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# The epidemiology of the common cold

## II. Cross-infection and immunity

BY O. M. LIDWELL AND R. E. O. WILLIAMS*
*Air Hygiene Laboratory, Central Public Health Laboratory, Colindale, London, N.W.9*

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### INTRODUCTION

In the previous paper we described the background of our studies of the common cold in four groups of office workers, and recorded the numbers of colds reported. In this paper we have attempted to analyse the relative importance of the recognizable contacts—in the office or at home—as sources of infection.

We were unable to employ any laboratory methods for identifying the causal agents of the colds that were studied, and so had to rely on statistical methods for evaluating cross-infection. In the family studies, with groups of two to seven individuals, it was possible to define the separate episodes of the disease in the family groups and so to measure the number of secondary infections apparently arising from each introduction. In the offices this was not possible. None of the rooms had less than twenty persons in them and most had about forty. In groups of this size it was rare to record no colds in a week, so that separate episodes of intra-office spread could not be distinguished. Various indirect methods for measuring the frequency of intra-office infection have been tested, but the results do not give a consistent estimate.

Except for some observations on the apparent immunity following a cold, all the data discussed in this paper are derived from the records obtained from the central executive offices of the Ministry of Pensions and National Insurance at Newcastle upon Tyne, and from the families of a number of members of the staff of these offices.

### CROSS INFECTION IN THE FAMILY

As we had complete information on the dates of onset for each infection we were able to adopt reasonably direct methods of assessing the cross-infection, and did not have to rely on the indirect methods used in a previous study (Lidwell & Sommerville, 1951). Some comparative calculations, however, show that estimates of the risk of cross-infection made by these indirect methods differ only insignificantly from those obtained by the methods described below.

* Present address: Wright–Fleming Institute of Microbiology, St Mary's Hospital Medical School, Paddington, London, W.2.

*Analysis of serial intervals*

The first procedure was to determine the range of serial intervals between two colds which was consistent with the second arising as the result of infection from the first.

If a series of events are distributed at random in a time series, then the probabilities of intervals of various lengths between two successive events will be distributed exponentially with the maximum fequency at zero interval. If we are concerned with events distributed into a series of discrete time intervals, e.g. days, this probability distribution takes the form of a simple geometric series, i.e.

$$f(i) = ar^i,$$

where $f(i)$ is the probability of an interval of $i$ days between two successive events and $a$ and $r$ are constants. The mathematical treatment of this series is conveniently straightforward and, in particular, a maximum likelihood estimate of both $a$ and $r$ can be obtained from a series of observed frequencies by means of the equations

$$N = a/(1-r) \tag{1}$$

and

$$r/(1-r) = \sum_{i=0}^{i=n} i\alpha_i + (n+1)\alpha'/(N-\alpha'), \tag{2}$$

where $N$ is the total number of intervals in the recorded series, $\alpha_i$ is the number of observed intervals of length $i$ and $\alpha'$ is the number of these intervals longer than $n$ days.

The observed distribution of serial intervals between colds in members of a household is shown in Table 1. This shows a clear-cut departure from the exponential form of a random series, having a hump in the distribution with a maximum at an interval of 2 days. Beyond 10–15 days, however, the distribution of frequencies does not differ significantly from an exponential form and it is reasonable to attribute the earlier hump to the results of cross-infection, with 2 days as the most frequent case to case interval. By applying equations (1) and (2) to the distribution at intervals of 15 days or longer an estimate can be made of the background of random colds over the shorter intervals. Subtracting these estimates from the observed frequencies gives an estimate of the number of presumptive cross-infections. (A small correction has to be made for the reduction in the number of members of the household at risk after an infection has been acquired by one of them.)

Some of the short intervals may arise from almost simultaneous exposure to a common source, either as multiple secondaries within the family or from some outside contact. However, it is unlikely that simultaneous infections contribute appreciably to the distribution, since over 85% of the apparent cross-infections are derived from episodes involving only two reported cases and the excess number of zero intervals is at most very small. The same is also true of any common agent, e.g. a weather disturbance which might be supposed to trigger off colds in members of the household.

