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A two year prospective study of hospital-acquired respiratory virus infection on paediatric wards

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SUMMARY

Over a 24 month period on six paediatric wards of different designs 169 cases of possible hospital-acquired respiratory virus infection were investigated. A variety of viruses was isolated from 82 cases, the most common being respiratory syncytial virus, influenza, parainfluenza, adenoviruses and rhinoviruses. A further 73 children developed respiratory symptoms between 3 and 300 days after admission but viruses were not demonstrable by the techniques used. These children were thought to have hospital-acquired infection nonetheless. Thirteen children were shown not to have acquired infection as the cause of their intercurrent illness. Most acquired infections occurred where toddlers were in cots in open wards. Children with trauma, including non-accidental injury, congenital malformations, mental retardation, failure to thrive or neoplasia were most likely to become infected. Almost 20% of children suffered from croup or lower respiratory tract illness as a result of their acquired infection. The figure was 41% if those less than 12 months old were considered alone. Most episodes settled quickly but in a few children investigations or surgery were delayed for a few days.

INTRODUCTION

In recent years several reports have described clinical and pathological aspects of hospital-acquired infection with respiratory syncytial (RS) virus (Ditchburn *et al.* 1971; Gardner *et al.* 1973; Hall *et al.* 1975), influenza A (Gardner *et al.* 1973; Hall and Douglas, 1975; Brocklebank *et al.* 1972), and parainfluenza viruses (Gardner *et al.* 1973; Downham, McQuillin & Gardner, 1974) in paediatric wards. Serious illness was often the result, particularly in infants and in children with other major medical problems.

To gather more information about hospital-acquired respiratory virus infections a prospective study was carried out on cases recognized over a 24 month period on six paediatric wards in two hospitals in Newcastle-upon-Tyne. The aims were (*a*) to assess the overall size of the problem of hospital-acquired virus infections in wards admitting children of different ages, (*b*) to discover the viruses associated with each hospital-acquired infection, (*c*) to document the types and severity of illness caused, (*d*) to determine whether or not the hospital-acquired infection delayed treatment of other conditions or discharge from hospital, (*e*) to note the number of infections occurring when RS virus or influenza A were not present in

the community, and (*f*) to compare hospital-acquired infection rates on different wards.

MATERIALS AND METHODS

Between 1 October 1974 and 30 September 1976 ward nursing and medical staff were asked to notify cases of possible hospital-acquired infection, i.e. onset of any respiratory symptoms more than 24 h after admission. Alternatively if virological studies were only requested some days after admission ward staff were asked whether hospital-acquired infection could have been the reason for sending samples. Minimum incubation periods of the viruses most commonly encountered were taken to be 5–8 days for RS virus, 1–2 days for influenza, 2 days for parainfluenza, 4–6 days for adenoviruses and 2 days for rhinoviruses (Rhodes and Van Rooyen, 1968). If a virus was subsequently demonstrated within the above incubation period the episode was excluded from the study.

In each case where hospital-acquired infection seemed possible a standard proforma was completed. The age of each child and the admission diagnosis, date of admission, date of onset of new symptoms, and details of those symptoms were noted. A record was also kept of all children with respiratory infection, however mild, and including febrile convulsions, who were on a ward during the preceding 14 days and who could have been in contact with the study child whether or not viral studies had been performed. Details of current respiratory illness in members of ward staff were obtained for each episode but viral studies were not performed on adults. The case notes of each study child were examined after discharge to ascertain the final diagnosis of the episode of hospital-acquired infection and the effect that this had on other treatment or delay in discharge.

Specimens of nasopharyngeal secretions and nose and throat swabs were obtained and examined by the fluorescent antibody technique and virus culture methods described elsewhere (Gardner & McQuillin, 1974).

Hospital-acquired infection rates for RS virus and influenza A were calculated for the six wards using a published formula adapted to take account of outbreaks of varying lengths on each ward (Weightman, Downham & Gardner, 1974).

RESULTS

During the 24 months of the study 169 episodes of possible hospital-acquired infection were documented out of a total of 10549 admissions (1·6%). The presence of a virus was demonstrated in 82 instances (48·5%). Seventy three children (43·2%) developed respiratory symptoms between 3 and 300 days (mean 21·9) after admission but no virus was demonstrable by the methods used. No viral studies were performed on one child. Most of the children from whom no virus was demonstrated were in hospital during the autumn and winter.

