AN INVESTIGATION OF ACUTE RESPIRATORY DISEASE IN CHILDREN ADMITTED TO HOSPITAL IN THE SOUTH WEST METROPOLITAN REGION

BY

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(RECEIVED FOR PUBLICATION FEBRUARY 5, 1962)

Acute respiratory disease in young children is exceedingly common and is responsible for an increase in the number of infants admitted to children's wards during the winter. Outbreaks have been reported in different parts of this country by Hubble and Osborn (1941), Garrow and Fawcett (1953), Heycock and Noble (1956) and Disney, Sandiford, Cragg and Wolff (1960). These workers and others (Morrison, Bass, Davis, Hobson, Madsen and Masters, 1957; Holland, Tanner, Pereira and Taylor, 1960b; Gardner, Stanfield, Wright, Court and Green, 1960) have indicated that knowledge of the causes is still incomplete, especially in children less than 1 year old. Most studies have been confined to the winter months and to small groups of children in localized areas.

The object of this investigation was to study, epidemiologically, cases of acute respiratory illness in children admitted to hospital over a wide area during both summer and winter months. Admissions to the children's wards of 10 general hospitals, seven in the London area, one at Guildford, one at Christchurch and one at Southampton, between February 1957 and March 1958 were included (see Appendix A). During this period the outbreak of Asian influenza in 1957 occurred, followed by two outbreaks of an acute lower respiratory tract illness predominantly affecting infants. The second of these was reported in the *Lancet* in 1958 (*Lancet*, 1958).

Method

Paediatricians at each hospital were asked to make a monthly return of all children under 5 years of age admitted each week with acute respiratory disease. Each case was classified according to age and sex and certain diagnostic categories as set out in Appendix B. In addition, the number of children treated in oxygen tents was obtained as an indication of the severity of illness.

Acute and convalescent stage specimens of blood for serological tests were obtained from a proportion of

children admitted to those hospitals in the London area. Efforts were made to obtain a sample of blood from each child as soon after admission to hospital as possible and again 14 days later. Satisfactory paired samples of serum were obtained from 106 (11.4%) of the 927 children under 5 years of age from the London area. Of these, 44 (41.5%) were less than 1 year old, whereas 409 (44.1%) of the whole group were under 1 year of age. It should be pointed out, however, that owing to the difficulty of obtaining blood samples from very young or acutely ill children, cases from which specimens of serum were tested do not represent a random sample of the whole group, and any conclusions reached from the serological results should be viewed with this in mind. In addition, paired samples were tested from 26 children aged 5-12 years, also from the London area.

Each convalescent stage sample of serum was first screened at a dilution of 1/8 for complement-fixing antibodies to the following antigens: influenza viruses A, B and C; adenovirus group; para-influenza virus 1 (Sendai virus); psittacosis virus; and *R. burnetii*. The method employed was similar to that described by Holland, Rowson, Taylor, Allen, Ffrench-Constant and Smelt (1960a). Specimens showing more than 50% fixation were titrated in parallel with their paired acute stage samples. A fourfold or greater rise in antibody titre was regarded as evidence of concurrent infection.

Findings

Information was supplied by the 10 hospitals during a period of 14 months, from February 1957 to March 1958 inclusive. The hospitals of the South West Metropolitan Region included in this study are situated in three areas; seven in London, two on the South Coast at Southampton and Christchurch, and one between London and the South Coast at Guildford. The number of cases admitted to hospital in these three areas is shown in Table 1. Out of a total of 1,488 admissions, 675 (45.4%) were less than 1 year old and 813 (54.6%) were between 1 and 4 years. In the general

TABLE 1
ADMISSION BY MONTHS AND AGE GROUPS IN YEARS

	London			Guildford			Southampton and Christchurch		
	Age		Total	Age		Total	Age		Total
	<1 Year	1-4 Years		<1 Year	1-4 Years		<1 Year	1-4 Years	
1957:									
February	42	43	85	3	11	14	13	26	39
March	36	46	82	6	3	9	20	13	33
April	14	19	33	1	4	5	17	12	29
May	7	24	31	2	0	2	10	15	25
June	19	32	51	1	1	2	13	13	26
July	11	25	36	0	1	1	2	6	8
August	10	19	29	6	0	6	5	11	16
September	19	32	51	4	0	4	2	17	19
October	18	49	67	2	8	10	13	34	47
November	11	29	40	1	4	5	13	22	35
December	32	37	69	1	7	8	40	23	63
1958:									
January	53	47	100	7	3	10	30	20	50
February	98	67	165	19	5	24	14	19	33
March	39	49	88	4	6	10	17	11	28
	409	518	927	57	53	110	209	242	451

