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SUDDEN UNEXPECTED DEATH IN INFANTS IN THE OXFORD RECORD LINKAGE AREA

AN ANALYSIS WITH RESPECT TO TIME AND PLACE

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Beckwith (1970) proposed the following definition of the syndrome of sudden unexpected death in infancy (SUD): 'The sudden death of any infant or young child, which is unexpected by history, and in which a thorough postmortem examination fails to demonstrate an adequate cause for death'.

As other causes of infant mortality are gradually being reduced, the entity sudden unexpected infant death (cot death) is coming more and more into prominence. It is thought to account for as many as 30% of deaths to infants between 1 and 12 months of age (Froggatt, Lynas, and MacKenzie, 1971a). It is now well established that the incidence increases in the cold months of the year, in both the northern and southern hemispheres (Valdés-Dapena, 1967; Froggatt *et al.*, 1971a; Steele, Kraus, and Langworth, 1967). Theories abound as to the cause of this syndrome—from a deficiency of magnesium (Caddell, 1972) or vitamin D (Kraus, Steele, Thompson, and de Grosbois, 1971) to parathyroid insufficiency (Geertinger, 1967), hypersensitivity to cow's milk (Gunther, 1972), viral infection (Ray, Beckwith, Hebestreit, and Bergham, 1970; Brandt, 1970), and myeloid leukaemia (Stewart, 1972).

The present study is undertaken in an attempt to test certain of these hypotheses against the epidemiology of the condition as observed over a five-year period in the Oxford Record Linkage Area. The study has been undertaken as a purely statistical exercise from the linked records in our files. At no time were the families of cases or controls contacted.

Although, therefore, deficient in data on aspects concerning the social environment, state of maternal care, and morbidity of the child in the period before death, these aspects have already been investigated thoroughly (Vaughan, 1968; Richards and McIntosh, 1972) and it is unlikely that further investigation would have brought anything new to light. The present study, on the other hand, has the advantage of large numbers, an unbiased recorder (the computer-based file), and the advantage of linking with details of delivery, hospital admissions to mother, index case and sibs, and the ability to control for several variables at once from the population of all births in the area. This first report of the study will be concerned with defining the population of index cases and analysing the incidence with respect to age at death, sex, date of death, and area of residence of the parents. It is intended that further papers will be concerned with the mother, the pregnancy and delivery, and a profile of the baby from birth to death.

Material and Methods

The Oxford Record Linkage Study (Acheson, 1967; Baldwin, 1972) was started in 1962. Since 1966 it has covered the area consisting of Oxfordshire and that part of Berkshire within the Oxford Regional Hospital Board area. Included are the two cities of Oxford and Reading, but the area is largely rural with several small towns, and a total population of some 800,000.

The following data are collected: *(a)* Information on all babies delivered in the area. (In the case of hospital births detailed descriptions of pregnancy and delivery, and of any abnormality or illness of the baby, are abstracted by trained clerks from the hospital notes. In the case of domiciliary deliveries the midwife who delivered the infant sends her notes to the Study, clerks then abstract and code the relevant information, including details of any pregnancy abnormality as well as of any illness or defect in the child). *(b)* The death certificates of all persons normally resident in the area, whether or not they died there. *(c)* The birth certificates of all infants delivered to women resident in the area. *(d)* Details of hospital admissions in the area.

For the purposes of the present study the death certificates of all children under the age of 5 years, resident in the area and dying in the period 1966-70, were examined. If the death had been unexpected and hence reported to the coroner, and necropsy failed to reveal any major pathology, it was accepted as being a case of SUD.

Meteorological information for each day of the five-year period was abstracted from the records of the meteorological station at RAF Abingdon. This happens to be geographically roughly in the centre of the Record Linkage Area.

Results

Incidence

In all, 206 deaths fulfilled the criteria described above and were accepted as cases of SUD. Over the period mid-1965 to mid-1970, 74,147 livebirths were delivered to women resident in the area. These are considered to be a fair estimate of the infants at risk of SUD in the period January 1966 to December 1970, and the incidence is thus estimated to be 2·78 per 1,000 livebirths, a figure in remarkable accord with the estimates of 2·8 of Froggatt, Lynas, and Marshall (1971b) in Northern Ireland, 2·87 of Peterson (1966) in Seattle, and 2·7 of Richards and McIntosh (1972) in Glasgow.

