

Epidemiology and aetiology of acute bronchiolitis in Hong Kong infants

R. Y. T. SUNG¹, R. C. K. CHAN², J. S. TAM², A. F. B. CHENG²
AND H. G. S. MURRAY²

*Department of ¹Paediatrics and ²Microbiology, Prince of Wales Hospital,
The Chinese University of Hong Kong, Shatin, N.T., Hong Kong*

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SUMMARY

The epidemiological, clinical and virological features of 1220 children with acute bronchiolitis admitted to the Prince of Wales Hospital, Hong Kong, from 1985 to 1988 are reported. They accounted for 6·6% of total paediatric admissions and provided a case incidence of bronchiolitis requiring admission to hospital of approximately 21 per 1000 children 0–24 months of age.

The clinical course and outcome was in general benign. The average hospital stay was 5 days and there were no deaths. Ten per cent of patients were repeatedly admitted to hospital with recurrent wheezing after discharge. Two infants developed bronchiolitis obliterans.

Respiratory syncytial virus (RSV) was shown by direct immunofluorescence, virus culture and serology to be the commonest cause of acute bronchiolitis in Hong Kong. Other aetiological agents included parainfluenza and influenza viruses, adenoviruses, and *Mycoplasma pneumoniae*.

In contrast to western countries, a seasonal variation of bronchiolitis was found with a peak incidence in the summer months. The significance of these observations is discussed.

INTRODUCTION

In a previous publication [1] respiratory syncytial virus (RSV) was found to be the commonest cause of bronchiolitis in infants and small children in Hong Kong. Contrary to the incidence in Western countries, the infection occurred most commonly during the summer months, showing a strong correlation with rainfall, humidity and temperature. In order to verify and extend these findings we undertook the 4-year cross-sectional study reported here.

PATIENTS AND METHODS

This study was done in the Prince of Wales Hospital (PWH), a large government teaching hospital which serves the eastern New Territories, which have a current population of about one million. There are 1360 beds in the hospital, including 114 beds for children aged between 1 month and 14 years. Most children who live in the catchment area and require hospital treatment are admitted into the paediatric wards of this hospital.

The diagnostic criteria for acute bronchiolitis adopted by the authors were: (1) age 24 months or younger, (2) signs of preceding or coexisting viral respiratory illness, such as coryza or fever, (3) expiratory wheezing of acute onset, (4) respiratory distress - dyspnoea or tachypnoea (respiratory rate > 40/min). A diagnosis of acute bronchiolitis was made when all four criteria were fulfilled. The presence or absence of history or signs of atopy did not affect the diagnosis.

Our investigation into the epidemiology of acute bronchiolitis was derived from demographic data, date of admission and length of hospital stay of patients discharged under the diagnosis of acute bronchiolitis (ICD code 466.1) [2] from 1 January 1985 to 31 December 1988. The number of monthly admissions with a diagnosis of acute bronchiolitis and their contribution to total admissions were analysed through clinical audit [3]. Patients repeatedly admitted with acute bronchiolitis were identified by the computer.

For the identification of aetiological agents samples of nasopharyngeal secretions (NPS) were collected with a mucous extractor on admission using the technique described by Gardner & McQuillin [4]. The specimens were immediately transferred to centrifuge tubes and centrifuged at 500 g for 10 min to deposit the cells present in the NPS. Each supernatant was inoculated into four different tissue cultures (LLCMK2, MDCK, HEP2, human foetal lung). The cells deposited from the specimen were washed with phosphate-buffered saline, transferred to a microscope slide, air-dried, fixed in acetone, and stained with FITC-conjugated monoclonal antibodies to RSV (IMAGEN; Boots Celltech Diagnostics, Slough, Berkshire, UK). The preparations were examined by incident-light fluorescence microscopy at a wavelength of 490 nm. Inoculated tissue cultures were incubated at 33 °C (LLCMK2 and MDCK) or at 37 °C (HEP2 and foetal lung) on a rotating drum (12 rev./h) and observed daily for cytopathic effect. The presence of RSV in the tissue cultures was confirmed by direct immunofluorescent staining (IMAGEN; Boots Celltech Diagnostics). Haemadsorption with guinea-pig red cells was routinely performed in LLCMK2 and MDCK tissue cultures to detect haemagglutinating viruses. Tubes were incubated up to 3 weeks and discarded if negative.

Paired sera taken at least 10 days apart were collected from the children whose parents consented to blood being taken. The sera were stored at -20 °C pending examination by the complement fixation technique for antibodies to RSV, influenza A and B, parainfluenza I, II and III, adenovirus, and mycoplasma. A fourfold or greater rise in antibody titre was taken as evidence of current or recent infection. All reagents for the complement fixation test were obtained commercially.

