

Parainfluenza virus infections in the Cirencester Survey: Seasonal and other characteristics

BY R. EDGAR HOPE-SIMPSON

*Epidemiological Research Unit, 86 Dyer Street, Cirencester,
Gloucestershire, England*

(Received 18 March 1981)

SUMMARY

Parainfluenza viruses were isolated 165 times during 14 years surveillance of the illnesses of a general practice population of around 3700. Type 1 isolations numbered 57, type 2 isolations 22 and type 3 isolations 86, representing annual rates of 33, 13 and 50 infections respectively per 10000 of population. Type 4 parainfluenza virus was not isolated. Three major classes of illness gave the following rates: sore throats (Throats) nine, acute febrile respiratory diseases (FRD) 23, acute non-febrile respiratory diseases (non-FRD) 71. The illnesses caused by the three types isolated were similar. Type 1 infections were most abundant in November and type 2 infections in December, and only 11·4 % of these types were isolated in the warm semester April through September. Type 3 infections were seasonally bi-modal, with a winter peak in January and an even greater prevalence (66 % of the total) in the warm semester. Type 3 infections in the warmer months and in the later years of the Survey were usually more severe. Type 3 virus may therefore be heterogeneous, one subtype possessing and the other lacking the genetic mechanism of 'cold-season' prevalence. Geographical discontinuity between summer and winter isolations strengthens the case for the existence of the two subtypes of type 3 parainfluenza virus.

Type 3 infections caused the majority of the infections in very young infants. Type 2 infections were widely distributed at all ages. Females were attacked more often than males: type 1, 68·4 %; type 2, 63·6 %; type 3, 53·5 %. Type 3 infections in males outnumbered those in females up to 60 years of age, whereas female predominance became apparent in types 1 and 2 before 10 years of age.

All types were widely and sparsely distributed, areas of prevalence changing from year to year. Recurrences occurred only twice, both with type 3 infections. Six persons suffered both a type 1 and a type 3 infection, and one person suffered both a type 2 and a type 3 infection.

INTRODUCTION

The present paper continues a series of studies of common pathogens isolated during the Cirencester Survey, a prolonged clinical and laboratory surveillance of the illnesses encountered by the two general practitioners serving a population of about 3700 in Gloucestershire, England. Some of the studies have been published (Hope-Simpson, 1979*b*, 1981*a*, 1981*b*) but the parainfluenza viruses have been

discussed only briefly in a general description of the findings of the first 5 years of the Survey (Hope-Simpson & Higgins, 1969). The present paper analyses the findings of 14 years.

Of the four types of parainfluenza virus described as causing human illness, only types 1, 2 and 3 were isolated. Each type exhibited peculiarities of distribution bespeaking specific differences in epidemiological behaviour. The absence of type 4 isolations shows that it too has a specific epidemiology differing from that of all the other types.

Winter prevalence is a familiar but unexplained feature of human respiratory illness. Particular attention has therefore been given in all three studies to the seasonal distribution of the causal agents. The findings reported here show that type 3 parainfluenza virus differs in seasonal distribution from the other types.

The advantages of a survey in a community that is fully and continuously characterized by age and sex are offset by certain difficulties that need to be remembered when assessing the conclusions. The numbers in the different morbidity classes were varying continuously and independently, so that random sampling was irrelevant and representative sampling was impossible. A high sampling rate from all relevant classes was therefore undertaken, but there is no information concerning the proportion of specimens from infected persons that failed to reveal the presence of the virus. The proportion of sick persons failing to consult the doctor is also unknown. Such errors vary throughout the Survey and from one morbidity class to another. The rates given in the Tables are therefore underestimated to an unknown and variable degree.

Nevertheless trends peculiar to each type of parainfluenza virus appear consistently enough to indicate that they must be considered to be regular features of their epidemiological behaviour.

METHODS

Population. In 1953 the secretary of the general practice constructed a register of persons on the National Health Service lists of the practice partnership, recording sex, year and date of birth, and dates of entry into the practice list and departure therefrom. The register has been kept up to date by a weekly correction for births, transfers in and out, and deaths. Each year, at 31 December, a census is taken of the number of persons of each sex at each year of age.

Morbidity. All the entries made by the doctors on the records of the patients were duplicated into a daily Journal from which one of the doctors has analysed the illnesses falling in three main classes: sore throats (Throats), acute febrile respiratory diseases (FRD) excluding those with such specific diagnoses as measles and whooping-cough, and acute non-febrile respiratory diseases (non-FRD) such as the common cold. The Journal, begun in May 1947, was terminated in mid-1975.