The proportion of the family infections which, on this analysis, should be

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regarded as cross-infection within the family is 309/907 or 34 %. About 84 % of these 309 fall within the range of intervals 1–5 days inclusive and since the number of actual intervals which fall within this range is approximately 310, all the colds that occur within 1–5 days after an initiating cold have been presumed to result from cross-infection for the purpose of the succeeding analyses. This compromise

Table 1. *The distribution of serial intervals between colds in a household. Data derived from sixty-three households in* 1955–56 *and fifty-eight households in* 1956–57. *Total person-weeks*, 17,507

| Interval (days) | Observed no. | Corrected no.* | Calculated no.† | Excess over calculated | Cumulative excess | Percentage |
|---|---|---|---|---|---|---|
| 0 | 12 | 12·0 | 10·5 | 1·5 | 1·5 | 0·5 |
| 1 | 59 | 59·3 | 10·2 | 49·1 | 50·6 | 16·4 |
| 2 | 91 | 91·9 | 10·2 | 81·7 | 132·7 | 43·0 |
| 3 | 62 | 63·0 | 10·0 | 53·0 | 185·7 | 60·1 |
| 4 | 60 | 61·2 | 9·8 | 51·4 | 237·1 | 75·9 |
| 5 | 34 | 34·9 | 9·8 | 25·1 | 262·2 | 85·0 |
| 6 | 25 | 25·8 | 10·0 | 15·8 | 278·0 | 90·1 |
| 7 | 22 | 22·8 | 10·1 | 12·7 | 290·7 | 94·2 |
| 8 | 16 | 16·7 | 10·2 | 6·5 | 297·2 | 96·3 |
| 9 | 11 | 11·5 | 10·2 | 1·3 | 298·5 | 96·8 |
| 10 | 14 | 14·8 | 10·2 | 4·6 | 303·1 | 98·2 |
| 11 | 13 | 13·8 | 10·4 | 3·4 | 306·5 | 99·3 |
| 12 | 10 | 10·7 | 10·4 | 0·3 | 306·8 | 99·4 |
| 13 | 12 | 12·9 | 10·4 | 2·5 | 309·3 | — |
| 14 | 9 | 9·7 | 10·4 | −0·7 | 308·6 | 100 |
| 15 | 6 | 6·5 | 10·2 | −3·7 | | |
| 16 | 11 | 12·0 | 10·0 | 2·0 | | |
| 17 | 8 | 8·8 | 9·8 | −1·0 | | |
| 18 | 9 | 9·9 | 9·6 | −0·3 | | |
| 19 | 6 | 6·6 | 9·3 | −2·7 | | |
| 20 | 10 | 11·1 | 9·1 | 2·0 | | |
| 21 | 13 | 14·6 | 8·9 | 5·7 | | |
| 22 | 6 | 6·8 | 8·7 | −1·9 | | |
| 23 | 12 | 13·6 | 8·5 | 5·1 | | |
| 24 | 6 | 6·8 | 8·3 | −1·5 | | |
| 25 | 3 | 3·4 | 8·1 | −4·7 | | |
| 26 | 6 | 6·9 | 7·9 | −1·0 | | |
| 27 | 9 | 10·4 | 7·8 | 2·6 | | |
| 28 | 9 | 10·5 | 7·6 | 2·9 | | |
| 29 | 5 | 5·9 | 7·4 | −1·5 | | |
| 30 | 4 | 4·7 | 7·2 | −2·5 | | |
| Over 30 | 220 | 307·5 | 307·5 | 0·0 | | |
| Indeterminate | 114 | — | — | | | |
| Total | 907 | | | | | |

* The 'Corrected no.'s' have been obtained by distributing the intervals of indeterminate length on the assumption that the probability of an interval being recorded as indeterminate, i.e. being unconcluded at the end of a period of observation, is proportionate to its length.

† The calculated figures have been derived by fitting a geometric series to the frequencies of 15 days and over, making allowance for the reduction in exposure to risk at the shorter intervals due to the duration of symptoms and the demand for at least one day clear of symptoms before a fresh cold could be recorded. A mean family size of four members has been taken for the calculation of this correction.

gives approximate compensation for the continual risk of colds being acquired from outside the household.

An analysis was also made of the distribution of serial intervals for four relationships between the first and the following case, namely adult to adult, adult to child, child to adult and child to child, and these are compared in Table 2 with that found for the distribution of time intervals preceding the development of symptoms after instillation of nasal washings.

Table 2. *Distribution of the intervals between a cold and one secondary to it according to the status of the individuals concerned*

| Donor | Recipient | Total intervals | Apparent no. of cross-infections | % cross-infections | Median interval (days) | Index of dispersion |
|---|---|---|---|---|---|---|
| Adult* | Adult | 338 | 64·2 | 19·0 | 3·3 | 1·7 |
| Adult | Adult | 214 | 41·7 | 19·5 | 3·1 | 1·9 |
| Adult | Child | 190 | 48·8 | 25·7 | 2·8 | 1·9 |
| Child | Adult | 206 | 94·5 | 45·8 | 2·9 | 1·9 |
| Child | Child | 297 | 106·4 | 35·8 | 2·5 | 1·7 |
| Any | Any | 907 | 308·6 | 34·0 | 2·8 | 1·8 |
| Nasal instillation† | Adult | — | — | — | 2·4 | 1·5 |

* Data for years 1954–55, 1955–56 and 1956–57; the following rows are for years 1955–56 and 1956–57 only.

