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Respiratory viruses transmission from children to adults within a household

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Background: The aim of this study was to examine the rate of transmission of influenza and other respiratory viruses from children attending an Emergency Department to their family members in the household using active surveillance.

Methods: A prospective hospital-based study was conducted over three consecutive winters (2006–2008) in children aged <1–15 years presenting with influenza-like illness (ILI). 168 children with ILI and their healthy families were recruited over three winter seasons.

Results: Respiratory viruses were detected in 101 (60.8%) children with ILI; in 91/166 (54.8%) a single pathogen was detected, and in the remaining 10 children more than one virus was detected concurrently. Influenza was the most common virus detected (34/101), followed by rhinoviruses (22/101) and adenoviruses (14/101). Of influenza viruses, 21/34 were influenza A and 13/34 influenza B. Meeting the clinical definition of ILI did not differentiate between influenza and other viruses. Clinical ILI developed within one week of follow up in 12% (26/205) of the family members who were swabbed. Viral pathogens were detected in 42.3% (11/26) of the symptomatic family members. In 6/11 cases the same virus was detected in the adult and child. The lower estimate of the household risk of transmission of respiratory viruses, based on concordant proven infection in both child and adult, from a single sick child to adult household contacts is therefore 3% per week.

Conclusion: This study provides quantitative, prospective data on rates of household transmission of infection from children to adults.

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1. Introduction

Acute respiratory infections (ARIs) are the leading causes of morbidity and mortality throughout the world, particularly in developing nations [1]. Respiratory syncytial virus (RSV) is the most common viral cause of lower respiratory tract infection in young children, followed by parainfluenza viruses (PIVs) types 1, 2 and 3, influenza virus A and B, and adenoviruses. However, the characteristics of viral transmission are poorly understood. Significant understanding is required about the role of household contacts, persistence and recurrence, re-infection, potentially predisposing risk factors, age-related risks, and the effect of prior exposure and past strain infection are not well defined. Insight into the aforementioned information will arm us with more potent way of tackling infectious viral epidemics and lower the burden of healthcare cost.

Household studies [2–5] and community studies [6–8] show RSV to re-infect repeatedly throughout life, which points to a potentially significant role for re-infections within the population that may be fundamental to RSV persistence within the community. Finally, RSV is typical of many viral infections with respect to inducing less than solid immunity, and being antigenically and genotypically diverse.

In addition to being the leading cause of upper and lower respiratory tract infections in infants and young children [9], RSV is the most common cause of bronchitis and pneumonia in children younger than one year of age [10]. The peak incidence of RSV infection occurs in children aged 2–8 months [11], with over half of all children being infected with RSV by their first birthday [12].

During each influenza season, it has been estimated that 30–40% of school-aged children develop symptomatic infection and that they are the main source for transmission to healthy adults and children, and to those in high-risk groups [13–18]. Of the children who develop symptomatic influenza infection, only a small
proportion are admitted to hospital and it is likely that hospital admissions may represent only a small part of the total influenza-associated morbidity [19,20].

Universal influenza vaccinations is not (yet) recommended for children; this is partly due to lack of data regarding the burden of laboratory-confirmed influenza in children making a meaningful cost effectiveness analysis of a universal influenza vaccination program difficult. Decisions regarding the introduction of influenza vaccine in healthy children require an accurate evaluation of influenza disease burden in the inpatient and outpatient settings, as well as the socioeconomic impact of the disease. The aim of this study was to examine the transmission of influenza and other respiratory viruses from children to their family member in the household. Our results give an estimation of the extent and impact of respiratory viruses, including influenza, in a cohort of children attending the emergency department but not admitted to hospital.

2. Methods

As described before [21], an initial prospective, cluster-randomized trial of the effect of mask use on respiratory virus transmission in households was conducted during two successive winter seasons between 2006 and 2007 in Sydney, Australia. The current study was conducted prospectively as an extension of the aforementioned over three consecutive winters between 2006 and 2008 in Sydney, Australia. The setting in which suitable families were identified was a pediatric health service comprising an emergency department of a pediatric hospital. The hospital acts as a specialized tertiary referral hospital for the western metropolitan area of Sydney, Australia, which has a population of 1.5 million people, and 15 local government areas. Over 70,000 sick children and their families are cared for each year in this area [22]. The study protocol was approved by the Human Research Ethics Committee of the Children’s Hospital at Westmead.

