

Viruses associated with acute respiratory infections in children admitted to hospital in Naples, 1979-82*

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A survey of the virological and epidemiological features of acute respiratory diseases in children admitted to hospital in Naples has been carried out; the results of three years of research are reported.

Between April 1979 and March 1982, 787 nasopharyngeal swabs were examined. There were 287 (36.5%) positive samples, with the highest isolation rate being found in children with bronchiolitis (39.5%).

Among the different viruses isolated, adenovirus was the most common (161 positive samples, 56%); this agent appeared regularly in the different age and disease groups, with a marked increase in prevalence during the winter of 1980. Isolations of herpesvirus, respiratory syncytial virus and enterovirus were less frequent; however, echovirus 3 caused an epidemic in the summer of 1980. Influenza and parainfluenza viruses were seen fairly infrequently; two cases of Reye's syndrome yielded strains of influenza B.

During the winter season of 1978-79 (December-February) there was an outbreak of respiratory illness in Naples, which caused several deaths in infants under the age of two years. An epidemiological and virological survey attributed the epidemic mainly to respiratory syncytial virus, although other respiratory viruses were also isolated (13-22).

During the epidemic, it became clear that there was a need for virological studies to complement the epidemiological data; this requirement appeared particularly important in the paediatric field. It was decided to carry out a virological survey on children hospitalized for acute respiratory disease or coma of unknown etiology and to monitor respiratory morbidity and mortality in Neapolitan children.

In this paper, the results of the first 3 years of laboratory surveillance are reported.

MATERIALS AND METHODS

The survey was started in April 1979; during the following 3 years we tested 787 nasopharyngeal swabs from children aged between 0 and 69 months, admitted to the Santobono Hospital in Naples.

Specimens were collected as soon as possible after hospital admission, inoculated into Hep-2 and/or Bristol HeLa cells, usually at the patient's bedside, and transferred to the laboratory in tryptose phosphate broth or veal infusion broth. Each swab specimen was pretreated with penicillin, streptomycin, and amphotericin, and then inoculated into African green monkey kidney (AGMK) and fetal human diploid cell (strain MRC-5) cultures and embryonated chicken eggs (amniotic). After the first year, AGMK cells were replaced by, or used together with, Madin-Darby canine kidney cells.

The cultural and diagnostic methods used have been described by Grist et al. (6) for the different cell cultures and by the Center for Disease Control (1) for embryonated eggs.

During the first year of the study, the virus strains were sent for typing to the Virus Reference Laboratory of the Central Public Health Laboratory in London; subsequently, virus typing was carried out in Naples using neutralizing antisera, kindly supplied by the Statens Seruminstitut, Copenhagen.

RESULTS

Hospital admissions for acute respiratory disease

Fig. 1 shows the number of children admitted to hospital with acute respiratory disease and the number of viral isolations made between April 1979 and March 1982. During the 3-year period, there was a clear seasonal variation in the number of admissions.

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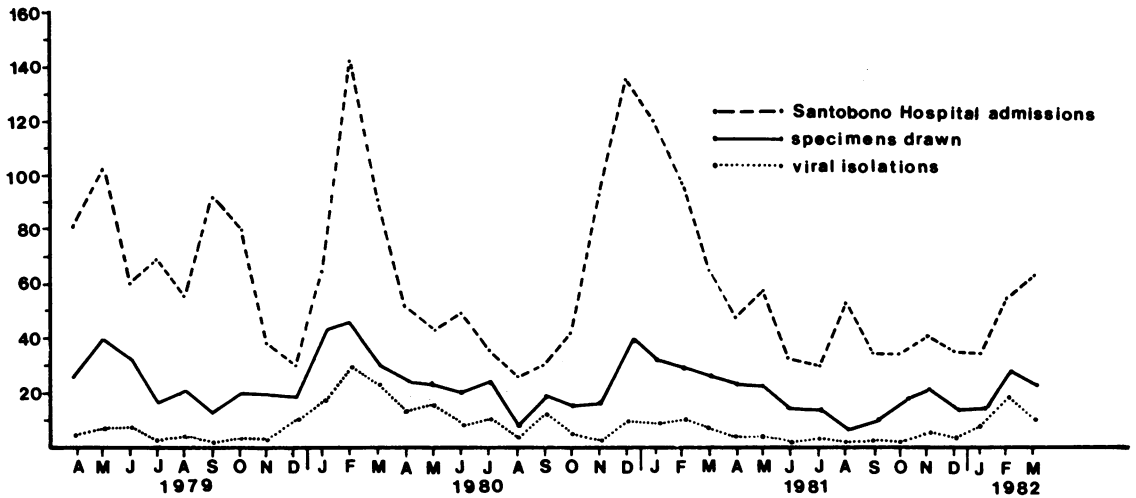


Fig. 1. Monthly variation in number of children admitted to hospital with acute respiratory disease, number of nasopharyngeal specimens taken, and number of virus isolations.

