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Aetiology and epidemiology of viral croup in Glasgow, 1966–72

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SUMMARY

A retrospective study of 258 children admitted to Ruchill Hospital, Glasgow, with croup between 1966 and 1972 indicated that the viruses most frequently associated with the syndrome were parainfluenza types 1 and 3 and influenza A. Most cases were admitted in the late autumn and winter months, with a small peak in May and June. This seasonal distribution mirrored the circulation of the main causative agents in the community, parainfluenza 1 being principally associated with the autumn cases, influenza A the winter cases and parainfluenza 3 the summer cases. Two of these 'croup associated' viruses showed regular periodicity, parainfluenza 1 occurring biennially in even years and influenza A in most years. The periodicity of parainfluenza 3 is as yet undetermined.

INTRODUCTION

Viral croup remains an important clinical disease of early childhood which often necessitates admission to hospital and occasionally results in death. Past investigation of the viral aetiology of the disease in North America showed association with parainfluenza viruses of types 1, 2, and 3 (Chanock, 1956; Chanock *et al.* 1958; Beale, McLeod, Stackiw & Rhodes, 1958; Cook *et al.* 1959). Other viruses (influenza A and B; adenovirus types 1, 2, 3, 5 and 7; coxsackievirus A9 and echoviruses 10 and 14) were associated with the syndrome in Melbourne, Australia (Forbes, 1961). More recently the role of respiratory syncytial (RS) virus as a causative agent was reported (Gardner, McQuillin, McGuckin & Ditchburn, 1971). Stark (1969) in his review of croup suggested that the parainfluenza viruses and influenza A and B were the commonest aetiological agents. The present paper reviews the viral aetiology and epidemiology of the cases of croup admitted to Ruchill Hospital in 1966–72.

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Table 1. *Age, sex and virological investigation of croup admissions* – 1966–72

Age – years	Sex M	Sex F	No. tested	No. positive
< 1	35	15	35	16
1	65	18	54	33
2	35	10	33	18
3	16	9	15	7
4	17	4	16	6
5–10	26	4	20	11
11–14	3	1	4	4
Total	197	61	177	95 (54%)

MATERIALS AND METHODS

Clinical records

Records of all croup cases in the 7-year-period notified to the Records Department at Ruchill Hospital were examined; only those with evidence of characteristic vibrant cough and obstructive stridulous respiration were included. The few cases of acute epiglottitis due to *Haemophilus influenzae*, which is also associated with the croup syndrome, were omitted. Of the 258 cases 76% were male and 52% were under 2 years of age (Table 1). The severity of illness varied considerably and two deaths occurred. Of those children in whom conventional treatment by humidification of the atmosphere failed to produce sufficiently rapid improvement, fourteen were treated with a corticosteroid, two were intubated and four had tracheotomy. Throat swabs were submitted from 177 (69%) of the 258 patients for virological investigation.

Virus isolation

Throat swabs were collected in virus transport medium (Grist, Ross, Bell & Stott, 1966) on admission and sent quickly to the Regional Virus Laboratory in the same hospital. Specimens were cultured in rolled monolayers of secondary rhesus monkey kidney and human embryo lung (WI-38 strain) at 33° C, and stationary Bristol HeLa cultures at 36° C. Agents which exhibited haemadsorption or cytopathic effects were identified by conventional methods (Grist *et al.* 1966).

RESULTS

Epidemiology of virologically positive croup cases

The monthly distribution of the 258 cases of croup admitted to Ruchill Hospital between January 1966 and December 1972 is shown in Part A of Fig. 1. Most cases were admitted in late autumn and early winter, 149 (58%) in the months of October, November, December and January. There was also a small peak in May and June. It is interesting to compare over the 7-year-period these monthly admissions of croup to Ruchill with details in Part B of the monthly isolations of the three principal croup associated viruses in the Glasgow area during that period. Part B gives the total isolations of these viruses at the Regional Virus

