Deaths Associated with Respiratory Tract Infection in Childhood*

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The number of children who die from respiratory tract infections has decreased markedly during the period in which antibacterial drugs have become available. The figures given in Table I illustrate this point clearly, but they also show that such deaths have by no means been eliminated and that the extent of the improvement is much less among infants than among older children.

TABLE I.—Numbers of Children Who Died in Newcastle upon Tyne from Lower Respiratory Tract Infections

Age in Years	No. of Deaths During			Approximate Ratio of Deaths 1931-5 to 1961-5
	1931-5	1946-50	1961-5	
<1	416	206	73	6:1
1-4	294	24	6	50:1
5-14	52	6	5	10:1
Total	762	236	84	9:1

This table is based on figures for deaths from bronchitis or pneumonia given in the appropriate Annual Reports of the Medical Officer of Health for the City and County of Newcastle upon Tyne. Virtually all deaths from non-tuberculous lower respiratory tract infections were included under these two diagnoses.

In the course of an extensive survey of respiratory tract infection in children in the Newcastle area we have obtained information about 22 children with such infections who died during the period October 1964 to December 1966 and who fulfilled the following conditions: that they were admitted to hospital before they died; that they came to necropsy; and that bacteriological and virological investigations of their infections were carried out either before or after death, or both. We have analysed our data in an attempt to find out why these children died, and have paid particular attention to information on three subjects: the presence of conditions which might have made the children unduly liable to succumb to infection; the nature of the infecting organisms; and any features of the children's clinical conditions which might suggest the mechanisms of death and measures that might have prevented it. These children are admittedly a selected group; "cot deaths," for example, were excluded by our criteria. Our information is incomplete at many points, but it is sufficient to provide a valid, even though only a partial, picture of respiratory tract infection as a continuing threat to the lives of young children.

Methods of Investigation

In addition to clinical examination and assessment the children were investigated as follows:

Bacteriology.—Nasal and cough swabs for bacterial culture were collected from 13 children shortly after they were admitted to hospital. No such swabs were collected from the other nine, many of whom died within a few hours of admission, but blood cultures were set up from two of them before they died. Heart and lung punctures were carried out within 15 minutes after death in 11 cases; the resulting fluids were inoculated into Robertson's cooked meat medium, which was placed in a 37° C. incubator as soon as possible

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and was subcultured to solid media when visible growth occurred. Necropsy tracheal or lung swabs were collected in 13 cases. In one case a small amount of broth was injected submucosally into the swollen epiglottis at necropsy and then withdrawn and used for inoculating cultures for *Haemophilus influenzae* (Jones and Camps, 1957).

Virology.—Nasal and cough swabs collected from 11 children shortly after admission were transported to the laboratory and examined there as previously described (Elderkin *et al.*, 1965). Lung tissue for virus culture was collected at necropsy, up to 48 hours after death, in 21 of the 22 cases. Such tissue was homogenized in 10 times its own volume of medium 199 and then lightly centrifuged, and the supernatant fluid was used for inoculating tissue cultures. The cell lines used for cultures of swabs and of lung tissue were HeLa, Hep II, rhesus monkey kidney, and human diploid cells (W.I.38).

Pathology.—Seven pathologists carried out necropsy examinations of children in this series, but two of us, who had carried out nine of the necropsies, each examined histological sections of lung from all 22 cases. Final pathological classification of respiratory tract conditions was based on the following combinations of findings: *epiglottitis*—oedema, hyperaemia, and neutrophil infiltration of the epiglottis; *bronchitis*—mucosal oedema, enhanced mucus formation, and neutrophil infiltration confined to the bronchi; *bronchiolitis*—inflammatory exudate in the intralobular air passages but little or none in the surrounding pulmonary alveoli, the inflammatory cells being in some cases mainly neutrophils within the lumina and in other cases mainly lymphocytes within the walls of the bronchioles; *pneumonia*—inflammatory exudate and infiltration involving the pulmonary alveoli. We hope to publish elsewhere further details of the pathological findings in the lungs.