Morbidity from Throats and non-FRD illnesses is available for the first 13 years of the survey, and that from FRD illnesses for the whole period of 14 years.

Specimens. The equipment for collecting specimens for virological examination, already described elsewhere (Hope-Simpson & Higgins, 1969), was available to the doctor at all contacts with the patients, whether in his consulting rooms or in their homes. The Public Health Laboratory was housed within the general practice

premises, so that little delay elapsed between the taking of a specimen and its arrival in the laboratory.

Specimens taken from well persons and from those with a complaint not falling in the three classes mentioned above formed a miscellaneous 'Other' class for which no morbidity figures are available. Most specimens, however, came from the morbidity classes Throats, FRD and Non-FRD.

Laboratory techniques. The techniques used routinely throughout the survey have already been published (Hope-Simpson & Higgins, 1969). Most strains of parainfluenza virus were isolated in the secondary cultures of monkey kidney cells, but strains were occasionally isolated in other systems such as Bristol HeLa cells.

Estimation of infection rate. The number of isolations of the virus is related through the number of specimens taken and the number of the illnesses seen to the background population as follows:

$$R = I \times \frac{M}{S} \times \frac{10000}{P},$$

where R is estimated annual rate per 10000 of the population, I is number of strains isolated, M is number of illnesses seen, S is number of specimens taken and P is number of person-years (persons multiplied by years of observation).

Example. Type 1 parainfluenza viral infections, 1 July 1962 to 30 June 1963.

$I = 8$ strains. $M = 1237$ sick in three morbidity classes.

$S = 446$ specimens. $P = 3573$ person-years.

$$R = 8 \times \frac{1237}{446} \times \frac{10000}{3573} = 62.10, \text{ say } 62 \text{ persons per } 10000 \text{ per annum.}$$

(The estimated rate R is lower than the true rate R^T because the efficiency of the techniques used for isolation of the virus (E) is less than 100%, and because M is less than the total morbidity M^T so that: $R^T = R \times 100/E \times M^T/M$. The values of E and M^T are not known.)

The analyses usually reckon the years from 1 July to 30 June to avoid breaking the sequence of winter months in which preliminary analysis had shown the greatest concentration of type 1 and type 2 infections. Type 3 has a peculiar seasonal distribution which has required a different secular analysis (Table 6).

RESULTS

Table 1 summarises the general practice population, illnesses in the three main morbidity classes and specimens taken during the survey.

Population. The population served by the general practice increased irregularly from 3511 in 1961-2 to 3919 in 1973-4 without seriously disturbing the age and sex composition.

The first 13 years have been totalled for use with Throats and Non-FRD classes which lack morbidity figures for 1974-5. The 14-year totals have been used with FRD illnesses.

Morbidity. Sore throats are estimated to have averaged nearly 900 cases per 10000 of the population per annum, the rate ranging from 444 in 1961-2 to 1218 in 1969-70.

Table 1. *Study population, morbidity and specimens*

| Morbidity class | Total | Annual mean | Range |
|----------------------------------|-------|-------------|------------|
| Throats | | | |
| No. of cases | 4287 | 328 | 156-475 |
| Rate/10000 person-years | — | 893 | 444-1218 |
| No. of specimens | 1458 | 106 | 27-173 |
| % of cases sampled | — | 32.2 | 17.3-43.1 |
| FRD | | | |
| No. of cases | 5398 | 386 | 232-579 |
| Rate/10000 person-years | — | 1022 | 641-1282 |
| No. of specimens | 3344 | 239 | 97-416 |
| % of cases sampled | — | 63.1 | 27.3-100.0 |
| Non-FRD | | | |
| No. of cases | 9424 | 725 | 594-809 |
| Rate/10000 person-years | — | 1962 | 1527-2634 |
| No. of specimens | 2120 | 161 | 68-246 |
| % of cases sampled | — | 22.2 | 8.8-33.1 |
| Other | | | |
| No. of specimens | 514 | 37 | 7-85 |
| Population (average of 13 years) | — | 3964 | 3511-3919 |

FRD illnesses, slightly more numerous, averaged more than 1000 cases annually per 10000 of the population, the rate ranging from 641 in 1966-7 to 1282 in 1961-2, the year of least sore throats.

Non-FRD illnesses were much more abundant, averaging 1962 cases per 10000 of the population annually, the rate ranging from 1527 in 1972-3 to 2624 in 1966-7, the year of minimum FRD illnesses.