Registered Causes of Death

Over the five-year period the sudden unexpected death in infancy had not been accepted as a registered cause of death, and indeed the rubric only occurred on one of the death certificates in the present study.

Table I shows that 62·6% were registered as dying of respiratory infection and a further 20·4% with inhalation of vomit. In the 13 cases registered as gastro-enteritis the infection had been mild, and in two cases the infant was thought to have recovered. Of the 11 other causes, one notable one was coded as constipation (the wording on the death certificate being inhalation of vomit due to constipation) and another was coded to dermatitis, the infant having had a nappy rash!

Table I

Registered Causes of Death

Registered Cause of Death	No.	%
Acute bronchitis or bronchiolitis ..	93	45·1
Bronchopneumonia	36	17·5
Inhalation of vomit: reflex inhibition ..	42	20·4
Gastroenteritis	13	6·3
Asphyxia (bedclothes, etc.)	6	2·9
Acute pulmonary oedema	5	2·4
Other	11	5·3
Total	206	100·0

Table II

Place of Death

Place of Death	No.	%
At home	135	65·5
At other address	10	4·9
En route to hospital (including 'brought' in dead)	14	6·8
Hospital	46	22·3
Other (health centre)	1	0·5
Total	206	100·0

Place of Death

From Table II it can be seen that over 70% of the infants died at home or at some other non-institutional address, 6·8% died en route to hospital, and 22·3% at hospital.

Sex and Age at Death

Of the 206 cases of SUD, 119 (58%) were male, a finding in accord with many previous studies (Valdés-Dapena, 1967; Strimer, Adelson, and Oseasohn, 1969; Froggatt *et al.*, 1971a). The distribution of the ages of these infants at death is shown in Table III, and it can be seen that our results support

Table III

Age at Death (completed week)	Male No.	Male Cum. %	Female No.	Female Cum. %	All No.	All Cum. %
0-1 ..	3	2·6	3	3·4	6	2·9
2-3 ..	5	6·8	3	6·9	8	6·9
4-5 ..	7	12·8	8	16·1	15	14·2
6-7 ..	4	16·2	9	26·4	13	20·6
8-9 ..	11	25·6	10	37·9	21	30·9
10-11 ..	13	36·8	6	44·8	19	40·2
12-13 ..	14	48·7	7	52·9	21	50·5
14-15 ..	7	54·7	3	56·3	10	55·4
16-17 ..	7	60·7	5	62·1	12	61·3
18-19 ..	2	62·4	3	65·5	5	63·7
20-21 ..	3	65·0	3	69·0	6	66·7
22-23 ..	2	66·7	3	72·4	5	69·1
24-25 ..	1	69·2	1	73·6	4	71·1
26-29 ..	3	71·8	6	80·5	9	75·5
30-33 ..	3	74·4	—	80·5	3	77·0
34-37 ..	5	78·6	3	83·9	8	80·9
38-41 ..	4	82·1	4	88·5	8	84·8
42-45 ..	2	83·8	1	89·7	3	86·3
46-51 ..	4	87·2	—	89·7	4	88·2
52-77 ..	6	92·3	4	94·3	10	93·1
78-103 ..	4	95·7	2	96·6	6	96·1
2 yr + ..	5	100·0	3	100·0	8	100·0
Total ..	117	100·0	87	100·0	204	100·0

In two instances the exact age at death was unknown.

those of a previous study (Ministry of Health, 1965) in finding a peak among female deaths at earlier age (6-9 weeks) than among the males (10-13 weeks). Overall, however, there is a typical distribution, 71% occurring in the first 6 months of life and less than 7% after the first year.

TABLE IV
SEX RATIO AND AGE AT DEATH

Age at Death (wk)	Total No.	Male : Female
0-5	29	1·06 : 1
6-11	53	1·02 : 1
12-17	43	1·90 : 1
18-51	55	1·29 : 1
52+..	24	1·67 : 1
Population at risk ..		1·08 : 1

Table IV shows the sex ratios for each age at death grouping and indicates that up to 12 weeks of age the infant has an equal risk of SUD regardless of its sex, but that thereafter the male is at greater risk than the female.

