Sudden unexpected death in infants in the Oxford Record Linkage Area

Details of pregnancy, delivery, and abnormality in the infant

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SUMMARY

One-hundred-and-seventy infants resident in the Oxford Record Linkage Area and dying suddenly and unexpectedly in the five-year period 1966-70 were linked with the records concerning their delivery. For each of these cases three controls were chosen, matched for maternal age, parity, social class, legitimacy, and place and year of delivery. The files of general hospital admissions were scanned to identify admissions to the mothers during the pregnancy, and admissions to the infants, for both index cases and controls.

Significant associations were found with short gestation, low birthweight, slight growth retardation, twin delivery, 'insult' during pregnancy, induction of labour, neonatal jaundice, congenital defects, subsequent hospital admission, and month of birth. There was no association with breast feeding but some evidence for contact with other cases during hospital admission.

INTRODUCTION

In the two previous papers (Fedrick, 1973, 1974) it was suggested that the cases of sudden unexpected death (SUD) occurring before 12 weeks of age differed epidemiologically from those dying later in several respects. The high proportion of males and excess of deaths in the winter were confined to the later deaths, as were associations with low social class. In the present paper we analyse further information concerning these infants.

One of the chief predictors of SUD in infants was stated by Carpenter (1972) to be the absence of breast feeding from birth. In all, 70% of his control infants had been breast fed during the first two weeks of life, compared with only 56% of the index cases. A similar finding was obtained in the

Canadian study of Steele, Kraus, and Langworth (1967), but in three more recent studies (Froggatt, Lynas, and MacKenzie, 1971; Kraus, Steele, Thompson, and de Grosbois, 1971; Rhead, Schrauzer, and Saltzstein, 1973) there were no significant differences between the series.

In no previous study, however, have the control infants been matched for those factors which we have already shown to have a strong association with the incidence of SUD, i.e., maternal age, parity, social class, and marital state (Fedrick, 1974).

As a result, we are able to show in the present paper that once these factors have been taken into account, there is no residual effect which can be considered to be associated with breast feeding at the time of discharge from hospital. We have no details for later periods.

A further finding in previous studies of SUD, where the families of the infant had been questioned soon after the death, was a significant increase in respiratory illness in the child in the two weeks prior to death. This, as Camps (1972) has pointed out, has all the defects of retrospective recall in parents and investigators motivated to find some cause for the child's death. In the present study we are only able to look at records of hospital admissions and details of neonatal morbidity and abnormality recorded on the Record Linkage files before the death had occurred. In this way our data will not suffer from bias, although they do lack detail of any illnesses that did not require hospital admission.

MATERIAL AND METHODS

As in the preceding paper, for most of the analyses only the 170 cases which were delivered in the Area and for whom details of the delivery were

on the Record Linkage files have been included. For each case three controls were chosen matched for maternal age, parity, civil state, social class, and hospital and year of delivery. For all cases and controls details of birthweight, type of delivery, complications of pregnancy, and infant abnormalities in the neonatal period were obtained from the maternity abstract. In addition, the files of general hospital admissions were scanned in order to ascertain whether the mother had been admitted to hospital for any other reason during the period of her pregnancy. Gestation was calculated as the number of completed weeks from the first day of the last menstrual period.

Information on whether the infant had been breast fed on discharge has not been routinely collected by the Record Linkage Study. It was, therefore, necessary to return to the hospital notes to obtain this information for the index cases and controls. This task was performed by clerks employed by the Study in the various hospitals without knowledge of the outcome of the baby.

A further part of the present study was concerned with the question whether the index infants were more likely than their controls to have been admitted to hospital. Here the question of period at risk was pertinent. For each control the 'period at risk' was taken to be only the number of days from its birth to that age which the index case with whom it was matched had survived. The general files were then searched for hospital admissions to all index cases during the period of their lives and to their matched controls during the relevant periods at risk.

RESULTS

MONTH OF BIRTH

It has already been suggested (Fedrick, 1973, 1974) that the infants dying before 12 weeks of age differ epidemiologically from those dying later. It was shown (Fedrick, 1973) that these younger cases of SUD did not present with the marked winter excess exhibited by the later deaths. When month of birth is considered there is an excess of births in the latter half of the year, and it is apparent that this is largely due to variation in the season of birth of the infants dying before 12 weeks (Table I).