FRD and Non-FRD illnesses exhibited a regular seasonal rhythm, with a high prevalence in the colder months. Sore throats showed no such regular seasonal trend.

Specimens. Specimens were taken from 32.2% of illnesses seen in the Throats class, the percentage ranging from 17.3 in 1961-2 to 43.1 in 1971-2. A much higher percentage of FRD illnesses, 63.1, was sampled varying from 27.3 in 1961-2 to 100% in 1971-2. The lowest sampling rate, 22.2%, was from non-FRD illnesses but the class is so large that the actual number of such specimens exceeded those from Throats. The percentage of non-FRD illnesses sampled ranged from 8.8 in 1973-4 to 33.1 in 1963-4.

Specimens were also collected from 514 persons who were either well or suffering from a complaint not classifiable in the three major morbidity classes. The number of those 'Other' specimens varied from seven in 1969-70 to 85 in 1961-2. Morbidity figures are not available for this miscellaneous class.

Isolations and infections (Table 2). Type 1 isolations numbered 57, giving an estimated annual average infection rate of 33 per 10000 of the population and varying from nil to 120 (1964-5). More than 90% of the viruses were isolated in 5 of the 14 years, none were isolated in 6 of the years and only one in the other 3 years. The well-known tendency for type 1 infection to be present in alternate years can be seen in this Table.

Type 2 virus was the scarcest with 22 isolations, an annual average of three

Table 2. Isolations and estimated infection rates by type and year

| Year | Type 1 | | Type 2 | | Type 3 | | Total | |
|---------|--------|-----|--------|----|--------|----|-------|-----|
| | N | R | N | R | N | R | N | R |
| 1961-2 | 1 | 15 | 1 | 15 | 2 | 29 | 4 | 59 |
| 1962-3 | 8 | 62 | 10 | 78 | 8 | 62 | 26 | 202 |
| 1963-4 | — | — | 1 | 7 | 12 | 86 | 13 | 94 |
| 1964-5 | 15 | 120 | 6 | 48 | 9 | 72 | 30 | 239 |
| 1965-6 | — | — | — | — | 2 | 18 | 2 | 18 |
| 1966-7 | 1 | 11 | 1 | 11 | 7 | 76 | 9 | 98 |
| 1967-8 | — | — | — | — | 11 | 86 | 11 | 86 |
| 1968-9 | 4 | 26 | — | — | 3 | 19 | 7 | 45 |
| 1969-70 | — | — | — | — | 3 | 25 | 3 | 25 |
| 1970-1 | 11 | 98 | 1 | 9 | 2 | 18 | 14 | 125 |
| 1971-2 | — | — | 1 | 5 | 5 | 27 | 6 | 32 |
| 1972-3 | 16 | 69 | — | — | 10 | 56 | 26 | 145 |
| 1973-4 | — | — | — | — | 11 | 80 | 11 | 80 |
| 1974-5 | 1 | NK | 1 | NK | 1 | NK | 3 | NK |
| Total | 57 | 33 | 22 | 13 | 86 | 50 | 165 | 95 |

N = number of strains, R = estimate of rate/10000/annum.

Note: The estimates of rate exclude 1974-5 for which some morbidity figures are not available. Two type 3 strains isolated in 1971-2 and 1973-4 from the class 'Other' are similarly excluded for lack of morbidity figures for the class. The final row gives the annual average estimated rate from 1961-2 to 1973-4.

infections per 10000 of the population varying from nil to 78 (1962-3). Six years produced no isolations and 6 years only one isolation. Most of the isolations were made in 1962-3 and 1964-5, more irregularly than type 1 viruses.

Type 3 virus, the most abundant, totalled 86 isolations, giving an estimated annual average of 50 infections per 10000 of the population, varying from 18 in 1965-6 to 86 in 1963-4 and again in 1967-8. In contrast to the other types, type 3 infections were much more constantly present.

Type and morbidity class (Table 3). All three types of virus were found in each morbidity class but only two parainfluenza viruses, both of type 3, were isolated from the miscellaneous 'Other' specimens. This finding suggests that detectable asymptomatic carriers of parainfluenza virus are uncommon, perhaps eight of type 3 virus per one million of the population, per annum.