2.1. Recruitment

Children aged <1–15 years presenting with ILI (an ILI was defined as fever >38 °C and cough and/or sore throat in the absence of a known cause), but who were not subsequently admitted to hospital were identified using an electronic triage system. Inclusion criteria for the families were that all household members were healthy at the time the child was presented to the emergency department (ED), and that they agreed to follow-up for the duration of the study.

2.2. Follow-up and case definition

An investigator-administered questionnaire was used to collect information on symptoms, relevant medical history including medication, influenza vaccination status and health related visits prior to the ED visit. A combined nose and throat swab was collected from the index child for nucleic acid testing using a multiplex PCR assay. All children were discharged from ED on the same day.

Two adult family members from the child’s direct household (i.e. parents/caregivers or siblings aged 16 years and older) were followed up for a week to determine if they developed an ILI. During this follow up period we also collected information regarding the course of the child’s illness, requirement for medical visits, and work absenteeism.

If the two family members developed respiratory disease symptoms on follow up (fever, myalgia, arthralgia, sore throat, cough, sneezing, runny nose, nasal congestion, and headache), a home visit was conducted on the same day and swabs were collected and tested for a range of respiratory viruses.

2.3. Laboratory testing

An in-house multiplex, real-time, reverse transcriptase polymerase chain reaction (RT-PCR; primer and probe sequences available on request) for influenza A and B, parainfluenzaviruses, RSV, picornavirus (enterovirus, rhinovirus), adenoviruses, coronaviruses 229E and OC43, and human metapneumovirus (hMPV) was performed [23]. The method was evaluated against respiratory virus antigen positive (by immunofluorescence) upper respiratory tract samples (55 cases of RSV, 35 influenza B, 60 influenza A, 45 parainfluenzaviruses, 25 hMPV, 50 adenoviruses), and PCR positive (all confirmed by sequencing) upper respiratory tract samples (68 cases of rhinovirus and 20 enterovirus infections), and 150 antigen negative samples. The sensitivity of the real-time PCR for RSV, influenza A, influenza B, parainfluenza, hMPV and adenoviruses was 15% higher than antigen detection by immunofluorescence (testing both the antigen positive and negative samples) and the specificity was 100%. All coronavirus positive samples in the study were confirmed by sequencing.

2.4. Statistical analysis

Data were analyzed using Epi InfoTM (CDC, USA, version 3.3.2). Descriptive statistics was used to describe age, symptoms, and vaccination rates, etc. Comparison among groups was made with the Fisher exact test for categorical variables. A paired t test p value <0.05 was considered significant.

3. Results

3.1. Study population

Demographic, clinical and laboratory information on 168 children with ILI and their families were analyzed (Table 1). Sixty-three percent of the children (107/168) attended some form of childcare, leaving 61 (36%) children with no structured exposure of this type to other children outside the home. 39/168 (23%) children had a

| Table 1 | Characteristics of children/families with and without a child with a laboratory-confirmed infection. |
|---------|-------------------------------------------------------------------------------------------------------|
| Demographic characteristic | Laboratory positive N (%) | Laboratory negative N (%) |
| Total children | 101 (50) | 67 (40) |
| Information about the child | | |
| Age, mean ± S.D. | 3.78 ± 3.49 | 3.93 ± 3.54 |
| Premature birth | 93 (92.1) | 66 (98.5) |
| Congenital abnormalities | 7 (6.90) | 8 (11.9) |
| History of asthma | 13 (12.9) | 7 (10.4) |
| School/day care attendance | | |
| Daycare | 67 (66.3) | 40 (59.7) |
| School | 43 (42.6) | 19 (28.4) |
| Up to date with childhood vaccines | 23 (22.8) | 21 (31.3) |
| Vaccinated against influenza | 2 (2.0) | 2 (3.0) |
| Information about the family | | |
| Family size, mean ± S.D. | 4.3 ± 1.35 | 4.19 ± 1.10 |
| Adult number, mean ± S.D. | 2.4 ± 0.90 | 2.34 ± 0.77 |
| Children in household, mean ± S.D. | 1.9 ± 0.93 | 1.87 ± 0.75 |
| Living arrangement | | |
| House | 72 (71.3) | 48 (71.6) |
| Unit | 19 (18.8) | 11 (16.4) |
| Other | 10 (9.90) | 8 (11.9) |
| Smoking in house | 17 (16.8) | 14 (20.9) |
| Vaccinated against influenza | 8 (7.90) | 10 (14.9) |
condition that put them at high risk for complications of influenza (e.g., asthma, congenital abnormalities, or premature birth).