RESULTS

Epidemiology

A total of 1220 children with acute bronchiolitis were admitted during the study period. These 1220 cases accounted for 6.6% of total admissions and 14% of all respiratory-tract infections (including upper and lower respiratory tract infections) (Fig. 1). The total admission number of 1985 was notably small compared to each of the following three years because the 24 h emergency service in the hospital did not commence until 1 September 1985. One hundred and

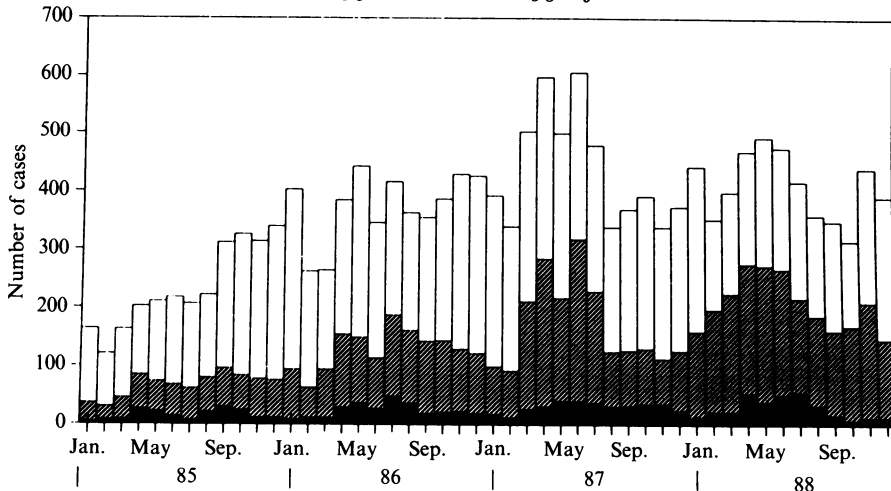


Fig. 1. Admission of acute bronchiolitis and respiratory tract infection from January 1985 to December 1988. ■, Acute bronchiolitis; ▨, respiratory tract infections; □, admission.

nineteen patients (9.8%) were admitted more than once with the same clinical diagnosis. Thirteen of these were admitted on four or more occasions and were followed up in our out-patients department. Three cases with a strong family history of asthma, three cases of bronchopulmonary dysplasia and two cases who developed bronchiolitis obliterans continued to have recurrent wheezing attacks (follow-up period 16 months to 4 years). Five patients who had clustered admissions during the first year after the initial episode of acute bronchiolitis had no further attacks of severe wheezing (follow-up period 14 months to 2 years). There were no fatal cases during the study.

More boys than girls were admitted with acute bronchiolitis, the male to female ratio being 2.24 to 1. The average age was 5 months and the mean duration of hospital stay 5 days (range 2–63 days). The mean interval between the onset of illness and admission was 3 days (range 1–11 days).

Viral studies

Nasopharyngeal secretions for rapid viral antigen tests and culture were collected on admission from 681 (56%) patients. Patients admitted during the weekends or after office hours were unable to have these investigations. Paired serum samples were obtained from only 62 of the 681 patients for serological study. Viruses were identified in 272 (40%) children. The results are shown in Fig. 2. RSV comprised 86% of the positive cases. Other respiratory viruses, including influenza and parainfluenza viruses, adenovirus and *Mycoplasma pneumoniae*, accounted for 0.4–5% each.

Seasonal variation of RSV isolation

During the course of the study marked seasonal variation in the rate of RSV isolation was found. There was a clear seasonal periodicity with RSV isolation peaking in summer and disappearing in winter. When the RSV isolation rate was compared with the number of specimens studied each month, it was found to be disproportionately low between October and January (Fig. 2).