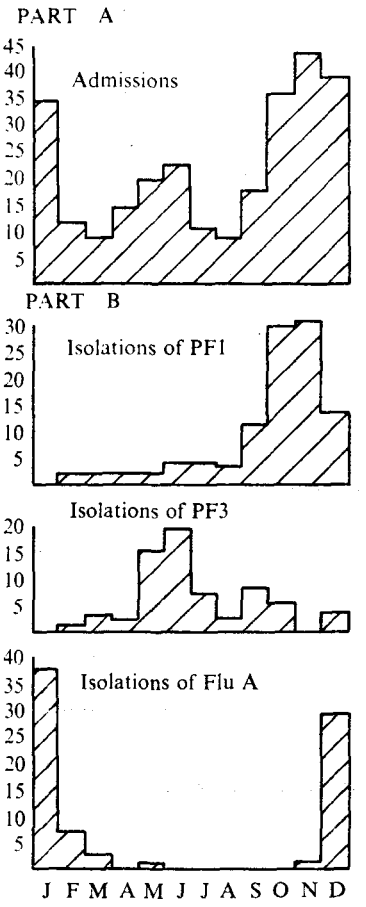

Fig. 1. Monthly distribution in 1966–72 of (A) croup admissions to Ruchill Hospital, (B) isolations from all sources of parainfluenza types 1 and 3 and influenza A viruses.

Laboratory from children under 15 years with a variety of respiratory illnesses in other West of Scotland hospitals as well as Ruchill and also in general practice. It can be seen that the peaks of croup admissions to Ruchill Hospital reflect the peaks of incidence of parainfluenza virus types 1 and 3 and influenza A virus in the community.

Table 2 lists the viruses isolated from 95 (54%) of the 177 croup patients in Ruchill Hospital from whom swabs were submitted. The viruses isolated in order of frequency were parainfluenza 1 (44), influenza A (18), parainfluenza 3 (14), herpes simplex (7) parainfluenza 2 (3), RS virus (3), adenovirus 1 (2), rhinovirus (2), and one each of adenovirus 5, echovirus 8 and poliovirus 1. In addition two unidentified viruses were isolated. Three of the 95 virologically positive cases were double infections (influenza A and adenovirus 1, influenza A and herpes simplex, and parainfluenza 1 and herpes simplex). During the same period eighteen croup cases (7%) were associated with clinical measles and three with chickenpox.

Over the 7 years, by far the commonest virus isolated in autumn was para-

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Table 2. *Monthly virus isolations from Ruchill croup admissions* 1966–72

	PF 1	PF 2	PF 3	Flu A	R.S.	Herp.	Other
Jan.	—	—	—	10	1	1	Ad. 1 Ad. 5
Feb.	1	—	—	2	—	—	Rh
Mar.	2	—	—	—	—	—	—
Apr.	1	—	—	—	—	1	Rh
May	2	—	3	1	—	—	—
June	2	—	5	—	—	1	—
July	1	—	—	—	—	—	—
Aug.	4	—	—	—	—	—	—
Sept.	5	—	5	—	—	—	—
Oct.	14	—	1	—	—	2	U.T.
Nov.	8	2	—	—	1	2	U.T. A. 1
Dec.	4	1	—	5	1	—	E. 8 P. 1

PF 1, PF 2, PF 3	Parainfluenza Virus Types 1, 2, 3
Flu A	Influenza A Virus
R.S.	Respiratory Syncytial Virus
Herp.	Herpes Simplex Virus
Ad. 1, Ad. 5	Adenovirus Types 1, 5
Rh.	Rhinovirus
E. 8	Echovirus Type 8
P. 1	Poliovirus Type 1
U.T.	Unidentified Agent

influenza 1, although September yielded five isolations of parainfluenza 3 (Table 2). The December cases yielded a mixture of viruses, the commonest being influenza A and parainfluenza 1, while in January influenza A predominated. The summer peak in May and June yielded mainly parainfluenza types 3 and 1. Thus during the periods May–June, October–November and December–January, the croup cases were of different viral aetiology – principally parainfluenza 3, parainfluenza 1 and influenza A respectively.