Of the 168 children with an ILI, 87% (146/168) reported having four or more symptoms. 59% (99/168) had a fever of ≥39°C. 153/168 (91%) reported having a cough, 146/158 (87%) had a congested nose, 81/168 (48%) had a sore throat and 82 (49/168) reported vomiting. Upper respiratory tract samples were collected from 166 children, with respiratory viruses detected in 101 (60%) children (Figs 1 and 2) (Table 2). In 91/101 cases a single virus was detected. As shown in Table 3, influenza and rhinoviruses were the most commonly detected viruses. The remaining ten children had dual or co-infection—adenovirus and rhinovirus in 4/166 (2.4%), rhinovirus and coronavirus OC43 in 2/166, and one child with each of influenza A and enterovirus, influenza A and rhinovirus, RSV and enterovirus, and adenovirus and hMPV.

No single symptom was predictive of influenza when compared to other viral causes of ILL. However, when compared with RSV,

### Table 2
Characteristics of families with and without a child with a laboratory-confirmed infection.

| Demographic characteristic | Laboratory positive (%) | Laboratory negative (%) |
|----------------------------|-------------------------|-------------------------|
| Total                      | 101 (60)                | 67 (40)                 |
| Age, mean ± S.D.           | 3.78 ± 3.49             | 3.93 ± 3.54             |
| Males/females              | 53/48                   | 34/33                   |
| Family size, mean ± S.D.   | 4.3 ± 1.35              | 4.19 ± 1.10             |
| Adult number, mean ± S.D.  | 2.4 ± 0.90              | 2.34 ± 0.77             |
| Children in household, mean ± S.D. | 1.9 ± 0.93 | 1.87 ± 0.75 |
| Living arrangement         |                         |                         |
| House                      | 72 (71.3)               | 48 (71.6)               |
| Unit                       | 19 (18.8)               | 11 (16.4)               |
| Other                      | 10 (9.90)               | 8 (11.9)                |
| Number of rooms, mean      | 3.1                     | 3.1                     |
| Race*                      |                         |                         |
| Caucasian                  | 40 (39.6)               | 26 (38.8)               |
| Asian                      | 27 (26.7)               | 22 (32.8)               |
| Indian                     | 15 (14.9)               | 9 (13.4)                |
| Middle Eastern             | 8 (7.90)                | 6 (9.0)                 |
| Other                      | 11 (10.9)               | 4 (6.0)                 |
| Language other than English| 39 (38.6)               | 24 (35.8)               |
| Smoking in house           | 17 (16.8)               | 14 (20.9)               |
| School/day care attendance | 67 (66.3)               | 40 (59.7)               |
| Daycare                    | 43 (42.6)               | 19 (28.4)               |
| School                     | 23 (22.8)               | 21 (31.3)               |
| Vaccinated against influenza|                        |                         |
| Adults                     | 8 (7.90)                | 10 (14.9)               |
| Child                      | 2 (2.0)                 | 2 (3.0)                 |
| Not fully vaccinated        | 9 (8.90)                | 6 (9.0)                 |
| Previously well            | 93 (92.1)               | 66 (90.9)               |
| Prematurity birth          | 7 (6.90)                | 8 (11.9)                |
| Congenital abnormalities    | 1 (1.0)                 | 3 (4.50)                |
| History of asthma          | 13 (12.9)               | 7 (10.4)                |

* Information relates to the participating adult interviewed.

