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Introduction of a cross-infection rate in children's wards and its application to respiratory virus infections

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SUMMARY

Statistical methods are described in detail for the calculating and comparing of cross-infection rates. In addition the use of these rates has been extended to study the influence of age and of different virus types on susceptibility to cross-infection in children's wards.

INTRODUCTION

Bacterial cross-infection in hospital is no longer the serious hazard it was in the past but in recent years attention has been drawn to the risks of virus cross-infection, particularly with respiratory viruses in children's wards (Sterner 1972; Ditchburn, McQuillin, Gardner & Court, 1971). In order to assess the extent of cross-infection, taking into account the days at risk of those children who enter hospital free of the infection and the days of possible infection imposed by those children who have the infection, a 'cross-infection rate' was devised (Gardner *et al.* 1973). In this paper the statistical methods for calculating and comparing cross-infection rates are described in detail. The use of the rates has been extended to study the influence of age and of different virus types on susceptibility to cross-infection.

METHODS

The period of study

The survey was undertaken from 14 December 1971 to 30 April 1972 when influenza A and respiratory syncytial (R.S.) viruses were epidemic.

Definition of cross-infection

Virus cross-infection was considered to have taken place when a child acquired an infection after being in the ward longer than the accepted shortest incubation period for the virus. For R.S. virus this period is 5 days and for influenza A, 1 day.

The wards

The wards studied for evidence of cross-infection with influenza A or R.S. virus were divided, as well as possible, into two groups – those of open design and those made up mostly of cubicles.

Group A wards (numbered for identification 1, 2, 3 and 4) had open sections with cots or beds for children over a year, together with a variable number of single cubicles which were used mainly for infants under 12 months, although, when necessary, older children were admitted. Group B wards (numbered 5, 6, 7 and 8) contained mainly single cot cubicles. A full description of the wards has been given previously (Gardner *et al.* 1973).

Virology and clinical categories of respiratory infections

The clinical category of each respiratory infection (Gardner *et al.* 1960), the types of specimens, methods of collection and laboratory techniques have been described elsewhere (McQuillin & Gardner, 1968; Sturdy, McQuillin & Gardner 1969; Ditchburn *et al.* 1971). In a previous paper (Gardner *et al.* 1973) the clinical picture and age incidence of illnesses produced by cross-infection have been described in detail. Examples to illustrate the ways in which cross-infection occurred in the wards were also given.

Cross-infection rate

When a cross-infection rate is being studied it is necessary to take into account not only the number of cross-infections which occur but also the number of susceptible child days and the number of child days of primary infection in the ward. Four factors which might have some bearing on the rate were not taken into account in these calculations:

1. the possibility of tertiary cases (becoming infected by a secondary case who had himself acquired the infection in the ward from a primary case),
2. the length of time of virus excretion by each infected child,
3. the adult carriage of viruses,
4. possible cases which occur after discharge from hospital.

The assumption has been made that these factors were similar in both groups of wards.

The formula for the rate is:

$$\text{Cross-infection per million susceptible days per infective day} = \frac{\text{Number of cross-infections} \times 10^6}{(\text{Number at risk} \times \text{mean stay}) \times (\text{Number of infected} \times \text{their mean stay})}.$$

The standard error of a rate R_1 is estimated as $R_1/\sqrt{n_1}$, where n_1 is the number of cross-infections in the ward or group of wards.

A difference between two rates may be tested for significance as follows:

$$z = \frac{R_1 - R_2}{\sqrt{\left[R_1 R_2\left(\frac{1}{n_1}+\frac{1}{n_2}\right)\right]}}$$

z is compared with the standard Normal deviate. For example, a z-value $>1{\cdot}96$ or $<-1{\cdot}96$ indicates a statistically significant difference between the rates at the 5% level.

It will be noted that this cross-infection rate, which is entirely valid for internal comparisons in this study, is nevertheless dependent upon the duration of the study itself. We would like to thank a referee for the suggestion that an alternative formula for comparison of studies of different durations could be achieved by multiplying our cross-infection rate by the duration of the study (in days).

RESULTS

During the 4 months of the study period, 154 children were admitted to hospital with illness due to R.S. virus infection and 13 acquired the infection in hospital. Over the same period, 56 children were admitted with illness due to influenza A virus and 15 acquired the infection in hospital. Table 1 shows in detail the numerical information required and the method of calculating the cross-infection rate of R.S. virus in both groups of wards. The nine cross-infections in Group A (open design) wards gave a rate of 7·1 and the four in Group B (cubicle) wards a rate of 4·2 cross-infections per million susceptible days per infective day.

These two rates were compared as follows:

$$z = \frac{7{\cdot}1-4{\cdot}2}{\sqrt{\left[7{\cdot}1\,.\,4{\cdot}2\left(\frac{1}{9}+\frac{1}{4}\right)\right]}} = 0{\cdot}884.$$

This value is less than the conventional 1·96 at $P = 0{\cdot}05$ and is thus not statistically significant.