Day of Death

A report by Cameron and Asher (1965) in Birmingham of an excess of deaths occurring on a Sunday prompted several authors to look at their data. Froggatt *et al.* (1971a) in Northern Ireland also reported more deaths on a Sunday, and Peterson (1966) in the U.S.A. had an excess on Saturday, but Richards and McIntosh (1972) found a peak on Tuesday, and the present data (Table V) show a peak incidence on Thursday, there being, if anything, fewer deaths than expected at the weekend.

TABLE V
DAY OF DEATH

Day of Week	Number Observed
Monday	27
Tuesday	25
Wednesday	28
Thursday	37
Friday	32
Saturday	30
Sunday	27
Total	.. 206

No. expected each day = 29·4
(χ^2 = 2·865; df = 5; P > 0·05)

Month and Year of Death

The now well documented increase in cases of SUD in the winter months is shown in Table VI. This trend is apparent in each of the five years, though it is less marked in 1967 and 1970. Using the test for seasonality of Edwards (1961), one obtains the hardly surprising finding that the seasonal distribution is highly significant (P < 0·001) with a peak in January.

TABLE VI
MONTH OF DEATH AND YEAR OF DEATH

Month	1966	1967	1968	1969	1970	Total
January ..	4	3	7	9	4	27
February ..	4	4	2	5	4	19
March	3	5	5	4	7	24
April	6	3	1	6	1	17
May	3	1	2	4	3	13
June	1	3	2	5	3	14
July	3	3	0	—	1	7
August ..	2	2	2	2	5	13
September ..	2	3	1	2	4	12
October.. ..	3	5	5	2	2	17
November ..	4	3	3	5	5	20
December ..	8	2	4	7	2	23
Total	43	37	34	51	41	206
May-October ..	14	17	12	15	18	76
November-April ..	29	20	22	36	23	130

TABLE VII
MONTH OF DEATH AND SEX, 1966-70

Month	Male	Female	Total
January	18	9	27
February	10	9	19
March	14	10	24
April	12	5	17
May	4	9	13
June	8	6	14
July	3	4	7
August	7	6	13
September	8	4	12
October	8	9	17
November	15	5	20
December	12	11	23
May-October ..	38	38	76
November-April ..	81	49	130
Total	119	87	206

All cases SUD : χ^2 = 23; df = 2; P < 0·001
Males only : χ^2 = 20; df = 2; P < 0·001
Females only : χ^2 = 4·4; df = 2; P < 0·05

TABLE VIII
YEAR OF DEATH AND SEX

	Male	Female	Total	Male : Female
1966 ..	28	15	43	1·87 : 1
1967 ..	18	19	37	0·95 : 1
1968 ..	18	16	34	1·13 : 1
1969 ..	31	20	51	1·55 : 1
1970 ..	24	17	41	1·41 : 1
Total ..	119	87	206	1·38 : 1

What is somewhat unexpected is the finding shown in Table VII. Here it is apparent that the seasonal distribution of date of death is far more marked for the males in the series than for the females. Similarly, Table VIII shows that there is marked variation in the sex ratio from year to year, there being some indication that the variation in the incidence of SUD is due to the variation in the incidence of male rather than female deaths.

TABLE IX
AGE AT DEATH AND SEASON

Age at Death (wk)	Date of Death November-April (a)	May-October (b)	(a)/(b)
0-11	46	36	1·28
12-17 ..	29	14	2·07
18-51 ..	37	18	2·06
52+	16	8	2·00

TABLE X
AGE AT DEATH AND YEAR OF DEATH

Age at Death (wk)	1966	1967	1968	1969	1970
0-11	15	16	16	15	20
12-17	10	7	4	13	9
18-51	12	12	9	15	7
52+	6	2	5	7	4
All 12+ ..	28	21	18	35	20

By considering the age at death (Tables IX and X), one can also see that there is far less seasonal effect in the deaths before 12 weeks than those later. Similarly, the secular variation in incidence is due to the cases occurring after 12 weeks.

Thus one obtains the impression of two distinct types of sudden unexpected infant death: that occurring mainly to infants under 12 weeks where there is little sex difference or seasonal or secular variation, and that where the infant is aged 12 weeks or more. Of the latter cases, twice as many occur during the winter as the summer months, there is a high proportion of males and a secular variation.

