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Variola minor in Bragança Paulista County, 1956: lack of evidence indicating the influence of contaminated classrooms on spread of the disease*

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SUMMARY

Space-time interaction analysis was applied to data from 101 elementary school children who contracted variola minor during an epidemic in Bragança Paulista County, Brazil. One school had two and the other three shifts of students occupying the same classrooms each day. There was no evidence found for excessive numbers of cases to occur among unvaccinated students occupying the same desks or seated near the desks occupied by cases occurring during another shift. Only three cases occurred among the 31 unvaccinated students occupying desks of students with variola from other shifts. Only one of these three subsequent cases occurred at a time interval suggestive of transmission. For the three models tested there was no evidence of space-time interaction between time of onset of the disease and location of desk for pairs of students from different shifts.

INTRODUCTION

In a previous report (Klauber & Angulo, 1974), space-time interactions among 101 cases of variola minor (alastrim) in two elementary schools were analysed by Mantel's permutational procedure (1967), which is a generalization of Knox's (1963) approach. The object of that investigation was to determine the extent to which various epidemiological units, e.g. classrooms or rows of desks, patterned the school outbreak. The approach was to compare total number of pairs of cases within given time and space units to expectation. In the present study, only the number of pairs of cases where one member of the pair is from one shift and the other from another shift using the same classroom, is compared to expectation. The intent here is to obtain evidence of possible indirect contagion by contaminated desks or classrooms.

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MATERIALS AND METHODS

The study schools

The two schools where most cases of variola minor occurred during the study epidemic were described in the previous report (Klauber & Angulo, 1974). This report also described the methods of data collection, and the critical time and space units chosen before the statistical analysis were also discussed. The same cases, but different statistical procedures, are used in the present report.

For the sake of clarity, some descriptions and definitions are reproduced here. The same classroom was used daily by two groups of students in the José Guilherme (JG) School and by three groups in the Jorge Tibiriçá (JT) School. All the classes attending during the same daily period are called a *shift*. Maps of classrooms were plotted for each shift and school. Save for one classroom of the JG School, all classrooms of either school had the same dimensions. The desk occupied by each student (the same every day) was identified. Desks were paired, one contacting the other on one side. Each desk-pair was placed immediately after the other, from the front to the rear of the classroom.

Statistical methods

Space-time interaction analysis

Space-time interaction was tested by the method of Klauber (1971) using the approach of Knox (1964). That is, Z the number of close pairs in both space and time, where each pair is composed of cases from different shifts, is evaluated relative to expectation E and to variance V, computed for three different randomization models. Values of Z, E and V were computed for two pairs of shifts: *JG* School, shift 1 *vs*. shift 2 and JT School, shift 1 *vs*. shift 3. It was impossible to have any pairs within the space and time units tried for the JT School, shift 1 *vs*. shift 3 and three additional pairs were available for shifts 2 *vs*. 3, only if a 30-day time unit were used, hence, these comparisons were eliminated.

An approximate standard normal statistic, corrected for continuity is given by

$$U = (\Sigma Z - \Sigma E \pm 0{\cdot}5)/\sqrt{(\Sigma V)},$$

where the summations are over the pairs of shifts to be combined and the sign of the continuity correction, 0·5, is chosen to reduce the difference between ΣZ and ΣE.

For each pair of shifts within each school three separate randomization distributions were considered. The three randomization models correspond to hypotheses of disease spread: (1) from the later shift to the earlier shift (earlier shift random); (2) from the earlier shift to the later shift (later shift random); and (3) both (1) and (2) (both sets random). The formulae for E and V are lengthy for all three models, and the reader is referred to Klauber (1971) for the details of the computations.

Space and time units

The critical time units between onsets of illness in two cases of variola minor would be approximately 11–16 days to allow for the actual variability in the periods of infectivity and incubation. In order to compensate for possible inaccuracies in the dates of onset, the following critical time units in days were tried: 11–16, 8–19, 5–22, 2–25 and less than or equal 30.