Findings

Nine of the 22 children were boys and 13 were girls. Eighteen were 6 months old or less and only three were more than a year old. Most of the illnesses were short—three days or less in eight cases and four to seven days in seven cases. Eleven children died within 24 hours of admission to hospital, four of them within the first two hours.

Classification of the patients according to the findings shown in Table II provides a satisfactory basis for a description of the main features of their illnesses. This is followed by a review of the treatment given and of certain additional aspects of their conditions to which we wish to draw attention.

Twenty-two Patients Classified According to Pathological and Microbiological Findings

The first six children (Cases 1-6) apparently died from bacterial infections. The first two had staphylococcal pneumonia with characteristic multiple lung abscesses. One of them (Case 1) had a pyopneumothorax when she reached hospital five days after the onset of her illness; she died two days later. The other (Case 2) did not receive any medical attention for nearly a week after he became ill; he died one hour after reaching hospital.

The child with epiglottitis (Case 3) was moribund when he reached hospital, having been treated for cardiac arrest during

the journey, and his breathing was maintained by positive-pressure ventilation from the time of his admission. He had had a mild coryzal illness for about a week but had been seriously ill for only a few hours—a common sequence of events in this often lethal disease (for references see Turk and May, 1967). *H. influenzae* type b, the expected causal agent, was isolated at necropsy from this child's grossly inflamed and swollen epiglottitis, but an additional and unexpected finding was the isolation of respiratory syncytial virus (R.S.V.) from his upper respiratory tract before death and also from his necropsy lung specimen.

A 1-month-old infant with multiple congenital haemangiomas of her face and liver (Case 4) died within 12 hours of becoming seriously ill with streptococcal septicaemia and pneumonia, probably secondary to infection of her facial lesions.

Each of the two remaining children in this group (Cases 5 and 6) had for several weeks before death received continuous antibiotic treatment for bacterial superinfection of pulmonary mucoviscidosis; and in each case highly antibiotic-resistant bacilli, such as had been found in the upper respiratory tract during life, were isolated from tracheal swabs taken at necropsy and were thought to have been responsible for the terminal pneumonia. Details of the antibiotic treatment are given below.

One child (Case 7) was admitted to hospital two days after she became ill. She had pneumonia, with radiological appearances suggesting that it was staphylococcal. She seemed to make good progress on treatment with cloxacillin and ampicillin, but eight days after admission she suddenly collapsed and died. Necropsy revealed that as well as pneumonia, which was showing evidence of resolution, she had an unexplained area of myocardial necrosis, and this was thought to have been responsible for her death.

Four children (Cases 8 to 11) all had pneumonia for which no bacterial cause was found. All were ill for less than five days, and all died within a few hours of admission to hospital. R.S.V. was isolated from necropsy lung specimens in every case. Two of the children had congenital heart abnormalities—endocardial fibroelastosis (Case 10) and a large ventricular septal defect associated with mongolism (Case 11)—and one (Case 9) was found at necropsy to have acute myocarditis.

Nine children (Cases 12 to 20) had bronchiolitis. In seven the illness lasted only two to five days; one of these (Case 16) had previously undergone right upper lobectomy for congenital emphysema. One child (Case 13) had been treated with tetracycline for bronchitis three weeks before admission, following which she vomited blood and remained unwell, with diarrhoea. When she came into hospital with an exacerbation of her respiratory tract condition two days before she died she was markedly dehydrated, and at necropsy was found to have a sagittal sinus thrombosis as well as bronchiolitis. The

remaining child (Case 15) had a patent ductus arteriosus and an atrial septal defect and had been intermittently ill for six of his 12 weeks of life; he died two days after admission. R.S.V. was isolated from three of these nine children.