AREA OF HOME ADDRESS

In the epidemiological study in Northern Ireland, the incidence of SUD was found to be much higher in Belfast and Londonderry than in the surrounding county areas (Froggatt *et al.*, 1971b), and most authors agree that the incidence is greatest in urban areas (Valdés-Dapena, 1967). In Ontario the reverse appears to be true, the incidence being highest in the north of the province, an essentially rural area, and lowest in the south-west, an area of large cities.

In the present study, too, there appeared to be marked geographical variation in the incidence of SUD. There was a much higher incidence in the two cities than in the rest of the area, but the rate in rural areas is higher than that in the small towns (urban areas) (Table XI). Throughout, however, the incidence in Oxfordshire was higher than that in Berkshire.

For infants dying under 12 weeks of age the rates were 1·35 per 1,000 for Oxfordshire and 0·97 for Berkshire (i.e., the rate was 39% higher in Oxfordshire than in Berkshire). For infants over 12 weeks at death the corresponding rates are 1·76 and 1·56 (a 13% increase). Thus it seems that the difference in incidence between Oxfordshire and Berkshire is largely due to a difference in incidence among the infants dying under 12 weeks.

CLUSTERING IN TIME AND SPACE

A previous study has found no evidence for clustering in space and time (Froggatt *et al.*, 1971a), and the present study was no exception. Using the method of Knox, adapted in the way previously explained (Fedrick and Wilson, 1971) one obtained

TABLE XI
AREA OF HOME ADDRESS AND RATE PER 1,000 LIVEBIRTHS

Area	Total Livebirths July 1965-June 1970	Cases SUD Under 12 wk No.	Under 12 wk Rate	12 wk+ No.	12 wk+ Rate	All No.	All Rate
County boroughs							
Oxford	8,064	15	1·86	16	1·98	31	3·84
Reading ..	12,152	16	1·32	25	2·06	42	3·46
All CBs	20,216	31	1·53	41	2·03	73	3·61
Municipal boroughs and urban districts							
Oxfordshire ..	7,031	10	1·42	9	1·28	19	2·70
Berkshire ..	6,804	4	0·59	8	1·17	12	1·76
All UD and MB ..	13,835	14	1·01	17	1·23	31	2·24
Rural districts							
Oxfordshire ..	16,820	18	1·07	31	1·84	49	2·91
Berkshire ..	23,276	19	0·82	33	1·42	53	2·28
All rural	40,096	37	0·92	64	1·59	102	2·54
Total	74,147	82	1·11	122	1·65	206	2·78

TABLE XII

EXAMINATION OF EVIDENCE FOR CLUSTERING IN TIME AND SPACE USING THE METHOD OF KNOX

	Pairs in Same Month	Pairs not in Same Month	Total
Pairs in same area ..	29	1,875	1,904
Pairs not in same area ..	340	18,871	19,211
Total	369	20,746	21,115

Expected no. pairs in same area and month

$$= \frac{1904 \times 369}{21,115} = 33 \cdot 3$$

29 pairs of cases occurring within the same month and the same area compared with the 33·3 expected (Table XII).

CLUSTERING IN TIME

Kraus, Steele, and Langworth (1967) in Canada reported a significantly greater number of pairs of SUDs occurring on the same day and an examination of the study in Northern Ireland (Froggatt *et al.*, 1971a) also reveals a greater number of days on which two or more cases occurred than expected. In the present study, over the five-year period there were 14 days on which two deaths occurred and one day on which three deaths occurred. Assuming a Poisson distribution, one would expect 10·8 days on which two or more deaths occurred. This, however, does not take account of the seasonal variation in the present data. In Table XIII we therefore compare results taking all winter months separately from the summer ones, and it becomes apparent that in both winter and summer there is a slight excess of days when two or more deaths occurred.