The critical space units reported (Klauber & Angulo, 1974) are: (1) the classroom, and (2) 'within one seat', i.e. students seated side-by-side, front to back or adjacent diagonally. Actually a number of other space units were tried, but these either gave similar results to those reported or yielded too small expectations to yield normal approximations in which we had confidence.

Seating position and disease occurrence

For the units, 'seated at the same desk', 'seated side-by-side' and 'seated front to back', an alternative analysis was used. For each school and shift each student who was unvaccinated for variola was counted in a 2 by 2 contingency table according to whether or not he contracted variola minor during the epidemic, and whether or not he was 'exposed', i.e. seated within the given space unit of a previously occurring case in a different shift (Table 1). The overall significance of an association between the factor, being seated at the same desk as a previous case from another shift (or other space unit association), and development of the disease was tested by combining the results for the five shifts using the Mantel–Haenszel chi square (one degree of freedom) procedure (1963)..

It should be pointed out that this second approach is not a test of space-time interaction. Each case occurring after another from a different shift within the space unit was checked for time difference in onset from that case (only pairs occurred) to see if transmission between them could possibly have occurred.

RESULTS

Same desk

An inspection of the seating maps and dates of onset indicated that 31 unvaccinated students occupied desks of students from other shifts who contracted the disease. Only three cases subsequently occurred among the 31 so 'exposed' to the index cases. The time intervals to onset of the index case were 13, 35 and 44 days, respectively. Thus, only one case conceivably could have resulted from fomites left at the desk.

The Mantel–Haenszel approach indicated no significant difference between observed versus expected cases (Table 1). The observed : expected ratio was 3:3·92 ($\chi^2 = 0{\cdot}06$).

Transversally attached desk

There were 37 unvaccinated students seated at desks attached to those on the left or right occupied by cases occurring during a different shift. Only one

Table 1. *Variola minor in two Bragança Paulista Schools*, 1956

(Number of cases occurring among unvaccinated students seated at desks where a case occurred previously from another shift*)

School		Shift 1			Shift 2		
		Case	Not-case	Total	Case	Not-case	Total
JG	'Exposed'	1	2	3	0	7	7
	'Not-exposed'	34	72	106	19	86	105
	Total	35	74	109	19	93	112

School		Shift 1			Shift 2			Shift 3		
		Case	Not-case	Total	Case	Not-case	Total	Case	Not-case	Total
JT	'Exposed'	0	2	2	0	13	13	2	4	6
	'Not-exposed'	30	60	90	3	84	87	12	98	110
	Total	30	62	92	3	97	100	14	102	116

* Summary $\chi^2 = 0{\cdot}06$; (observed cases)/(expected cases among 'exposed') = $3/3{\cdot}92 = 0{\cdot}77$.

Table 2. *Variola minor in two Bragança Paulista Schools*, 1956

(Number of cases occurring among unvaccinated students seated at desks transversally adjoining a desk where a case occurred previously from another shift*)

School		Shift 1			Shift 2		
		Case	Not-case	Total	Case	Not-case	Total
JG	'Exposed'	0	4	4	0	11	11
	'Not-exposed'	35	70	105	19	82	101
	Total	35	74	109	19	93	112

School		Shift 1			Shift 2			Shift 3		
		Case	Not-case	Total	Case	Not-case	Total	Case	Not-case	Total
JT	'Exposed'	0	5	5	0	10	10	1	6	7
	'Not-exposed'	30	57	87	3	87	90	13	96	109
	Total	30	62	92	3	97	100	14	102	116

* Summary $\chi^2 = 4{\cdot}58$, $P = 0{\cdot}032$; (observed cases)/(expected cases) = $1/5{\cdot}93 = 0{\cdot}17$.

case occurred after the index case among the 37 so 'exposed' and the onset was 64 days after that of the index case.

The Mantel–Haenszel approach yielded an expected number of cases of 5·93, which was statistically significantly different from the one observed at the 5% level; $\chi^2 = 4{\cdot}58$ (Table 2).