Thirteen children (7·7%) were eventually thought not to have hospital-acquired respiratory infection as their intercurrent illnesses developed and other causes became clear on clinical, laboratory and radiological assessment. Diagnoses in this group included inhalation of vomit, streptococcal and meningococcal septicaemias,

Table 1. *Types of virus isolated, ages of patients and delay before infection*

Virus	Number of cases	Mean age in years ± S.D. (range)	Mean days in hospital before infection ± S.D. (range)
RS virus	25	1·8 ± 2·0 (0·2- 9·0)	16·9 ± 11·1 (5–47)
Influenza	18	4·5 ± 4·0 (0·1–12·0)	29·9 ± 58·4 (2–249)
Type A	17	—	—
Type B	1	—	—
Parainfluenza	12	1·0 ± 0·8 (0·2–2·0)	14·6 ± 10·6 (4–36)
Type 2	2	—	—
Type 3	10	—	—
Adenovirus	10	1·2 ± 0·9 (0·2–3·5)	26·7 ± 17·3 (6–53)
Type 1	7	—	—
Type 2	2	—	—
Type 7	1	—	—
Rhinoviruses	9	1·2 ± 0·9 (0·1–2·5)	11·9 ± 5·0 (6–20)
Enterovirus	3	0·5 ± 0·3 (0·1–0·8)	33·7 ± 41·2 (6–81)
Others (Mumps, Herpes simplex)	5	4·0 ± 3·3) (1·2–9·0)	14·8 ± 16·8 2–44)

postcardiotomy syndrome, uncontrolled diabetes mellitus, asthma, urinary infection and mumps, the latter developing within 3 weeks of admission. Almost two thirds of the 156 children thought to have hospital-acquired infection were male.

The main admission diagnoses of those children who became infected were typical of those seen on general childrens' wards. Those with trauma (non-accidental injury 26, road accidents and fractures 9), congenital malformations (congenital heart disease 16), mental retardation (15), failure to thrive (13) or neoplasia (solid tumours 6, leukaemia 3) were most affected.

Episodes of acquired infection most often presented with rhinorrhoea (60%), fever (54%), cough (34%), wheezing (14%), pharyngitis (13%), otitis media (10%) or vomiting (10%).

Table 1 shows the viruses associated with the episodes of illness investigated, the mean age of the patients in each group and the mean delay between admission and the onset of new symptoms. RS virus and influenza were the two main pathogens detected. Children who had hospital-acquired infection with influenza or 'other viruses' tended to be older than the rest. Forty-four percent of the children with RS virus infection were less than 12 months old compared with only 16·6% of those with influenza. There were only 5 months during the 2 year study when RS virus or influenza A were not in the community as judged by the virus laboratories' records. During these 5 months there were 25 cases of hospital-acquired infection, 12 (48·0%) being virus positive.

Table 2. *Final clinical features of episodes of infection*

Virus (total number)	Cold and Pharyngitis	Otitis media	Croup	Bronchitis	Bronchiolitis	Pneumonia	Influenza	PUO	Others (Mumps Gastroenteritis
RS virus (25)	11	3	1	11	3	2	—	—	1
Influenza (18)	6	4	—	3	—	—	10	2	—
Parainfluenza (12)	8	1	1	4	—	—	—	1	—
Adenovirus (10)	9	2	—	—	—	1	—	—	—
Rhinovirus (9)	7	1	1	—	—	1	—	1	—
Enterovirus (3)	—	—	—	1	—	—	—	1	1
Other viruses (5)	3	—	1	—	—	—	—	—	1
Virology negative (73)	50	1	2	11	—	2	—	7	4

Children judged to have hospital-acquired infection had been in the same ward at the same time as other children with the same virus, and therefore potentially in contact in 94·4% of influenza, 92% of RS virus, 41·7% of parainfluenza, 20% of adenovirus (one case each of types 1 and 7) and 11·1% of rhinovirus infections. The echovirus outbreak was small and all 3 affected children had been contacts of one child with this virus.