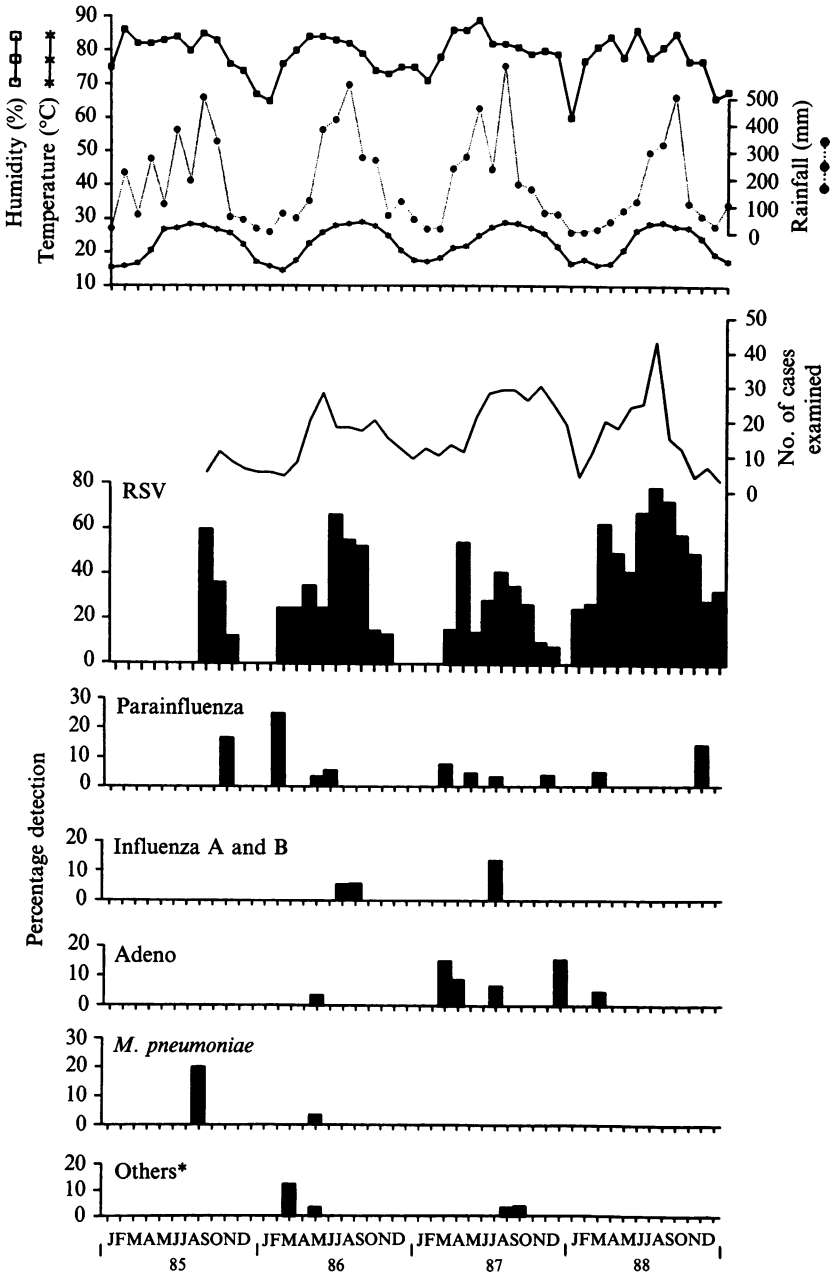


Fig. 2. Viruses identified in 265 children with acute bronchiolitis by direct antigen detection (IF), viral culture or serology. *Others include cytomegalovirus in 13 cases, coxsackie virus in 1 case and herpes simplex virus in 1 case.

The isolation rate showed significant positive correlations with rainfall ($P < 0.001$), mean relative humidity ($P < 0.001$) and mean temperature ($P < 0.001$) (Fig. 2).

DISCUSSION

In the knowledge that the contribution of acute bronchiolitis to total paediatric admissions during the 3-year study period was fairly constant at around 6.5% and

the population of 2 years or under in the catchment area was about 16000 [5], it is possible to derive a crude estimate of approximately 21 cases of bronchiolitis per 1000 children requiring admission to hospital. This is higher than the estimate of 10 per 1000 infants, up to 12 months of age, in Washington, DC [6], but close to Martin and colleagues' estimate in northeast England, where 1 in 50 live-births are admitted to hospital with severe RSV infection [7]. There are, however, many pitfalls in direct comparison of incidence data from different studies, notably the great variation in diagnostic criteria employed [8, 9]. In our diagnostic criteria for acute bronchiolitis we did not exclude cases who had previous wheezing episodes, and it is possible that patients with early onset asthma might have been included.

Mortality from bronchiolitis among infants less than 1 year of age was reported to be 4–7% for infants hospitalized in the 1960s [10, 11]; however, it has dropped to less than 1% in the last decade [12]. There were no deaths from bronchiolitis in PWH during the study period; this may reflect an ethnic difference or a different viral aetiology.

The average age of 5 months is similar to that found in other hospital-based studies [6, 13]. A community-based study has shown that the occurrence rates of acute bronchiolitis are similar for children under 6 months of age, 6–12 months of age and 12–24 months of age [14]. However, the authors noted that 56% of patients admitted to the local hospital because of acute bronchiolitis were under 6 months of age. These figures are consistent with the widely held view that very young children with bronchiolitis are more severely ill and in greater need of hospital care than older children. The male predominance observed in this study is in agreement with reports from other parts of the world [13, 14].

In our study, 119 (9.8%) patients had recurrent wheezing severe enough to warrant two or more admissions within the 4-year study period. This observation is in agreement with the general consensus that recurrent wheezing after acute bronchiolitis in infancy is common [15–18]. Thirteen of the 119 patients had four or more admissions under the same diagnosis, 'acute bronchiolitis'. Of these 13 patients, 2 developed bronchiolitis obliterans, 3 suffered bronchopulmonary dysplasia and 3 patients subsequently developed asthma. The remaining five patients, who were followed up from 6 months to 32 months, were frequently readmitted within several months of the initial attack of acute bronchiolitis but remained free of wheezing episodes thereafter. These results indicate that the bronchial hyperreactivity induced by, or associated with, acute bronchiolitis causes more problems in early infancy than later in the child's development.