TABLE 2
SEX INCIDENCE IN DIFFERENT DIAGNOSTIC GROUPS

Diagnostic Category	A	B	C	D	E	F	G	H	Total
Males	268	21	46	119	87	36	176	55	808
Females	201	8	11	60	67	25	148	50	570
Male : female ratio ..	1.3	2.6	4.2	2.0	1.3	1.4	1.2	1.1	1.4

population, there are four times as many children 1 to 4 years of age as there are under 1 year of age, hence, in this study, there were proportionately more children under 1 year of age. In both age groups there was a preponderance of males.

The number of admissions in each diagnostic category is shown in Table 2. Males outnumber females in every group but they do so most in laryngo-tracheo-bronchitis (Category C), in which the male:female ratio is 4.2:1. A greatly increased incidence in males of acute infections of the larynx has also been noted by other workers (Rabe, 1948; Morgan, Turner, Rhodes, Peach, Zaiman and Duncan, 1956; Vargosko, Chanock, Huebner, Luckey, Kim, Cumming and Parrott, 1959).

When the numbers of children admitted each month to the three regions are compared (Table 1) it can be seen that the greatest number of admissions in London and Guildford was in February 1958, whereas in Southampton and Christchurch the greatest number was in December 1957. During these months the number of admissions greatly exceeded the total for any other month, including October 1957, when there was an epidemic of Asian influenza.

The Autumn Asian Influenza Epidemic. During the autumn Asian influenza epidemic there was a five-week period when there was an increase in the total number of admissions both in London and in Southampton and Christchurch. In London the increase began in week 38 and lasted until week 42; in Southampton and Christchurch it began one week later in week 39 and lasted until week 43. During these weeks the increase in the number of admissions of children under 1 year of age was less than in those aged 1 to 4 years. The ratio of infants to young children admitted was 1:1.9 (32:61) in London, 1:2.7 (3:8) in Guildford and 1:3.4 (13:44) in Southampton and Christchurch. Acute upper respiratory tract infection was the most commonly used diagnostic category. During the epidemic, 161 children were admitted and of these 72 were diagnosed as having upper respiratory tract infections (Category A), 16 as having laryngitis or laryngo-tracheo-bronchitis (Categories B and C), and 73 as having lower respiratory tract infections (Categories D, E, F, G and H). A diagnosis of bronchiolitis was made only twice. Most of the illnesses seem to have been mild, since relatively few children, especially in the age group under 1 year, required

TABLE 3

CHILDREN REQUIRING TREATMENT IN OXYGEN TENTS

	London		Guildford		Southampton and Christchurch	
	Age		Age		Age	
	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years
1957						
February	11	3	0	0	1	2
March	12	3	0	0	9	5
April	7	0	0	0	2	0
May	2	3	0	0	2	3
June	2	2	0	0	3	1
July	1	1	0	0	0	0
August	1	0	1	0	2	3
September	3	1	0	0	1	4
October	1	2	0	0	6	8
November	1	1	0	0	6	2
December	4	4	1	2	24	3
1958						
January	13	3	3	0	13	1
February	26	7	1	0	8	4
March	10	2	1	0	8	3
	94	32	7	2	85	39

oxygen tents. Nevertheless, during October 1957, in Southampton and Christchurch, more children aged 1 to 4 years required oxygen than in any other month of this investigation (see Table 3).

Comparable figures for admissions in other years are not available, but the number of notified deaths from influenza, pneumonia and bronchitis in London for the five weeks has been compared with the same period in the preceding five years and the following year (Table 4). During all years the mortality figures for children under 1 year of age greatly exceeded those for the age group 1 to 4 years, the ratio being 4.9:1 (49:10). During the 1957 influenza epidemic, however, this excess was much less, the ratio being 1.6:1 (11:7).