PLACE OF BIRTH (matched cases only)

There was significant variation in the incidence of SUD with hospital of delivery ($P < 0.02$), and it seemed that, in general, the larger the hospital, the higher the incidence of subsequent SUD (Table II). Further analysis showed that the variation was not due to variations of parity, age, and social class in

TABLE I
MONTH OF BIRTH OF ALL CASES OF SUD (MATCHED AND UNMATCHED)

Month of Birth	Death		
	< 12 Weeks	12 Weeks +	All
Jan.—March ..	17	28	45
April—June ..	12	29	41
July—Sept. ..	21	28	49
Oct.—Dec. ..	30	34	64
Total	80	119	199

For seven unmatched cases the month of birth was not recorded on the death certificate.

TABLE II
RATES OF SUD PER 1,000 LIVE BIRTHS ACCORDING TO SIZE OF HOSPITAL OF DELIVERY

Size of Hospital (deliveries/year)	SUD		
	< 12 Weeks	12 Weeks +	All
Over 800 ..	1.23 (53)	1.59 (69)	2.82 (122)
400–800 ..	0.73 (5)	1.32 (9)	2.05 (14)
Less than 400 ..	0.45 (4)	1.03 (9)	1.48 (13)

Numbers of cases are shown in parentheses

these hospitals but was, to a certain extent, a function of the catchment area. The latter factor was unable to account for all the variation however.

CLUSTERING IN TIME AND PLACE OF BIRTH

Altogether 149 of the SUD infants were delivered in one of the 15 maternity units in the Area. Considering all possible pairs, there were 107 in which the interval between births was less than ten days, and 1,917 pairs in which both members of the pair were born in the same hospital. Thus, using the method of Knox (1964), the expected number to be delivered within ten days of one another at the same hospital was 18.6, insignificantly different from the observed number of 22.

In contrast, analysing the two groups of cases of SUD separately, one found among the group of deaths occurring by the 12th week six pairs born at the same hospital within seven days of one another compared with an expected 3.17 ($P \sim 0.1$). Among the older deaths, however, there were only five observed pairs with 4.7 expected.

An interesting point concerning the six pairs of infants who died before the 12th week is that in five of the pairs the deaths occurred at ages within two weeks of one another. Adding this factor into a

specification of clustering in the young group of deaths gives an expected number of 1.3 compared with the observed five.

A similar calculation among the older deaths yielded two pairs observed to be born within seven days of one another at the same hospital and dying within two weeks of one another, compared with an expected 0.62.

MULTIPLE BIRTHS

In 1968 in the Oxford Record Linkage Area 265 of 13,886 livebirths (1 in 52) were twins. In the present series of 170 cases of SUD linked with the birth information, eight were twins (expected 3.3). In other words, the risk to a twin would appear to be over twice as high as that to a singleton. There were no concordant pairs.

Of the eight twins, four had died by the 12th week, and in all four the index case was the first to be delivered. Of those dying later, there was an equal distribution of first and second twins.

GESTATION AND BIRTHWEIGHT

Bergman (1970) studied 119 cases of SUD in King County, Washington. From his paper one can calculate that the incidence of SUD in an infant delivered before 35 weeks' gestation was 12.4 per 1,000 compared with 2.05 overall. In all, 16 (13%) of his cases fell into this category. Similarly, in Canada, Steele *et al.*, (1967) studied 66 cases of SUD, 26% of which were delivered before 37 weeks compared with only 6% of the population.

It can be seen from Table III that in the present series the relative risk of death with SUD, given the maternal age, social class, and parity distributions,

is greater with shorter lengths of gestation. Note, however, that this effect appears to be confined to the deaths occurring after 12 weeks of age. The other striking finding is the consistent excess of cases where the gestation was apparently unknown. This might indicate a certain lack of organization in the mother in that she does not habitually keep a record of the dates of her menstrual periods.

There is also a rise in the relative risk of SUD with decreasing birthweight, the effect, as with gestation, being most apparent among the later group of deaths (Table IV).

