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# A study on the virus aetiology of mild respiratory infections in the primary school child

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When a child first attends school he or she immediately joins a group of children highly susceptible to a wide range of infectious agents. The chances of spread of viruses introduced into such a community are very high indeed and each year it can be predicted that outbreaks of the common infectious diseases will almost certainly occur.

The viruses of measles, rubella, chicken-pox and mumps are known to be the aetiological agents of these well-defined clinical illnesses. But besides these there are now known to exist a large number of other viruses which have been found associated with respiratory illness in other populations.

Among the school populations studied by various workers (Bransby, 1951; Norris, 1951; Nisbet, 1956) it seems that children were absent with a respiratory illness between once and twice a year and they lost anything between 2 and 10 days of schooling each year as a result. In a survey of respiratory viral disease McDonald (1963) estimated that among school children respiratory illness accounted for a third of all absence and about three-fifths of time lost.

Since the importance of these new viral agents among the primary school population has not yet been determined a study was undertaken to establish which of these many agents could be found circulating among school children. It was hoped to estimate how much illness was caused by these viruses, how easily they spread and to what extent they were responsible for the loss of school time.

## MATERIALS AND METHODS

### *Population studied*

In this country the majority of children attend day schools, and since one of our objects was to observe a population as normal as possible we avoided residential schools where the opportunities for viruses to spread and cause disease are greatly increased, compared with the more usual day school from which young children return to their homes each afternoon.

A local primary school was chosen since it was conveniently near the laboratory and the headmaster was co-operative. The school was recently built, light, airy and warm in winter and mainly served the surrounding housing estate which

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consisted of modern houses for small middle or lower middle class families. Children from all social classes were represented.

Altogether between 265 and 300 children of both sexes and aged between 4½ and 11 years attended the school. They were divided up into eight forms, the first three with the youngest children considered the infants and the rest referred to as the juniors. Class rooms held groups of between 30 and 40 of each age and although there was a common hall for morning assembly and the mid-day meal and a common playground, on the whole each age group tended to keep to itself.

The school year began in September and, with breaks of 2–3 weeks at Christmas and Easter, ended in the middle of July. Permission was obtained from all but a very few of the parents for the children to participate in the study.

*Laboratory methods*

Visits were made to the school on alternate mornings of the week and any child who was considered by his form teacher, or who considered himself, to be suffering from a cold or other minor respiratory ailment presented himself for examination. Each of us attended in rotation so that differences in clinical criteria and swabbing technique would not influence any long-term trends in the findings. A brief history of the illness was obtained and swabs taken from both the nose and throat. These swabs were broken off into 2 ml. of transport medium consisting of Hanks's salt solution with 0·2% bovine serum albumin. The specimens were taken to the laboratory and inoculated without delay into cultures of HeLa, monkey kidney, human embryo kidney and human diploid lung cells (strain WI-38); blood agar and mycoplasma agar plates were also inoculated. Pools of three specimens were prepared for subcutaneous and intracerebral inoculation into newborn mice. Specimens were then stored in an electric refrigerator at −70° C.

Occasionally cultures of human embryo kidney cells were not available for inoculation on the day the swabs were taken and specimens were then tested after having had one cycle of freezing and thawing.

When inoculated cultures became contaminated or if the cultures themselves were considered unsatisfactory owing, for example, to the presence of latent $SV_5$ virus in monkey kidney, the specimens were thawed and re-inoculated into fresh cultures.

The production, maintenance and examination of all cultures followed a routine pattern and viruses were identified by standard methods as described in a collaborative study of acute respiratory illness (Report, 1965).

Plates of mycoplasma agar prepared according to the method used by Chanock *et al.* (1962) were inoculated with approximately 0·1 ml. of pooled nose and throat swab extract, and examined at intervals during 18 days incubation aerobically at 37° C. The strains of *Mycoplasma pneumoniae* isolated were identified by fluorescent staining with specific serum.

No attempts were made to obtain blood samples for serology since it was clear that the attendance of children for swabbing would fall sharply if a procedure such as venepuncture were to be suggested. Much of the success of the scheme depended on the willing voluntary co-operation of the children themselves.

The study continued for two consecutive years and besides attempts at virus isolation a record was made throughout this period of the number of children who were absent from school.

## RESULTS

Over the 2-year period of the survey swabs were taken from 207 children. In all 782 illnesses were investigated, the numbers in consecutive years being 394 and 388. From these 59 viruses were isolated, 27 in the first year and 32 in the second making a final isolation rate of 8%.