For influenza A the 14 cross-infections in the Group A wards gave a rate of 31·0 cross-infections per million susceptible days per infective day, and in Group B wards one cross-infection gave a rate of 12·4. The difference between these two rates was not significant ($z = 0{\cdot}917$).

None of the individual wards experienced a large number of cross-infections and comparisons made between them were not statistically significant in either Group A or Group B for either type of infection.

When the ages of the children were considered some significant differences in the cross-infection rates emerged. For these comparisons the 'susceptible child days' were those for the particular age group but the infective figure was that for all ages. Table 2 shows in detail the method of calculating the cross-infection rates in three age groups, under 1 year, one year to 4 years, and 5 years and over.

Table 3 shows the numbers and rates of cross-infection for each age group in the two types of ward. From this, comparisons can be made between the age groups for both R.S. virus infection and influenza A. Comparison may also be made between the two types of infection at each age group. The period and places of survey were the same for both infections, and they were both epidemic during this time.

Table 1. *Calculations for cross-infection rates of R.S. Virus for Group A (open design) wards and Group B (cubicle) wards*

					Under 1 year		1 – 4 years		≥ 5 years					
	Total number admitted	Number at risk	Mean stay of those at risk (days)	Number of susceptible days	Number admitted with R.S. virus infection	Mean stay (days)	Number admitted with R.S. virus infection	Mean stay (days)	Number admitted with R.S. virus infection	Mean stay (days)	Number of infective (days) (5) × (6) + (7) × (8) + (9) × (10)	(4) × (11)	Number of cross-infections	Cross-infection rate $\frac{(13) \times 10^6}{(12)}$
Col. no.	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)
							Group A							
Ward 1	370	351	5·8	2,036	15	10·8	4	9·0	—	—	198	403,128	3	7·4
Ward 2	323	306	7·0	2,142	13	10·9	2	11·5	2	12·0	189	404,838	2	4·9
Ward 3	95	81	10·5	850·5	7	11·1	6	4·3	1	6·0	110	93,555	0	0
Ward 4	309	275	6·7	1,842·5	23	6·7	11	3·9	—	—	196	361,130	4	11·0
												1,262,651	9	

Cross-infection rate for all Group A wards $= \frac{9 \times 10^6}{1,262,651} = 7{\cdot}1$

							Group B							
Ward 5	124	93	15·0	1,395	31	6·74	—	—	—	—	209	291,555	2	6·9
Ward 6	125	116	9·0	1,044	9	6·8	—	—	—	—	61	63,684	1	15·7
Ward 7	288	273	6·0	1,638	12	12·0	2	12·0	—	—	168	275,184	0	0
Ward 8	224	208	7·0	1,456	15	14·1	1	8·0	—	—	219	318,864	1	3·1
												949,287	4	

Cross-infection rate for all Group B wards $= \frac{4 \times 10^6}{949,287} = 4{\cdot}2$

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Table 2. *Calculations for cross-infection rates of R.S. virus for three age groups in Group A (open design) wards*

	Under 1 year				Under 1 year		1–4 years		≥ 5 years					
	Total number admitted	Number at risk	Mean stay of those at risk (days)	Number of susceptible days	Number admitted with R.S. virus infection	Mean stay (days)	Number admitted with R.S. virus infection	Mean stay (days)	Number admitted with R.S. virus infection	Mean stay (days)	Number of infective (days) (5) × (6) + (7) × (8) + (9) × (10)	(4) × (11)	Number of cross-infections	Cross-infection rate (13) × 10⁶ / (12)
Col. no.	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)
Ward 1	50	35	5·8	203	15	10·8	4	9·0	—	—	198	40,194	2	49·8
Ward 2	42	29	7·0	203	13	10·9	2	11·5	2	12·0	189	38,367	2	52·1
Ward 3	18	11	10·5	116	7	11·1	6	4·3	1	6·0	110	12,760	0	0
Ward 4	102	79	6·7	529	23	6·7	11	3·9	—	—	196	103,684	2	19·3
												195,005	6	

Cross-infection rate for children under 1 year in Group A wards $= \frac{6 \times 10^6}{195{,}005} = 30{\cdot}8$

		1–4 years												
Ward 1	124	120	5·8	696	15	10·8	4	9·0	—	—	198	137,808	0	0
Ward 2	115	113	7·0	791	13	10·9	2	11·5	2	12·0	189	149,499	0	0
Ward 3	36	30	10·5	315	7	11·1	6	4·3	1	6·0	110	34,650	2	57·7
Ward 4	207	196	6·7	1313	23	6·7	11	3·9	—	—	196	257,348	0	0
												579,305	2	

Cross-infection rate for children aged 1 to 4 years in Group A wards $= \frac{2 \times 10^6}{579{,}305} = 3{\cdot}5$