Epidemiology of the croup-associated viruses

The important 'croup-associated' viruses in the Glasgow area are parainfluenza 1, parainfluenza 3 and influenza A. As previously mentioned Fig. 1 shows the monthly distribution of the seven years' isolations of these viruses from all sources by the Regional Virus Laboratory. Parainfluenza 1 was most prevalent in the months of October–November, coinciding with the maximum admission of croup cases infected with that virus. Similarly the peak of parainfluenza 3 in May–June coincides with the months of maximum admission of parainfluenza 3 croups. December and January were the months in which influenza A was most prevalent in the Glasgow area, again coinciding with the maximum admission of croup cases associated with this virus. Analysis of the diagnoses of cases from which parainfluenza viruses were isolated demonstrates the varying degree of croup-association of parainfluenza viruses which were isolated from children with

Table 3. *Croup-association of parainfluenza viruses isolated at the Regional Virus Laboratory from all sources from children under* 15.

		Parainfluenza 1		Parainfluenza 2		Parainfluenza 3	
		Total	Croup	Total	Croup	Total	Croup
Ruchill Hospital respiratory admissions 1966–72		59	44 (75 %)	5	3 (60 %)	38	14 (37 %)
Sources outside Ruchill Hospital 1966–72		43	20 (47 %)	—	—	27	7 (26 %)
Combined cases by year:	1966	8	1 (13 %)	1	1 (100 %)	2	0 (0 %)
	1967	2	1 (50 %)	—	—	6	2 (33 %)
	1968	25	15 (60 %)	—	—	7	2 (29 %)
	1969	2	0 (0 %)	—	—	29	11 (38 %)
	1970	24	21 (88 %)	—	—	11	1 (9 %)
	1971	—	—	3	1 (33 %)	7	3 (43 %)
	1972	41	27 (65 %)	1	1 (100 %)	3	2 (67 %)
Total	1966–72	102	64 (63 %)	5	3 (60 %)	65	21 (32 %)

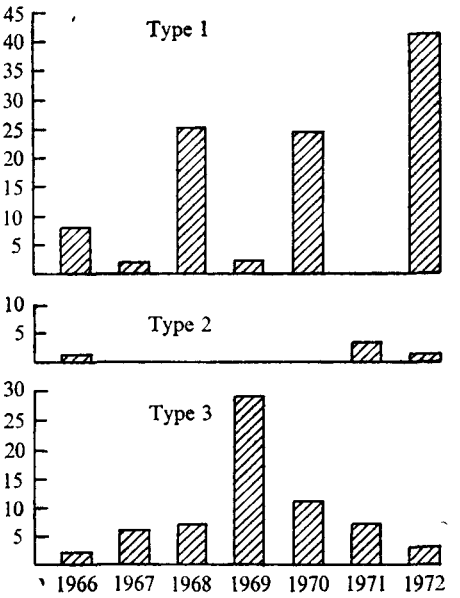

Fig. 2. Parainfluenza isolations 1966–72, Regional Virus Laboratory, Ruchill Hospital.

respiratory infections admitted to Ruchill Hospital and also from swab submissions from all sources outside the Hospital. Table 3 clearly shows an annual variation in the croup-association of the parainfluenza viruses from all sources. Also, although 63 % of the total parainfluenza 1 isolations were croup-associated, only 32 % of total parainfluenza 3 isolations were from croup cases. Parainfluenza 2 was a rare cause of croup in the Glasgow area (three cases) and had a 60 %

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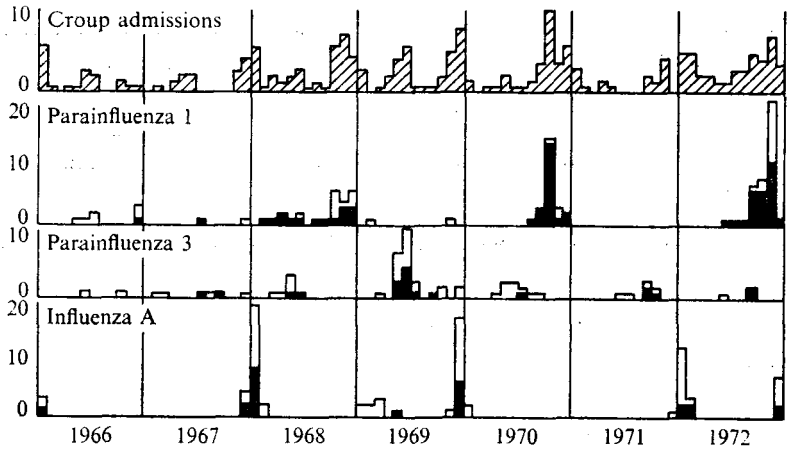