Table 3. *Variola minor in two Bragança Paulista Schools*, 1956

(Number of cases occurring among unvaccinated students seated at desks adjoining longitudinally a desk where a case occurred previously from another shift*)

School		Shift 1 Case	Shift 1 Not-case	Shift 1 Total	Shift 2 Case	Shift 2 Not-case	Shift 2 Total
JG	'Exposed'	0	5	5	0	13	13
	'Not-exposed'	35	69	104	19	80	99
	Total	35	74	109	19	93	112

School		Shift 1 Case	Shift 1 Not-case	Shift 1 Total	Shift 2 Case	Shift 2 Not-case	Shift 2 Total	Shift 3 Case	Shift 3 Not-case	Shift 3 Total
JT	'Exposed'	2	11	13	0	12	12	1	14	15
	'Not-exposed'	28	51	79	3	85	88	13	88	101
	Total	30	62	92	3	97	100	14	102	116

* Summary $\chi^2 = 6{\cdot}57$, $P = 0{\cdot}011$; (observed cases)/(expected cases) = 3/10·22 = 0·29.

Longitudinally adjoining desk

There were 58 unvaccinated students seated at desks directly in front of or behind desks of cases from other shifts. Three out of these 58 students had onset of variola subsequent to that of the index case. The time differences between the onsets of the index and subsequent cases were 5, 26 and 29 days.

The Mantel–Haenszel chi square was almost statistically significant at the 1 % level; $\chi^2 = 6{\cdot}57$. A total of 10·22 cases would be expected among the 58, where three were observed (Table 3).

Evidently, there is no evidence favouring the possibility that the disease was transmitted via fomites from one class period to another. Quite the contrary, if there was an effect of a desk being infected, it was to reduce the likelihood of an unvaccinated student contracting the disease, if seated at (or adjacent to) that desk.

Between-class space-time interaction

The space-time interaction tests showed no significant excess of observed pairs compared to expectation. The greatest O/E ratio was 3/2·43 = 1·24, which occurred using the later shift as the random set, a time unit of 5–22 days and the space unit, 'within one seat in any direction'. Out of the 30 O/E ratios, 25 had values less than one, confirming the impression from the previous analyses that if there was any effect, it was tendency towards fewer than expected cases occurring in different shifts, that could be possibly related. At the 5 % level (Table 4), there was only one significant difference in observed versus expected pairs 11/18·44 = 0·60. By chance, one would expect on the average 1·5 such significant differences out of 30 tests.

Table 4. *Variola minor in two Bragança Paulista Schools*, 1956

(Analysis of between-shift clustering, number of pairs of cases/expected within indicated space and time distances by sets assumed random)

Time unit	Space unit	Random set: Earlier shift	Later shift	Both
11 ⩽ T ⩽ 16 Days	Same room	10/12·14 = 0·82	10/9·55 = 1·05	10/12·23 = 0·82
	Within 1 seat	1/1·46 = 0·69	1/1·14 = 0·88	1/1·54 = 0·65
8 ⩽ T ⩽ 19 Days	Same room	11/18·44 = 0·60*	11/15·38 = 0·72	11/20·25 = 0·54
	Within 1 seat	1/2·49 = 0·40	1/1·56 = 0·64	1/2·55 = 0·39
5 ⩽ T ⩽ 22 Days	Same room	18/29·96 = 0·72	18/21·90 = 0·82	18/28·44 = 0·63
	Within 1 seat	3/3·45 = 0·87	3/2·43 = 1·24	3/3·58 = 0·84
2 ⩽ T ⩽ 25 Days	Same room	28/33·99 = 0·82	28/28·98 = 0·97	28/37·80 = 0·74
	Within 1 seat	3/4·75 = 0·63	3/2·92 = 1·02	3/4·76 = 0·63
T ⩽ 30 Days	Same room	37/43·82 = 0·84	37/36·79 = 1·01	37/47·23 = 0·78
	Within 1 seat	4/5·68 = 0·70	4/3·83 = 1·04	4/5·94 = 0·67

* Observed statistically significantly different from expectation at the 5% level.

The three randomization models yielded slightly different results. When the earlier shift cases were considered fixed, i.e. the source of disease spread, and later shift cases random, the O/E ratios averaged close to one (0·94). When the later shift cases were considered fixed and the earlier shift cases random or both sets random, all these O/E ratios were less than one and averaged 0·69.