Epidemic Bronchitis. The outbreaks of acute respiratory infections in December 1957 and February 1958 differed in many respects from the

TABLE 5

COMPARISON OF DIAGNOSES DURING BRONCHITIS AND INFLUENZA EPIDEMICS

Diagnostic Category	Bronchitis Epidemics		Autumn Influenza Epidemic	
	Number	Per Cent.	Number	Per Cent.
A	45	17.9	76	44.7
B	2	0.8	7	4.1
C	13	5.2	11	6.5
D	44	17.4	18	10.6
E	29	11.5	17	10.0
F	25	9.9	2	1.2
G	84	33.3	30	17.6
H	10	4.0	9	5.3
Total	252	100	170	100

autumn Asian influenza epidemic. Whereas the Asian influenza epidemic led to a relative increase in the number of admissions in children aged 1 to 4 years, the bronchitis epidemics led to the greatest increases in the admission rate of children under 1 year of age. The ratio of infants to young children admitted was 1.5:1 (98:67) in London, 3.8:1 (19:5) in Guildford, and 1.7:1 (40:23) in Southampton and Christchurch. Whereas Asian influenza frequently led to hospital admission with uncomplicated involvement of the upper respiratory tract, in the December and February outbreaks the diagnoses recorded (Categories D, E, F and G) suggested diffuse involvement of the lower respiratory tract with bronchitis as the common factor in more than two-thirds of the cases (Table 5).

Although the outbreaks in London and Guildford in February 1958 and in Southampton and Christchurch in December 1957 affected the same age group and involved the lower respiratory tract predominantly, there was one difference between them; the term acute bronchiolitis was not once recorded in the December outbreak on the South Coast nor in February in Guildford, whereas this diagnosis was made 25 times during February 1958 in London. It is doubtful whether this represented

TABLE 4

EFFECT OF AUTUMN INFLUENZA EPIDEMIC ON NUMBER OF NOTIFIED DEATHS FROM INFLUENZA, PNEUMONIA AND BRONCHITIS IN LONDON (ADMINISTRATIVE COUNTY)

Week No.	1952		1953		1954		1955		1956		1957		1958	
	Age		Age		Age		Age		Age		Age		Age	
	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years
38	1	0	1	0	0	0	2	0	0	1	1	0	2	0
39	4	0	1	0	2	0	1	1	4	0	3	0	2	0
40	1	0	3	1	3	0	1	0	0	2	2	4	0	2
41	3	1	1	0	2	0	2	0	4	0	2	2	1	0
42	1	0	1	0	1	1	1	0	3	1	3	1	1	0
	10	1	7	1	8	1	7	1	11	4	11	7	6	2

TABLE 6

EFFECT OF FEBRUARY EPIDEMIC ON NUMBER OF NOTIFIED DEATHS FROM
INFLUENZA, PNEUMONIA AND BRONCHITIS IN LONDON (ADMINISTRATIVE COUNTY)

Week No.	1952		1953		1954		1955		1956		1957		1958	
	Age		Age		Age		Age		Age		Age		Age	
	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years
5	5	2	2	1	5	3	5	2	5	0	7	1	6	5
6	3	1	8	5	7	1	5	2	4	0	5	1	5	0
7	1	1	5	1	1	0	6	2	3	2	4	0	10	0
8	3	2	8	2	4	0	2	1	5	1	1	1	5	1
Total	12	6	23	9	17	4	18	7	17	3	17	3	26	6

a true difference in the clinical picture; more probably it was due to a personal preference for interchangeable clinical terms.

The 1958 February bronchitis epidemic in London was unusually severe, more than twice as many infants being admitted as in February 1957. Table 3 shows the number of children requiring treatment in oxygen tents each month in London and in Southampton and Christchurch. This contrasts strikingly with the small number needing oxygen tents during the autumn Asian influenza epidemic in September and October.