Viruses detected in the present study are compared with those detected in other major studies in Table 1. In general, our results are comparable with those found in two major longitudinal studies carried out in North Carolina [19] and Colombia [20]. The very high isolation rates reported in the Newcastle and Singapore studies may be a consequence of collecting specimens only during RSV epidemics. In all the studies where an aetiological agent was detected, RSV was shown to be the commonest pathogen of acute bronchiolitis. Cytomegalovirus, coxsackie virus and herpes simplex virus isolated from a few patients in our study are unlikely to have been the cause of the bronchiolitis.

In the first 4 years of the study RSV was identified as the aetiological agent of bronchiolitis in only a small proportion of children admitted from October to January. Although other viruses may have been responsible for some of these

Table 1. *A summary of viruses detected in six studies of acute bronchiolitis*

Geographical location of study [ref.]	Pts no.	Total no. of viruses isolated (% of total patients)	R.S.V.	P1 + P3*	Adeno-virus	Rhino-virus	<i>Mycoplasma pneumoniae</i>	Influenza A and B	Other
N. Carolina [19]	909	203 (22%)	90 (44.3)	54 (26.6)	27 (13.3)	9 (4.4)	6 (3.0)	—	17 (8.4)
Newcastle, UK [9]	726	611 (84%)	553 (90.5)	23 (3.8)	14 (2.3)	11 (1.8)	0	7 (1.1)	3 (0.5)
Colombia [20]	339	73 (22%)	41 (56)	9 (12.3)	16 (21.9)	—	1 (1.4)	5 (6.8)	1 (1.4)
Washington, DC [21]	48	24 (50%)	20 (83.3)	3 (12.5)	1 (4.2)	—	—	—	—
Singapore [13]	58	48 (83%)	24 (50)	10 (21)	1 (2.0)	—	4 (8.3)	1 (2.0)	8 (16.7)
This study	681	272 (40%)	113 (75.8)	7 (4.7)	9 (6.0)	—	4 (2.7)	6 (4.0)	10 (6.7)

* Parainfluenza 1 and parainfluenza 3. † Number in parentheses indicates percentage of total isolates.

cases, the number of isolations were too few to enable any conclusions to be drawn. The misdiagnosis of some cases of asthma as acute bronchiolitis would provide an alternative explanation for the unexpectedly low RSV isolation rate. The highest admission rate for asthma in Hong Kong occurs between October and December [22]. It is estimated that 10% of asthmatic children begin to have symptoms in the first year of life [23] and the differential diagnosis of asthma and acute bronchiolitis can be difficult in a small infant.

The monthly admission pattern is in sharp contrast with that reported in the UK [9], the US [6, 14] or Australia [24], where epidemics of acute bronchiolitis invariably occur in winter and early spring. In Hong Kong acute bronchiolitis was prevalent in the middle part of the year, between April and October.

Notwithstanding the short duration of this study, we believe that the seasonal variations in the isolation of RSV reflected in the data are valid, since the weather conditions during the study period were typical for Hong Kong. Indirect support for our finding can be found in a 4-year retrospective study of admissions of patients with acute bronchiolitis to a large general hospital in Kowloon from 1980 to 1984, where admissions were high in the summer but low in winter [22]. Furthermore, according to the statistics of the Medical and Health Department of Hong Kong collected during 1976–85, the number of in-patients treated in seven government hospitals for acute bronchiolitis and bronchitis was greater in late spring and summer and lowest in winter (personal communication). Although this seasonal distribution is different from that reported from Western countries, similar observations have been reported from Trinidad [25] and South India [26].

The higher incidence of RSV infection in Hong Kong in the hot rainy season may be related to the atmospheric conditions or to the degree of environmental pollution which might change with the weather or with human behaviour. In the absence of the relevant data in the Shatin area we can only speculate on the significance of air pollution in transmission of RSV. Crowding, however, could be an important factor favouring transmission of the virus. The rain and heat of the Hong Kong summer might discourage people from going outdoors and the crowded indoor living conditions thus facilitate viral transmission. A similar explanation could also explain the prevalence of RSV infection during the winter months in colder climates. Whatever the explanation, the seasonality of RSV infection has clinical implications for hospital management. With a high summer incidence in Hong Kong, greater pressure on bed occupancy and demands on oxygen tents can be expected. Also, knowledge of the existence of an 'epidemic' period should make it easier to test the efficacy of antiviral agents now becoming increasingly available for treatment of RSV infection.

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