DEATHS IN CHILDHOOD DUE TO INFECTION

BY

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Considerable attention has recently been paid to the group of sudden deaths in early childhood described as "cot deaths". Whereas Banks (1958) attributed most of the cases in his series to acute bacterial or viral infection, Valdes-Dapena and Hummeler (1963) and Cooke and Welch (1964) were able to elucidate only approximately one-quarter of their cases. However, where definite diagnoses could be made, infection predominated. This was also the experience of Coe and Hartman (1960). In contrast, relatively little attention is now paid to the role of infection in the general mortality of childhood. Yet throughout this period, infection remains not only the principal source of morbidity but is also a leading cause of death.

From Table I it can be seen that in Scotland, while the total number of deaths in the adult group aged 15 to 55 years has almost halved over the past 30 years, there has been an 11-fold drop in the number of deaths which can be ascribed to infection, so that these now represent only 7 per cent. of the total mortality. Among infants aged 3 months to 1 year the total mortality is now less than one-sixth of its former level and there has been a 10-fold drop in infective deaths, yet more than 50 per cent. of all

deaths are still apparently due primarily to infection. In the age group 1 year to 15 years, the total mortality is now also less than one-sixth of its former level, but there has been a 20-fold decrease in the number of infective deaths. Nevertheless, infection still seems to account for one-quarter of all deaths in this age group. The total numbers in each of the three age groups are closely comparable during the two periods under consideration.

NATURE OF FATAL INFECTIONS IN CHILDHOOD

Table II (overleaf) gives the main certified causes of the deaths in childhood which can be ascribed to infection for the periods 1930 to 1932 and 1960 to 1962. While there have been marked falls in the death rates from all the infective causes in both age groups, certain infective conditions are now relatively more important. Thus pneumonia and bronchitis in the younger age group formerly accounted for 46.5 per cent. of infective deaths but now represent 66.5 per cent. A similar relative increase is seen in the older age group. In this age group too deaths due to gastro-enteritis formerly constituted 4.0 per cent. of infective deaths, but now account for 9.2 per cent. Similar proportionate increases are seen in the case of meningococcal infections in both age groups.

A detailed inquiry into the factors underlying infective deaths in childhood at the present time is facilitated in the Edinburgh area by the existence of a Regional Paediatric Pathology Service. In 1962, the total population in the area was 737,178 (1.3 per cent. of the population of Great Britain), of whom approximately 169,000 were aged from 3 months to 14 years. Rather more than three-quarters of the population is urban. It is estimated that comprehensive pathological investigations are carried out on more than 80 per cent. of children who meet non-violent deaths locally. "Cot deaths", however, when

TABLE I

DEATHS AMONGST CHILDREN AND ADULTS IN SCOTLAND ATTRIBUTABLE TO INFECTION DURING THE PERIODS 1930-32 and 1960-62¹

Age Groups	Approximate Triennial Totals (millions)	No. of Deaths			
		1930-32		1960-62	
		Total	Infective ^a	Total	Infective ^a
3 to 11 mths	0.2	9,681	8,155 (84)	1,480	770 (52)
1 to 14 yrs	3.7	15,641	11,592 (73)	2,273	554 (24)
15 to 55 yrs	8.2	44,211	18,160 (41)	23,673	1,601 (7)

¹ Calculated from the Annual Reports of the Registrar General for Scotland and from supplementary data supplied by the Registrar General.

^a Percentages of total deaths given in parentheses.

TABLE II
DEATHS ATTRIBUTABLE TO INFECTION AMONGST
CHILDREN IN SCOTLAND DURING PERIODS
1930-32 and 1960-62¹

Certified Causes of Death	Infective Deaths in Age Groups*			
	3 to 11 mths		1 to 14 yrs	
	1930-32	1960-62	1930-32	1960-62
Pneumonia	3,187 (1,770.5)	441 (220.5)	3,059 (85.0)	220 (5.9)
Bronchitis	602 (334.4)	71 (35.5)	292 (8.1)	53 (1.4)
Gastro-enteritis ..	1,201 (667.2)	91 (45.5)	462 (12.8)	51 (1.4)
Measles	663 (368.3)	6 (3.0)	1,587 (44.1)	5 (0.1)
Whooping Cough ..	816 (453.3)	10 (5.0)	941 (26.1)	1 (<0.1)
Tuberculosis	424 (235.5)	3 (1.5)	1,882 (52.3)	16 (0.4)
Diphtheria	69 (38.3)	0	1,018 (28.3)	0
Scarlet Fever	30 (16.7)†	0	411 (11.4)	0
Influenza	120 (66.7)†	22 (11.0)	205 (5.7)	15 (0.4)
Cerebro-spinal Fever and Meningococcal Infections	223 (123.9)	26 (13.0)	314 (8.7)	25 (0.7)
Other Infective Conditions‡	820 (455.5)	100 (50.0)	1,421 (39.5)	168 (4.5)
Totals	8,155 (4,530.6)	770 (385.0)	11,592 (322.0)	554 (15.0)