### Table 3
Characteristics of families with and without a child with a laboratory-confirmed infection.

| Demographic characteristic | Laboratory positive (%) N = 101 | Laboratory negative (%) N = 67 |
|----------------------------|---------------------------------|---------------------------------|
| Reported symptoms           |                                 |                                 |
| Chills                      | 32 (31.7)                       | 24 (35.8)                       |
| Cough                       | 95 (94.1)                       | 58 (86.6)                       |
| Nasal congestion            | 89 (88.1)                       | 57 (85.1)                       |
| Sore throat                 | 47 (46.5)                       | 35 (52.2)                       |
| Ear ache                    | 17 (16.8)                       | 14 (20.9)                       |
| Sneezing                    | 69 (68.3)                       | 33 (49.3)                       |
| Lethargic                   | 72 (71.3)                       | 54 (80.6)                       |
| Loss of appetite            | 70 (69.3)                       | 48 (71.6)                       |
| Abdominal pain              | 33 (32.7)                       | 19 (28.4)                       |
| Vomiting                    | 52 (51.5)                       | 30 (44.8)                       |
| Diarrhea                    | 25 (24.8)                       | 18 (26.9)                       |
| ≥4 symptoms                 | 88 (87.1)                       | 58 (86.6)                       |
| Previous medical visit      |                                 |                                 |
| GP                          | 74 (73.3)                       | 50 (74.6)                       |
| Emergency department        | 9 (8.90)                        | 7 (10.4)                        |
| Antibiotics prescribed      | 42 (41.6)                       | 24 (35.8)                       |
| Laboratory diagnosis        |                                 |                                 |
| Influenza A                 | 21 (20.8)                       | –                               |
| Influenza B                 | 13 (12.9)                       | –                               |
| RSV                         | 7 (6.90)                        | –                               |
| PIV types 1–3               | 8 (7.90)                        | –                               |
| Adenoviruses                | 14 (13.9)                       | –                               |
| hMPV                        | 8 (7.90)                        | –                               |
| Rhinoviruses                | 22 (21.8)                       | –                               |
| Coronaviruses               | 5 (5.0)                         | –                               |
| Picornoviruses              | 6 (5.9)                         | –                               |
| Other*                      | 7 (6.9)                         | –                               |
| 2 Viruses detected          | 10 (9.9)                        | –                               |
| Impact of virus             |                                 |                                 |
| Missed school               | 40 (39.9)                       | 23 (34%)                        |
| One family member missed work*| 60 (36%)                       | 18 (37%)                        |
| Both families missed work   | 20 (12%)                        | 12 (18%)                        |
| Family member who reported an ILI  | 6 (4%)                         | 5 (7%)                          |

* Including Enteroviruses.

Fig. 1. Number of laboratory confirmed respiratory viruses in children participating in study, 2006–2008.

3.2. Transmission rate to adults family members

ILL developed within one week of follow-up in 12% (26/205) of the adult family members of the 101 children with a viral
pathogen detected. Viral pathogens were detected in 42.3% (11/26) of the symptomatic family members. In all 11 cases only a single pathogen was isolated: two cases each of RSV and adenovirus, and one case each of PIV-3 and coronavirus OC43. Other viruses detected included picornaviruses (4/11 rhinoviruses, 1/11 uncharacterized non-sequenced picornavirus). In 6/11 cases, the virus detected for the adult family members was the same as what was detected in their child. Only one case was detected where the patient had a laboratory-confirmed infection and the child did not. The lower estimate of the household risk of transmission of respiratory viruses, based on concordant, proven infection in both child and adult, from a single sick child to adult household contacts is therefore 3% per week. It is known that adults have a lower rate of laboratory detection of viral infections compared to children, and this was confirmed in our study, with only 42% of symptomatic family members compared to 60% of symptomatic children, being PCR positive for a respiratory virus. Based on symptoms, the rate of transmission could be as high as 12% per week. Of the adult family members interviewed, 38% (128/336) took time off work to care for their child. In some cases, two adults took time off (26/128, 25%).

We found that among the healthy children ≤15 years of age meeting a clinical case definition of ILI, 60% were found to have a laboratory-confirmed respiratory virus. The results of this study demonstrated that influenza A, rhinoviruses and picornaviruses were the most commonly detected viruses from pediatric outpatients using an ILI definition that included a fever ≥38 °C.

In a previous study based on epidemiology surveillance data it was estimated that influenza accounted for 24–35% of excess outpatient visits observed in children less than 3 years of age during the winter [24]. In response to this finding was the assumption by Tsolia et al. that even if other viruses are co-circulating in the community it appears that influenza predominates and is the main cause of respiratory morbidity in outpatients [25]. This may be true in other settings but in our cohort, influenza A and B only accounted for 37% of the laboratory-confirmed illnesses. A range of different viruses were detected.

4. Discussion

This study provides quantitative, prospective data on rates of household transmission of infection from children to adults, and shows that defined ILI symptoms may not differentiate between infection with influenza or other respiratory viruses. The results confirm that during winter, influenza viruses are not the only respiratory pathogens which are responsible for a febrile illness and hospital visits in this cohort of children. While these viruses were not serious enough to require the child to be admitted to hospital, taking into account lost days from work and school, hospital admissions and mortality rates in infants and the elderly, the health and economic costs are considerable. Children often carry these viruses to their homes and spread infection to younger siblings or to their parents, whereas those admitted to hospital tend to shed the virus abundantly for prolonged periods, thus potentiating spread [10].