Two children (Cases 21 and 22) collapsed and died unexpectedly while under treatment for what appeared to be relatively mild respiratory tract infections, of 19 and 11 days' duration respectively. In each case the only respiratory tract abnormality found at necropsy was a mild bronchitis, not apparently sufficient to explain death; but one child, a mongol, was found to have a small atrial septal defect and the other to have endocardial fibroelastosis. R.S.V. was isolated from the upper respiratory tract of the first of these two children before he died.

Antibiotic Treatment

Only seven of the 22 children had been treated with antibiotics before coming to hospital. The two with mucoviscidosis had both received penicillins. One of them (Case 5), who had had phenoxymethylpenicillin for two days before admission, was treated with benzylpenicillin and cloxacillin throughout her three weeks in hospital and with polymyxin B (to which her *Pseudomonas* was sensitive *in vitro*) for the last four days. The other (Case 6) had been on ampicillin for several weeks before admission, and received benzylpenicillin, cloxacillin, and chloramphenicol during her five days in hospital; her *Proteus* was resistant to the penicillins but chloramphenicol-sensitive. Five children had been treated with tetracyclines before admission. These included one with staphylococcal pneumonia and pyopneumothorax (Case 1), who had been so treated for two days and who received cloxacillin (to which her staphylococcus was sensitive) and benzylpenicillin for the two days that she was in hospital; the child mentioned above as having had tetracycline three weeks before admission (Case 13), who received cloxacillin and chloramphenicol during her two days in hospital; and three others (Cases 11, 17, and 22) whose tetracycline treatment had lasted for one to three days and who died within 12 hours of reaching hospital.

Six of the 15 children who received no antibiotics before coming to hospital (Cases 2, 4, 8, 9, 14, and 20) died within 12 hours of admission, and the details of their treatment are thus of little importance. The child with haemophilus epiglottitis (Case 3) was treated with an appropriate antibiotic (ampicillin) but was moribund before this treatment began. It seems likely that one child (Case 7) was being successfully treated for staphylococcal pneumonia with cloxacillin, as already described, when she died from myocardial necrosis. The remaining seven children (Cases 10, 12, 15, 16, and 18–20), received benzylpenicillin, cloxacillin, ampicillin, tetracyclines, or combinations of these drugs for periods of between

TABLE II.—Pathological and Microbiological Findings

Case No.:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Age in months	1	36	21	1	4	5	1	1	1	4	6	1	2	3	3	4	5	6	9	22	2	4
Necropsy findings:																						
Epiglottitis			x																			
Bronchitis																						
Bronchiolitis												x	x	x	x	x	x	x	x	x	x	x
Pneumonia	x	x	m	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Congenital abnormalities																						
{ Heart																						
{ Other																						
Myocardial lesions																						
Potential pathogens isolated:																						
Bacteria ante mortem from	S	—	—	PS	Pr	S	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
{ Upper respiratory tract																						
{ Blood culture				A	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Bacteria post mortem from	S	S	H	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
{ Epiglottitis																						
{ Heart/lung punctures	S	S	—	A	P+	Pr	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
{ Tracheal/lung swabs																						
Viruses ante mortem from upper	—	—	R	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
{ Respiratory tract																						
{ Lung tissue	—	—	R	—	—	—	—	R	R	R	R	R	—	R	—	R	—	—	—	—	R	—

m = Pneumonia of minor degree, thought to have been less important than findings marked x. S = *Staphylococcus aureus* (all 3 isolates from Case 1 were of the same phage-type). P = *Pseudomonas pyocyanea*. Pr = *Proteus* sp. H = *Haemophilus influenzae* type b. A = *Streptococcus pyogenes*, Lancefield Group A. R = Respiratory syncytial virus. — = Cultures carried out but no relevant organisms isolated. + = Various intestinal-type Gram-negative bacilli, isolated only from necropsy lung swabs and therefore of doubtful significance.

16 hours and five days, but there is no evidence that they were suffering from bacterial infections.

Among the patients with no bacterial explanation for their infections (Cases 8–22) there were only four who had received antibiotics (tetracyclines in every case) before coming to hospital.