		5+ years												
Ward 1	196	196	5·8	1137	15	10·8	4	9·0	—	—	198	225,126	1	4·4
Ward 2	166	164	7·0	1148	13	10·9	2	11·5	2	12·0	189	216,972	0	0
Ward 3	41	40	10·5	420	7	11·1	6	4·3	1	6·0	110	46,200	0	0
Ward 4	—	—	—	—	—	—	—	—	—	—	—	—	—	—
												488,298	1	

Cross-infection rate for children aged 5 years and over in Group A wards $= \frac{1 \times 10^6}{488{,}298} = 2{\cdot}0$

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Table 3. *Numbers and rates of cross-infection for each age group in Group A and B wards*

Age	R.S. Virus Number	R.S. Virus Rate	Influenza A Number	Influenza A Rate
	Group A wards			
< 1 year	6	30·8	1	11·2
1 to 4 years	2	3·5	11	55·2
≥ 5 years	1	2·0	2	12·4
All ages	9	7·1	14	31·0
	Group B wards			
< 1 year	4	8·3	1	23·8
1 to 4 years	0	0	0	0
≥ 5 years	0	0	0	0
All ages	4	4·2	1	12·4

Group A wards

The difference between the R.S. virus cross-infection rates of 30·8 for children under one year and 3·5 for children aged one to 4 years in the open design wards is significant ($z = 3{\cdot}22$, $P < 0{\cdot}01$). Comparing the rate of 30·8 for children under a year with the rate of 2·0 for children aged 5 years and over gives $z = 3{\cdot}40$, which is significant at the 0·1 % level.

Comparing the age groups for influenza A in the open design wards the children aged one to 4 years had a cross-infection rate of 55·2 which was not significantly higher than the rate of 11·2 for children under a year ($z = 1{\cdot}69$), but was significantly higher than the rate of 12·4 for children aged 5 years and over ($z = 2{\cdot}13$, $P < 0{\cdot}05$).

A comparison between the R.S. virus cross-infection rates and those for influenza A in the open design wards shows that only for the children aged one to 4 years are they significantly different; 3·5 compared with 55·2 gives $z = 4{\cdot}84$, $P < 0{\cdot}001$.

Group B wards

No cross-infections occurred in children aged over a year and with only four R.S. virus and one influenza A cross-infection occurring in the children under 1 year, the numbers are too small to make valid comparisons using the above method. An exact test based on the binomial distribution shows that there is no significant difference between the two groups.

A comparison can be made between the cross-infection rates in the two types of wards for children under one year; the difference between the R.S. virus rate of 30·8 in the open wards and 8·3 in the cubicle wards was statistically significant ($z = 2{\cdot}2$, $P < 0{\cdot}05$). For influenza A the rate of 11·2 for children under one year in the open wards was not significantly different from the rate of 23·8 in the cubicle wards ($z = 0{\cdot}55$).

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DISCUSSION

The calculation of the cross-infection rate is simple and, as we have suggested in a previous paper (Gardner *et al.* 1973), could be of value in monitoring an existing situation or measuring the effect of a new one. Comparisons between cross-infection frequency in different centres might be made. If studies of different lengths were being compared, then for each study the cross-infection rate, as defined in this paper, should be multiplied by the duration of the particular study.

When separate age groups were compared some significant differences in the cross-infection rates emerged. Children under a year, in the open design wards had a significantly higher rate of R.S. virus cross-infection than children under a year in the cubicle wards. Within the open design wards the rate of R.S. virus cross-infection was significantly lower among children over one year of age than among children under one year. This difference seems likely to be due to two factors. In the first place, illnesses due to R.S. virus infection are usually less severe in older children (Chanock *et al.* 1961), so that some children in this group may have acquired illnesses so mild that they escaped surveillance. Secondly, it may be that immune defences in older children reduce the quantity of virus antigen in the respiratory tract to levels which defy identification.

There is a contrasting pattern of cross-infection rates for influenza A. The rate for children aged 1–4 in Group A wards is the highest of the three age groups and, though not reaching statistical significance when compared with the rate for children under a year, is significantly higher than that for children of 5 years and over. It has been noted that children admitted to hospital with illnesses caused by influenza A infection are most commonly aged between 1 and 2 years (Brocklebank, Court, McQuillin & Gardner, 1972). This age distribution is in contrast to that for R.S. virus, which most often results in hospital admission during the first year of life (Public Health Laboratory Reports, 1972, 1973); and this is also the case, although to a lesser extent, for the other two most commonly identified respiratory viruses, parainfluenza virus types 1 and 3 (Downham, McQuillin & Gardner, 1973). No information is yet available about the age distribution of children with influenza A infection who are not admitted to hospital. However, the findings of this cross-infection study support the impression that children under the age of a year are in some way less susceptible to infection by this virus and are usually less severely ill than older children if they do become infected. Why the relationship between age and influenza A infection should differ from that for the other common respiratory viruses is a matter for speculation, but it may point to important contrasts in mechanisms of pathogenesis and immunity.

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