Respiratory symptoms were present in members of ward nursing or medical staff at the time of hospital acquired infection in 88·9% of influenza, 83·3% of parainfluenza, 77·7% of rhinovirus, 68% of RS virus and 50% of adenovirus infections. Illness was also present in ward staff in 70% of those from whom no virus was demonstrated.

The final diagnoses in the episodes of hospital-acquired infection are shown in Table 2. Croup or lower respiratory involvement occurred in 19·2% of all children and in 40·7% of those less than 12 months old. Three children with acute lymphoblastic leukaemia became infected, two aged 23 months and 6 years with RS virus and one aged 12 years with influenza A. The child with influenza remained well except for pyrexia, the 23 month old with RS virus had an upper respiratory infection with bronchitis but no wheezing and the 6 year old had an upper respiratory infection and pyrexia treated with intravenous antibiotics. None had been nursed in a laminar flow unit. All were better within seven days. Five other immunosuppressed children (four on prednisone, two on azathioprine and one on mustine) aged from 2 to 12 years became infected, two with RS virus and three with influenza. All settled without specific treatment and discharge home was not delayed by these episodes.

For the group of 156 children as a whole respiratory symptoms settled quickly and did not delay discharge home, although in several cases the symptoms did take up to a week to disappear. Some children were in hospital because of injuries or social problems and these conditions kept them in after the infection had settled. Discharge was delayed in 22 children (14·1%) and four were readmitted

Table 3. *The number and type of beds available on each ward with the results of virological studies carried out*

Ward	Total beds	Single cubicles	Mother and child rooms	Open Ward: Toddler cots	Open Ward: Beds	Age (years)	Hospital-acquired infection: Virus positive	Hospital-acquired infection: Virus negative
A	29	8	4	4	13	0–15	15	13
B	31	7	4	6	14	0–15	31	17
C	16	16	0	0	0	0–1	8	10
D	16	4	0	12	0	0–6	25	20
E	22	0	6	0	16	0–15	2	13
F	22	2	2	0	18	0–15	1	1

with respiratory symptoms less than five days after discharge. Antibiotics were started to treat the infection in 11 children, but some occurred during antibiotic therapy for other reasons.

One child of 20 months admitted with RS virus pneumonia died. RS virus alone had been cultured from respiratory tract secretions during life but at autopsy 13 days later, adenovirus type 1 was cultured from the trachea and both lungs. RS virus was still demonstrable on immunofluorescent staining. In three instances children had to be operated on for suspected neoplasia during the acquired infection and in a further case surgery was delayed for two days. Other investigations on four children had to be delayed because of acquired infection.

Basic details of the six wards studied with the number of episodes of possible hospital-acquired infection investigated on each are shown in Table 3. Overall the lowest hospital-acquired infection rate expressed as a percentage of hospital-acquired infection per total admissions was 0·1% in each 12 month period on ward F. For the other wards the figures were, ward A, 1·1 and 1·0%, ward B, 1·6 and 2·3%, ward C, 1·3 and 3·9%, ward D, 5·1 and 3·3%, and ward E, 0·4 and 1·1%. On ward D during the first 12 months of the study 13·7% of the children admitted below the age of one year became infected and viruses were identified in 50% of these. The figure for those over the age of one year was 3·7%. The following year the corresponding figures were 1·4 and 3·6%.

For comparison of hospital-acquired infection rates for RS virus and influenza A the duration of study on each ward was from the day on which the first demonstration of the virus was made to the day of discharge of the last known child with that virus. This period varied from 2 days to 194 days. Not all wards had outbreaks of acquired infection with these two viruses in each 12 month period.

Comparison between the hospital-acquired infection rates for RS virus in 1974–5 showed no significant differences. In 1975–6 ward C with three acquired RS virus infections, a study period of 171 days and a calculated hospital-acquired infection rate of 1604·7 was significantly different to ward D with four acquired RS virus infections in a study period of 105 days and an infection rate of 8317·5 ($P < 0·05$). Ward B with five acquired RS virus infections, a study length of 169 days and an infection rate of 1215·9 also differed significantly from ward D

($P < 0{\cdot}001$). Ward D in 1974–5 had two acquired RS virus infections in 140 days with an infection rate of 1428·0 and was significantly different to the same ward in 1975–6 ($P < 0{\cdot}05$).