Other Forms of Treatment

All 22 children were treated with oxygen at some time, either in tents or by intermittent positive-pressure respiration. Intravenous fluids were given to five, including three who were hyperpyrexial on admission (rectal temperature 105° F. (40.6° C) or more). Ice-packs were used in treatment of one of these and of two other hyperpyrexial children. (In contrast to these, eight children had rectal temperatures of 100° F. (37.8° C.) or less on admission; we have found no correlation between temperature levels and pathological or microbiological findings.) Nine children were given digoxin for cardiac failure; these included four of the seven children with congenital or acquired heart lesions, but not the two whose cardiac abnormalities were unsuspected before necropsy (Cases 21 and 22) nor the child with a ventricular septal defect (Case 11) whose hopeless condition on arrival in hospital is described below. Eight children received hydrocortisone or prednisone; further information about six of these is given below.

Mode of Death

As indicated in our introduction, we have been concerned to discover not only why these children died—that is, the aetiology of their fatal illnesses—but also how they died, in the hope of seeing whether their lives could have been saved by measures other than those which were employed.

Cardiac Arrest.—This occurred in three cases. The heart of the child with a patent ductus arteriosus (Case 15) stopped suddenly while she was undergoing bronchoscopy for treatment of massive pulmonary collapse, having been successfully treated in this way twice in the preceding 24 hours; cardiac massage was ineffective. The heart of the child with epiglottitis (Case 3) also stopped suddenly, while he was on the way to hospital, but it responded to massage; however, he never breathed spontaneously after admission, and by the next day had ceased to show any evidence of cerebral function. One other child (Case 19) had a similar story except that his heart stopped and was started again by external massage on four occasions during his last three days.

Cardiac Failure.—One child (Case 10) suddenly became deeply cyanosed and showed signs of cardiac failure several hours after admission. He was treated with digoxin and hydrocortisone but died 10 hours later. Necropsy confirmed that he was in cardiac failure as well as having pneumonia, and also revealed that he had endocardial fibroelastosis. (As already stated, eight other children were treated for cardiac failure, but in none of these cases was it a principal cause of death.)

Sudden Collapse.—Thirteen children collapsed suddenly, becoming pale, hypotonic, and unresponsive to stimuli, with shallow irregular or gasping respirations but without cardiac arrest. These 13 included only one of the six children whose deaths were apparently due to bacterial infection. This child (Case 1) and six others (Cases 7, 8, 12, 16, 21, and 22) all died within minutes of collapsing. The remaining six children in this group (Cases 9, 13, 14, 17, 18, and 20) survived for periods ranging between one hour and two days; four of them were treated with hydrocortisone or prednisone after they collapsed, with little or no appreciable effect. One of those who died quickly had received prednisone for 36 hours before her terminal collapse. Four of the 13 children had convulsions—one as a prelude to terminal collapse and the others between collapse and death.

Gradual Deterioration.—Four children with bacterial pneumonia (Cases 2, 4, 5, and 6) became progressively more ill after admission and died without any notable terminal features to their illnesses. However, one of them (Case 4) was in a collapsed state when admitted six hours before she died, and may have been so as the result of a sudden episode. Finally, the child with mongolism and a large ventricular septal defect (Case 12) reached hospital moribund, with a rectal temperature of 108° F. (42.2° C.) and extensive bilateral pneumonia. He died two hours later.

Seasonal Incidence

Table III shows that most of the deaths occurred during the winter months, and that nearly all of those not attributable to bacteria occurred at times when bronchiolitis is commonest in this community (Elderkin *et al.*, 1965) and when R.S.V. was widely distributed, as judged by the frequency with which we isolated it from children with respiratory tract infections who were admitted to hospitals in this city.

Discussion

It is clearly necessary to be cautious when drawing conclusions from the findings presented here. As we have said, these 22 children are not representative of all who die while suffering from respiratory tract infections; and there are obvious limitations to a discussion of treatment which is based solely on data about fatal cases. However, despite these reservations a number of important facts and indications can be discerned among our findings.