Comparable figures for admissions for previous years are not available, but the severity of the epidemic is reflected by the number of notified deaths from influenza, pneumonia and bronchitis in London in February 1958. The number of deaths from influenza, pneumonia and bronchitis reported in the Registrar-General's weekly returns in the two age groups was compared each week with the number of admissions to those hospitals in the London area taking part in this investigation. Not only was there an increase in the number of deaths and admissions throughout February 1958 as compared with other months, but the greatest number of admissions and deaths also occurred in the same week (week 7). The number of notified deaths from influenza, pneumonia and bronchitis in London in February 1958 was also compared with the numbers in February during the previous six years. Table 6 shows that there was an unusually high death rate in 1958 in children under 1 year of age, whereas the figures for children aged 1 to 4 years was not excessive by comparison.

Serological Findings. Table 7 shows that a serological diagnosis was made in 23 (17.4%) of the cases tested. Of these, 15 (11.4%) were due to influenza virus A; one (0.8%) was due to influenza virus C, and seven (5.3%) were due to a virus of

the adenovirus group. In the screening test 91 (69.0%) did not show any evidence of antibodies to the antigens used, but 18 (13.6%) had antibody titres of 1/16 or higher to either influenza virus A, influenza virus C or a virus of the adenovirus group, but no significantly rising titres to any of these. It is probable that, owing to the difficulty of accurately determining the date of onset, the first sample of blood was sometimes taken too late in the illness to show a rising titre, and that the illness was in fact due to the virus to which antibodies were found in the serum. On the other hand, some of the cases in this group may have had antibodies remaining from past infections.

Children with influenza A and adenovirus infection respectively form two contrasting groups which differ in seasonal incidence, in age and in type of illness. Cases of influenza A were found only between September 1957 and January 1958, when Asian influenza was prevalent in Southern England. By contrast, cases of adenovirus infection were distributed throughout the period of this study.

TABLE 7
RESULTS OF COMPLEMENT-FIXATION TESTS

	Age Group			
	<1 Year	1-4 Years	5-12 Years	All Ages
Number of children tested	44	62	26	132
*Positive influenza A	2 (1)	5 (4)	8 (3)	15 (8)
*Positive influenza C	0	1	0 (2)	1 (2)
*Positive adenovirus	1	6 (10)	0 (3)	7 (13)
†Negative to all antigens	40	37	14	91

* Numbers refer to cases showing fourfold or greater rises in complement-fixing antibody. Numbers in brackets refer to cases with a titre of 1/16 or higher but without a fourfold rise. Seven of these showed antibodies to more than one virus.

† Convalescent specimen with complement-fixing antibody titre less than 1/8 to influenza A, B and C, adenovirus group, para-influenza virus 1 (Sendai virus), psittacosis virus, and *R. burnetii*.

The number of influenza virus A infections increased with age, whereas the number of adenovirus infections did not (Table 7). In influenza A, the incidence of infection in those under 1 year was 4.5% (2/44 cases), in children aged 1 to 4 years it was 8.1% (5/62 cases) and in children aged 5 to 12 years it was 30.8% (8/26 cases).

In adenovirus infections, however, six of the seven cases were in the age group 1 to 4 years, an incidence of 9.7% (6/62 cases), and not one case was diagnosed in the 26 children aged 5 to 12 years.

Influenza A seemed to affect predominantly the upper, and adenovirus infection the lower respiratory tract. More than half (8/15) of the cases of influenza A were diagnosed as upper respiratory tract infections (Category A), two as acute laryngo-tracheo-bronchitis (Category C) and only five as either bronchitis or pneumonia (Categories D, E and G).

Only one adenovirus infection was diagnosed as an upper respiratory tract infection and one as acute laryngo-tracheo-bronchitis, whereas five were diagnosed as either bronchitis or pneumonia (Categories D, G and H). Serological results were entirely negative in 90.9% (40/44 cases) of children under 1 year of age, which indicates that the cause of most respiratory illnesses in this age group has not been found.

The agent responsible for the epidemic which occurred in London in February 1958 was not identified.

