ANENCEPHALUS IN BELFAST INCIDENCE AND SECULAR AND SEASONAL VARIATIONS, 1950-66

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Anencephalus is one of the most common major congenital malformations of the central nervous system observed in Caucasian populations today, and the highest incidence in the world so far reported occurs in the city of Belfast, Northern Ireland (Stevenson, Johnston, Stewart, and Golding, 1966; Elwood and Warnock, 1969). Analyses of the official statistics of the Registrar General for Scotland for 1939-56 (Edwards, 1958) and data from Birmingham, England (Record and McKeown, 1949; Leck and Record, 1966; Leck and Rogers, 1967) and from South Wales (Laurence, Carter, and David, 1968a) have demonstrated periodic variations in the incidence of this malformation from year to year.

The aims of the present investigation are to examine the incidence of anencephalus in Belfast and to test certain hypotheses relating to secular variations in this annual index which occurred over the period from 1 January 1950 to 31 December 1966. During this time 584 anencephalic stillbirths and infant deaths were observed in a population of 147,825 total (live and still) births of 28 or more weeks gestation. Seasonal incidence is analysed using data for 1956-66 as this information is incomplete for the years prior to 1956.

METHODS AND POPULATION STUDIED

The primary source of material for this study was the records of the maternal and child health division of the Belfast Health Department. Since 1957 a voluntary arrangement between this municipal Department and the University Departments of Social and Preventive Medicine and Medical Statistics has enabled additional antenatal and obstetric data to be recorded on all births using methods similar to those in Birmingham (Charles, 1951) and Aberdeen (Baird, Walker, and Thomson, 1954). Infant death data by cause are not routinely collected and these were ascertained specifically for this investigation. Stillbirths have been legally registered in this part of the United Kingdom only since 1961, but this study was possible because of the existence of Belfast Health Department records

relating to all stillbirths which occurred in the city prior to 1961 (Warnock, 1969).

The population studied consisted of all livebirths and stillbirths of 28 or more weeks' gestation delivered to mothers whose permanent address at the time was within the statutory boundary of Belfast. The diagnosis, anencephalus (W.H.O., 1957), includes this malformation alone or in association with one or more abnormalities. Incidence rates are calculated per 1,000 total (live and still) births (Table I).

TABLE I

INCIDENCE OF ANENCEPHALUS PER 1,000 TOTAL (LIVE AND STILL) BIRTHS IN BELFAST, NORTHERN IRELAND, 1950-66

Year of Birth	No. of Total Births	Anencephalics			Incidence per 1,000 Total Births
		No. of Stillbirths	No. of Infant Deaths	Total	
1950	9,114	25	8	33	3.62
1951	9,059	29	5	34	3.75
1952	8,781	28	1	29	3.30
1953	8,805	22	6	28	3.18
1954	8,562	33	3	36	4.20
1955	8,342	28	5	33	3.95
1956	8,460	24	3	27	3.19
1957	8,519	33	6	39	4.58
1958	8,439	33	5	38	4.50
1959	8,424	25	5	30	3.56
1960	8,895	29	7	36	4.05
1961	8,993	38	9	47	5.23
1962	8,827	27	11	38	4.30
1963	8,953	21	8	29	3.24
1964	8,845	34	6	40	4.52
1965	8,488	32	2	34	4.01
1966	8,319	24	9	33	3.97
1950-66	147,825	485	99	584	3.95

Many estimates of the incidence of anencephalus are based on ascertainment from hospital births, and the relationships between these rates and those calculated from ascertainment of all cases occurring in all births in the communities served by the hospitals in question are usually unknown. The importance of recognizing this bias is shown in the Belfast 1950-66 data (Fig. 1) and in more detail for 1961-66 (Table II). The incidence rates were calculated as follows: for the subgroup 'births in hospital',

FIG. 1. Incidence of anencephalus per 1,000 total (live and still) births ascertained from three groups in Belfast, 1950–66. One further group, 'births in other units', is not shown (see text).

from the numbers of anencephalics and total births delivered in the Royal Maternity Hospital and the Jubilee Maternity Hospital, which are responsible for approximately 50% of all deliveries to city residents annually; for the group 'home births only', from the numbers of anencephalics which occurred exclusively in domiciliary confinements; and for the group 'all births', from the total numbers of anencephalics and births to Belfast residents in 1950–66 (Table I). The last-mentioned group includes the other two categories and also a third group of births (not shown in Fig. 1) corresponding to deliveries in other lying-in units as listed in Table II. From the 1961–66 data, if the population incidence (4.21 per 1,000) is taken as a standard of 100, then ascertainment using the commonest source via teaching hospital births gives a rate 50% above the Belfast community figure. Consideration of home deliveries