TABLE XIII

COMPARISON OF OBSERVED NUMBER OF DAYS WITH SUDDEN INFANT DEATHS WITH THAT EXPECTED FROM A POISSON DISTRIBUTION ACCORDING TO SEASON OF DEATH

No. of Cases SUD	No. of Days Observed	No. of Days Expected
November-April		
0	787	784·9
1	109	112·6
2	9	8·1
3+	1	0·4
Total	906	906·0
May-October		
0	849	847·1
1	66	70·0
2	5	2·9
3+	0	0·0
Total	920	920·0

TABLE XIV

DISTRIBUTION OF AGES AT DEATH IN PAIRS OCCURRING ON THE SAME DAY

Ages of Pair	Observed Distribution of Pairs	Expected Distribution of Pairs*
Both under 12 wk	5	2·75
One under 12 wk / One 12+ wk ..	6	8·17
Both 12+ wk ..	6	6·08
Total	17	17·00

*Given 17 pairs of cases of SUD from the population of 206 cases

TABLE XV

COMPARISON OF OBSERVED NUMBER OF DAYS WITH SUDDEN INFANT DEATHS WITH THAT EXPECTED FROM A POISSON DISTRIBUTION ACCORDING TO AGE AT DEATH

No. of Cases SUD	No. of Days Observed	No. of Days Expected
Under 12 weeks		
0	1,749	1,745·8
1	72	78·3
2	5*	1·8
3+	0	0·1
Total	1,826	1,826·0
12+ weeks		
0	1,709	1,708·0
1	113	114·1
2	3	3·8
3+	1	0·1
Total	1,826	1,826·0

*$P < 0 \cdot 05$

An examination of the area of residence of all the deaths involved revealed that two pairs occurred on the same day in the same area compared with 1·53 expected.

When the ages of death of the 31 cases occurring in pairs or trebles on the same day were examined one found that 16 (i.e., 52%) were under 12 weeks of age compared with 38% of the rest of the series. An examination of the way in which these young infants appear to be responsible for the slight clustering effect we have shown is demonstrated in Tables XIV and XV.

THE WEATHER

It has been noted that the increased frequency of the SUD syndrome during the winter months is associated with colder weather in Australia as well as in North America and Europe. In Table XVI are listed the mean measurements of each of the various meteorological factors for each month over the five-year period, and the correlation with the frequency of SUD. It can be seen that there is,

TABLE XVI

CORRELATION OF MONTHLY METEOROLOGICAL MEASUREMENTS WITH MONTHLY RATE OF SUD

	Mean Max. Temperature during Day (°C)	Mean Min. Temperature during Night (°C)	Mean Daily Rainfall (mm)	Mean Wind (mph)	Mean Daily Hours of Sunshine	Total Days with Snow	Pressure at 2 am (mm)	Relative Humidity %	Rate SUD per 30 Days
January ..	6·53	2·04	1·86	8·08	1·58	22	1012·45	79·35	5·23
February ..	6·53	0·98	1·72	9·13	2·80	31	1009·94	71·20	4·09
March ..	9·40	1·89	0·93	9·51	4·03	20	1016·13	61·91	4·64
April ..	12·00	3·60	1·89	8·50	5·02	12	1014·29	59·08	3·40
May ..	16·00	6·79	2·33	7·24	5·97	0	1013·64	58·90	2·51
June ..	20·70	9·95	1·49	6·99	7·67	0	1017·35	54·16	2·80
July ..	21·20	11·71	2·15	6·72	6·17	0	1017·76	56·28	1·36
August ..	20·56	11·66	1·99	6·70	5·28	0	1015·41	57·56	2·51
September ..	18·38	10·07	1·83	6·90	4·32	0	1014·83	61·33	2·40
October ..	15·12	8·22	2·05	7·32	3·04	0	1014·08	69·17	3·29
November ..	9·08	3·54	2·10	8·01	2·20	3	1011·35	76·87	4·00
December ..	6·27	1·52	1·96	7·67	1·48	28	1015·53	76·64	4·45
r	—0·911**	—0·890**	—0·422	0·745*	—0·766*	0·779*	—0·499	+0·771*	

r = correlation coefficient obtained when the monthly measurement is compared with the monthly incidence of SUD
df = 10 ** $P < 0·001$ *$P < 0·01$

as predicted, a striking negative association with temperature as well as with hours of sunshine, and positive correlations with wind speed, relative humidity, and snowfall.