¹ See footnote 1, Table I.

* Average crude death rates per 100,000 living shown in parentheses.

† Additional data from Annual Reports of Medical Officers of Health for Scottish burghs.

‡ Including septicaemia and meningitis (except meningococcal and tuberculous); other infections of central nervous system; other respiratory infections; rheumatic fever and acute nephritis; urinary infections.

reported to the Procurator-fiscal, are usually investigated by the forensic pathology service.

Deaths occurring during the first 3 months of life have been excluded from the survey, for although infection is particularly important during this period, many neonatal and early post-neonatal infective deaths have a multiple and often controversial aetiology.

Out of 184 deaths above the age of 3 months which were investigated, 42 (22.9 per cent.) were due to infection in previously healthy children. The group consisted of 23 boys and 19 girls. Table III summarizes the findings. Three "cot deaths" are included; two were due to pneumonia and one to tracheobronchitis. The only controversial cases included in the group are those of two older children who developed fatal peritonitis following undiagnosed appendicitis. Of the forty deaths, 23 are believed to have been preventable. In six of these cases, the duration of serious illness before the family doctor was called in exceeded 2 days, and the general practitioners' own written comments confirmed that significant parental negligence was present. The remaining "preventable" deaths followed illnesses of more than one day's duration where the family doctor had been in attendance, but a clinical diagnosis had not been made and treatment—if given—had been inadequate. Detailed social histories were unfortunately not available, but the case records indicate that the distribution of social groups was as in the general population.

TABLE III
SUMMARY OF FINDINGS IN 42 DEATHS DUE TO INFECTION

Diagnostic Group	No. of Cases				Predominant Organism
	Total	Aged <1 yr	Preventable		
			Parental	Medical	
Septicaemia	10	6	—	1	Meningococcus (7); pneumococcus (1)†; tubercle bacillus (from miliary lesions) (1); Streptococcus pyogenes (1)
Bronchiolitis and Pneumonia ..	9	6	1	4	Haemophilus influenzae (1); Staphylococcus aureus (5); Streptococcus pyogenes (1); (resp. syncytial lesions)‡ (1)
Gastro-enteritis	8	5	4	3	Enteropathogenic Escherichia coli "0·26" (1); Coxsackie virus A9 and B3
Tracheo-bronchitis	7	3	1	4	Haemophilus influenzae (5); Staphylococcus aureus (1); Streptococcus pyogenes (1)
Peritonitis	2	—	—	2	
Meningitis	2	1	—	2	Meningococcus (1); pneumococcus (1)
Meningo-encephalitis	2	—	—	—	Coxsackie virus B4; (measles)‡
Whooping Cough	1	1	—	(1)*	
Chicken Pox	1	1	—	—	
Totals	42	23	6	17	

* Infant of 4 months (not immunized).

† From haemorrhagic adrenal glands.

‡ Virus not isolated.

In the aetiology of a further 51 deaths (27·8 per cent.), infection was important but either it was superimposed upon a condition with a poor prognosis, or the evidence for a diagnosis of primary infection was incomplete. Table IV summarizes the findings in this group. Several of these additional cases would have been ascribed to primary infection in the absence of full pathological investigation or if less stringent criteria had been used. Thus, in two fatal cases of staphylococcal pneumonia, fibrocystic disease of the pancreas was diagnosed histologically. Likewise, three children who died of bronchopneumonia had congenital heart disease that had not been diagnosed before death. In another two cases, *Staph. aureus* was cultivated from the blood and lungs of children who died suddenly in their cots, but diagnoses of "primary infection" were not entirely acceptable since there was no histological evidence of infection in the lungs or elsewhere. Similarly, in another case of sudden death, *Strept. pyogenes* was isolated from the lungs, but there were no other signs of acute infection. Most of the remainder of this group were children with congenital lesions of the heart, central nervous, or other system who died, often unexpectedly, of bronchopneumonia (in one case following measles). A previously healthy child died in a coma 2 weeks after the onset of measles, but there was no histological evidence of meningo-encephalitis. Another child with severe burns died of septicaemia due to a "hospital" staphylococcus, and four others developed fatal surgical sepsis after operations upon congenital malformations.