DISCUSSION

A noteworthy finding is the very low frequency of variola minor among susceptible students occupying desks of students from other shifts who contracted variola during the study epidemic. This frequency becomes even lower when the length of the interval between the presumptive source and receptor cases is considered, unless a very long period of infectivity is admitted. In this regard, the time span covered by onsets of subsequent cases in defined social units indicate that, in real situations, the infectivity period of smallpox, particularly of variola minor, is rather limited (Dixon, 1948, 1962*a*; Anderson, Foulis, Grist & Landsman, 1951; de Salles-Gomes, Angulo, Menezes and Zamith, 1965; Angulo, Rodrigues-da-Silva & Rabello, 1967). This factual evidence contradicts the rather long periods postulated, without citation of supporting evidence, in textbooks, review articles, etc.

Further support to the above findings comes from the following facts: (*a*) a very low frequency of variola among susceptible students occupying one desk whose paired (contacting on one side) desk was occupied during another shift by a student who developed variola. This frequency becomes nil when the interval between onsets of the presumptive and receptor cases is considered; (*b*) a similar but less defined finding is made when desks placed immediately (no space between them) behind or in front of the desk occupied by a student who contracted variola are considered.

In a recapitulation, the analysis disclosed that contaminated desks, rather than increasing the likelihood of susceptible students developing the disease, showed a tendency towards fewer than expected cases occurring in different shifts, that could be possibly related. More support comes from space–time interaction analysis even though three randomization models yielded slightly different results. The object of the present study was to obtain evidence for possible contagion between students from different shifts using the same classroom. If such contagion had been evident it would not prove that the disease had been transmitted by fomites in the classroom, but rather it would admit it as a possibility. There was a tendency for students to queue outside the classroom before their shift and pass the members of the previous shift on the way to their desks. The negative findings of this study also indicate lack of evidence for this latter mode of transmission.

In the literature reviewed, only a single report of the spread of smallpox in a school was found. Although evidence of spread of variola minor in this, a primary school, was obtained, no suggestion of the influence of contaminated desks was found (Angulo, Rodrigues-da-Silva & Rabello, 1964). This intuitive examination of a small school outbreak is in full agreement with the results of the present statistical analysis. Studies resembling the present one are just intuitive examinations of the relative position of beds with cases in hospitals where smallpox was introduced (Eastwood, 1955; de Jongh, 1956; de Salles-Gomes *et al.* 1965; Angulo & de Salles-Gomes, 1967). No formal (analytical) approach was used in these studies. The possible role of fomites in those hospital outbreaks was examined without conclusive evidence of this self-suggestive mode of spread. As a matter of fact, when that role has been especially investigated in large as well as small epidemics occurring in other types of communities, negative results were also obtained (Clark *et al.* 1944; Dixon, 1948; Angulo, Rodrigues-da-Silva & Rabello, 1964). In this regard, handling bed-linen, clothing and similar objects used by or in physical contact with smallpox patients occurs in every house, hospital, etc., where patients are nursed. In spite of this enormous frequency, exceptionally few instances of spread through fomites have been reported (Corbin, 1915; Stallybrass, 1931; Ministry of Health, 1934; Parker, 1952).

In his intuitive study of a hospital-ward outbreak, Eastwood (1955) came to the conviction that fomites were not operative. Rather, aerial spread through droplet-infected dust impelled by moving the patient's beddings and clothings was the only plausible explanation for the observed spatial distribution of spread. Dixon (1962*b*), in reviewing a vast amount of published evidence on patient nursing and corpse handling, is also inclined to incriminate the infected dust rather than the body or corpse itself. In a recent study of two funeral-associated outbreaks of smallpox, Hopkins, Lane, Cummings & Millar (1971) found a 100% attack rate among corpse washers. Yet, Hopkins *et al.* also pointed out evidence suggesting that transmission might well have occurred before corpse handling. From a review of the literature, the impression is obtained that the evidence incriminating fomites is only circumstantial and that no conclusive demonstration has been made.

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