Rapid virus diagnosis in paediatric units by postal service

Respiratory syncytial virus infection in Cumberland

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Downham, M. A. P. S., Elderkin, F. M., Platt, J. W., McQuillin, J., and Gardner, P. S. (1974). *Archives of Disease in Childhood*, **49**, 467. **Rapid virus diagnosis in paediatric units by postal service: respiratory syncytial virus infection in Cumberland.** A method for the diagnosis of respiratory virus infections in children at a distance from a central laboratory, using the rapid immunofluorescent technique, has been devised. A respiratory syncytial virus (RSV) epidemic in a predominantly rural area was shown by using this method to study children admitted to two Cumberland hospitals. The incidence of infection, as reflected by hospital admissions, and the clinical patterns of the illnesses produced are compared with those experienced in hospitals serving a predominantly urban population.

Respiratory syncytial virus (RSV) has been found to be a major cause of acute respiratory illness in young children admitted to hospital (Chanock *et al.*, 1961; Holzel *et al.*, 1963, 1965; Elderkin *et al.*, 1965). On Tyneside, this experience has been recorded over a number of years (Gardner, 1971; Public Health Laboratory Service Report, 1972, 1973), and Fig. 1 shows the RSV epidemics for the past 3 winters. If the extent of RSV infection on Tyneside, as reflected by hospital admissions, is similar for the country as a whole, some 30,000 children could be admitted annually with lower respiratory tract illnesses caused by this virus, the majority concentrated into a 3-month epidemic period. To date, however, virus investigation of children admitted to hospital has largely been confined to the major conurbations, and little information is available about respiratory illness in areas of lower population density. Because of the increasing concern about the quantity and severity of the illnesses caused by RSV infection, it was felt important to investigate the extent of these infections in a predominantly rural area. A comparison of the incidence and patterns of illness

in such an area with those known to exist in large conurbations might also shed further light on the pathogenesis of severe RSV infections.

We hoped that in the process of collecting this specific information about RSV we might develop a technique which would make it possible for paediatricians in any area to carry out virus investigation in all children admitted with acute respiratory illnesses. Virus laboratories equipped for complete surveillance of all respiratory admissions are not generally available in areas of lower population density, and referral of specimens to a central laboratory for conventional isolation techniques is made difficult by the distances involved. The immunofluorescent method of virus diagnosis (Gardner, 1973; Brocklebank *et al.*, 1972; Downham, McQuillin, and Gardner, 1974) seemed to offer a possible solution to this problem, with the added advantage of giving a rapid result. The collaboration of colleagues has enabled us to test the feasibility of using this method to provide a virus diagnostic service at a distance from the central laboratory.

This paper describes the successful establishment of such a service for the two paediatric units in Cumberland, and gives the findings for RSV in the

FIG. 1.—Monthly identifications of respiratory syncytial virus in Tyneside hospitals.

epidemic period from December 1972 to April 1973, during which time RSV was identified in 64 children admitted to Cumberland hospitals. Comparisons are made with the RSV epidemic on Tyneside during the same period (Public Health Laboratory Service Report, 1973).

Methods

Study group. The group consists of all children admitted with acute respiratory illness to children's wards in Cumberland hospitals. The study started on 1 December 1972 and is continuing. The area is served by two children's departments, at Carlisle and at Whitehaven, and all children are admitted to one or the other. The total population of the area is approximately 310,000 with an annual live birth rate of about 4500. It is estimated that the Carlisle department receives its admissions from a population of 175,000 (East Cumberland), while the Whitehaven department serves the remaining 135,000 (West Cumberland). Carlisle is the largest centre of population (71,000); the only other towns with populations of over 10,000 are Workington (28,000), Whitehaven (26,000), Maryport (11,000), and Penrith (11,000).

Virus diagnosis. Nasopharyngeal secretions are aspirated from all children admitted with acute respiratory illnesses within 24 hours of admission, or within 48 hours for children admitted at weekends.