In Australia, timely community-level information about respiratory tract infection is scarce. Lambert et al. [26] examined the burden of respiratory illness during winter in a cohort of urban children. They reported that the risk factors for ILI included younger age, fewer people residing in the household, structured exposure to other children outside the home, and a higher household income. While we cannot comment on risk factors for ILI, we found that being ≤1 year of age was significant for being diagnosed with a respiratory illness. As documented in this study, the rate of laboratory-confirmed illness was not related to the number of people living in the house. This is in comparison to many other studies in developed settings, which have found that the rate of infections within the household decreases with increasing household incomes, thought to be a reflection of household crowding [27].

Our findings are however, in line with the results from the previous Australian study ref, who also reported that there was no significant relationship between crowding and reported illness.

These results have global relevance to respiratory disease control planning. Blocking transmission of respiratory viruses is an important part of halting spread of disease and epidemics. Using barriers such as face masks and gloves, isolating people known to be infected as well as introducing hygiene measures (e.g. hand washing) are effective ways of containing respiratory virus epidemics. This is particularly important for children because it will help to protect them as well as reduce the chance of transmission to other household members.

While the children in our study were not admitted to hospital with respiratory illness, these events consumed considerable resources, both in social and family terms. 73% of the cohort had visited their local GP, 40% had received antibiotics and in 38% of cases, a family member had missed work to care for the sick child. In Australia, the minimum cost of a visit to a GP’s office is estimated as AU$33.20 (standard consultation rebate from Medicare). For this cohort of children, the cost of these visits would amount to AU$4070. The costs calculated here do not capture the full cost attributable to the illness. The direct out-of-pocket costs to individuals can be substantial and includes costs for pharmaceuticals (both over-the-counter and prescribed), travel related costs for GP visits and hospital visits, and gap payments for GP’s consultation. In addition, there are the costs associated with lost economic production. Of the family members interviewed, 38% took time to care for the child. Previous studies have shown that parental work loss for the
care of sick children forms a substantial proportion of the total cost of influenza in children [28,29]. Cohen and Nettleman [28] found that the mean duration of work loss (3.2 days) due to influenza in these children would translate into US $300 in lost wages (assuming US $93 for a day’s salary for a parent in the United States).

In our study, we found a high proportion of probably inappropriate antibiotic use in the community, since about 42% of the patients, most of whom had a viral infection identified as the cause of their febrile illness, received antibiotics prior to presenting to hospital. This is similar to the results from Tsolia et al. [30] who also found an excess of antibiotic use in their cohort of outpatient children (>6 months to <14 years) with influenza. They found that the most common reason for justified antibiotic administration was acute otitis media. In our study, 37% of the children who were PCR positive for influenza received antibiotics. In the comparator study, influenza accounted for 37% of all antibiotic courses given to outpatients with febrile respiratory infection during the period studied. The study by Neuzil et al. [31] also analyzed excess antibiotic use attributable to influenza. They found an average of 0.072 excess courses of antibiotics per preschool-aged child. The inappropriate or excess use of antibiotics could theoretically be reduced and perhaps avoided by inclusion of rapid influenza testing for evaluation of febrile infants on assessment during the influenza season as early antiviral treatment has been shown to reduce both the use of antibiotic treatment and the length of hospital stay [32]. As only 31% of the children recruited were under one year of age, the use and role of antivirals in these children could be considered. A recent study indicated that antiviral use in hospitalized children under 12 months of age is safe [33].

In 2008 the American Advisory Committee on Immunization Practices (ACIP) recommended routine influenza immunization in all children aged 6 months to 18 years [18]. The recommendation of childhood influenza vaccination by the ACIP was justified along several grounds. Major factors included the burden of childhood disease, healthcare utilization, and caregiver absenteeism. While this vaccine may not have protected all the children in our cohort, it may have prevented 32 cases of influenza in the cohort. Vaccines to protect against RSV and parainfluenzaviruses may also be available in the future. For family members, aside from recommending the use of the influenza vaccine, masks and hand washing may be other methods of preventing the spread in these households.

There are some considerations when interpreting the findings of this study. While this study was conducted over three consecutive winters, the study recruited from only one site, and was limited to examining children whose family members had agreed to participate in the study. Although we may have missed children with a potential respiratory illness, we were able to prospectively examine the impact of the child’s illness on the family members as in order to be recruited, the family members had to have been symptom-free prior to the date of recruitment.

5. Conclusion

Our results demonstrate that during winter influenza viruses are not the only respiratory pathogens which are responsible for illness and hospital visits in children. While these viruses were not serious enough to require the child to be admitted to hospital, they were responsible for excess GP, ED visit and antibiotic use. This study has provided solid estimates of transmission rates of respiratory viruses between children and family members.

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