Congenital Abnormalities

Nine of the 22 children had major congenital abnormalities, which probably helped to determine the fatal outcome in each case. Of the five children with congenital heart abnormalities, one (Case 10) died mainly as a result of congestive cardiac failure, one (Case 15) from cardiac arrest during bronchoscopy, and two (Cases 21 and 22) from sudden collapse for which their relatively mild respiratory tract infections did not provide sufficient explanation; the fifth child had extensive bilateral

TABLE III.—Comparison between Months of Death of the 22 Children and Monthly Totals of R.S.V. Isolations from Children Admitted to Newcastle Hospitals with Respiratory Tract Infections

	1964			1965												1966											
	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D
Time of deaths																											
Cases 1 to 7															1	1				2				1		1*	1
with R.S.V. isolations ..			1	2	1	1			1						1			1							2	2*	1
Other cases	1						1																				
Numbers of R.S.V. isolations																											
from children with respira-																											
tory tract infections ..	2	6	21	17	8	12	6	4		4	2	2	1	3	7	7	6	2							5	23	9

* Case 3 (*H. influenzae* and R.S.V.) is recorded in both lines.

pneumonia, but his large ventricular septal defect must have added to his respiratory distress. Pulmonary mucoviscidosis commonly leads, as in two cases in this series, to a prolonged and ultimately unsuccessful fight against bacterial superinfection. Congenital facial haemangiomas were probably the portal of entry of the streptococci which killed one child. Lobectomy for congenital emphysema, even when carried out in infancy, leads to permanent impairment of vital capacity, and presumably also of ability to survive serious pulmonary infection (DeMuth and Sloan, 1966).

The frequent association of congenital abnormalities with death during respiratory tract infection in early childhood was noted in a previous report from Newcastle (Elderkin *et al.*, 1965) and has also been found by G. A. Neligan (personal communication, 1967) in follow-up studies of 13,430 single legitimate live births occurring in Newcastle during 1960–2. Of these children, 108 died between the ages of 1 month and 1 year, and of those who came to necropsy 18 were found to have had respiratory tract infections at the time of death, with associated major congenital abnormalities in five cases.

There is nothing original about the observation that children with congenital abnormalities, particularly those of heart or lungs, have a reduced chance of surviving respiratory tract infections; but the high proportion of children with such abnormalities in these series of fatal cases is noteworthy, and helps to explain why respiratory tract infections continue to have a relatively high mortality rate among young children.

Pathogenic Organisms

Only 6 of the 22 deaths in our series were demonstrably attributable to bacterial infections; one other child died from an unexplained complication of a pneumonia probably caused by staphylococci. The pneumococcus, principal agent of fatal respiratory tract infections in pre-antibiotic days, apparently played no part in our series. Our failure to find possible bacterial causes for the illnesses of 15 of the 22 children is all the more significant because only four of them had received antibiotics before coming to hospital. Furthermore, in many cases we were able to culture heart blood and lung aspirate collected a few minutes after death, and we think it unlikely that bacteria responsible for fatal pulmonary infections would commonly escape detection by such means.

R.S.V. was isolated from 3 of the 11 children from whom appropriate upper respiratory tract swabs were collected during life, and from necropsy lung tissue of 8 out of 21 children. The first of these findings can be compared with figures from a survey of our own, to be published in more detail elsewhere, in which we isolated R.S.V. from the upper respiratory tract swabs of only 4 out of 295 children admitted to hospital with no clinical respiratory tract infection; but we have no information about the frequency with which this virus can be isolated from the lungs of children who die from non-respiratory causes. The significance of our high rate of isolation of R.S.V. from the 22 fatal cases is enhanced by the fact that we isolated no other viruses from their respiratory tracts, despite the wide range of culture procedures used. It is of interest that we isolated R.S.V. from the lungs of all four children who died of non-bacterial pneumonia, but from the lungs of only three of the nine who died of bronchiolitis. The latter condition is known to be predominantly due to R.S.V., in Newcastle (Elderkin *et al.*, 1965) as elsewhere (Chanock *et al.*, 1961; Beem *et al.*, 1962), and though we do not know of conclusive evidence that it is also the predominant cause of fatal bronchiolitis, it seems likely that this is so. A possible explanation of our findings is that R.S.V. survives better in pneumonic lung than in bronchiolitic lung after the death of the patient, but there are many other possibilities.