TABLE II

DISTRIBUTION BY PLACE OF BIRTH, 1961–66

Type of Unit and Place of Birth	No. of Total Births	No. of Anencephalics	Incidence per 1,000 Total Births
Teaching hospitals:			
Royal Maternity	8,236	72	8.74
Jubilee	17,059	95	5.57
Mater ¹	3,070	12	3.91
Non-teaching hospital	2,752	12	4.36
General practitioner units	7,940	12	1.51
Private beds	1,290	1	0.77
Home deliveries	11,947	17	1.43
Total	52,425	221	4.21

¹Voluntary non-N.H.S. Roman Catholic Unit

gives a correspondingly low rate of 1.43 per 1,000 which is less than one-quarter of the incidence in hospital births. The Liverpool 1960–62 data show a greater bias, the anencephalic rate in hospital deliveries (4.3 per 1,000) being over 10 times that in home deliveries (Smithells, Chinn, and Franklin, 1964). The presence of this bias in hospital estimates, which may be large or small compared with the community rate, means that analyses of anencephalic rates in hospital series reported from various parts of the world are difficult to interpret.

LONG-TERM SECULAR VARIATIONS

The incidence of anencephalus in all births in Belfast, 1950–66, averages 3.95 per 1,000 and the rate exceeds 4.00 in several individual years. The range of variation is some 65%, from a minimum of 3.18 in 1953 to a maximum of 5.23 in 1961.

The secular trends in incidence in Belfast are compared with trends in Birmingham, 1950–65 (Leck, 1966) (Fig. 2), Scotland, 1950–65 (using the Registrar General's statistics) (Fig. 3), and South Wales, 1956–62 (Laurence *et al.*, 1968a) (Fig. 4). Because relevant statistics on all births in Dublin are not available incidence rates based on anence-

FIG. 2. Incidence of anencephalus (stillbirths and infant deaths) per 1,000 total births in Belfast and Birmingham, 1950–65.
FIG. 3. Incidence of anencephalus (stillbirths and infant deaths) per 1,000 total births in Belfast and Scotland, 1950–65.

FIG. 4. Incidence of anencephalus (stillbirths and infant deaths) per 1,000 total births in Belfast and South Wales, 1956-62.

phalic stillbirths and infant deaths observed in obstetric teaching hospitals in Belfast and Dublin, 1950-65, are compared. The Dublin data are from the annual reports of the Rotunda Hospital and Coombe Lying-in Hospital which are published in the *Irish Journal of Medical Science*, these two units being responsible for about 60% of births in that city each year (Leck and Rogers, 1967). Prior to 1960 the Rotunda Hospital records are based on a statistical year commencing 1 November and not 1 January, two months later, so that the years of birth and incidence rates in Dublin hospitals demonstrated in Fig. 5 are not strictly related for this earlier period. The Belfast data are from two units, the Royal Maternity and the Jubilee Hospitals, as mentioned in relation to Figure 1.

The mean incidence in Birmingham, 1950-65 (2.16), is significantly lower than in Belfast (3.95) ($D = 1.79$; $S.E. = 0.06$) and secular variations show a maximal rate of 2.80 in 1956-57, after which the incidence declined to reach a minimum of 1.56 in 1962-63 (Fig. 2). In Belfast the lowest incidence (3.24) occurred a decade earlier in 1952-53 and the highest (4.64) in 1960-61. Overall trends show an increasing incidence in Belfast but a decline in Birmingham.

Data for Scotland are compared using the official statistics of the Registrar General for all anencephalic stillbirths (I.C.D.Y. 38.0) and infant deaths (I.C.D. 750) which occurred in that country during 1950-65 (Fig. 3). Virtually all infant deaths attributed to I.C.D. 750 in Scotland are due to anencephalus (Registrar General Scotland, 1968). The reason for this selection was because in the period 1950-65 some 16% of anencephalics in Belfast were liveborn compared with 7% in Scotland and 9% in Birmingham (Leck, 1966). If, as in previous studies of the

FIG. 5. Incidence of anencephalus (stillbirths and infant deaths) per 1,000 total births in obstetric teaching hospitals in Belfast and Dublin, 1950-65.