For influenza A the significant differences in 1974–5 were between ward A with three acquired infections in 40 days with a hospital-acquired infection rate of 1845·1 and ward D with five acquired infections in 58 days and an infection rate of 18345 ($P < 0{\cdot}001$). In 1975–6 ward B had six acquired infections in 90 days with an infection rate of 2930·4 and ward C had two acquired infections in 10 days with an infection rate of 20408 ($P < 0{\cdot}01$).

DISCUSSION

Less than 2% of children of all ages developed respiratory symptoms suggestive of new infection while in hospital but in certain wards the risks were increased. Most hospital-acquired infections occurred on wards where there were children in the 0–6 year age range, especially if toddler cots were not in cubicles and the toddlers were free to roam as in ward D. However, 18 episodes of hospital-acquired infection occurred in a 16 cot cubicle unit for those less than one year old. These episodes were probably due to spread by staff or relatives as the children stayed in their cubicles. The young child is most at risk of severe illness from acquired infection (Gardner *et al.* 1973; Hall & Douglas, 1975).

The viruses commonly associated with virus positive hospital-acquired infections were RS virus and influenza, a finding demonstrated by others (Ditchburn *et al.* 1971; Brocklebank *et al.* 1972). Besides these two winter viruses, rhinoviruses were also mainly detected in winter but other viruses occurred sporadically throughout the year.

The majority of infections resulted in upper respiratory symptoms and otitis media only. However, 19% of children had croup, bronchitis, bronchiolitis or pneumonia, potentially fatal conditions if superimposed on a major medical illness which led to the initial admission (Gardner *et al.* 1967; Gardner *et al.* 1973; Hall & Douglas, 1975).

The children most at risk of acquiring infection were those whose hospital stay was in any case likely to be prolonged for social or medical reasons. The new infection did not materially alter the length of their time in hospital. Others have also noted that for RS virus the longer the hospital stay the greater the chance of acquired infection (Hall *et al.* 1975). In a few cases important investigations had to be delayed for a few days, and in others major surgery was thought urgent enough to justify operating during the episode of infection, exposing the child to extra risk.

Although RS virus and influenza were the viruses most commonly demonstrated and, particularly for RS virus the most persistent in the community, in their absence a number of hospital-acquired infections occurred and about 50% were virus positive.

Allowing for the fact that the hospital infected population was an abnormal one with a great excess of underlying medical illness, it was still apparent that

most of the children who became infected developed only mild upper respiratory symptoms. This supports the view that most respiratory viral infections cause only minor illness in most children. Even the children with malignant disease or on immunosuppressives were not severely ill. Such children do from time to time become fatally infected with common respiratory viruses (Craft *et al.* 1977). It has previously been shown that when children die with respiratory infection they often have a predisposing malformation or disease such as congenital heart disease or mental handicap (Gardner *et al.* 1967).

The hospital acquired infection rate on any ward is dependant on more subtle factors than just open or cubicle design and the age range of the children admitted. This becomes apparent from study of ward B. No hospital acquired influenza A occurred in 1974–5 but in 1975–6 quite a large outbreak happened – five cases in four days. One child freely excreting the virus was in contact with a large group of susceptible children. Why this sequence of events was not repeated several times in the two month epidemic is not clear. In general those wards with all cubicle design (ward C) or with no open ward toddler cot facilities (wards E and F) were less often the sources of infection.

During the months November to April each year when RS virus or influenza are prevalent it should in theory be possible to reduce hospital-acquired infection with these viruses by admitting each child with respiratory infection to a cubicle unit and screening for the presence of these viruses by immunofluorescence (Gardner *et al.* 1973). This would only partly deal with the problem as adults, staff and parents carry these viruses (Hall & Douglas, 1975; Hall *et al.* 1975; Sims *et al.* 1975). In addition many hospital-acquired infections occur with viruses for which rapid diagnosis is not available and viruses may not be isolated even by culture techniques. The isolation of children in the toddler age range is generally accepted as being psychologically undesireable for the child, so that unless facilities are increased for mothers to be admitted and isolated with their children, or high nurse/child ratios are available in isolation units for children it seems that viral hospital-acquired infection will continue to be common. In the majority of children mild illness will be the result. Those under one year old and those with neoplasia or on immunosuppressive drugs will continue to be at risk of serious illness.

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