† Sartwell (1950), computation based on the data of C. H. Andrewes.

The median intervals and the indices of dispersion were obtained graphically by plotting, on probability paper, the cumulative fraction of apparent cross-infections against the logarithm of the interval. An interval of, e.g., 3 days is reckoned to include intervals from $2\frac{1}{2}$ to $3\frac{1}{2}$ days. The relationship obtained was substantially linear and straight lines were drawn by eye from which the median was read off and the index of dispersion computed as the antilogarithm of half the span between the logarithms of the intervals corresponding to 16 and 84% of the apparent cross-infections.

The median interval between the first reported symptoms of a cold and the appearance of such symptoms in a presumed secondary infection is only slightly longer than the corresponding interval following experimental nasal inoculation with infective washings. This suggests strongly that infectivity is maximal about the time of onset of symptoms, which is in accord with observations on the isolation of virus following experimental inoculation (Tyrrell & Bynoe, 1961). The slight increase in the index of dispersion found under natural conditions, compared with the experimental data, is no more than would be expected from the uncertainties as to the precise moment of effective contact in the household. The small but definite increases in the median interval for cross-infections involving adults compared with those in which only children are concerned probably reflect variations in the opportunities for contact, although the greater susceptibility and, perhaps, also infectiousness of the child may play some part.

*Cross-infection in relation to age and sex*

The households were grouped into four classes. All adult, adult and schoolchildren, adult and infant, and adult with both schoolchildren and infants; and the individual members of the household were classified as husband, wife, other adult, schoolchild or infant. The colds reported were grouped into 'episodes', an episode being defined as a group of one or more colds with no interval between successive colds exceeding 5 days. In Table 3 are shown the number of occasions on which the various classes of person apparently initiated an episode in the household, i.e were the first to report a cold in an episode. Where symptoms of a cold were reported for two or more individuals on the same day at the start of an episode

Table 3. *The rate of acquisition of colds from outside the household and the fraction of colds acquired within it*

| | Status of individual | | | | | |
|---|---|---|---|---|---|---|
| Household type | Husband | Wife | Other adult | Schoolchild | Infant | Any |
| l adult | 2·5 (1672) | 2·9 (1672) | 3·9 (1597) | — | — | 3·1 (4941) |
| | 8·7 (46) | 18·3 (60) | 6·1 (66) | — | — | 11·1 (172) |
| cluding | 2·9 (2630) | 2·8 (2630) | 4·3 (1666) | 3·8 (5145) | — | 3·3 (12071) |
| choolchildren only | 25·2 (103) | 37·3 (118) | 36·1 (72) | 36·7 (313) | — | 34·8 (606) |
| cluding infant(s) only | 2·6 (894) | 3·9 (894) | 1·2 (423) | — | 5·8 (1400) | 4·0 (3611) |
| | 29·5 (38) | 38·6 (57) | 58·3 (12) | — | 43·0 (142) | 42·2 (249) |
| cluding both infant(s) | 2·5 (1344) | 2·5 (1344) | 0·5 (206) | 5·9 (1713) | 4·3 (1563) | 3·8 (6170) |
| nd schoolchild(ren) | 30·6 (49) | 47·7 (65) | 50 (2) | 22·3 (130) | 47·3 (127) | 36·5 (373) |
| ıy | 2·7 (6540) | 2·9 (6540) | 2·9 (3892) | 4·4 (6858) | 5·0 (2963) | 3·5 (26793) |
| | 25·4 (236) | 36·0 (300) | 25·0 (152) | 32·5 (443) | 45·0 (269) | 33·6 (1400) |

In each cell the top row gives the number of introductions per 100 weeks followed by the aggregate mber of weeks of exposure (in brackets). The lower row gives the percentage of infections which appear be cross-infections acquired within the household, followed by the total number of infections (in ackets).