In a further four cases—which are excluded from the group with "associated" infections—children suffering from acute leukaemia developed terminal infections due to hospital strains of *Staph. aureus*.

The remaining 87 cases (47·3 per cent.) were those in which infection played no significant part. They

consisted of 48 deaths due to congenital abnormalities, thirteen due to malignant conditions (including eight additional cases of leukaemia and three cases of nephroblastoma), and 26 due to miscellaneous causes such as status asthmaticus and epilepticus, acute intussusception, aplastic and haemolytic anaemias, and ulcerative colitis. In all, 29 out of a total of 80 children in the survey who died from congenital abnormalities, survived until after their first birthday.

DISCUSSION

The child population covered by this inquiry into "natural" death is approximately one-eighth of the Scottish total. Taking into account the 20 per cent. of cases in this area which were not investigated by the Regional Paediatric Pathology Service, our findings multiplied by a factor of ten might be expected to represent the Scottish pattern as a whole. Certain discrepancies, however, are encountered when comparing the present results with those calculated from the Registrar General's Reports for Scotland (Tables I and II). The total number of deaths which we could ascribe to primary infection, although high, was actually lower than would be expected from our interpretation of the National returns; but it is now widely appreciated that information derived from death certification must be regarded with caution, particularly in relation to childhood mortality (Emery and Irvine, 1958). Many of the cases which we have not accepted as primarily infective (Table IV) would have been certified as such if stringent pathological and bacteriological criteria had not been applied. In the individual categories, only the group of septicaemias—notably meningococcal—was larger than might have been expected, but it should be noted that several of our cases were not diagnosed clinically.

TABLE IV
SUMMARY OF FINDINGS IN 51 DEATHS IN WHICH INFECTION WAS ASSOCIATED WITH OTHER DISEASES

Underlying Condition		No. of Cases	No. aged <1 yr	Site of Terminal Infection				
				Chest	Urinary Tract	Blood	Meninges	Other
Congenital Lesions	Central Nervous System	12	5	7	1	1	1	2*
	Heart	7	4	7	—	—	—	—
	Alimentary System	6	4	4	—	—	1	1
	Uro-genital System	5	2	—	3	2	—	—
Other Chronic Diseases		8†	3	6	—	—	—	2
Atypical Gastro-enteritis		2	2	1	—	—	—	1‡
Multiple Abnormalities		1	—	1	—	—	—	—
Severe Burns		1	—	—	—	1	—	—
Laryngocele		1	1	—	—	—	—	1§
Not fully elucidated		8	2	4	—	2	—	2
Totals		51	23	30	4	6	2	9

* Measles meningo-encephalitis; *Esch. coli* (0·26) enteritis.

‡ Death following aspiration of neomycin.

† Including three with fibrocystic disease.

§ Produced asphyxia.

In contrast to our findings, the recent survey of childhood mortality carried out by Dunn and Macgregor (1964) indicates a less important role for infection. Their report, which is based on data collected from various sources, covers a relatively small, semi-rural population group, and includes perinatal mortality. The authors deal with infection in passing, and ascribe fourteen out of a total of 84 deaths to this cause. Pneumonia accounted for ten of the cases, most of which were in newborn premature babies. Only four children were reported to have died of infection after their first birthday. Dunn and Macgregor (1964) also observed that congenital malformations accounted for very few deaths after the first year of life. On the other hand, in our investigation, half of the children who died from congenital lesions in association with infection were aged one year or over, and indeed more than one-third of all deaths due to congenital malformations were in the older group.