TABLE IV
COMPARISON OF BIRTHWEIGHTS OF CASES OF SUD AND THEIR CONTROLS

Birthweight	(a) No. of Cases of SUD	(b) No. of Controls	3(a)/(b)
—4lb 8oz	8 (2)	11 (5)	2.2
—5lb 8oz	13 (6)	28 (14)	1.4
—6lb 8oz	52 (22)	88 (38)	1.8
—7lb 8oz	45 (19)	176 (70)	0.8
—8lb 8oz	32 (15)	145 (65)	0.7
8lb 9oz+	17 (7)	55 (18)	0.9
Unknown	3 (0)	7 (3)	(1.3)
Total	170 (71)	510 (213)	1.0

Number dying under 12 weeks and the corresponding number of controls shown in parentheses.

Although there was no evidence for severe growth retardation among the index cases, there was a suggestion that these infants were somewhat smaller for gestation than their controls (Table V). This finding, which is statistically significant, was apparent for both the cases dying before 12 weeks and those occurring later. The implication is that the majority of cases in the present series were slightly, but not severely, retarded in growth.

ABNORMALITIES OF PREGNANCY

Although the mothers of the index cases seemed to be less likely than their controls to have suffered from pre-eclamptic toxæmia during pregnancy (Table VI), there was a slight excess of women with antepartum haemorrhage and threatened abortion among the women whose infants died before the 12th week, though statistical significance was not reached. This group was also notable for a slight excess of cases of prematurely ruptured membranes (PRM).

The most striking finding, however, was with a reported insult during pregnancy, either in the form of an infection or obstetrical or other trauma (listed in Appendix Table 1). This occurred in six of 170 index pregnancies compared with only three

TABLE III
COMPARISON OF GESTATION OF CASES OF SUD AND CONTROLS

Gestation (completed weeks)	(a) No. of Cases of SUD	(b) No. of Controls	3(a)/(b)
Under 32	2 (0)	1 (0)	6.0
32-34	5 (1)	12 (5)	1.3
35-37	16 (6)	39 (21)	1.2
38-40	79 (36)	233 (92)	1.0
41+	31 (14)	158 (67)	0.6
Unknown	37 (14)	67 (28)	1.7
Total	170 (71)	510 (213)	1.0

Number dying under 12 weeks and the corresponding number of controls shown in parentheses

TABLE V
PROPORTION OF CASES WITH BIRTHWEIGHT 6LB 8OZ AND BELOW
(CASES OF KNOWN BIRTHWEIGHT ONLY)

Gestation (wk)	Males				Females			
	Cases		Controls		Cases		Controls	
Under 37	6/9	(67%)	13/17	(76%)	3/4	(75%)	10/18	(56%)
37-38	9/16	(56%)	11/32	(34%)	5/12	(42%)	8/23	(35%)
39-40	6/34	(18%)	25/104	(24%)	14/26	(54%)	18/88	(20%)
41+	4/16	(25%)	5/76	(7%)	4/14	(29%)	13/79	(15%)
Unknown	13/21	(62%)	9/40	(23%)	9/15	(60%)	13/24	(54%)
All	38/96	(40%)	63/269	(23%)	35/71	(49%)	62/232	(27%)

Test for consistency: Males $t=2.3$; $P<0.02$

Females $t=3.0$; $P<0.005$

TABLE VI
CERTAIN ABNORMALITIES PRESENT DURING PREGNANCY IN LABOUR AND POSTPARTUM

Abnormality	Death <12 wk		Death 12 wk+	
	Cases	Controls	Cases	Controls
Toxaemia	4	20	8	33
Threatened abortion	1	2	2	2
Antepartum haemorrhage	4	3	3	10
Postpartum haemorrhage	2	5	1	10
Anaemia	4	10	8	19
Puerperal pyrexia	1	5	5	6
Maternal distress	0	5	0	2
Fetal distress	1	11	5	16
Premature rupture of membranes	3	3	3	8
Pyelitis or urinary infection	1	5	2	3
Vaginal infection	1	0	1	2
Puerperal infection	1	3	1	6
Diabetes	0	2	0	0
Thrombophlebitis	1	0	1	1
Glycosuria	0	3	3	2
Psychiatric disorder	0	2	2	1
Abnormal uterus	2*	0	0	0
'Insult' in pregnancy	2	1	4	2
Total no. of mothers	71	213	99	297

*1 bicornuate uterus; 1 arcuate uterus

of 510 controls, a statistically significant difference ($P=0.012$). Note that four of the insults to the index mothers occurred in the third and fourth months.

INDUCTION OF LABOUR

Closely relevant to the study of the gestation of an infant is the question whether labour was allowed to start spontaneously or whether it was induced. Taking gestation into account, analysis showed that there was an increased rate of induction, but only among the infants dying before the 12th week (Table VII). The majority of the inductions were surgical.