Table 4. *Cross-infection in households—apparent risk according to the status of the individuals*

| | Donor | | | | | |
|---|---|---|---|---|---|---|
| Recipient | Husband | Wife | Other adult | School-child | Infant | Any |
| Husband | | 0·065 (12) | 0·102 (7) | 0·069 (19) | 0·063 (9) | 0·070 (47) |
| Wife | 0·112 (19) | — | 0·117 (8) | 0·158 (43) | 0·152 (21) | 0·140 (91) |
| Other adult | 0·045 (3) | 0·056 (5) | 0·099 (10) | 0·085 (10) | 0·030 (1) | 0·072 (29) |
| Schoolchild | 0·098 (19) | 0·173 (31) | 0·112 (7½) | 0·308 (62) | 0·114 (8½) | 0·178 (128) |
| Infant | 0·173 (13½) | 0·274 (24½) | 0·250 (2) | 0·380 (40½) | 0·396 (27½) | 0·307 (108) |
| Any | 0·107 (54½) | 0·135 (72½) | 0·110 (34½) | 0·179 (174½) | 0·147 (67) | 0·145 (403) |

The apparent risk is given as the number of occasions on which a cold was reported following the introction of the cold into the household by the indicated type of donor, divided by the number of exposures that type of donor, including only those apparent secondary infections reported within 1–5 days after e date of the first symptoms in the donor. The numbers in brackets after each fraction are the number apparent cross-infections on which the values of the risk are based.

these were counted as separate introductions, but any subsequent colds belonging to the same episode in other members of the household were divided equally between the individuals apparently initiating the episode when computing the cross-infections due to them. The numbers of introductions are given in the table as a fraction of the total number of weeks' exposure to risk. This fraction represents the apparent rate of acquisition of colds from sources outside the household. The number of colds apparently acquired in the household is also given as a fraction of the total number of colds experienced by the members of the particular class.

The risk of acquiring a cold following its introduction into the household can be estimated in terms of the ratio of the number of colds so acquired to the number of exposures to this risk. It is not possible to distinguish between primary and secondary cross-infections in an episode, so this ratio has been computed both for the first apparent cross-infection following an introduction and also for all the apparent cross-infections comprising the episode. The first will give an underestimate and the second an overestimate of the risk of infection from exposure to a single infection. The two sets of ratios only differ by about 15% and the lower value is given in Table 4.

Table 5. *Susceptibility, infectiousness and contact*

| Secondarily infected case | Introducing case: Husband | Wife or mother | School-child(ren) | Infant(s) | Relative susceptibility | Relative outside contact |
|---|---|---|---|---|---|---|
| Husband | — | — | — | — | 1·00 | 0·027 |
| Wife or mother | 5·4 | — | — | — | 1·82 | 0·016 |
| | | | | | (1·25) | (0·023) |
| Schoolchild(ren) | 5·4 | 6·6 | 12·9 | — | 1·53 | 0·029 |
| Infant(s) | 6·0 | 7·1 | 5·7 | 12·6 | 2·88 | 0·017 |
| Relative infectiousness | 1·00 | 1·46 | 1·56 | 1·09 | — | — |

The figures in the body of the table representing variation in the degrees of contact are obtained by dividing the cross-infection risk by the product of susceptibility and infectiousness and multiplying the quotient by 100. The symmetrical pairs of values have then been averaged.

The figures for relative outside contact have been obtained by dividing the 'introduction rates per week', taken from the penultimate row of table 3, by the relative susceptibilities. The bracketed figures below the second row are derived by assuming that the true relative infectiousness for wives and mothers, independently of contact differences, is the same as that of their husbands and dividing their apparent susceptibility by 1·46. The ratio 1·46:1 then indicates the extent to which the wives and mothers came into more effective contact with the other members of the household than these did with each other.

It is not possible to separate entirely the effects of susceptibility and infectiousness on these figures but an approach may be made by assuming a similar degree of contact between the several members of the household and comparing the secondary attack rates in the way described by Brimblecombe, Cruickshank, Masters, Reid & Stewart (1958). Some check on the consistency of this procedure is obtained by calculating the values obtained by dividing the observed risk of

cross-infection between two members of the household by the product of the relative infectiousness of the donor and the relative susceptibility of the recipient. The results of these calculations are given in Table 5. It will be seen that the quantities calculated as above are in fact substantially constant, except with respect to cross-infection between schoolchildren and between infants when they are about twice as large as for other relationships between donor and recipient. This difference might be interpreted as indicating closer contact between children of the same age group than between them and other members of the household.

In considering the values of infectiousness and susceptibility given in the table it must be remembered that they include any systematic difference in degree of contact. It would, for example, seem quite probable that the wives and mothers appear to be more infectious than their husbands because they are in more intimate contact with the other members of the household. This greater contact would also increase their apparent susceptibility to infection to much the same extent. The reduced figure for the susceptibility of wives and mothers obtained by assuming that their apparent increase in infectiousness is entirely due to increased contact is only 25% greater than the susceptibility of their husbands—a figure which is in substantial agreement with laboratory findings and with the differential incidence between men and women living and working in comparable circumstances.