The maximum values were generally registered in February–March, but there were a large number of admissions in December 1980, probably as a result of the intensely cold weather that followed the severe earthquake of 23 November of that year. Usually the virus isolation rate showed similar variations, with high rates during the winter season; the highest value (33 positive samples out of 50) was recorded in February 1980.

Isolation rate according to age and illness

Isolation rates among the different illness groups and age groups are reported in Table 1. Most of the samples (91.7%) were taken from children under 2 years old; 84.6% were from infants under one year, and over 50% of the cases were aged between 0 and 6 months. Three-quarters of the patients had tracheitis, bronchitis, pneumonia, bronchopneumonia, or bron-

Table 1. Virus isolation rates^a by clinical diagnosis and age of patients in children with acute respiratory infections

Clinical illness	Age group (months)				Total
	< 1	1–6	7–12	> 12	
Upper respiratory tract infection	0/0	13/30 (43.3)	6/20 (30.0)	7/18 (38.9)	26/68 (38.2)
Tracheitis/ Bronchitis	0/1	26/78 (33.3)	20/54 (37.0)	9/29 (31.0)	55/162 (33.9)
Pneumonia/ Bronchopneumonia	1/3 (33.3)	33/97 (34.0)	26/62 (41.9)	7/16 (43.7)	67/178 (37.6)
Bronchiolitis	0/1	72/176 (40.9)	34/82 (41.5)	10/35 (28.6)	116/294 (39.5)
Uncertain	0/4	7/28 (25.0)	10/29 (34.5)	6/24 (25.0)	23/85 (27.1)
Total	1/9 (11.1)	151/409 (36.9)	96/247 (38.9)	39/122 (32.0)	287/787 (36.5)

^a No. positive/no. examined. Figures in parentheses give percentage positive.

chiolitis; this last represented the largest group for all ages.

Overall, 36.5% of the samples were positive, with some variations among the different groups. The highest isolation rate (43.7%) was found in subjects aged over 12 months admitted for pneumonia or bronchopneumonia; for all age groups, children with bronchiolitis provided the highest isolation rate (116 out of 294 specimens (39.5%)).

in isolation rate in November 1981 (6 cases).

Enteroviruses were isolated from 37 swabs (4.7%): poliovirus from 4 (1 type 1, 1 type 2, and 2 type 3), coxsackievirus from 10 (6 type B3 and 4 type B5), and echovirus type 3 from 23 swabs. The polioviruses came from recently immunized children. Coxsackieviruses were isolated from children with respiratory and enteric symptoms. Echovirus was isolated in 22 cases during the summer of 1980 (mostly in Sep-

Table 2. Relationship between clinical illness and infective agent in children with acute respiratory infections

Clinical illness	Virus isolated														Total no. of samples
	None		Adenovirus		Herpesvirus		Enterovirus		Respiratory syncytial virus		Influenza-virus		Para-influenza virus		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Upper respiratory tract infection	42	61.8	8	11.8	9	13.2	2	2.9	0		5	7.4	3	4.4	68 ^a
Tracheitis/Bronchitis	107	66.0	32	19.7	7	4.3	11	6.8	1	0.6	0		4	2.5	162
Pneumonia/Broncho-pneumonia	111	62.4	45	25.3	9	5.1	6	3.4	5	2.8	2	1.1	0		178
Bronchiolitis	178	60.5	62	21.1	12	4.1	13	4.4	26	8.8	1	0.3	3	1.0	294 ^b
Uncertain	62	72.9	14	16.5	4	4.7	5	5.9	0		0		0		85
Total	500	63.5	161	20.5	41	5.2	37	4.7	32	4.1	8	1.0	10	1.3	787

^a One swab contained adenovirus and influenza virus.

^b One swab contained adenovirus and respiratory syncytial virus.

Virus isolations

The viruses isolated are reported in Table 2. Adenoviruses were detected in 161 samples (20.5%), representing 55.7% of all isolations. They were isolated once in association with respiratory syncytial virus and once with influenza A virus. The adenoviruses were found particularly in children affected with pneumonia and bronchopneumonia (25.3%); the highest isolation rate for adenovirus was seen in January–May 1980, when as many as 47.2% of samples were positive for adenovirus. Adenovirus type 2 was found most often (77.0%), followed by type 1 (15.5%), type 7 (4.3%), type 5 (2.5%), and type 11 (0.6%) (Table 3).