LABOUR AND DELIVERY

There were no significant differences between the duration of labour of the index cases compared with their controls, nor in the method of delivery.

TABLE VII
PROPORTION OF CASES AND CONTROLS FOR WHICH LABOUR WAS INDUCED, BY TIME OF DEATH
(CASES OF KNOWN GESTATION ONLY)

Gestation (wk)	Death <12 wk				Death 12 wk+			
	Cases		Controls		Cases		Controls	
Under 37	1/2	(50%)	2/17	(12%)	1/11	(9%)	3/18	(17%)
37-38	5/16	(31%)	3/23	(13%)	4/12	(33%)	12/34	(35%)
39-41	13/36	(36%)	25/124	(20%)	9/46	(20%)	35/174	(20%)
42+	2/3	(67%)	15/21	(71%)	3/6	(50%)	13/32	(41%)
All	21/57*	(37%)	45/185	(24%)	17/75	(23%)	63/258	(24%)

*Test for consistency: $t=1.85$

TABLE VIII
MORBIDITY IN NEONATAL PERIOD

Symptom or Diagnosis	Death under 12 wk		Death 12 wk +	
	Cases	Controls	Cases	Controls
Jaundice with no sign of incompatibility ..	2	6	8*	10
Prematurity ..	2	5	10**	10
Rheus isoimmunization ..	0	1	0	2
Respiratory distress ..	0	1	1	3
Cerebral irritation ..	0	2	0	0
Feeding difficulties ..	0	1	2	2
Cyanotic attacks ..	0	0	1	0
Mild infection ..	0	1	1	3
Systolic murmur ..	1	1	0	2
Mild birth injury ..	0	2	0	5
White asphyxia ..	0	3	4	3
Blue asphyxia ..	7	23	10	34
Total no. of infants ..	71	213	99	297

*P<0.05 **P<0.02

MORBIDITY IN THE NEONATAL PERIOD

In Table VIII are listed the details (other than congenital abnormality) of symptoms or diagnoses recorded for cases and controls during the neonatal period. Altogether there were significantly more illnesses recorded for the index cases who died at 12 weeks or later than for their controls. As can be seen, this was largely accounted for by the association of the later cases of SUD with prematurity (requiring special care), and a hitherto unreported association with jaundice in the neonatal period.

CONGENITAL ABNORMALITIES

Of the 71 infants dying before 12 weeks, six (8.5%) had congenital defects mentioned on the maternity abstract, two of which were major defects. This compares with eight of the 213 controls (3.8%), two being major abnormalities (Appendix Table II). Six of the 99 (6.1%) infants dying after the 12th week had defects compared with seven of the 297 controls (2.3%).

For the most part the defects are necessarily minor, the definition of sudden unexpected death employed having required that no major pathological condition be present that might have contributed to the death. Nevertheless the difference between the number of defects apparent in cases and controls is statistically significant (P<0.01).

FEEDING OF THE INFANT

As can be seen from Table IX, there is no appreciable difference between the proportion of index cases who were breast fed on discharge from hospital compared with their controls.

TABLE IX
TYPE OF INFANT FEEDING ON DISCHARGE
(Cases where this information was not obtained have been excluded)

Type of Feeding	Cases		Controls	
	No.	%	No.	%
Breast only	56 (20)	36.4	140 (59)	34.2
Breast + bottle	7 (6)	4.5	17 (7)	4.2
Bottle only	91 (40)	59.1	252 (103)	61.6
Total	154 (66)	100.0	409 (169)	100.0

Number of infants dying before 12 weeks and corresponding number of controls are shown in parentheses

SUBSEQUENT HOSPITAL ADMISSION

Excluding those admissions during which the terminal event occurred, there were altogether 18 admissions to 17 (10%) of the 170 cases of SUD which had been matched with controls, and three admissions to three of the 36 cases which had not been matched. This compares with only 19 admissions to 16 (3%) of the 510 controls in the relevant periods at risk.

Obviously the longer the period at risk, the more likely is an infant to have entered hospital, and this is demonstrated by the fact that none of the 213 infants matched with the deaths occurring before 12 weeks had entered hospital during their period at risk whereas 5% of the 297 controls of the later deaths had done so (Table X). The causes for these hospital admissions are listed in Appendix Tables IIIA and IIIB.