The distribution of viruses in the various age groups is shown in Table 1. The viruses most frequently isolated were rhinoviruses followed by herpes simplex, respiratory syncytial and influenza $A_2$ virus. Two strains of a haemadsorbing virus were isolated in monkey kidney cultures from two children in different classes, aged 9 and 11 years, who were swabbed on the same day. These viruses were serologically identical with $SV_5$ virus. Since the same agents were re-isolated later in human embryo kidney cultures from the original stored specimens, they have been included under the name of para-influenza 5 virus.

Table 1. *Viruses isolated in different age groups*

| | Age in (years) | | | | | | |
|---|---|---|---|---|---|---|---|
| | 4–5 | 6 | 7 | 8 | 9 | 10–11 | Total |
| No. of children in age group | 50 | 50 | 32 | 30 | 30 | 70 | 262 |
| No. of children swabbed (on one or more occasions) | 24 | 35 | 29 | 27 | 25 | 67 | 207 |
| No. of illnesses swabbed | 92 | 142 | 111 | 72 | 151 | 214 | 782 |
| | Viruses isolated | | | | | | |
| Influenza $A_2$ | 0 | 0 | 0 | 1 | 2 | 3 | 6 |
| Para-influenza 1 | 0 | 1 | 1 | 0 | 0 | 2 | 4 |
| Para-influenza 3 | 0 | 1 | 1 | 0 | 1 | 0 | 3 |
| Para-influenza 5 | 0 | 0 | 0 | 0 | 1 | 1 | 2 |
| Respiratory syncytial | 2 | 2 | 0 | 0 | 0 | 3 | 7 |
| Herpes simplex | 1 | 3 | 0 | 0 | 1 | 3 | 8 |
| Adenovirus | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| Enterovirus | 0 | 1 | 1 | 0 | 0 | 1 | 3 |
| Rhinovirus | 2 | 2 | 7 | 1 | 5 | 6 | 23 |
| *M. pneumoniae* | 0 | 0 | 1 | 0 | 0 | 1 | 2 |
| Total viruses | 5 | 10 | 11 | 2 | 10 | 21 | 59 |
| Percentage of illnesses yielding virus | 6 | 7 | 10 | 3 | 7 | 10 | 8 |

The highest number of viruses was isolated from the 7-year and 10–11-year-old age groups. The variety of viruses was greatest in this latter group where all but para-influenza 3 virus were found.

The number of children investigated in the younger age groups was considerably lower than in the older. The reason for this is not clear; it may be that the younger children were less often suffering from a cold but it is possible that the older children understood the scheme better and attended with more enthusiasm.

Table 2 indicates the seasonal distribution of virus isolations and broadly the myxoviruses were found in the winter months and the picorna viruses (enteroviruses and rhinoviruses) from late spring through to autumn. Herpes simplex was absent through spring and summer except for a single isolation in June.

Table 2. *Monthly virus isolations, November 1962–July 1964*

| Virus | Sept. | Oct. | Nov. | Dec. | Jan. | Feb. | Mar. | Apr. | May | June | July | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Influenza $A_2$ | . | . | . | . | . | 3 | 2 | 1 | . | . | . | 6 |
| Para-influenza 1 | . | . | 1 | 1 | . | 2 | . | . | . | . | . | 4 |
| Para-influenza 3 | . | 3 | . | . | . | . | . | . | . | . | . | 3 |
| Para-influenza 5 | . | . | . | . | . | 2 | . | . | . | . | . | 2 |
| Respiratory syncytial | . | . | . | 1 | 4 | 1 | 1 | . | . | . | . | 7 |
| Herpes simplex | . | 1 | 1 | 1 | . | 2 | 2 | . | . | 1 | . | 8 |
| Adenovirus | . | . | . | . | . | . | 1 | . | . | . | . | 1 |
| Enterovirus | 1 | . | 1 | . | . | 1 | . | . | . | . | . | 3 |
| Rhinovirus | 2 | 1 | 3 | 2 | 1 | . | . | 2 | 1 | 7 | 4 | 23 |
| *M. pneumoniae* | . | . | 1 | . | 1 | . | . | . | . | . | . | 2 |
| Total | 3 | 5 | 7 | 5 | 6 | 11 | 6 | 3 | 1 | 8 | 4 | 59 |