Herpesviruses were isolated in 41 cases (5.2%). These viruses were found mostly in upper respiratory tract infections. Herpesviruses were detected throughout the three years with only a slight increase

Table 3. Serotypes of adenovirus isolated from children with acute respiratory infection

Period	Serotype					Total
	1	2	5	7	11	
April–Sept. 1979	3	10	1	1	0	15
Oct. 1979– March 1980	3	55	2	1	1	62
April–Sept. 1980	7	21	1	3	0	32
Oct. 1980– March 1981	7	15	0	1	0	23
April–Sept. 1981	3	3	0	1	0	7
Oct. 1981– March 1982	2	20	0	0	0	22
Total	25	124	4	7	1	161

tember, when there were 14 positive samples out of 20 pharyngeal swabs (70%). Of these 22 patients, all were affected with upper respiratory tract infection, 11 had enteric symptoms, 5 suffered convulsions, 3 had hepatosplenomegaly, 1 had myocarditis, and 1 died with acute meningoencephalitis. During the same period many virological examinations performed on swabs taken from outpatients (children and adults) suffering from an influenza-like illness gave positive results for echovirus type 3.

Respiratory syncytial virus has been isolated only rarely since the outbreak in the winter season of 1978-79; during the present study only 32 children gave positive results for this virus. The highest number of isolations occurred in February 1982 (8 strains). Respiratory syncytial virus was found frequently in babies suffering from bronchiolitis (26 out of 32).

Influenza A and B viruses were found in February 1981 and in May-June 1979, respectively. The former were A/USSR/90/77(H1N1)-like and were isolated during the winter of 1980-81. Influenza B strains isolated were similar to B/Johannesburg/9/75, which showed some drift away from B/Hong Kong/8/73. The children positive for this strain were all suffering from severe clinical illness and two developed Reye's syndrome.

Parainfluenza 3 virus was detected in only 10 cases (1.3%) most of whom had upper respiratory tract infection.

Seasonal variations

The seasonal variations are shown in Fig. 2. It is evident that the adenoviruses spread during the winter of 1979-80; respiratory syncytial virus was not found during the spring and summer of 1979 and 1980; during these seasons enteroviruses were frequently isolated. However the data are inconclusive because of the short observation time; there is a need for studies over a longer period.

DISCUSSION

Some etiological, clinical, and epidemiological data have emerged from the present survey, but it should be noted that there was a lack of rigorous standardization of clinical diagnosis and that only cases requiring hospital treatment were examined. In consequence, the results can only give some indication of the true distribution of respiratory viruses in the Naples area and, above all, of their relationship to the clinical illnesses observed. Within these terms, the data indicate that all the isolates were associated with several types of respiratory infection, although there seemed to be a strong relationship between respira-

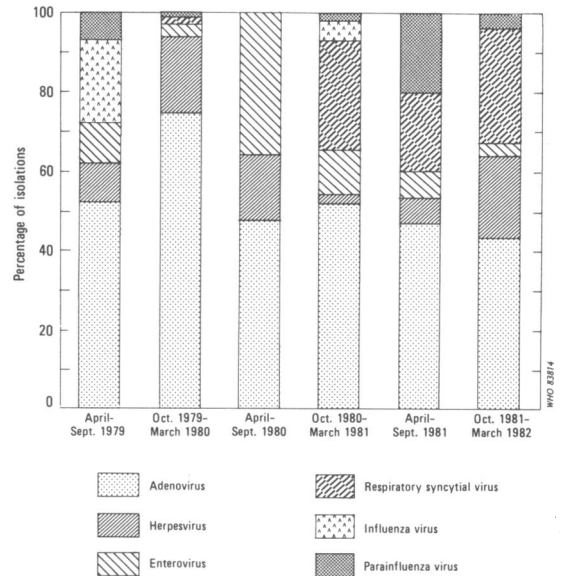


Fig. 2. Percentage distribution of viral isolates from children with acute respiratory disease.

tory syncytial virus and bronchiolitis and between herpesvirus and disease of the upper respiratory tract.

The rate of adenovirus isolations was higher than those recently obtained in other surveys in Italy (2, 9, 17, 19) and elsewhere (8, 14, 15). The results of typing showed that adenovirus type 2 was the most prevalent, with an endemic distribution as previously observed by Fox et al. (4).

The outbreak caused by echovirus type 3 was interesting. The epidemiological findings indicated that the strains were widespread during the summer of 1980. Although there are relatively few descriptions of similar events, it seems that the clinical and epidemiological features of the outbreak were the usual ones (12, 18, 20). The frequency of these epidemics is perhaps underestimated.