Table 3 gives a good illustration of the misleading effect of the isolation figures. Nearly the same number of parainfluenza viruses were isolated from FRD (73) as from non-FRD (76) illnesses, but these represent an annual rate of 23 FRD infections and 71 non-FRD infections respectively per 10000 of the population. The 14 viruses isolated from Throats represent a rate of only nine such infections annually per 10000 of the population. All three types of parainfluenza virus were associated most commonly with non-FRD illnesses even though more type 1 viruses were isolated from specimens from FRD cases, 28 as compared to 25. Table 3 shows that type 1 viruses must nevertheless have caused twice as many non-FRD as FRD illnesses.

The year 1973-4 was remarkable for the finding that five of the nine type 3 isolations came from patients suffering sore throat, all in the second quarter of the year.

Table 3. *Type of parainfluenza virus by morbidity class*

| | Type 1 | | | Type 2 | | | Type 3 | | | Total | | |
|-------------------------|-------------|-------|-------|-------------|-------|-------|-------------|-------|-------|-------------|-------|--------|
| | Annual mean | Range | Total | Annual mean | Range | Total | Annual mean | Range | Total | Annual mean | Range | Total |
| Throat | 4 | 0-3 | 0-2 | 1 | 0-1 | 0-1 | 9 | 0-6 | 0-5 | 14 | 1 | 0-5 |
| No. of cases | — | 2 | 0-16 | — | 1 | 0-11 | — | 6 | 0-35 | — | 9 | 0-35 |
| Rate/10000 person-years | 28 | 2 | 0-10 | 12 | 0-9 | 0-5 | 33 | 2-4 | 0-9 | 73 | 5-2 | 0-18 |
| FRD | — | 9 | 0-38 | — | 4 | 0-32 | — | 10 | 0-40 | — | 23 | 0-89 |
| No. of cases | 25 | 1-8 | 0-8 | 9 | 0-6 | 0-6 | 42 | 3 | 0-11 | 76 | 5-4 | 1-15 |
| Rate/10000 person-years | — | 23 | 0-82 | — | 8 | 0-61 | — | 39 | 0-116 | — | 71 | 15-153 |
| Other | 0 | — | — | 0 | — | — | 2 | 0-1 | 0-1 | 2 | 0-1 | 0-1 |
| No. of cases | 57 | 4-1 | 0-16 | 22 | 1-6 | 0-10 | 87 | 6-2 | 1-12 | 165 | 11-8 | 2-30 |
| Rate/10000 person-years | — | 33 | 0-120 | — | 13 | 0-78 | — | 50 | 18-86 | — | 95 | 18-239 |

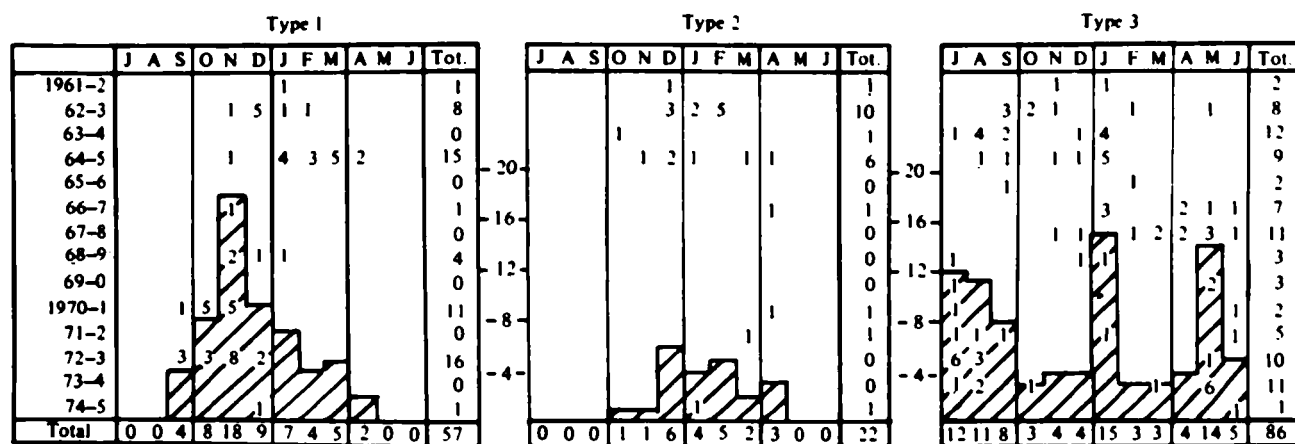


Fig. 1. Seasonal distribution of parainfluenza viruses. Number of strains isolated by type, year (July through June) and calendar month. Numerals within the frames indicate number of strains isolated each month. Horizontal totals are annual totals, vertical totals are calendar month totals. The bar diagrams summarize the monthly totals on the scale shown between the frames.