A polyethylene nasogastric feeding tube (size 8) is attached to a plastic mucus extractor connected to a suction pump, providing a maximum negative pressure of 26 lbs/in². With the suction turned on, the feeding tube is passed through each nostril in turn into the region of the nasopharynx. An adequate quantity of secretion is usually obtained within a few seconds. The mucus extractor containing the secretion is immediately placed in a dish of ice and taken to the hospital laboratory (Public Health Laboratory, Cumberland Infirmary,

Carlisle, and the Microbiology Laboratory, West Cumberland Hospital).

The mucus extractor is centrifuged at 1500 r.p.m. for 10 minutes, and then its top is removed with a red-hot platinum wire or scalpel blade. Any clear supernatant present is removed and the remainder suspended in 3 to 4 ml phosphate buffered saline. The suspension is pipetted until all mucoid particles are evenly dispersed, and then centrifuged at 1500 r.p.m. for 10 minutes, and the supernatant discarded. The cell deposit is resuspended in a small volume of fresh phosphate buffered saline, just sufficient to give a suspension which is no longer sticky; excessive dilution must be avoided. Small drops of the suspension are spread on pre-etched slides at evenly spaced intervals (2–3 drops per slide), and the smears are allowed to dry in air. As soon as dry, the smears are fixed in acetone at 4 °C for 10 minutes. The slides are then packed in slide boxes suitably padded to prevent breakage, and posted to the Department of Virology in Newcastle.

Slides not posted immediately are stored at –20 °C, and some slides are kept for up to 7 days when an urgent result is not required. On arrival in Newcastle the slides are stained and examined by the immunofluorescent method described by McQuillin and Gardner (1968) and the result telephoned to the relevant Cumberland hospital. In this way it is possible to give a virus diagnosis within 36 hours of the child's admission.

Clinical classification. All illnesses are classified into one of five clinical categories—pneumonia, bronchiolitis, bronchitis, croup, and upper respiratory infection syndrome. The criteria for these categories are the same as those which have been in use in Newcastle for many years (Gardner *et al.*, 1960).

Results

During the first 5 months of the study, from 1 December 1972 to 30 April 1973, RSV was identified in 32 out of 45 specimens (71%) received from East Cumberland, and in 32 out of 74 specimens (43%) received from West Cumberland. It must be emphasized that these specimens were in no way selected for a likely RSV aetiology, but were taken from all children of all ages admitted with any type of acute respiratory illness. The smaller number of respiratory admissions in East Cumberland so far, despite its larger population, appears to be genuine, and was not due to incomplete surveillance. The proportion of illnesses for which RSV was responsible varied for different categories of illness, and was highest for bronchiolitis (East Cumberland 88%; West Cumberland 94%). Table I shows the part played by RSV for each of the five clinical categories in the two Cumberland Hospitals, and compares the findings for Tyneside hospitals during the same period, where 334 identifications of RSV were made out of a total number of 683 specimens

TABLE I

Contribution made by RSV to different categories of respiratory illness in East Cumberland, West Cumberland, and Tyneside

	East Cumberland			West Cumberland			Tyneside		
	Total respiratory admissions	RSV admissions	RSV % of total	Total respiratory admissions	RSV admissions	RSV % of total	Total respiratory admissions	RSV admissions	RSV % of total
URIS	12	6	50	24	7	29	298	87	29
Croup	4	3	75	10	1	10	36	9	25
Bronchitis	10	7	70	10	3	30	88	33	38
Bronchiolitis	17	15	88	18	17	94	216	187	87
Pneumonia	2	1	50	12	4	33	45	18	40
Total	45	32	71	74	32	43	683	334	49

URIS, upper respiratory infection syndrome.

TABLE II

Numbers of children admitted to hospital with RSV infections, compared with the populations served by the 3 centres

	Total population	Population under 5 yr	RSV cases	RSV cases per 1000 children under 5 yr
East Cumberland	175,000	13,500	32	2.37
West Cumberland	135,000	10,400	32	3.07
Tyneside	605,000*	40,000	334	8.35

*This figure is based on the Newcastle Regional Hospital Board's analysis of the geographical origin of cases admitted to hospitals in Newcastle and Gateshead.