The most significant finding to emerge from the present work is the observation that more than half of the deaths due to primary infection were evidently preventable. The remaining nineteen cases in Table III were due to fulminating infections—notably with *H. influenzae*, meningococci, and *Staph. aureus*. It is arguable, however, that a number of these children might have been saved by prompt tracheostomy and intravenous therapy to combat infection and shock. Junior medical staff in hospital are often not aware of the rapidity with which acute infections may kill children. However, in all the deaths described as “preventable”, mismanagement occurred outside hospital, and in only about one-quarter of the cases was any parental negligence involved. Failures in diagnosis were important in a large proportion of cases. Thus, the two cases in which bacterial meningitis was not diagnosed clinically emphasize the importance of “atypical” presenting features such as convulsions and vomiting in children, who often do not show other well-developed signs of meningeal irritation (Heycock and Noble, 1964). Similarly, the cases of “missed” appendicitis are instructive (Jackson, 1963).

Some of the other cases included in Table III are of special interest. Thus six of the seven cases of Waterhouse-Friderichsen syndrome in the septicaemic group were proved to be of meningococcal origin, but in one child the adrenals yielded a pure culture of pneumococci—apparently a rare cause of the syndrome (Thorn, 1953). Nevertheless, Margaretten, Nakai, and Landing (1963) have shown that the syndrome can be due to a wide variety of bacteria other than the meningococcus. The death of a non-immunized infant, aged 4 months, from whooping

cough, emphasizes the danger of this infection in infants who are excluded from current immunization schedules on account of age.

The isolation of Coxsackie viruses in gastro-enteritis is of doubtful significance, and, while viruses of Group A have been incriminated in infantile diarrhoea (Hodes, 1960), the general role of viruses in sudden deaths amongst children remains problematical (Valdes-Dapena and Hummeler, 1963).

Hospital cross-infection was a decisive factor in several of the cases included in Table IV. In many others in this group the terminal infection was not treated energetically, though it would be unreasonable to describe many of these deaths as “preventable”. However, prevention should have been possible in the case of the child who asphyxiated following infection of an undiagnosed laryngocele. A possible hazard of neomycin therapy may have occurred in another case included in Table IV. The aspiration of a relatively small volume of neomycin by an infant with severe gastro-enteritis was followed by respiratory depression and collapse. The dangers of neomycin in anaesthetized patients are well established, but the effects might not always be due to synergism with other drugs (*British Medical Journal*, 1963).

The progress made against infection during the past 30 years is Medicine's greatest achievement to date. As indicated in Table II, deaths due to the specific infectious diseases and to infections of the chest and intestinal tract have all shown a spectacular decline during this period. The marked reduction in mortality and morbidity amongst children is a direct result of the introduction of antibacterial drugs, active immunization, and social improvements—although the importance of each factor varies in the case of individual diseases. It is understandable, therefore, that infection as a cause of disease and death should now be regarded with such complacency in the medical profession and by the general public. There is indeed a widespread feeling that in Great Britain deaths due to infection have reached an irreducible minimum. Nevertheless, it is likely that more than 1,000 children above the age of 3 months die here each year as a result of primary infection. In at least another 2,000 deaths in this age group, infection plays a significant part. The present investigation suggests that many of these children need not die.

SUMMARY

During the period 1960–62, infective conditions were certified as the primary cause of death in 1,324 Scottish children aged 3 months to 14 years (representing 38 per cent. of deaths in this group).

In the Edinburgh area during the period 1961–63, full investigations were carried out on 184 deaths in this age group. In 42 cases death was due to primary infection in previously healthy children. At least 23 of the deaths were preventable; in six cases parental neglect was evident, and in all but one of the remainder there were serious delays in diagnosis and treatment. Fulminating septicaemia, meningitis, or respiratory infection occurred in a further nineteen children, but even in this group, energetic emergency measures might have altered the outcome in more than one-third of the cases. In order of incidence, the bacterial infections were due to meningococci, *H. influenzae* and *Staph. aureus*, *Strept. pyogenes*, and pneumococci; there were single cases of tuberculosis, whooping cough, and specific coliform enteritis; three viral deaths occurred and two viral isolations of doubtful significance were made.

In another group of 51 deaths (27·8 per cent.), infection was either superimposed on a condition with a poor prognosis (forty cases) or there was insufficient evidence for a diagnosis of “primary infection” (eleven cases). Out of 32 children in this group who had congenital malformations, sixteen had survived their first year. A further thirteen with similar lesions also reached at least their first birthday but died without evidence of infection.

Discrepancies between our results and those based on death certification are discussed; and the plea is

made for a wider recognition of the large number of preventable deaths in childhood which are still due to infection.

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