Table 3. *Symptoms in virus positive children*

| Virus isolated | No. of of cases | Nasal discharge | Sore throat | Cough |
|---|---|---|---|---|
| Influenza $A_2$ | 6 | 5 | 2 | 1 |
| Para-influenza 1 | 4 | 4 | 1 | 1 |
| Para-influenza 3 | 3 | 3 | — | 3 |
| Para-influenza 5 | 2 | 2 | — | — |
| Respiratory syncytial | 7 | 6 | — | 2 |
| Herpes simplex | 8 | 8 | 1 | 4 |
| Adenovirus | 1 | 1 | — | — |
| Enterovirus | 3 | 3 | 2 | 2 |
| Rhinovirus | 23 | 17 | 5 | 7 |
| *M. pneumoniae* | 2 | 1 | — | 2 |
| Total | 59 | 50 | 11 | 22 |

*Mycoplasma pneumoniae* was isolated from two cases seen in the winter of 1962–3. Many other strains of mycoplasmas were isolated but as the object was to identify Eaton agent these were not investigated further. *Streptococcus pyogenes* was isolated from two children, one type 4 in January 1963 and the other, type 12, in the following July. This low frequency may be due to the fact that only when $\beta$-haemolytic colonies were present in large numbers were they reported as present and investigated further.

Table 3 shows the presenting symptoms associated with the viruses isolated. The most frequent feature was a nasal discharge which was found in 50 cases, nearly half of whom had a cough as well. Only eleven children complained of a sore throat. Four of the six children with influenza $A_2$ virus infection had no more than mild nasal symptoms as had most of the children with para-influenza 1 virus. In contrast all the three children with para-influenza 3 virus had an associated cough. One of the children with para-influenza 5 virus developed laryngitis and lost his voice. He was absent from school for 2 days as a result.

Most of the infections with respiratory syncytial virus were mild, although two children had a cough and one developed a very bad cold and cough.

Four of the eight cases from whom herpes simplex was isolated had a cough as well as nasal discharge. The rhinovirus infections presented predominantly with nasal discharge, but a third had coughs and a fifth had sore throats.

In both cases where *Mycoplasma pneumoniae* was isolated the main symptom was a persistent cough and it was found possible to re-isolate the organism 1–2 months later.

Table 4. *Virus positive children*

The relation of time absent from school with virus type.

| | Days absent | | | | | |
|---|---|---|---|---|---|---|
| Virus isolated | None | 1 | 2 | 3 | 4 | 5 |
| Influenza $A_2$ | 5 | . | 1 | . | . | . |
| Para-influenza 1 | 4 | . | . | . | . | . |
| Para-influenza 3 | . | 1 | 2 | . | . | . |
| Para-influenza 5 | 1 | . | 1 | . | . | . |
| Respiratory syncytial | 5 | . | . | 1 | . | 1 |
| Herpes simplex | 6 | . | 1 | 1 | . | . |
| Adenovirus | 1 | . | . | . | . | . |
| Enterovirus | 2 | 1 | . | . | . | . |
| Rhinovirus | 21 | . | . | . | . | 2 |
| *M. pneumoniae* | 2 | . | . | . | . | . |
| Total | 47 | 2 | 5 | 2 | . | 3 |

Table 5. *Common infectious diseases, 1962–3*

| Class | No. of children | Measles | Chicken pox |
|---|---|---|---|
| 1 | 26 | 17 | 0 |
| 2 | 38 | 14 | 3 |
| 3 | 36 | 8 | 0 |
| 4 | 30 | 0 | 0 |
| 5 | 39 | 2 | 0 |
| 6 | 36 | 2 | 0 |
| 7 | 25 | 0 | 0 |
| 8 | 35 | 0 | 0 |
| Total | 265 | 43 | 3 |

Table 4 shows the relationship between school absences, which were determined by examination of the attendance books, and the type of virus in the 59 virus positive children. In 47 (80 %) there was no associated absence from school either before or after the illness. The remaining 12 (20 %) children were absent for varying periods, but none over 5 days. In all three cases where para-influenza 3 was isolated an absence of 1 or 2 days was noted. Para-influenza 1 virus which is often regarded as the more virulent of the two was not associated with school absence in any of the four cases. The longest absences were found in two of the rhinovirus positive children. Neither of the children from whom *Mycoplasma pneumoniae* was isolated was absent from school.