TABLE III

Illnesses caused by RSV infections in children admitted to hospital

	East Cumberland		West Cumberland		Tyneside	
	No. of RSV illnesses	% of total RSV illnesses	No. of RSV illnesses	% of total RSV illnesses	No. of RSV illnesses	% of total RSV illnesses
URIS	6	19	7	22	87	26
Croup	3	9	1	3	9	3
Bronchitis	7	22	3	9	33	10
Bronchiolitis	15	47	17	53	187	56
Pneumonia	1	3	4	13	18	5
Total	32	100	32	100	334	100

URIS, upper respiratory infection syndrome.

(49%). When the number of children admitted to hospital in each area with RSV illnesses was compared with the child population of the area, a much lower incidence was found for both East Cumberland and West Cumberland than for Tyneside (Table II).

Clinical patterns. Table III shows the distribution of RSV illnesses between the five clinical categories for the three centres. The

pattern of illnesses caused by RSV in Cumberland appears to be similar to that on Tyneside.

There was 1 death among the Cumberland children admitted with RSV infection; a 3-month-old baby with Down's syndrome admitted with bronchiolitis to the West Cumberland Hospital died a few hours later. Of the 334 children with RSV illness on Tyneside, 2 died, one aged 2½ months with bronchiolitis and one aged 4 months with pneumonia; neither had congenital abnormalities.

TABLE IV

Age distribution of children admitted to hospital with RSV infections

	0-6 mth	7-12 mth	1-2 yr	2-3 yr	3-4 yr	Over 4 yr	Total
East Cumberland	19 (59)	4 (13)	3 (9)	1 (3)	2 (6)	3 (9)	32
West Cumberland	20 (63)	4 (13)	3 (9)	2 (6)	1 (3)	2 (6)	32
Tyneside	213 (64)	48 (14)	33 (10)	21 (6)	14 (4)	5 (2)	334

Note: Percentage in parentheses.

Age. The age distribution of the children admitted with RSV infection also appears to be similar in the three centres (Table IV).

Timing of epidemic. Fig. 2 shows the fortnightly identifications of RSV in East Cumberland, West Cumberland, and Tyneside hospitals for the 5-month period. The timing of the epidemic in the three areas is notably similar, though in both parts of Cumberland it took slightly longer for the peak to be reached than in Newcastle, and the fall-off of cases at the end of the epidemic was less sharp.

Discussion

We have shown that both virus diagnosis and rapid virus diagnosis can be operated successfully in

hospitals distant from a laboratory practising the necessary techniques. This has important implications for the diagnosis and management of individual patients in such hospitals, and for research into the epidemiology of virus infections. The first results of this study show that between December 1972 and April 1973 a large proportion of acute respiratory admissions to children's wards in Cumberland was due to RSV infection. The clinical patterns of the illnesses were similar to those on Tyneside. Bronchiolitis in Cumberland, as on Tyneside, so far appears to be almost exclusively associated with RSV (Table I). The age distribution of children admitted with RSV infection is also very similar to that seen on Tyneside, with approximately 75% aged under 1 year.

A notable difference between Cumberland and Tyneside is the smaller number of RSV illnesses admitted to Cumberland hospitals per head of population (Table II). At this stage we can only speculate whether this reflects a lower incidence of severe infection in Cumberland, or whether it is because fewer infected children are admitted to hospital.

Variations in both incidence and clinical patterns for different types of population may prove to be important for the better understanding of the pathogenesis of RSV infection, and in particular the hypothesis that severe illness may represent an allergic response to reinfection (Gardner, McQuillin, and Court, 1970).

This is the first time that the extent of RSV infection has been measured in hospitals serving a relatively scattered population. We hope that the findings will help towards a realistic assessment of the effects of RSV infection in the country as a whole, and emphasize the need for further research into incidence, pathogenesis, and methods of control.

This investigation would not have been possible without the co-operation of the pathologists in Cumberland, Dr. D. G. Davies at the Public Health Laboratory, Carlisle, and Drs. D. Smith and P. J. Whitehead at

FIG. 2.—Fortnightly identifications of respiratory syncytial virus, as percentages of total identifications of RSV for the 5 months, December 1972 to April 1973.

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