revealed that the cases not included in the study had a similar age, sex and infection source distribution to those that were. Therefore it is unlikely the exclusion of these cases would have introduced any systematic bias into the study. Finally, this study was small in comparison to some of the previous studies overseas, but similar in size to the 2 previous Australian studies. In contrast to these 2 studies, we collected data from cases with a broad range of severity over a short period of time, allowing a unique insight into pertussis transmission to infants during an epidemic. It should also be noted that PCR testing has replaced serology and culture confirmation due to its higher sensitivity, and confirmation by PCR was an inclusion criteria for the infants in this study. It not known what affect this had on the comparability to previous studies that included index cases that were confirmed by laboratory methods other than PCR testing, however there is no reason to assume it would have impacted the range of infection sources identified.

The recent pertussis epidemic in Australia, and New South Wales in particular, has underlined the necessity to reinforce control strategies, of which vaccination remains the most potent tool. The most significant shortcoming of the current pertussis immunisation schedule is that no protection is provided to infants less than 2 months of age. Universal adult vaccination would be an effective strategy to protect infants too young to be immunised, but very difficult to implement, and further safety and efficacy data are required before maternal and neonatal vaccination can be implemented.[17] Therefore the only available option at present to protect infants too young to be immunised themselves is

to encourage vaccination for those most likely to transmit infection, including not just parents, but siblings and other non-household contacts. Most importantly, our data highlight the role of siblings around 3 and 4 years of age as potential reservoirs of pertussis infection and reinforces the importance of both timely vaccination and the need to consider amending the immunisation schedule to minimise infection in this age group.

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