Seasonal distribution (Fig. 1)

Type 1 and type 2 viruses showed a strong predilection for the colder months. More than 61% of type 1 viruses were isolated in the fourth quarter of the year, most of them in the months of November. Type 2 viruses were almost all isolated in the fourth and first quarters, the latter showing the higher prevalence. Only 11.4% of type 1 and type 2 viruses were isolated in the warm semester, April to September.

The seasonal distribution of type 3 isolations was strikingly different from that of the other types. Figure 1 shows two seasons of high prevalence of type 3 infections, one in January and the other, more prolonged, from May to September. Most type 3 Throats illnesses occurred in the warm semesters. It is surprising to find that about 70% of FRD illnesses associated with type 3 virus occurred in the warm half-year whereas the milder non-FRD type 3 illnesses were almost equally divided. About 66% of type 3 viruses from all classes of illness were isolated in the warm semester.

Sex distribution (Table 4). Parainfluenza viruses were found 50% more frequently in female than in male patients but the sex distribution differed by age and by type of virus. More than twice as many females as males suffered type 1 infections and the female preponderance was only a little less in type 2 infections, whereas type 3 infections in females exceeded those in males by only a small margin.

Type 2 infections were fairly evenly divided between the sexes up to the age of 10 years and the female preponderance then appeared rapidly.

Type 3 infections were more commonly isolated from males until the age of 60 years and thereafter type 3 infected females overtook them. Males formed about 49% of the practice population and were in the minority up to the age of 29 and again over 70 years of age. Males exceeded females between the ages of 30 and 69. The difference between the numbers of the sexes was never more than 2 or 3% from equality except amongst those over the age of 70 when females predominated heavily in the small population of that age.

Age distribution (Table 5). Parainfluenza virus infection was predominantly a

Table 4. Sex distribution of parainfluenza viruses in broad age groupings

| Age group | Type 1 | | Type 2 | | Type 3 | | Total | | | | | |
|--------------|--------|--------|--------|------|--------|--------|-------|--------|--------|----|----|------|
| | Male | Female | % male | Male | Female | % male | Male | Female | % male | | | |
| 0-11 months | 4 | 6 | 40.0 | 2 | 1 | 66.7 | 14 | 10 | 58.3 | 20 | 17 | 54.0 |
| 1-9 years | 8 | 21 | 27.6 | 2 | 4 | 33.3 | 16 | 18 | 47.1 | 26 | 43 | 37.7 |
| 10-90+ years | 6 | 12 | 33.3 | 4 | 9 | 30.8 | 10 | 18 | 35.7 | 20 | 39 | 33.9 |
| Total | 18 | 39 | 31.6 | 8 | 14 | 36.4 | 40 | 46 | 46.5 | 66 | 99 | 40.0 |

Table 5. Parainfluenza virus isolations by type in broad age groupings

| Age group | Type 1 | | Type 2 | | Type 3 | | Total | |
|--------------|--------|-------|--------|-------|--------|-------|-------|-------|
| | No. | % | No. | % | No. | % | No. | % |
| 0-11 months | 10 | 17.5 | 3 | 13.6 | 24 | 27.9 | 37 | 22.4 |
| 1-9 years | 29 | 50.9 | 6 | 27.3 | 34 | 39.5 | 69 | 41.8 |
| 10-90+ years | 18 | 31.6 | 13 | 59.1 | 28 | 32.6 | 59 | 35.8 |
| Total | 57 | 100.0 | 22 | 100.0 | 86 | 100.0 | 165 | 100.0 |

childhood ailment, 22% coming from babies under a year old and 60% from children under 10 years of age. The three serotypes showed different distributions within this general picture.

Type 1 viruses showed 17.5% from babies under 1 year old and 68% from those under 10 years old. Type 2 viruses showed only 13.6% from those under a year old and only 40.9% from those under 10 years old. Type 3 viruses showed 27.9% from the babies of under a year and 67% from persons under 10 years old. They showed a relatively high prevalence in infants, 11.6% of the isolations coming from those of less than 5 months old.

All three types showed a slight upturn of the number of infections in elderly persons.

Geographical distribution. The numerical key to the villages and districts served by the general practice (Table 6) is used to indicate the geographical distribution of the isolations of the three types of parainfluenza virus. All three types were widely and thinly distributed in most of the years in which they were prevalent. The annual geographical pattern differed from year to year, and from type to type when more than one virus was prevalent in the same year.