R.S.V. infection was the presumptive cause of death in four cases of pneumonia and in three cases of bronchiolitis, and was

found in the upper respiratory tract of one other child who died with only minor pathological changes in his respiratory tract. The isolation of R.S.V. as well as *H. influenzae* type b from the respiratory tract of the child with epiglottitis may have been coincidental; but since pathogenic collaboration between viruses and this bacterial species has been postulated in various conditions and demonstrated in some (see Turk and May, 1967), the suggestion that R.S.V. plays a part in the aetiology of haemophilus epiglottitis cannot be dismissed out of hand.

Speed of Diagnosis and Treatment

Several of the children were desperately ill before they reached hospital, and in some cases before any medical help was sought. Of the two who died of staphylococcal pneumonia, one might have survived if she had received a more appropriate antibiotic than tetracycline during the early days of her illness, and the other if he had come under medical care before he had been ill for a week. Haemophilus epiglottitis is virtually always a necropsy diagnosis in Britain (Jones and Camps, 1957; Johnstone and Lawy, 1967), but in those parts of the U.S.A. where the condition is well known, promptly diagnosed, and treated by immediate tracheotomy and administration of appropriate antibiotics the recovery rate is high (Berenberg and Kevy, 1958). We suspect that more young children die of haemophilus epiglottitis in this country than the number of recognized and reported cases indicates, and that prompt recognition and treatment might save quite a number of lives. However, the one child with this condition in our series was moribund within about half an hour of being found in a state of severe respiratory distress, and his life could have been saved only by remarkably rapid and well-informed action. The fulminating course of the case of streptococcal septicaemia and pneumonia also left very little time for diagnosis and treatment, especially as there were no strong clinical indications of the nature of the infecting organism. It is impossible to assess the extent to which earlier diagnosis and treatment might have improved the prognosis of any of the children whose infections were apparently not bacterial.

Antibiotic Treatment

Apart from the suggestions made in the preceding paragraph it does not appear that better use of existing antimicrobial drugs would have prevented the deaths of any of the children in this series; but it seems likely that if effective antiviral agents become available there may be a further considerable fall in the mortality rate of respiratory tract infections in early childhood.

Other Forms of Management

Sudden and substantially irreversible collapse was a prominent clinical feature of the illnesses of many of these children, as it was in many of the cases of bronchiolitis reported by Hubble and Osborn (1941) and by Disney *et al.* (1960). The mechanisms underlying such collapse are obscure, and we do not know what parts dehydration and hypoxia play in its production. Some of the children in our series were given intravenous fluids and all received oxygen, but hardly any biochemical investigations were carried out to determine the extent of their need for such treatments and the adequacy of the measures employed. Morrison (1955) showed that oxygen tents, as commonly used, may fail to supply enough oxygen to children with acute respiratory tract infections. Simpson and Flenley (1967) confirmed that administration of 40% oxygen cannot be relied upon to produce normal levels of arterial oxygen tension in such cases; they also showed that clinical signs of respiratory distress are not to be trusted as indices of blood-gas levels, and that uncorrected respiratory acidosis in such

children carries a poor prognosis. Their work thus suggests that repeated direct measurements of arterial blood-gas and pH levels might do much to improve the management of children with severe respiratory tract infections; we would add that repeated electrolyte determinations might also be of value. The use of modern microtechniques greatly reduces the extent to which such investigations disturb a sick child. The mortality rate associated with respiratory tract infections in childhood seems more likely to be reducible by such an approach than by any other at present available to us.