The most striking difference between the causes of admission of the two series was in the proportion of cases with respiratory infection. This was true of nine of the 170 matched index cases (5%) and

TABLE X
HOSPITAL ADMISSIONS TO INDEX CASES AND CONTROLS IN PERIOD AT RISK

	No. of Hospital Admissions	No. of Children involved	Proportion of Children involved
Death under 12 wk			
Cases ..	6	5	5/71* (7%)
Controls ..	0	0	0/213 (0%)
Death 12 wk +			
Cases ..	12	12	12/99** (12%)
(matched)			
Controls ..	19	16	16/297 (5%)

*Exact probability = 0.001
** χ^2 with Yates's correction = 4.15, P<0.05

only six of the 510 controls (1%) (exact probability = 0.005); three index cases had bronchiolitis compared with only one control. Note that all three infants admitted with bronchiolitis had died within eight days of discharge.

LINKAGES

It may be noted that among the infants admitted to hospital there were several linkages in time and place.

LINK 1. Infant N was admitted to hospital X on 2 February 1970 and died suddenly and unexpectedly that day. The following day patient 2 was admitted to the same hospital with a chest infection. He was discharged on 8 February and died suddenly 12 days later.

LINK 2. Patients 1 and 7 were discharged from hospital X on the same day. They died within four days of one another, eight and 12 days after leaving hospital.

LINK 3. Patient 8 was in hospital Y for five days. During this time one of the index cases (aged 2 years) was brought into hospital in extremis and died. Patient 8 was discharged apparently well but collapsed and died two days later.

LINK 4. Patient 16 was admitted to hospital Z (a hospital for infectious diseases) on 25 November with Sonne dysentery and the malabsorption syndrome, aged 14 months. Some two weeks later her 4-week-old sibling (case 3) was admitted to hospital X with bronchiolitis. She was transferred to hospital Z on 14 December and also developed Sonne dysentery. Patient 16 was discharged on 21 December and died five weeks later, patient 3 was discharged on 3 January and died six days later.

It is somewhat provoking that these small clusters involved five of the six infants who died within 14 days of discharge from hospital, and two of the three admissions with bronchiolitis. It must also be noted that there were only 20 hospital admissions altogether to index cases in the five-year period, involving five hospitals. The probability that two of these cases should have the same date of discharge from the same hospital would seem very remote.

DISCUSSION

In the past, low birthweight has been considered to be a major predisposing factor in the syndrome of SUD, high rates for low birthweight infants having been demonstrated by Steele *et al.* (1967) and Peterson (1966). Richards and McIntosh (1972), however, found a rate only twice as high among

infants of birthweight under 2,500g compared with heavier infants, and Froggatt, Lynas, and Marshall (1971) concluded after a complex discriminant analysis that although birthweight may be correlated with SUD it is not *per se* an important determinant of it. This appears to receive support from the present series.

On the other hand, the slight but significant growth retardation detectable at the birth of the present series compared with their matched controls cannot be dismissed altogether. This was not due to an increase in the incidence of pre-eclamptic toxæmia in the present series as there were actually fewer index mothers with this condition than would be expected from the control data.

One could speculate that the finding might be due to an increased incidence of smoking mothers in the index series. Unfortunately, this item of information has not been collected routinely by the Study, but two previous reports (Steele *et al.*, 1967; Rhead *et al.*, 1973) have shown a significant excess of women who smoked during pregnancy among mothers of SUD cases. If indeed there was an excess of smoking mothers in the present series, one would expect the lower incidence of toxæmia that we have found, it having been previously demonstrated that the smoking mother has a reduced likelihood of developing toxæmia (Butler and Alberman, 1969, among others).

The association with delivery in large hospitals, especially in the group of early deaths, suggests either an infective aetiology in that the larger the number of deliveries the more likely is the infant to come into contact with a reservoir of infection, or possibly some practice, perhaps in the management of labour or in the giving of drugs to the mother or infant, might differ in the larger hospitals. It is probably not an effect of the women in the SUD series being referred to larger hospitals because of the incidences of factors such as pre-eclampsia and difficult delivery. These were no greater in the SUD series than in controls.

Apart from an increased incidence of jaundice and special care due to prematurity among some of the index cases, there was little difference in the inability of the infant to withstand the trauma of birth compared with his control. Indeed, he did slightly better, probably due to the fact that he was slightly smaller.