Discussion

It is of special interest that by chance the period of this study should have included not only an epidemic of Asian influenza but also two outbreaks of an acute lower respiratory tract illness affecting infants. In the influenza epidemic, infants seemed, relatively, to be spared as judged by the number of hospital admissions, the number of notified deaths and the serological evidence. Influenza was most common in schoolchildren, whereas adenovirus infections were most frequently diagnosed in children aged 1 to 4 years. We have followed Garrow and Fawcett (1953) in using the term 'epidemic bronchitis' to describe the outbreaks which chiefly affected infants. Those affected suffered an acute diffuse involvement of the lower respiratory tract as implied by the terms acute bronchitis, bronchiolitis or bronchopneumonia. Since the cause of epidemic bronchitis is unknown, it is not possible to say whether the same or different agents were responsible in each area. Something can be said, however, about their timing and extent:

Southampton and Christchurch on the South Coast, 24 miles apart, were affected simultaneously in December 1957, but neither Guildford, which is some 50 miles inland, nor London were involved at that time. Two months later in February, London and Guildford both experienced an outbreak which did not, however, extend to the South Coast. Although outbreaks of epidemic bronchitis are relatively localized, they are probably the commonest cause of admission of infants to hospital in this country.

Summary

An investigation of acute respiratory illness in children admitted to 10 hospitals in the South West Metropolitan Region is described. Seven hospitals were situated in the London area, one at Guildford and two on the South Coast. The period of study lasted 14 months and included the Asian influenza epidemic and also two outbreaks of epidemic bronchitis.

Serological tests were carried out on 132 children in the London area.

Asian influenza virus infection was more common in children over 5 years of age than in those aged 1 to 4 years, and infants were rarely affected. The influenza epidemic involved London and the South Coast simultaneously. About half of all admissions were for uncomplicated upper respiratory tract infections. Only a few children required treatment in oxygen tents.

Infection with influenza virus was limited to the time of the Asian influenza epidemic, whereas adenovirus infections occurred throughout the period of study and were most commonly diagnosed in children aged 1 to 4 years, who had been admitted with bronchitis or pneumonia.

Epidemic bronchitis occurred as two separate and circumscribed outbreaks, one on the South Coast in December 1957 and one in London in February 1958. The London outbreak extended as far as Guildford. Infants were predominantly affected and were diagnosed either as acute bronchitis, as bronchiolitis or as bronchopneumonia.

Evidence is presented that epidemic bronchitis caused more admissions, more severe illness and, in London, more deaths among young children than did the 1957 Asian influenza epidemic.

We are grateful to Dr. B. D. R. Wilson for help with planning this investigation; to the paediatricians of the South West Metropolitan Regional Paediatric Society for their co-operation, and to Miss P. M. Davis, F.I.M.L.T., for technical assistance.

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APPENDIX A

Hospitals Taking Part in This Investigation

London Area

Kingston Hospital, Surrey
 Lambeth Hospital
 Royal Waterloo Hospital
 St. James's Hospital, Balham
 St. Thomas's Hospital
 Victoria Hospital for Children
 Westminster Children's Hospital

Outside London

Christchurch Hospital
 St. Luke's Hospital, Guildford
 Southampton Children's Hospital

APPENDIX B

Definition of Diagnostic Groups

All admissions of children under 5 years of age were recorded by weeks of admission on a form under *one* of the following eight diagnostic groups.

- A. Acute upper respiratory tract infection (1)
- B. Acute laryngitis (2)
- C. Acute laryngo-tracheo-bronchitis
- D. Bronchitis, wheezy, recurrent or complicating other conditions (3)
- E. Acute bronchitis
- F. Acute bronchiolitis (4)
- G. Bronchopneumonia
- H. Lobar or segmental pneumonia

- (1) Including tonsillitis, but excluding primary herpes simplex stomatitis, diphtheria, uncomplicated otitis media, uncomplicated cervical adenitis, and infectious mononucleosis.
- (2) Including laryngeal stridor with upper respiratory tract infection and acute epiglottitis.
- (3) Other conditions include asthma or eczema, congenital heart disease, fibrocystic disease, bronchiectasis, etc.
- (4) With or without radiological changes.
 Measles, whooping cough and pulmonary tuberculosis were excluded.

By 'uncomplicated' was meant unassociated with an acute respiratory tract infection. It was not intended to exclude children with an acute respiratory infection and incidental otitis media.