Summary

Of 22 children with respiratory tract infections who died in Newcastle and Durham hospitals during a 27-month period, 19 were less than 1 year old. Nine had major congenital abnormalities. Bacterial infections were apparently responsible for only 6 of the 22 deaths. Respiratory syncytial virus was the only potential pathogen isolated from eight of the children; it was isolated from necropsy lung specimens in seven of these cases, including all four cases of pneumonia with no apparent bacterial cause; and it was also isolated from the upper respiratory tract and the lung of a child with haemophilus epiglottitis. No other viruses were incriminated in any of the 22 cases. Sudden and substantially irreversible collapse was a common feature, especially in the cases not apparently caused by bacteria. Investigation of the blood-gas levels and

biochemical changes in such children is suggested as the most promising approach to improved management.

We gratefully acknowledge the use of clinical notes and reports by numerous colleagues at the Royal Victoria Infirmary (11 cases), Newcastle General Hospital and Dryburn Hospital, Durham (five cases each), and Walker Gate Hospital, Newcastle (one case); also of necropsy reports on the five Dryburn Hospital patients by Dr. J. E. Ennis and on eight of the infirmary patients by Drs. T. Ashcroft, C. Ashton, A. R. Morley, and A. Talerman; and of histological sections of the lungs from all these patients. We are indebted to many of our laboratory colleagues for technical assistance, and also to the Scientific and Research Subcommittee of the United Newcastle upon Tyne Hospitals for their continued support. During this work one of us (M. D. H.) held a research grant from the Medical Research Council.

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Further Experience of Reactions, Especially of a Cerebral Nature, in Conjunction with Triple Vaccination: A Study Based on Vaccinations in Sweden 1959-65

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The previous report concerning reactions in conjunction with triple vaccination in Sweden during the period 1954-8 (Ström, 1960) aroused considerable attention and also criticism (Malmgren *et al.*, 1960; Hellström, 1962). To question the propriety of recommending universal vaccination against whooping-cough in all circumstances and in all countries was naturally a serious matter. Even if the predominant view is still that pertussis vaccination is of such value that it should be universally recommended, certain authorities (Wilson and Miles, 1964; Herrlich, 1965; Ehrengut, 1966) express some doubt on the point.

However, one absolute requirement must be that the complications occurring in connexion with vaccination are carefully observed and recorded. It is also important to note whether in due course the incidence or the severity of the side-effects is reduced. A further requirement is to ascertain whether the complications that may occur are likely to affect the incidence and fulfilment of vaccination.

Material.—A study was made of children under the control of child welfare clinics. Every vaccination clinic was sent an annual questionnaire for notification of reactions that had occurred. All children's hospitals in the country were asked to report annually concerning treated cases of postvaccinal complications. For the years 1962-4, furthermore, special reports were requested from the welfare clinics on whether vaccination had been carried out.

Results

Table I shows the various types of cerebral reactions observed. Of the 167 cases 81 were admitted to hospital.

TABLE I.—Cerebral Reactions in Conjunction with Triple Vaccinations 1959-65

Year	Cerebral Injury	Convulsions	Hyps-arrhythmia	Shock	Irritability + Abnormal Spinal Fluid	Abnormal Screaming	Total
1959	1	7	1	3		4	16
1960		5	1	7		3	16
1961		12		3		1	16
1962	1	12		5		1	19
1963		9	2	9		1	21
1964	1	11		11		4	27
1965		24		16	2	10	52
	3	80	4	54	2	24	167

Cerebral injury was thus reported in three cases, which are described in some detail.

Case 1.—The child was said to have developed normally. The first injection was given at the age of 5 months. The patient was febrile for two to three days, and for one week was very drowsy. The second injection, given six weeks later, produced the same reaction, but the child then became extremely listless, "did not react to anything," and convulsive attacks started one week after the injection. The attacks increased in frequency and duration and were followed by rapid mental regression. E.E.G. showed great paroxysmal activity. While the child was in hospital, at 7 months

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