Table 6 examines the secular and geographical distribution of type 3 viruses by half-years October to March (cold semester) and April to September (warm semester). From 1961-2 till 1967-8 type 3 viruses were isolated in numerous areas in both warm and cold semesters, 27 from 11 areas in cold semesters and 25 from ten areas in warm semesters. From 1968-9 onwards the picture changed, only five viruses, each from a different area, were isolated in the cold semesters, whereas 29 were isolated from 13 areas during the warm semesters.

It is not easy to trace a connexion between affected areas in consecutive semesters. In the same semesters also the areas are highly variable from one year to the next. The geographical patterns seem to be continually changing.

Recurrent isolations in persons. No person was found to have suffered a second infection with type 1 or type 2 virus. Type 3 viruses were twice isolated a second time at intervals of around 3 and 4 years.

A second infection by a different type was found seven times (Table 7) including SR who also had a second homotypic infection.

Recurrent isolations in households. In eight households more than one person was found to be infected with type 1 virus at an interval compatible with a household outbreak. No such sequence was found for type 2 strains, but there were four for type 3 strains (Table 8).

Six households are recorded with multiple infections with strains belonging to different types of parainfluenza virus (Table 9).

Table 7. Reinfection of same person with different types of the virus

| Initials | Born | Type | Date | Type | Date | Interval (months) |
|----------|----------|------|----------|------|----------|-------------------|
| S.C. | 8. 7.67 | 3 | 26. 7.72 | 1 | 11.10.72 | 2.5 |
| S.G. | 10. 8.64 | 1 | 15. 3.65 | 3 | 21. 6.71 | 75.0 |
| B.G. | 8. 4.63 | 3 | 16. 8.63 | 1 | 30.10.70 | 86.5 |
| A.M. | 30. 4.67 | 3 | 10.10.62 | 1 | 30.11.66 | 49.8 |
| K.R. | 18. 9.68 | 3 | 7. 1.72 | 1 | 8. 9.72 | 8.0 |
| S.R. | 3. 3.69 | 1 | 26.10.70 | 3 | 24. 7.72 | 21.0 |
| | | | | 3 | 13. 5.75 | 54.6 |
| A.L. | 25.10.11 | 2 | 2. 4.65 | 3 | 13. 5.74 | 109.4 |

Table 8. Households with more than one person infected by same virus type

| Type 1 infections | | | | | |
|--|----------|----------|----------|----------|-----------------|
| Household | Born | Attacked | Born | Attacked | Interval (days) |
| 1 | 14. 4.70 | 20.11.72 | 7. 1.72 | 20.11.72 | 0 |
| 2 | 31. 8.60 | 17.12.62 | 7.11.62 | 24.12.62 | 7 |
| 3 | 16. 1.60 | 21. 1.65 | 9. 1.63 | 21. 1.65 | 0 |
| 4 | 5. 7.64 | 21. 4.65 | 10. 5.42 | 23. 4.65 | 3 |
| 5 | 18. 9.68 | 8. 9.72 | 23. 7.44 | 13. 9.72 | 5 |
| 6 | 26. 3.37 | 29. 3.75 | 21.10.60 | 29. 3.75 | 0 |
| 7 | 11. 6.62 | 5. 3.65 | 23.11.63 | 5. 3.65 | 0 |
| 8 | 21.12.68 | 9.10.72 | 4.10.70 | 13.10.72 | 4 |
| | | | | | (years) |
| 9 | 8.10.64 | 15. 3.65 | 2.10.68 | 19.11.70 | 5 |
| 10 | 15. 5.60 | 30. 1.65 | 24. 4.55 | 9.11.70 | 5 |
| Type 2 infections: No households outbreaks | | | | | |
| Type 3 infections | | | | | |
| Household | Born | Attacked | Born | Attacked | Interval (days) |
| 1 | 13. 3.61 | 10. 8.63 | 8. 4.63 | 16. 8.63 | 0 |
| 2 | 20. 5.60 | 4. 1.65 | 27. 3.64 | 4. 1.65 | 0 |
| 3 | 21. 4.61 | 5. 7.62 | 29. 1.64 | 7. 7.72 | 2 |
| 4 | 15. 9.71 | 2. 8.72 | 31. 1.52 | 8. 8.72 | 6 |
| | | | | | (years) |
| 5 | 12. 6.65 | 4.12.67 | 13. 9.67 | 18. 7.72 | 4 |
| 6 | 22. 2.68 | 21. 3.68 | 16. 2.67 | 3. 7.69 | 1 |