At least three mechanisms have been suggested: (i) that what is demonstrated is the usual increase in respiratory infection with a drop in temperature; (ii) that a sort of diving reflex is brought into play by sudden cooling of the child's face (Steinschneider, 1970); and (iii) that a deficiency of vitamin D is enhanced by lack of sunshine (Kraus *et al.*, 1971). A further suggestion that a sudden lowering of the relative humidity could result in the dehydration of the infant and be a factor in the aetiology of SUD does not appear valid from the monthly figures.

If cooling has a direct effect in causing the death one would expect to find factors such as a drop in temperature and high winds (with their added cooling effect) in the period preceding the death. In Glasgow, however, no association was found between the occurrence of an SUD and low temperature (Richards and McIntosh, 1972). In the Canadian study (Kraus *et al.*, 1967) an association was found during the months December to March between the occurrence of death among infants aged 18 weeks or over and a sudden drop in temperature of at least 10°F on a day with little or no precipitation.

Looking at the data in the present series for the months December to March, of the 606 days under observation only 32 (5·3%) were demonstrated to have a minimum temperature some 10°F below that of the preceding day, no rain having fallen. Of the 86 days on which an SUD had occurred, only 3 (3·5%) conformed to this pattern, and in only 9 more could it be said that this feature of the weather had occurred in the preceding three days. When only the infants aged 18 weeks or over were considered the lack of association was equally apparent (of the 37 days of death only 1 (2·7%) was associated with this weather pattern and in only 3 others had it occurred int he preceding three days).

Two Canadian studies have shown an excess of death occurring up to five days after a day on which high winds had been recorded (Kraus *et al.*, 1967; Kraus *et al.*, 1971). In the present study no such finding could be demonstrated nor did an examination of any of the other factors indicate that the weather on the day of deaih, or in the preceding days, was consistently abnormal in any way, apart from a significant relationship with days with no sunshine, confined to the group of deaths under 12 weeks (Table XVII).

TABLE XVII

RELATIONSHIP OF OCCURRENCE OF SUD WITH DAYS WITH NO SUNSHINE AT ALL

	Days with No Sunshine			
	November to April		May to October	
	Observed	Expected	Observed	Expected
Deaths under 12 wk				
Day of death ..	19	12·6*	8	3·2**
1 day before death ..	13	12·6	8	3·2**
2 days before death ..	12	12·6	6	3·2
Deaths 12 wk+				
Day of death ..	24	23·1	3	3·6
1 day before death ..	24	23·1	5	3·6
2 days before death ..	18	23·1	4	3·6

* $P < 0·04$
** $P < 0·02$

DISCUSSION

The frequently reported distribution of SUD with season and age of the infant has been demonstrated, and two different forms of the syndrome postulated: one predominantly found in infants under 12 weeks of age where sex ratio is roughly that of the population at risk and there is variation with area but little or no variation with season or year; the second, found in infants over 12 weeks of age, has a marked preponderance of males and is responsible for seasonal and secular variation.

An analysis to detect clustering in time and space was negative, suggesting perhaps that an acute infectious disease with short incubation period could not have been a feature of many of these deaths. On the other hand, there did appear to be an excess of days on which two or more deaths under 12 weeks occurred at widely separated places. This possibly points to some environmental association, but examination of the meteorological records has so far revealed little of interest, apart from an association with lack of sunshine among the infants dying under 12 weeks of age. This would support the hypothesis of Kraus *et al.*, (1971) of a deficiency in calciferol, the form of vitamin D produced on exposure of the skin to sunlight.

The geographical fluctuations in incidence also reflect a possible environmental influence, but one has first to eliminate other factors such as social class, maternal age, and parity, to be described and analysed more fully in a subsequent paper.

SUMMARY

Two hundred and six cases of sudden unexpected death in infancy (SUD) occurring in the Oxford Record Linkage Area over the five-year period 1966-70 have been analysed. The overall incidence was 2·78 per 1,000 livebirths and was shown to vary with area of residence, year, and season. Two types of death were postulated: that occurring in infants under 12 weeks of age where there was significant clustering in time of death, an association with days with no sunshine, an unremarkable sex ratio, little seasonal variation but variation with area of residence; and that occurring in infants of 12 weeks or more where there was a marked preponderance of males and a striking increase in incidence in the winter months.

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