Summary

A survey has been made of 1,230 cases of acute bronchiolitis of infancy occurring in a children's hospital over an eight-year period.

It is postulated that bronchiolitis is an acute infection of the whole respiratory tract in babies, caused by the viruses of the common cold, and that secondary infection of some degree is almost inevitable. It is suggested that this dual mechanism of infection applies in other illnesses and other age groups.

The clinical features consist of signs of infection of the upper respiratory tract followed by persistent cough and marked bronchospasm. There are often crepitations at the lung bases and there may be cyanosis and restlessness. The signs vary with the stage of the illness, and it is suggested that acute bronchiolitis cannot be separated clinically from bronchopneumonia in infancy. The acute phase of bronchiolitis seldom lasts for more than a week, but cough and wheeze can persist for another fortnight.

The suggested plan of treatment emphasizes the need for broad-spectrum antibiotics in all cases. Some babies

can be treated at home, and one of the main indications for admission to hospital is the need for oxygen therapy.

The mortality during the period under discussion has been 5.5%. This includes many babies with serious congenital abnormalities. Three out of four babies admitted with bronchiolitis are under 6 months of age, and the death rate is highest in this age group. There is no significant morbidity in infants who recover, and second attacks are rare.

Tables giving details of age, mortality, radiological findings, and treatment are presented.

We wish to record our appreciation of the work done by the medical and nursing staffs of this hospital in the management of these sick babies, and we wish to thank Miss B. D. Stuart for her secretarial assistance.

REFERENCES

- Disney, M. E., Sandiford, B. R., Cragg, J., and Wolff, J. (1960). *Brit. med. J.*, **1**, 1407.
Heycock, J. B., and Noble, T. C. (1956). *Ibid.*, **1**, 438.
McKerrow, C. B., Oldham, P. D., and Thomson, S. (1961). *Lancet*, **1**, 185.
Morrison, B. (1955). *Ibid.*, **2**, 737.

RESPIRATORY SYNCYTIAL VIRUS IN EPIDEMIC BRONCHIOLITIS OF INFANTS

BY

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During the winter of 1956-7 an investigation into epidemic bronchiolitis of infants in Birmingham was carried out (Disney *et al.*, 1960). In the course of it throat swabs, stools, and aspirated lung juices were collected from 73 infants. These were examined by culture in chick embryos, HeLa cells, human amnion cells, and monkey-kidney cells for evidence of a causative virus. Acute and convalescent sera were also examined by the complement-fixation test (C.F.T.) for antibody to influenza, parainfluenza, adeno, Q fever, and psittacosis-lymphogranuloma venereum viruses. No evidence for a causative virus was found (Sandiford, 1960).

After storage for five years at -30° C. some of the sera have been reinvestigated for complement-fixing antibody to respiratory syncytial virus (R.S.V.), which was unknown as a human pathogen at the time of the original investigation.

Materials and Methods Used

The antigen was prepared from the Randall strain of R.S.V. grown on a monocellular layer of R.S.V.-sensitive HeLa cells in a "medical flat" until there was a marked cytopathic effect. The bottle's contents were then frozen and thawed thrice and suspended debris was centrifuged out. The supernatant fluid was titrated, "chessboard" fashion, against rabbit R.S.V. antiserum supplied by Dr. S. Clarke, of Bristol Public Health Laboratory. The optimum dilution of antigen proved to be 1 in 2, and this dilution was used in the C.F.T.s which were carried out in "perspex" plates by overnight fixation at 4° C.

Screening tests on the convalescent sera at a dilution of 1 in 8 were first put up. In cases which showed at

least a 2-plus reaction both acute and convalescent sera were then titrated, starting at a 1 in 2 dilution with the former and at 1 in 8 with the latter.

Results

Thirty-two pairs of sera were available for testing, of which seven were eliminated by the screening test. Of the 25 pairs which were then titrated, 22 showed a fourfold or greater rise in complement-fixing antibodies between individual members of a pair (see Table).

Complement-fixation Tests for Respiratory Syncytial Virus on Infants' Sera

Age	Antibody Rise	Days after Onset during which Rise Occurred
7 months ..	<2 to 128	4-14
4 " ..	<2 " 64	6-16
5 " ..	<2 " 64	8-18
5 " ..	<2 " 64	3-13
3 " ..	<2 " 32	5-15
4 " ..	<2 " 128	5-15
2 " ..	4 " 8	4-11
2 " ..	2 " 8	8-17
5 " ..	<2 " 256	3-13
18 " ..	<2 " 256	5-15
9 " ..	<2 " ≥ 256	8-18
6 " ..	<2 " 128	6-16
3 weeks ..	≥ 16 " 16	4-14
5 months ..	<2 " 256	5-15
12 " ..	<2 " ≥ 256	3-13
5 " ..	8 " 32	4-14
4 " ..	<2 " 32	4-14
3 " ..	2 " 16	4-13
11 " ..	<2 " 256	9-19
2 " ..	4 " 16	2-19
2 " ..	<2 " 256	6-16
1 month ..	4 " 8	3-13
2 months ..	4 " 16	3-13
7 " ..	<2 " 64	1-10
5 " ..	<2 " 16	10-20

Results are recorded as reciprocals of the reacting titres. $\geq$ Means equal to or greater than the recorded titre.