An estimate of the relative exposure to infection outside the family can be made by dividing the introduction rate for individuals of a given class by the susceptibility of that class. The figures thus obtained are subject to the uncertainty in the discrimination between variations in susceptibility and variations in degree of contact between different members of the family but they do suggest that, in these families, the greater extent to which the children introduced infection into the family compared with the adult members was largely a reflexion of their greater susceptibility to infection and not a consequence of greater exposure.

Taken as a whole the picture of the sources of infection for the household, and the risk of cross-infection within it derived from the data for the Newcastle families, differs from that obtained in the village community (Lidwell & Sommerville 1951) in that the school and the schoolchildren no longer appear to be the most important agents in the spread of the infection. It differs from that obtained by Brimblecombe *et al.* in the London district of Paddington in the greater part that seems to have been played by the mother in spreading the infection in the Newcastle households, possibly through closer contact with the several members of the family. These two differences are not difficult to explain plausibly in terms of the different social arrangements in the three localities. In the village, contact between adult members of the community was much less than in the urban environments so that the school was the most constant place of association. The degree of crowding and overcrowding in Paddington was certainly greater than in Newcastle where the population studied was entirely middle class and this crowding may well have led to a more uniform degree of contact between all members of the family. The aggregate risk of cross-infection does not, however, appear to have been any greater in the Paddington homes and the total attack rates are about the same in all the three studies.

## CROSS-INFECTION IN THE OFFICE

The size of the community comprising the individual office in these observations, usually about forty persons, made estimation of the extent of cross-infection much more difficult than for the household. It was not possible to break up the sequence of colds into episodes, since there was not often a sufficiently long interval between successive cases. Two different methods have been used in the attempt to evaluate the amount of apparent cross-infection. The first utilizes the observed serial intervals between successive cases, that is, it is strictly analogous to the first method employed for the family analysis, but it could only be applied to groups within the rooms and not to the whole of the room population. The second method involved an attempt to detect an excess of colds, during the 5 days following the onset of cold, among those working in the same room as the index case.

### *Analysis of serial intervals*

The distribution of serial intervals for the offices, each room being treated as a separate unit, is such that nearly 90% of the intervals are of less than 8 days. The remaining 10% cannot be used to determine the distribution of the randomly occurring colds in the same way as was done for the household data employing the intervals exceeding 14 days, because these intervals are mostly derived from those periods of time when the rate of occurrence of colds was low. This difficulty can, to some extent, be avoided by using smaller groups. By dividing each of the two working sections of each office into two halves, groups of about nine or ten individuals working in relatively close proximity to each other were defined. A similar number of groups of about the same size were artificially constructed by selecting in alphabetical sequence one person from each of the nine offices under observation during the 2 years (1954–55 and 1956–57) for which this analysis was undertaken. The distribution of the serial intervals in the two sets of groups was then obtained, treating each group as a separate unit. Comparison of these two distributions (Table 6) shows a greater proportion of shorter intervals, of 7 days or less, for the groups working together. This excess is of the order of 14% of the total infections reported, whether the excess is computed by assuming a random distribution of the longer intervals and following the method of calculation described earlier, or is derived by comparison with the distribution of intervals found in the artificially constructed groups all of whose members work in different rooms. Following the hypothesis employed in analysing the data for serial intervals within the families this 14% of excess short intervals would be regarded as presumptive cross-infections.

The distribution of these intervals within the first 7 days is, however, noticeably different from that found in the family data. In particular the peak frequency is found at or about an interval of 1 day only, instead of at about 2 days. The distribution closely resembles that which would be expected from simultaneous infection from a common source, on the supposition that the development of the secondary infections followed the pattern suggested by the distribution of serial intervals in the family data. There does not, however, appear to be any reason for

assuming that this is in fact the cause of the difference between the two distributions nor are we able to suggest any other plausible explanations either in terms of a recording artefact or as a consequence of the larger size of the group involved.

Table 6. *The distribution of serial intervals between infections in sub-groups, half-sections, of the offices*

| Interval (days) | Half-sections | | Excess, observed less calculated | Constructed* 'control' groups | Excess, observed less control |
|---|---|---|---|---|---|
| | Observed | Calculated | | | |
| 0 | 92 | 84·5 | 7·5 | 45 | 47 |
| 1 | 157 | 78·5 | 78·5 | 81 | 6 |
| 2 | 120 | 73·3 | 46·7 | 93 | 27 |
| 3 | 91 | 68·2 | 22·8 | 85 | 6 |
| 4 | 73 | 63·4 | 9·6 | 66 | 7 |
| 5 | 71 | 58·9 | 12·1 | 58 | 12 |
| 6 | 71 | 54·8 | 16·2 | 56 | 15 |
| 7 | 63 | 56·8 | 6·2 | 51 | 12 |
| 0–7 | 738 | 538 | 200 | 536 | 202 |
| 8 and over | 661 | (661) | — | (661) | — |

The calculated figures have been derived in a similar way to that described for the family serial intervals, but in this case the calculated distribution has been fitted to the data for 8 days and over.