Table 9. Household infections with different types of the virus

| House | Type | Attacked | Type | Attacked | Type | Attacked | Interval (months) |
|-------|------|----------|------|----------|------|----------|-------------------|
| 1 | 1 | 30.11.61 | 3 | 10.10.62 | 2 | 4. 1.65 | 10, 27, 37 |
| 2 | 3 | 16. 8.63 | 1 | 30.10.70 | | | 86 |
| 3 | 3 | 16. 8.63 | 1 | 30.10.70 | | | 86 |
| 3 | 2 | 13.12.61 | 1 | 16.11.70 | | | 107 |
| 4 | 3 | 3. 7.68 | 1 | 6.11.70 | | | 27 |
| 5 | 1 | 30. 1.65 | 3 | 15. 5.67 | 1 | 9.11.70 | 28, 42 |
| 6 | 3 | 7. 6.72 | 1 | 8. 9.72 | | | 3 |
| | | | 1 | 13. 9.72 | | | 3 |

DISCUSSION

The three types of parainfluenza virus resembled one another in the patterns of illness they caused and in the proportion of each type that was isolated from each class of illness, about 45% from FRD illnesses and the same proportion from non-FRD illnesses, and about 10% from sore throats. No isolations were obtained from well persons and very few from those with 'Other' ailments, a finding that suggests that carriers were either uncommon or difficult to detect.

The difference between the types was most striking in the seasonal distribution. Type 1 and type 2 infections were winter-seasonal with 90% of infections in the cold semester October to March, and no isolations during most months of the warm semester April to September. Type 3 virus, on the other hand, was found to have a bi-modal seasonal distribution with 34% of infections in the cold semester peaking sharply in January, and 66% in the warm semester without a definite peak. No cumulated months lacked type 3 virus isolations.

The agents of acute respiratory disease that have so far been shown to exhibit winter prevalence are influenza viruses, parainfluenza viruses and respiratory syncytial virus (Hope-Simpson, 1975). All seasonal phenomena are determined by variations in solar radiation (Woodbury, 1954) but the mechanism whereby the influence is mediated to control common human respiratory illness is not yet elucidated. The relationship of season and latitude to epidemic influenza has been explored in some detail (Hope-Simpson, 1979*a*, 1979*b*, 1981*a*, *b*).

When related viruses, presumably sharing a common ancestry, share a similar peculiarity of seasonal distribution, the mechanism is likely to be a common inheritance, and all the related winter-seasonal viruses are therefore likely to possess a basically similar mechanism causing their seasonal distribution. Their genetic composition should differ in this character from that of related myxoviruses not showing winter-seasonal prevalence (Hope-Simpson, 1975).

The finding that parainfluenza viruses of type 1 and type 2 possess this winter control character whereas type 3 viruses do not, seems to offer an opportunity for discovering the molecular basis of the control mechanism. Furthermore the seasonal bi-modality of type 3 infections suggests that two subtypes of type 3 may exist, one possessing and the other lacking the character whereby winter prevalence is mediated.

Two other peculiarities of type 3 viruses indicate the possible co-existence of the two subtypes. First is the unexpected finding that nearly 70% of type 3 infections in the warm semester were of the more severe febrile class whereas the proportion of febrile to non-febrile type 3 infections in the cold semester was only 34%, a picture consistent with a milder winter subtype and a more virulent subtype lacking the mechanism of 'winter-control'. Secondly the geographical distributions of type 3 isolations show striking discontinuities between the two semesters. If the area sequences are followed year after year from the left of Table 6 (cold semester) to right (warm semester) and back again, geographical dislocation is encountered more often than not when crossing from semester to semester. For example, in 1961-2 areas 7, 16 are followed by areas 4, 12, 13. Again in 1966-7 area 17, 17 is succeeded by areas 13, 14, 16, 20 and those in 1967-8 by areas 11, 11, 12, 20, 21. If one of the subtypes were seasonally uncontrolled complete dislocation

would not be expected, and the winter areas differ from summer areas to a degree great enough to support the hypothesis of the two subtypes. Area 11, common in the winter isolations, appears only twice in summer, whereas area 12 appears only five times in the winter isolations but 13 times in summer. An alternative explanation was sought unsuccessfully in the ages of the persons infected at different seasons. In the warmer months some 15% of school-age children were infected at the expense of the younger children, but this age pattern fails to explain the geographical and other findings.

The term winter- or cold-seasonal is a verbal convenience applicable in temperate latitudes, but may be epidemiologically misleading. Acute respiratory diseases show seasonal prevalences in parts of the world where seasonal temperature changes are minimal.