The over-all relationship of respiratory virus isolations with attendance rates is shown in Figs 1 and 2. No significant fall occurred in association with the presence of any of the viruses isolated. The significant alterations are correlated with one

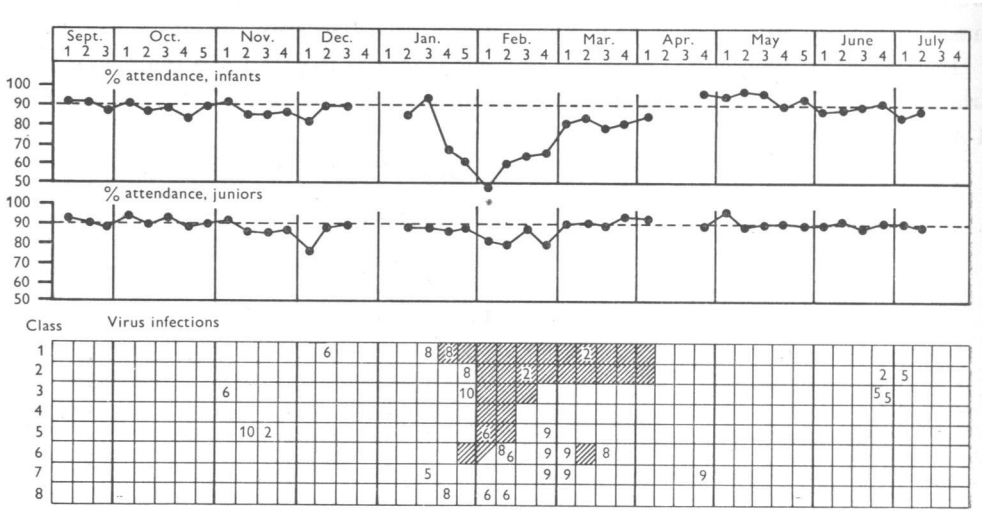


Fig. 1. Courtland School, 1962–3. For key to numbers, see Fig. 2.

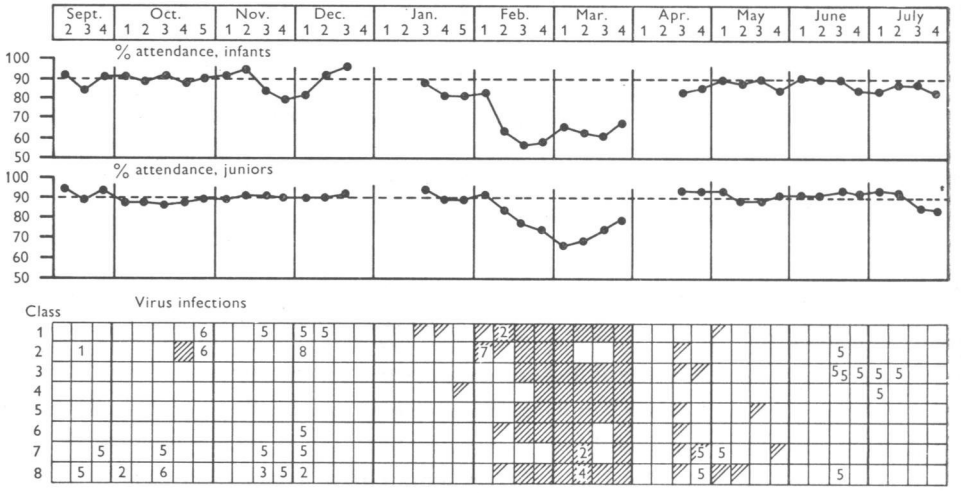


Fig. 2. Courtland School 1963–4

1 = Coxsackie B 3 2 = Herpes simplex 3 = echovirus 4 = adenovirus
5 = rhinovirus 6 = para-influenza 7 = Coxsackie A 9, 8 = Resp. syncytial
9 = influenza $A_2$ 10 = *M. pneumoniae*

or other of the common infectious diseases which are indicated by the shaded areas.

In 1962–3 the sharp fall in attendance in the winter months corresponded exactly with the course of an epidemic of measles which as can be seen in Table 5

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affected predominantly the younger age groups. The junior school was barely affected and attendance was maintained at a normal level.

In 1963–4 the winter months were marked by outbreaks of mumps, chicken-pox and rubella. Table 6 shows the occurrence of these diseases in both infants and juniors which reflects clearly in the drop of attendance in all classes, seen in Fig. 2.