* The numbers of intervals have been reduced by a constant factor in order to give the same number of intervals of 8 days and over as were observed in the half-sections.

Table 7. *Cross-infection in the offices in relation to proximity*

| Position of 'recipient' relative to 'donor' | Cases obs. (1) | 1–5 days calc.* (2) | Excess, obs. − calc. (3) = (1) − (2) | Excess, as % of total cases (4) = (3)/32·45 | Average no. in relation specified (5) | Apparent risk × 100 (6) = (4)/(5) |
|---|---|---|---|---|---|---|
| Adjacent | 175 | 120·2 | 55 | 1·7 ± 0·4 | 0·69 | 2·4 ± 0·6 |
| Same table (not adjacent)† | 299 | 295·1 | 4 | 0·1 ± 0·5 | 1·70 | 0·1 ± 0·3 |
| Back to back | 243 | 202·3 | 41 | 1·2 ± 0·5 | 1·15 | 1·1 ± 0·4 |
| Rest of section | 2689 | 2555·3 | 134 | 4·1 ± 1·8 | 14·7 | 0·3 ± 0·1 |
| Other section | 3008 | 3062·0 | − 54 | − 1·6 ± 2·1 | 17·6 | − 0·1 ± 0·1 |
| Same room | 6414 | 6234·9 | 179 | 5·5 ± 2·8 | 35·8 | 0·15 ± 0·08 |
| Total cases | 3245 | | | | | |

* The calculated values were obtained by dividing the aggregate number of cases observed in the other rooms during the 1–5 days following each index case by the corresponding total number of individual exposures to risk in these rooms and then multiplying the result by the number of individual exposures to risk in the specified position. The figures in this column and in column (1) sometimes exceed the total number of cases since a particular cold might, and often did, occur within 1–5 days after several other colds and so might be recorded more than once as each of these was taken as the index case.

† There was often a considerable barrier, in the shape of bookshelves and filing boxes running across the middle of the tables, so that the staff were in much closer contact with those sitting behind them at the next table, with whom they could easily communicate by rocking back on their chairs.

The approximate values of the standard deviations given in the table are based only on the component of variation due to the finite numbers of observations.

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*Cross-infection in relation to proximity*

For each reported cold the number of persons at risk in the following 1–5 days and the number of these reporting a cold in this period has been tabulated in relation to their working position in the office at the time. As a control on the rate of acquisition from outside those working in other rooms were also included as a group in the analysis. These data are summarized in Table 7. It will be seen that there is some evidence of increased risk of cross-infection to those sitting close to the person reporting a cold but that the aggregate effect deduced in this way appears rather small; the estimated errors are, however, considerable.

*Evidence from overall incidence rates*

The results of the regression analysis made on the data derived from the family study (Lidwell & Williams, 1961) showed that those wives and mothers who did not go out to work and who did not have children living in the home experienced fewer colds than women of the same age, living in households which did not include children, who went out to work. The extent to which this can be taken as evidence for the acquisition of colds at the place of work is limited by the fact that the incidence of colds reported in the family study was only 88 % of that for the offices, when allowance is made for the distribution in the family population of the factors included in the general office regression analysis.

There were 30 person-years of observation on such wives and mothers who did not go out to work and these reported only thirty-four colds. On the basis of the experience of those women of similar age, living in households without children, who worked in the Ministry Offices, the expected number of colds would have been fifty-seven, which is reduced to fifty if an allowance is made for the generally lower number of colds reported by the persons included in the family study. The thirty-four colds reported are less than 70 % of the lower of these two estimates of the number expected but the difference is only just significant at the 0·02 probability level. The apparent increase of 30 % or more in the number of colds experienced by those women, who, having no children in the house went out to work, over those who did not do so may be compared with the estimates of 14 and 6 % for the fraction of colds acquired at work derived from the cross-infection analyses described above.

## IMMUNITY

It has usually been thought that the common cold is a disease that confers little or no immunity to reinfection (Reed, 1934, Commission on Acute Respiratory Diseases, 1947). The recent work by Jackson & Dowling (1959) on attempted reinfection of volunteers with nasal washings has, however, challenged the established view and the even more recent work on isolation of the viruses has revealed a number of immunologically distinct strains (Tyrell & Parsons, 1960; Hobson & Schild, 1960). In the circumstances no purely epidemiological study of immunity is likely to be very profitable, but it may be worth recording some observations on the apparent immunity resulting from the colds recorded in our study.