There were very few isolates of respiratory syncytial virus during the first year of the study; towards the end of the 3-year period, a few strains were detected. Many authors have indicated that respiratory syncytial virus is the most important and widespread respiratory agent in children (3, 5, 7, 11, 16, 23). The low number of isolates in the present study may be related to the wide distribution of the virus during the winter of 1978-79, reflecting perhaps a periodic pattern of circulation; alternatively, the methods used for detection of the virus may not have been sufficiently sensitive.

The isolation of influenza B/Johannesburg-like strains was quite unexpected. This subtype was first isolated in South Africa in 1975 (21), and in 1979 several countries reported its isolation from sporadic cases or small outbreaks marked by an unusual severity of disease (23). In Italy this strain has been isolated only in Naples from children admitted to hospital with severe or fatal illness. This confirms the usefulness of attempting the isolation of influenza virus in all children admitted to hospital.

The data on other isolates did not show a marked clinical or epidemiological relationship. There are reasonable doubts of some false negative results for

parainfluenza virus, because of the lack of primary cells, which are rarely available in the Naples area.

Finally, the most significant result of the present survey was the unusually high rate of recovery of adenoviruses, which were found to be the most common viral agent in children hospitalized with acute respiratory infection. More surveillance is needed, particularly with the aid of immunofluorescence techniques to improve the detection of respiratory syncytial virus and parainfluenza virus and to obtain a more reliable picture of the viruses circulating in the area.

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RÉSUMÉ

VIRUS ASSOCIÉS AUX INFECTIONS RESPIRATOIRES AIGÜES PARMI LES ENFANTS HOSPITALISÉS À NAPLES, 1979-82

L'hiver 1978-79 a été marqué à Naples par une flambée épidémique d'infections respiratoires qui a frappé en particulier les nourrissons de moins de 2 ans. Le principal germe isolé à l'époque a été le virus respiratoire syncytial. Après cette épidémie, une enquête virologique a été entreprise sur les enfants hospitalisés pour une maladie respiratoire aiguë. Le présent article est consacré aux résultats des trois premières années de surveillance en laboratoire.

Entre avril 1979 et mars 1982, 787 prélèvements rhinopharyngés ont été examinés; tous les échantillons provenaient d'enfants âgés de 0 à 69 mois, admis à l'hôpital Santobono de Naples. Le nombre d'hospitalisations, le nombre d'échantillons, et le taux d'isolement ont été plus élevés au cours des deux hivers.

Deux cent quatre-vingt-sept échantillons se sont révélés positifs (36,5%), les adénovirus étant les germes les plus courants (161 échantillons, 56%); on a observé ces virus dans tous les groupes d'âge et tous les groupes nosologiques et noté une hausse sensible de leur fréquence pendant la période janvier-mai 1980 (47,2% de la totalité des échantillons contenaient alors des adénovirus). L'adénovirus de type 2 était le plus fréquent (77,0%), suivi du type 1 (15,5%), du type 7 (4,3%), du type 5 (2,5%) et du type 11 (0,5%).

Les isolements de virus respiratoire syncytial ont été moins nombreux qu'on ne s'y attendait (32 prélèvements); ils ont

en général été effectués pendant la saison d'hiver, chez des enfants atteints de bronchiolite.

Au total, 41 échantillons contenant le virus de l'herpès ont été isolés, en particulier chez des sujets atteints d'infection des voies respiratoires supérieures; aucune variation saisonnière bien nette n'a été mise en évidence. Parmi les entérovirus isolés se trouvaient 4 poliovirus, 10 virus coxsackie et 23 échovirus type 3. L'échovirus type 3 a été à l'origine d'une épidémie pendant l'été 1980, à la fois chez des enfants hospitalisés et des malades traités en ambulatoire.

Les virus grippaux et paragrippaux ont été rarement décelés: les souches de virus grippal A isolées étaient analogues au type A/URSS/90/77 (H1N1), tandis que les souches de virus grippal B étaient analogues à B/Johannesburg/9/75. Deux cas de syndrome de Reye ont donné des souches de virus grippal B.

Deux éléments remarquables ont été mis en évidence par cette enquête: le taux élevé d'isolement d'adénovirus (20,5%) dans la population étudiée, et le faible taux d'isolement de virus respiratoire syncytial alors qu'au cours des épidémies antérieures dans cette région, il avait été l'agent étiologique. En conclusion, l'article insiste sur l'importance de la surveillance permanente des infections respiratoires aiguës, en particulier dans les régions défavorisées des pays industrialisés.

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