There was, however, a significant increase in the incidence of congenital defects in the index cases compared with controls. This might tie up with the finding of an increase in the number of women in the index series who had suffered some viral or traumatic insult during pregnancy. It is well known

that often the presence of an external anomaly is associated with other internal defects. It seems feasible to postulate that a small proportion of cases of SUD might be due to internal defects not spotted at necropsy.

A full discussion will appear at the end of the present series of papers.

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REFERENCES

- BERGMAN, A. B. (1970). Sudden infant death syndrome in King County, Washington: epidemiologic aspects. In *Sudden Infant Death Syndrome*, edited by A. B. Bergman, J. B. Beckwith, and C. G. Ray. University of Washington Press.
- BUTLER, N. R. and ALBERMAN, E. D. (1969). *Perinatal Problems: The Second Report of the 1958 British Perinatal Mortality Survey*. E. & S. Livingstone, Edinburgh and London.
- CAMPS, F. E. (1972). in Camps and Carpenter, p. 1.
- and CARPENTER, R. G. (Ed.) (1972). *Sudden and Unexpected Deaths in Infancy (Cot Deaths)*. John Wright, Bristol.
- CARPENTER, R. G. (1972). in Camps and Carpenter, p. 7.
- FEDRICK J. (1973). Sudden unexpected death in infants in the Oxford Record Linkage Area: An analysis with respect to time and place. *Brit J. prev. soc. Med.*, **27**, 217.
- (1974). Sudden unexpected death in infants in the Oxford Record Linkage Area: The mother. *Brit. J. prev. soc. Med.*, **28**, 93.
- FROGGATT, P., LYNAS, M. A., and MACKENZIE, G. (1971). Epidemiology of sudden unexpected death in infants ('cot death') in Northern Ireland. *Brit. J. prev. soc. Med.*, **25**, 119.
- , —, and MARSHALL, T. K. (1971) Sudden unexpected death in infants ('cot death'). Report of a collaborative study in Northern Ireland. *Ulster med. J.*, **40**, 116.
- KNOX, G. (1964). Epidemiology of childhood leukaemia in Northumberland and Durham. *Brit. J. prev. soc. Med.*, **18**, 17.
- KRAUS, A. S., STEELE, R., THOMPSON, M. G., and DE GROSBOIS, P., (1971). Further epidemiologic observations on sudden unexpected death in infancy in Ontario. *Canad. J. publ. Hlth*, **62**, 210.
- PETERSON, D. R. (1966). Sudden, unexpected death in infants: an epidemiologic study. *Amer. J. Epid.*, **84**, 478.
- RHEAD, W. J., SCHRAUZER, C. N., and SALTZSTEIN, S. L. (1973). Sudden death in infancy and vitamin E deficiency. *Brit. med. J.*, **4**, 548.
- RICHARDS, I. D. G. and MCINTOSH, H. T. (1972). Confidential inquiry into 226 consecutive infant deaths. *Arch. Dis. Childh.*, **47**, 697.
- STEELE, R., KRAUS, A. S., and LANGWORTH, J. T. (1967). Sudden, unexpected death in infancy in Ontario: I. Methodology and findings related to the host. *Canad. J. publ. Hlth*, **58**, 359.

APPENDIX 1

LISTING OF CASES WHERE SOME INSULT HAD OCCURRED DURING PREGNANCY

Case	Insult	Time of Insult	Death of Case
Index cases			
1	Mumps	2 wk	11 wk
2	Appendicectomy	4 mth	8 wk
3	Appendicectomy	4 mth	50 wk
4	Rubella	4 mth	66 wk
5	Severe fall	3 mth	13 wk
6	Influenza	8 mth	16 wk
Controls			
1	Influenza	39 wk	—
2	Drug overdose	18 wk	—
3	Tooth extraction	5 wk	—

APPENDIX 2

CONGENITAL ABNORMALITIES PRESENT: SINGLE CASES

Cases	Controls
Death under 12 wk Hare lip and cleft palate Ileal atresia Extra digit L. hand R. talipes Bilateral clicking hips L. clicking hip	Hare lip and cleft palate Cleft palate Tag on hand Talipes Large lax scrotum Odd-shaped ears Odd transverse palmar crease Single umbilical artery
Death 12 wk + Oesophageal atresia Down's syndrome Bilateral webbed toes 4 umbilical arteries Small bony prominence in R. temporal region Birthmark	Hypospadias (2 cases) Minimal talipes Mongolian spot Skin tag on hand Bilateral accessory digits Prominent ears