At any time it was possible to subdivide the population according to the period which had elapsed since the last reported cold. The experience of these groups in the particular week could then be compared to some reference group. Two reference groups were used for this purpose, the whole population at risk at the time, or the group last reporting a cold 10–14 weeks previously. The analysis was carried out separately for males and females and for those over and those under 30 years of age. Data obtained from the London offices as well as the Newcastle offices were used but no significant differences between these groups was found.

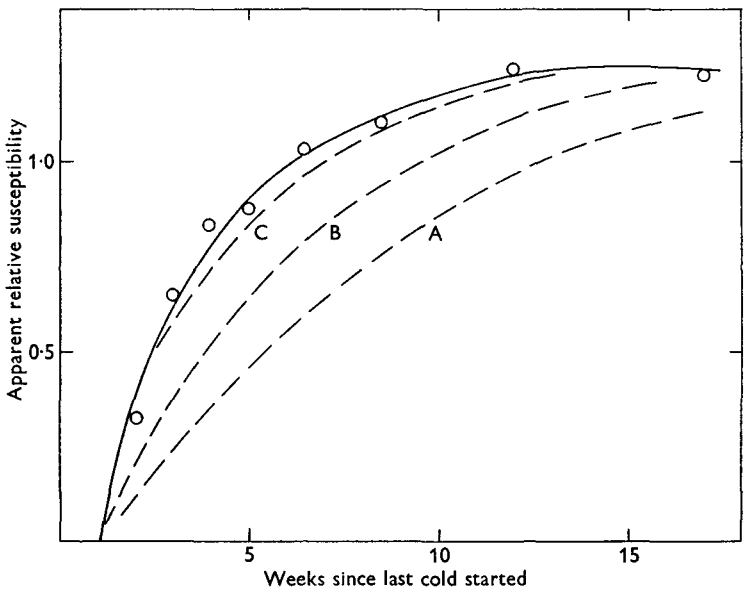


Fig. 1. Apparent immunity to reinfection with the common cold. The relative susceptibility to a further attack of the common cold is given as the ratio of the attack rate on those who had last reported a cold the indicated time previously, to the attack rate on the whole populations to whom the particular analysis refers. Full line: Data from 3 years' observation in the London offices together with 6 years' observation in the Newcastle offices, 1924 person-years in all. Broken lines: data from those persons who were included in all 3 years' observation in the London offices. A. Persons reporting five colds or less in the 3 years, 212 person-years. B. Persons reporting six, seven or eight colds in the 3 years, 309 person-years. C. Persons reporting nine colds or more in the 3 years, 224 person-years.

Since a new cold was not reported unless the individual had been free from symptoms for several days (the shortest recorded clear interval was 3 days) the figures could be corrected to allow for the reduction in the population at risk which this involves. As the median duration of symptoms, however, was no more than 10 days the effect of any such correction is limited.

It is apparent from the data which are presented in Fig. 1 that some form of relative insusceptibility persists for 8–10 weeks. An apparent fall in relative susceptibility beyond 14 weeks is probably an artefact arising from non-homogeneity in the population.

## DISCUSSION

Our studies were completed before the isolation of virus from patients with the common cold had given any real hope that it would shortly be possible to use laboratory methods to complement epidemiological studies. It is clear that, in the future, no purely epidemiological methods will suffice. Meanwhile our studies serve to supplement previous analogous investigations in various communities.

The pattern of cross-infection and the relative infectiousness and susceptibility of the various members of the household was not dissimilar to that reported in previous studies. However, while schoolchildren apparently introduced the infection into the household more frequently than adults, their role in this respect was not nearly so evident as in the village studied by Lidwell and Somerville. This is in accord with the finding that the presence of children in the household only increased the number of colds experienced very slightly if at all. Infants appeared to be responsible for rather more introductions per individual than schoolchildren. This seemed to be a reflexion of their greater susceptibility, for when allowance was made for this, their outside contact rate appeared to be not much more than half that of the schoolchildren, which in its turn was similar to that of the working adults.

The proportion of their colds that the Newcastle office workers apparently acquired at home was only about 10% when there were no children in the household, but was nearly 30% when there were children. This home contribution represents about 18% for the office population taken as a whole. The proportion of the colds traceable to office contacts is estimated at between 5 and 30%. The effect of public transport was considered in the previous paper and appeared to be trivial. We have therefore only succeeded in accounting for perhaps about one-third of the colds experienced, in terms of known contacts, even though the range of contacts explored might be expected to cover all those of any great importance.