Table 6. *Common infectious diseases, 1963–4*

| Class | No. of children | Chicken pox | Mumps | Rubella | Measles |
|---|---|---|---|---|---|
| 1 | 41 | 14 | 12 | 6 | 4 |
| 2 | 34 | 18 | 1 | 1 | 3 |
| 3 | 35 | 10 | 3 | 5 | 1 |
| 4 | 33 | 8 | 5 | 3 | 0 |
| 5 | 39 | 11 | 6 | 3 | 0 |
| 6 | 35 | 10 | 6 | 6 | 0 |
| 7 | 39 | 5 | 2 | 4 | 0 |
| 8 | 44 | 5 | 5 | 2 | 0 |
| Total | 300 | 81 | 40 | 30 | 8 |

Table 7. *Rhinovirus serotypes*

| Date | Age of child (years) | Serotype |
|---|---|---|
| 1963 | | |
| 24 Jan. | 9 | Not identified |
| 27 June | 7 | NIH 151–1 |
| 27 June | 7 | 16/60 |
| 4 July | 6 | Thompson |
| 17 Sept. | 10 | HIL 181 |
| 24 Sept. | 9 | NIH 151–1 |
| 15 Oct. | 10 | 16/60 |
| 15 Nov. | 10 | 16/60 |
| 22 Nov. | 4 | Unidentified |
| 24 Nov. | 10 | Unidentified |
| 3 Dec. | 9 | B 632 |
| 6 Dec. | 5 | B 632 |
| 1964 | | |
| 28 Apr. | 10 | NIH 363 |
| 28 Apr. | 9 | 16/60 |
| 1 May | 9 | NIH 363 |
| 23 June | 7 | 16/60 |
| 23 June | 10 | MRH |
| 23 June | 6 | Not identified |
| 23 June | 7 | Not identified |
| 30 June | 7 | 16/60 |
| 7 July | 7 | NIH 151–1 |
| 7 July | 7 | 16/60 |
| 7 July | 8 | Not identified |

The distribution of the viruses isolated in the course of the study is indicated in Figs. 1 and 2. There is no evidence of any substantial alteration in attendance associated with the presence of any of these agents in the community.

The isolations of influenza $A_2$ virus coincided with the identification of the virus from cases of clinical influenza, many moderately severe, in other parts of London.

Among the 23 strains of rhinovirus seven different serotypes were identified. Their distribution by time and age is shown in Table 7. The strain 16/60 was found most often followed in frequency by NIH 151–1. Although rhinoviruses appeared to cluster in summer and autumn, the serotypes at any one time were heterogeneous.

## DISCUSSION

In this study, if a child became ill at home he would, particularly if he was a young child, quite possibly not attend school and would not be included in this survey. In this way some of the more severe clinical infections with viruses must inevitably have been missed, and it might partly account for the low rate of streptococcal infection. The design of the study meant that on the whole only the mildest infections were sampled.

Perhaps for this reason the number of viruses isolated from these primary school children was low compared with the rate obtained in concurrent studies on children with respiratory illness in hospital or attended at home by their general practitioner, where something like 30% yielded virus (Report 1965). However, all the viruses found associated with the more severe respiratory disease were found circulating at some time or other among the children at school.

There was no evidence of epidemic spread of these viruses and the pattern was one of sporadic infections, of a continuous flow of candidates with colds throughout the whole period, yielding a variety of different associated viruses.

Throughout the survey there was virtually never 100% attendance at school and a remarkably constant figure around 90% was noted except for sharp falls in the early months of each year due to the common infectious diseases.

This pattern could be related to the widespread immunity now known to exist in the pre-school child to many of these newer respiratory viruses which appear to be highly efficient infecting agents even when the children are dispersed in small families. The viruses causing the common infectious diseases appear to be less efficient as spreaders since a high proportion of children reach school age still susceptible to them. It is only when the situation becomes favourable to the virus with multiple non-immunes in a close community that epidemics occur.

The cause of the 10% absenteeism has not been definitely determined. The reason given by parents in the majority of cases where a child is absent for a day or two is a bad cold. From the evidence that is presented here it is clear that there were sufficient viruses circulating in this population throughout the year to account for most of these illnesses and we suggest that they may have been responsible for the low but steady rate of absenteeism observed.

## SUMMARY

A survey of mild respiratory disease in a primary school was undertaken over a 2-year period to determine which of the newer respiratory viruses were responsible for these illnesses.

The over-all isolation rate was low but a wide variety of viral agents was isolated.

None of these caused epidemics but it is suggested they may be the cause of a low but constant absentee-rate throughout the year.

We would like to thank the Area Medical Officer of Middlesex County Council Health Department and the Borough Education Officer, Hendon, for making this study possible and the Headmaster and Staff of Courtland School, Mill Hill, for their willing participation. We are grateful to the children and their parents for their co-operation.

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