APPENDIX 3A
LISTING OF ALL HOSPITAL ADMISSIONS TO INDEX CASES

Case	Age at Admission	Reason for Admission	Duration of Stay (days)	Sex	Time from Discharge till Death	Age at Death
1	2 d	Resection of ileal atresia	26	M	12 d	5 wk
2	5 wk	Chest infection	5	M	12 d	8 wk
3	4 wk	(1) Chest infection—bronchiolitis	3			
4	4 wk	(2) Sonne dysentery	20	F	6 d	9 wk
5	8 wk	Cyanotic attack	5	F	33 d	9 wk
		Acute bronchiolitis	8	M	3 d	10 wk
6	4 wk	Upper respiratory tract infection	1	M	7 wk	12 wk
7	11 wk	Bronchiolitis	3	F	8 d	13 wk
8	15 wk	Strangulated inguinal hernia	5	M	2 d	16 wk
9	2 wk	Failure to thrive, dysmaturity	16	F	5½ mth	28 wk
10	4 wk	Bronchopneumonia				
		Social problem	10	M	5 mth	30 wk
11	21 wk	Upper respiratory tract infection				
		'Wheezy bronchitis'	22	F	2½ mth	34 wk
12	1 d	Oesophageal atresia	NS	M	NS	36 wk
13	18 wk	Bullous impetigo	8	F	5 mth	40 wk
14	8 wk	Upper respiratory tract infection	11	F	10 mth	56 wk
		Gastro-enteritis	1			
15	8 mth	Convulsions—cause unknown	1	M	3 mth	51 wk
16	15 mth	Sonne dysentery	27	F	5 wk	73 wk
		Malabsorption syndrome				
17	16 mth	Bronchopneumonia	5	F	22 mth	3 yr
Unmatched cases						
18	9 mth	Vomiting—?due to lax cardia of stomach	17	M	7 mth	69 wk
		Poor weight gain				
		Retardation of development				
19	17 mth	Fractured tibia	3	M	4 wk	79 wk
20	4 yr 2 mth	Asthmatic bronchitis	7	M	8 wk	4 yr 4 mth
		Bilateral basal pneumonia				

Cases 3, 4 and 16 were sibs, 4 and 16 being in the same hospital at the same time.

APPENDIX 3B
LISTING OF HOSPITAL ADMISSIONS TO CONTROLS DURING THEIR 'PERIOD AT RISK'

Control	Age at Admission	Reason for Admission	Duration of Stay (days)	Sex	Time from Discharge till End of Period at Risk	Period at Risk
1	5 wk	Pyloric stenosis	21	M	4 wk	12 wk
2	6 wk	Bronchopneumonia	10	F	5 wk	13 wk
3	2 wk	Infected finger	5	M	3½ mth	19 wk
4	11 wk	Acute bronchitis	5	M	2½ mth	23 wk
5	8 wk	Upper respiratory tract infection	10	M	3½ mth	24 wk
6	7 wk	(1) Upper respiratory tract infection				
		Urinary infection	37	M	—	—
7	14 wk	(2) Urinary tract infection	4	M	2½ mth	25 wk
8	3 wk	Vomiting—? urinary infection	10	F	5 mth	26 wk
9	6 mth	Tonsillitis	1	F	20 d	30 wk
10	7 wk	Bronchiolitis	13	M	7 mth	40 wk
11	1 wk	Purulent conjunctivitis	19	M	8 mth	40 wk
12	6 mth	Acute gastro-enteritis	5	M	3 mth	40 wk
13	8 wk	Pyloric stenosis	8	M	14 mth	73 wk
14	4 mth	Upper respiratory tract infection	7	M	13 mth	78 wk
		Bilateral inguinal hernia	6	M	15 d	92 wk
		Bilateral otitis media				
15	10 mth	(1) Blocked tear ducts	0	F	—	2 yr
	14 mth	(2) Blocked tear ducts	0	F	—	2 yr
	18 mth	(3) Blocked tear ducts	0	F	6 mth	2 yr
16	2 wk	Paraphimosis	1	M	2 yr	2 yr 3 mth