Section of Pædiatrics

President M E MacGregor MD

Meeting October 27 1967
held at the Queen Elizabeth Hospital for Children, Hackney, London, to mark the Centenary of the Hospital

Failure to Thrive in Infancy and Early Childhood

A Follow-up Study of the Respiratory Distress Syndrome

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Little is known as yet of the long-term prognosis of infants who recover from the respiratory distress syndrome of the newborn. By 1964 a clinical impression had been gained at Queen Elizabeth Hospital for Children that infants who had made an apparently complete recovery from the acute illness showed an increased liability to serious lower respiratory tract infection during the first year of life. In 1965 an attempt was made to inquire into the subsequent history of these infants.

Material

During the years 1960–4 112 infants were discharged from hospital after recovering from the respiratory distress syndrome (RDS). Letters were sent to the parents of these children at their last known address; if there was no response information was sought from general practitioners, executive councils and maternity hospitals – several mothers had attended with subsequent pregnancies. Because the infants had originally been admitted from many scattered maternity departments the geographical distribution of the recovered infants was very wide, and it was not thought justified at that time to appeal for help to the many local health departments involved.

Of the 112 children 60 attended the follow-up clinic at least once; 7 of these were subsequently rejected because the original diagnosis could not be substantiated from the case notes. Ten cases were added during 1965 making a total of 63 children seen out of a potential total of 122.

Table 1
Age grouping of 122 cases of respiratory distress syndrome (RDS)

Year of birth	*No. of cases of RDS discharged from hospital*	*No. seen at follow up in 1965*
1960	2	2
1961	8	4
1962	21	8
1963	23	14
1964	58	25
1965	10 (not complete year)	10
Total	122	63

Table 1 shows the age grouping of the whole group and of the 63 children who attended.

Procedure

When a child was first seen a full history was taken, paying special attention to respiratory disease and including details of family structure and living accommodation. The child was examined clinically, and a chest X-ray was taken unless there was evidence of an acute respiratory infection in which case X-ray was postponed until recovery from the episode. Chest X-ray was not repeated unless the first follow-up film showed an abnormality.

Lung compliance was measured in 3 infants under the age of 3 months. This was undertaken in the Neonatal Research Group Laboratory at the London Hospital using the Cross body plethysmograph to measure respiratory volumes, and an œsophageal balloon to record changes in intrapleural pressure.

Peak flow rates were measured in 10 of the older children using a Wright peak flow meter.

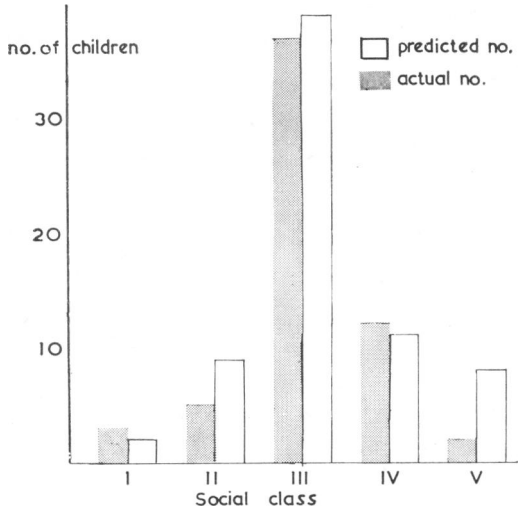

Fig 1 *Distribution of 63 children compared with predicted distribution according to 1951 population census*

These 63 children cannot be regarded as a necessarily representative group. Parents were told that their co-operation was needed to obtain information; it was in no way suggested that their child's health necessitated attendance at the clinic – although advice was given when appropriate. It seems probable that some parents attended because they were already anxious about their child's health and welcomed the invitation to hospital. A considerable proportion appeared to be motivated by an active social conscience. Some children were already attending other hospitals (the only known case of retrolental fibroplasia and the only known case of mental retardation occurring in the 122 children were attending elsewhere). The younger children in particular were attending clinics at the maternity hospitals and welfare centres and their mothers were naturally reluctant to visit yet another doctor.

In view of the hospital's location in East London it was thought that the group would include a disproportionately large number in Social Classes IV and V (General Register Office 1960) and that this would distort the findings of disease incidence. This did not occur; the distribution of Social Class corresponds closely to the 1951 Census figures for the general population (Fig 1).

It was expected that a high proportion of the group would have been prematurely born, and that these infants would show an increased illness rate in the first year of life (Drillien 1964). Forty-six of the 63 infants weighed less than 2·5 kg at birth; 5 of these were born at or near term.

Although mothers were apparently able to remember all but trivial illnesses in their child's first year, they could not be expected to recall all respiratory illness in subsequent years. Respiratory illness was graded by the most severe episode in a given year. The number of individual disease incidents was not counted; for example a child having one attack of bronchitis and two or three severe colds in one year is only recorded as having bronchitis.