Discussion

R.S.V. was first found in human beings by Chanock *et al.* (1957), who isolated it from two children with pneumonia. Since then its association with many cases of bronchiolitis has been shown by workers in America, and Peacock and Clarke (1961) have recorded its isolation from two cases in this country.

To ensure isolation, specimens should not be frozen before being cultured, and a special strain of tissue culture cells known to be sensitive to R.S.V. must be used. These factors would account for failure to isolate it from the infants in the Birmingham outbreak of 1956-7. All specimens were frozen several times before they were put on to tissue cultures and those used were probably insensitive to R.S.V. But the fact that 68.7% of the 32 convalescent sera tested have shown significant, and mostly very considerable, rises in complement-fixing antibody to R.S.V. indicates that it was the primary cause of the bronchiolitis in the majority of the infants in this outbreak.

As might be expected, better serological responses were given by the older infants, though one only 2 months old attained a titre of 1/256. The reactions shown by the infant of 3 weeks with titres of 1/16 in both sera must have been due to maternal antibody, as were possibly those shown by the two with titres of 1/4 and 1/8 in their paired sera; otherwise this common difficulty in interpreting serological reactions in the very young was refreshingly absent.

Respiratory infection, often of the common-cold type, is frequently present in other members of the household when an infant goes down with bronchiolitis. R.S.V. in older children and adults, many of whom have demonstrable antibodies, usually produces a common-cold type of infection. It is possible that further investigation of winter respiratory infections will show that epidemics of infantile bronchiolitis occur when the prevailing virus in the general population is R.S.V., while the sporadic cases may be associated with other types of respiratory virus.

Summary

Stored sera collected during an investigation of epidemic infantile bronchiolitis in 1956-7 have been investigated for evidence of respiratory syncytial virus infection. The original investigation had failed to show any evidence of a virological cause for the condition.

Out of 32 pairs of sera tested for complement-fixing antibodies to respiratory syncytial virus, 22 have been found to show significant rises of titre.

Thus it is shown that respiratory syncytial virus must have been the main aetiological factor in the outbreak.

REFERENCES

- Chanock, R., Roizman, B., and Myers, R. (1957). *Amer. J. Hyg.*, **66**, 281.
 Disney, M. E., Sandiford, B. R., Cragg, J., and Wolff, J. (1960). *Brit. med. J.*, **1**, 1407.
 Peacock, D. B., and Clarke, S. K. R. (1961). *Lancet*, **2**, 466.
 Sandiford, B. R. (1960). *Mth. Bull. Minist. Hlth Lab. Serv.*, **19**, 74.

The 1962 New Zealand health stamps (1d. from the sale of each stamp is diverted to the maintenance of health camps for children) were placed on sale on October 3. The stamps depict New Zealand birds in their natural colours. The 3½d. denomination shows the kakariki (parakeet) and the 4d. denomination the tieke (saddleback).

ADULT LEUKAEMIAS AND DIAGNOSTIC X RAYS

BY

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The present investigation was designed to detect possible associations between exposure to medical x rays and the subsequent development of malignant diseases in adults, and was modelled on a recent survey of childhood cancers (Stewart, Webb, and Hewitt, 1958).

Method

The earlier survey was restricted to children under 10 years who died between 1953 and 1955, and histories were obtained from parents. The adult survey was restricted to men and women over 20 years of age who were in hospital during 1958-60, and histories were obtained by interviewing patients. On both occasions the survey populations were recruited on a national basis and interviewed on a regional basis; cases and controls were matched for age, sex, and district, and data were collected by medical officers of health (survey doctors). The effects of observer error were randomized by an arrangement which ensured that each interviewer contributed an equal amount to case and control data.

In the childhood survey, leukaemias and cancers were notified by the General Register Office, and each dead child was matched with a live child of the same age and sex who was born in the same district. Both parents were interviewed by the same doctor (case/control pairs), and controls were obtained by asking clerks in charge of local birth registers to compile "short lists" of possible controls (that is, live births with the necessary matching characteristics).

In the adult survey, only leukaemias and lymphosarcomas were notified in the first instance. Details of these cases were supplied by hospital consultants who also undertook to find cancer patients of the same age and sex in the same or near-by hospitals. These "case pairs" were converted into "survey trios" by the addition of healthy controls, who were obtained by asking clerks to local executive councils to compile short lists of possible controls from local registers of N.H.S. patients. Survey trios in different regions were interviewed by different doctors, but each member of a given trio was seen by the same doctor. The leukaemia classification was based on pathologists' reports, copies of which were included in the survey data.

X-ray Data

Survey records of x-ray exposures and illnesses were confined to events which occurred during adult life and preceded the malignant disease (cases) or equivalent date for controls. These so-called *closing dates* marked the onset of symptoms and corresponded to "onset dates" in the childhood survey. For each x-ray attendance

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