There are a number of ways in which such a result might be produced. First, the contacts that were not included in the analysis might be in fact the more important. This seems unlikely in terms of number or intimacy. Secondly, a number of the reported colds might really be non-infectious conditions such as allergic rhinitis. It is likely that a few such have in fact been included but again it seems unlikely that they can have been more than a small proportion of the total. The analysis of the symptom patterns discussed in the previous paper does not suggest that any sizeable group of this kind could be distinguished. Thirdly, the infection might be acquired from a contact within the home or office, but no symptoms develop until the infection was stimulated by some other event such as a weather change, chilling, emotional stress, etc. It is not easy to produce evidence against this possibility, but experimental attempts to stimulate colds by the application of stresses have failed (Andrewes, 1950; Dowling, Jackson, Spiesman & Inonye, 1958; Jackson, Dowling, Anderson, Riff, Saporta & Turck, 1960).

A fourth possibility is that a considerable number of infections produce symptoms too slight to be reported. That some such effect occurs is most probable; to be of sufficient magnitude to account for the observed colds it would be necessary to assume that there are between one and two such trivial infections for every reported

cold and that these are as infectious as the reported colds. A number of studies of minor upper respiratory infections have recorded every detectable disturbance of the upper respiratory tract even though this was only transitory (e.g. Dingle, Badger, Feller, Hodges, Jordan & Rammelkamp, 1953; Simpson, 1958; McNamara, Thomas, Strobl & Kilbourne, 1960). As would be expected the number of events recorded in this way is considerably larger, by two to three times, than the number of colds reported under the conditions and with the criteria we have used, but there is no means of determining whether these additional disturbances were congruent with those infections usually included under the heading of the common cold. Cytopathological changes in the nasal epithelial cells following challenge with a 'common cold' virus have, however, been observed in a proportion of those volunteers who did not develop a clinical infection (Jackson *et al.*, 1960). If asymptomatic infections occur with any substantial frequency among adults it is also possible that at least part of the apparently greater susceptibility of the younger age group is to be attributed to a greater liability to develop obvious symptoms following infection. The whole question of asymptomatic infections should be capable of straightforward solution by direct experimental observations if regular recovery and detection of the virus is possible by the methods reported by Tyrrell & Parsons (1960).

Finally, if the virus can survive for some days or weeks on textiles or other fomites and lead to infection when material from these reaches the upper respiratory tract, then the proportion of infections transmitted in this way will not be traceable as cross-infections by any of the methods of analysis we have employed. It is also possible that unusually large bursts of dispersal from these sources could explain the distribution of serial intervals between colds in the offices which, as described earlier, appear to contain a substantial proportion of intervals most easily attributed to common source infection.

Our attempts to partition the number of colds experienced by our office workers according to the contacts from which they derive have not been very successful, but they suggest that the proportion of colds acquired at work was not likely to have exceeded one-half of the total so that the reduction that could be expected, at best, from any attempt to prevent the transmission of infection within the office environment was limited.

The data on reinfection after a cold clearly indicate a degree of reduced susceptibility to some extent for at least 8 weeks. If the results of Jackson & Dowling (1959) are of general application and infection confers a solid immunity against the homologous strain of virus for periods of at least a year, but no immunity against heterologous strains, then this may be interpreted as indicating the average time for one strain to be replaced by another in the population under observation. But if this is so and especially if inapparent infections are at all common, the number of distinct virus strains must be very large, for some people suffer five or six colds in a season of 40 weeks. The fact that the people who have the greatest number of colds in the year appear to regain their full susceptibility to infection after a cold more rapidly than those who have fewer colds in the year may well be evidence of some additional non-specific immunity factors.

SUMMARY

Analysis by epidemiological methods of the spread of the common cold among office workers and their families has failed to account for more than a fraction of the infections as a consequence of known exposure to infected individuals. Infections too mild to be recorded as colds, survival of the virus in the environment and its subsequent dispersal are considered as possible explanations of this.

The distribution of serial intervals between colds suffered by members of the same family indicates that the median interval between the onset of an infection and the first symptom in infection apparently arising from it as cross-infections was between $2\frac{1}{2}$ and $3\frac{1}{2}$ days. This is only slightly longer than the median interval, 2·4 days, observed between nasal installation and the onset of symptoms in experimental infections.

There is some epidemiological evidence that susceptibility to the common cold is reduced during the weeks following a cold.

We should like to repeat, in this the second paper in this series, our thanks to the Ministry of Pensions and National Insurance and to the Shell Petroleum Company, to those members of their staffs and to the nurses and others who helped us in this investigation.

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