The following classification of respiratory illness was adopted:

Serious respiratory illness: Bronchiolitis or bronchopneumonia invariably requiring hospital admission on medical grounds and associated with severe constitutional disturbance.

Bronchitis: Cough, with pyrexia and general malaise often associated with wheeze and sometimes with dyspnœa.

Chesty colds: A description often used by mothers – coryza, with cough and short-lasting anorexia and general malaise. Minor colds were not included.

Findings

Respiratory disease (Table 2): The retrospective classification of respiratory illness cannot be entirely satisfactory, but the diagnosis of serious respiratory illness is supported by hospital records and is least open to doubt. Eleven children suffered such an illness in the first year of life, 4 of these were full-term infants and 7 premature. Spence *et al.* (1954) used the term pneumonia to

Table 2
Respiratory illness in first year of life

Birth weight (kg)	*No. of children*	*Most serious respiratory illness in first year of life*			*Total affected as percentage of children at risk●*	*Drillien (1964): No. of disease incidents per 100 children at risk*
		Pneumonia or bronchiolitis	*Bronchitis*	*Chesty cold*		
<2·04	29	5	3	2	34·5	72·4
2·05–2·5	17	2	1	4	41	59·7
>2·5	17	4	3	4	64·5	46·8

● These figures must underestimate the number of disease incidents (*see* text)

describe 'an acute respiratory illness with severe constitutional disturbance, rapid breathing, frequent short and ineffectual cough, movement of the nostrils and sometimes cyanosis'. It seems reasonable therefore to compare the incidence of bronchopneumonia and bronchiolitis in this series with the incidence of pneumonia reported by Spence from Newcastle. Out of 1,011 children under the age of 1 year in Newcastle 5% suffered pneumonia whereas 17·5% of the 63 children in the present series suffered bronchopneumonia or bronchiolitis. This difference is significant ($P < 0·001$) and even if the 11 cases are related to the 122 potential propositi (assuming there was no serious respiratory illness among the children not seen) the incidence is still significantly increased ($P < 0·05$). The incidence of bronchitis, severe colds and specific fevers was similar in both groups.

Drillien (1964) reported the number of disease incidents per 100 children at risk for each year of life and found the highest number of disease incidents among the children of lowest birth weight. The figures for the present series must underestimate the number of disease incidents as in effect only one disease incident (the most severe) was noted for each child. It is surprising therefore to find in the present series that there was more respiratory illness in the heavier birth weight group than was reported by Drillien.

The number of children over the age of 1 year whose history was adequately documented was too small to allow comparisons.

In the present group the incidence of respiratory disease was not shown to be associated with low income, home crowding or severity of initial illness.

Physical signs: The only abnormal physical sign occurring with any frequency was a sulcus above the rib margin; this had persisted past the age of 2 in 9 out of 27 children so affected.

Chest X-rays: Dr C J Hodson reported on all the films. Air trapping was the commonest abnormal finding in children under the age of 1 year; it was seen in 7 out of 18 of these children but did not usually persist on repeat X-ray. One infant (birth weight 1·25 kg) showed definite persistent emphysema to the age of 9 months.

Pulmonary fibrosis as described by Shepard *et al.* (1964) was not seen in any of these children.

Growth: The rate of weight gain was satisfactory throughout the group apart from minor feeding problems. One child had been investigated as a case of failure to thrive after a severe episode of gastroenteritis.

Lung function tests: The studies on compliance in the younger children will be the subject of a later communication. Lung compliance was lower than expected in all cases. Peak flow rates in 10 children aged 2½–5 years was well within the normal range reported by Rivera & Snider (1962).

Thus there is evidence to suggest that infants who have survived the respiratory distress syndrome of the newborn show an increased susceptibility to serious respiratory illness in the first year of life and that this risk is not related to birth weight. There is no evidence to suggest that any handicap remains after the first year.

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Demonstrations

Hereditary Metabolic Disorders Involving the Urea Cycle

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Three types of hereditary enzyme defects in the biosynthesis of urea have been described in the last ten years. The first was argininosuccinic aciduria resulting from a deficiency of argininosuccinase (C) (Table 1); the second, hyperammonæmia, arising from a deficiency of ornithine transcarbamylase (A); and the third, citrullinæmia, arising from a defect in argininosuccinate synthetase (B). A fourth possible type, deficiency of arginase (D), has not yet been described, although inhibition of this enzyme by lysine has been postulated as the cause of chronic ammonia intoxication in lysine intolerance. Examples of the first two types are presented.

Case 1 *Argininosuccinic Aciduria*
This male infant appeared normal till the second day of life when he became lethargic and reluctant to feed. His condition deteriorated, he became cyanotic, developed grunting respiration and