Virus latency with seasonal reactivation has recently been proposed to explain the seasonal features of epidemic influenza (Hope-Simpson 1979*b*, 1981*a*). No direct evidence of influenza virus latency has yet been adduced although influenza virus has been grown for long periods in persistent state in cell culture (Gavrilov *et al.* 1972; Golubev *et al.* 1975). It is therefore of great interest that outbreaks of parainfluenza virus infection have been reported in a South Polar station months after loss of outside human contact (Parkinson *et al.* 1981). The cause of the illnesses was proved serologically and virologically (Muchmore *et al.* 1981), and was explained as brought about by reactivation of parainfluenza virus latent in members of the party.

Seasonal distribution was not the only feature in which the types of parainfluenza virus differed from each other. Type 2 was the least frequently isolated, type 3 the most abundant, nearly four times as common as type 2. Fewer of the type 1 infections (14%) and of the type 3 infections (30%) than of type 2 infections (60%) occurred in persons over 10 years old. Type 3 viruses caused 65% of all the parainfluenza virus infections in infants of less than a year old.

All three types were widely but thinly distributed and appeared annually in many geographical areas in an unrelated and haphazard manner and more infections occurred in the urban areas.

The Cirencester Survey was carried out in collaboration with Doctors P. G. Higgins, G. E. D. Urquhart and A. P. C. H. Roome, the staff of the Public Health Laboratory at Cirencester and the staff of the Cirencester General Practice. The work was performed during tenure of grants successively from the Medical Research Council and the Department of Health and Social Security. I am grateful for the help of Miss Joyce Dawson and Mrs Bettie Neal, medical secretaries; of Miss Hazel Spurrier and her staff at the Medical Library at Princess Margaret Hospital, Swindon; of the staff of the Photographic Department there, and to Dr Sylvia Reed for helpful criticism.

REFERENCES

- GAVRILOV, V. I., ASHER, D. M., VYALUSHKINA, S. D., RATUSHKINA, L. S., ZMIEVA, R. G. & TUMYAN, B. G. (1972). Persistent infection of continuous line of pig kidney cells with a variant of the WSN strain of influenza A₀ virus (36405). *Proceedings of the Society for Experimental Biology and Medicine* **140**, 109.
- GOLUBEV, VON D. B., PARAMONOVA, M. S., MEDVEDEVA, M. N. & POLJAKOV, YU. M. (1975). Influenza A₂ neuraminidases and their changes during persistence of viruses in tissue cultures. *Zeitschrift für gesamte Hygiene* **21**, 324.
- HOPE-SIMPSON, R. E. (1975). Viruses in acute respiratory diseases. In *Viral Diseases* (ed. A. T. Proudfoot), pp. 36–53. Edinburgh: *Royal College of Physicians of Edinburgh*.
- HOPE-SIMPSON, R. E. (1979a). The influence of season upon type A influenza. In *The Impact of Weather and Climate on Animals and Man (Period 1973–1978)*, (ed. Solco W. Tromp). London: Heyden.
- HOPE-SIMPSON, R. E. (1979b). Epidemic mechanisms of type A influenza. *Journal of Hygiene* **83**, 11–26.
- HOPE-SIMPSON, R. E. (1981a). The role of season in the epidemiology of influenza. *Journal of Hygiene* **86**, 35.
- HOPE-SIMPSON, R. E. (1981b). *Streptococcus pyogenes* in the throat. *Journal of Hygiene* **87**, 109–129.
- HOPE-SIMPSON, R. E. & HIGGINS, P. G. (1969). A respiratory virus study in Great Britain – review and evaluation. *Progress in Medical Virology* **11**, 354–407. Basel: Karger.
- MUCHMORE, H. G., PARKINSON, A. J., HUMPHRIES, J. E., NAN SCOTT, E., MCINTOSH, D. A., SCOTT, L. V., COONEY, M. K. & MILES, J. A. R. (1981). Persistent parainfluenza virus shedding during isolation at the South Pole. *Nature* **289**, 187.
- PARKINSON, A. J., MUCHMORE, H. G., MCCONNELL, T. A., SCOTT, L. V. & MILES, J. A. R. (1980). Serologic evidence for parainfluenza virus infection during isolation at South Pole Station, Antarctica., *American Journal of Epidemiology* **112**, 334.
- WOODBURY, A. M. (1954). *Principles of General Ecology*, New York, pp. 120–134.