Fig. 3. Monthly croup admissions and total isolations of parainfluenza and influenza viruses 1966–72. ■, isolates from croup cases. □, isolates from other respiratory infections.

croup-association. The 172 isolations of parainfluenza viruses over the 7 year period were from a wide variety of respiratory syndromes in children under 15 years of age. Of this total 70 were submitted from either other hospitals in the West of Scotland (26) or general practice (44).

Annual variations occur in croup admissions and in prevalence of the viruses in the community. Fig. 2 shows the annual isolations of parainfluenza viruses from all sources over the period under investigation. Parainfluenza 1 shows a biennial pattern of raised prevalence in alternate 'even' years, maximal in 1968, 1970 and 1972. Fig. 3 compares over the 7-year period the incidence each month of croup admissions with total isolations of parainfluenza viruses 1 and 3 and influenza A. Thus the only years with peaks of croup in the months of October and November are 1968, 1970 and 1972 with 18, 19 and 16 admissions respectively. During the years of low prevalence of parainfluenza 1, autumnal croup admissions were considerably reduced, e.g. four in 1967. Although there were eight croup admissions in October–November 1971, a year without any evidence of parainfluenza 1 activity, four cases were associated with 'sporadic' viruses (two measles, one each of parainfluenza viruses 2 and 3). Similarly although 1969, another year of low parainfluenza 1 prevalence, had ten late autumn cases, this period with November in particular was marked by RS virus activity. Nevertheless, only one isolation of RS virus was obtained from croup cases during that period. The year 1969 also provides interest by demonstrating an unusually high peak of admissions in early summer which corresponds with the period of maximum isolation of parainfluenza 3 virus during the 7 years. High prevalence of croup in December–January coincides with influenza A activity. Influenza was not detected in the Glasgow area during the winter of 1966-67 when croup admissions were fewer than in any of the other winters (only one in December 1966 and none in January 1967).

DISCUSSION

The dominant importance of parainfluenza and influenza viruses as causes of croup in Glasgow has been shown by the correlation between peak periods of incidence of the disease (reflected in Ruchill Hospital admissions) and peak periods of prevalence of parainfluenza 1, parainfluenza 3 and influenza A viruses as shown by their isolation from general respiratory illnesses as well as croup patients. Unusually low prevalence of these croup-associated viruses correlates with unusually low incidence of croup, as in winter 1966-67.

The maximum number of admissions (43) in the 7-year-period was in the month of November when the total number of virus isolations was not high. Virological studies of other respiratory diseases in the Glasgow area show that this is often a peak month for RS virus activity (Grist, Ross & Stott, 1967; Grist, 1970; Martin *et al.* 1971), and perhaps the high incidence of the disease in November may partly be due to this virus, in keeping with the report from Newcastle that RS virus is an important aetiological agent in croup (Gardner *et al.* 1971).

The outbreak of croup associated with parainfluenza 1 in October 1970, was reflected both by increased admissions of croup cases and also by an increased percentage of the croup-association of parainfluenza 1 isolations during that period. A similar phenomenon was shown by parainfluenza 3 in May–June, 1969. Table 3 shows that the percentage croup-association of parainfluenza infections fluctuates from year to year, tending to be highest when the viruses are more prevalent. Although this might suggest periodic variation in virulence of the viruses, it seems more likely that the figures reflect a sampling bias in favour of hospital admissions, and therefore virological investigation, of children in whom croup is the manifestation of the currently epidemic virus. Thus a raised incidence of croup in any year probably reflects a raised incidence of one of the relevant virus infections in the community, with increased opportunity to infect and help initiate croup in susceptible children. Why some individuals react to the virus in this way remains at the moment speculative, as must consideration of other possible aetiological factors in the croup syndrome.

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