Scottish Registrar General's statistics (Record, 1961; Leck and Record, 1966), anencephalic stillbirths only were considered, this would result in Belfast having an 84% ascertainment of cases, hence underestimating the frequency of this malformation. It appears that the phenomenon of a large proportion of live-born anencephalics, almost one-fifth of all cases, is not peculiar to Belfast but occurs in other areas of Ireland (Elwood, 1970). Both Scotland and Belfast experienced maximal peaks in 1960-61 and the trends show small increases in incidence which are of similar order in the two areas.

Data from the South Wales survey of central nervous system malformations show a marginally significant difference in mean incidence (3.54) compared with Belfast (4.21) for 1956-62 ($D = 0.67$; $S.E. = 0.32$). Again the overall trend is a small increase in incidence in South Wales as in Belfast (Fig. 4).

The Dublin data, relating to anencephalic stillbirths and infant deaths which occurred in obstetric teaching hospitals, show a lower mean incidence in 1950-65 (4.35) compared with a similar hospital sample in Belfast (6.20) ($D = 1.85$; $S.E. = 0.34$). This may be a real difference or else a reflection of other unknown factors causing relatively more anencephalics to be born in these units in Belfast. Both cities experienced an overall increase in incidence during the period of observation (Fig. 5).

Edwards (1958), in his analysis of the long-term variations in the incidence of anencephalic stillbirths

TABLE III
INCIDENCE OF ANENCEPHALUS IN FIRST BIRTHS AND IN ALL SUBSEQUENT BIRTHS, 1961-66

Type		1961	1962	1963	1964	1965	1966	1961-66
First births	Total births	2,719	2,622	2,627	2,508	2,437	2,460	15,373
	Anencephalics	18	7	9	15	9	7	65
	Incidence	6.62	2.67	3.42	5.98	3.69	2.84	4.23
All subsequent births	Total births	6,274	6,025	6,326	6,337	6,015	5,859	37,052
	Anencephalics	29	31	20	25	25	26	156
	Incidence	4.62	4.99	3.16	3.94	4.17	4.44	4.21
All births	Total births	8,993	8,827	8,953	8,845	8,488	8,319	52,425
	Anencephalics	47	38	29	40	34	33	221
	Incidence	5.23	4.30	3.24	4.52	4.01	3.97	4.21

in Scotland, 1939-56, attributed them largely to changes in the incidence of this malformation in first births compared with all other birth ranks and in winter births compared with those in summer. The Belfast data were analysed in a similar manner to determine whether these explanations accounted for any of the variations in total incidence observed, the contributions to the total incidence from that occurring in first births and in all other birth ranks being considered for the period 1961-66 (Table III). The range of variation in the incidence of first births (3.95) is greater than in all subsequent births (1.83), thus agreeing with the Scottish findings, but the variations in total annual incidence in Belfast are not entirely confined to first births. Another difference noted is that the increased risk in first births demonstrated in Scotland, Birmingham (Record and McKeown, 1949), and Rhode Island, U.S.A. (MacMahon, Pugh, and Ingalls, 1953) is not present in Belfast, the incidence in first births averaging 4.23 and 4.21 in all subsequent births for 1961-66 (Table III). Also there is a lower proportion of male anencephalics in first births than in later births in Scotland, while the reverse is found in Belfast (Table IV).

The contributions to the total annual variations in incidence in summer births, defined from April to September, and in winter, defined as the following six months from October to March in Belfast, indicates some agreement with the findings for Scotland (Table V). A higher incidence in winter than in summer births occurs in the two areas, but

the range of variation in incidence in Belfast summer births (3.20) and in winter births (2.78) is less than in Scotland.

These two series cover different time periods, and in Belfast the proportion of male anencephalics varies according to parity and also from year to year (Table IV). However, the evidence suggests that the long-term secular variations in Belfast are due to a greater contribution to the total variation from that occurring in winter births, although to a lesser extent than was found in Scotland. Different sex ratios are not the reason because these are almost identical (26.4% male anencephalics in Scotland and 25.8% in Belfast) but differences in the association of anencephalus with parity are more likely explanations because no increased risk in first births is present in Belfast. The distributions of mothers by parity, age, and family size in Belfast and Birmingham (Elwood, 1969) are significantly different and this is probably the case between Belfast and Scotland although it is not formally examined here.

SEASONAL VARIATION

The Belfast data for 1956-66 (Table VI) were analysed for seasonal variation by testing, first, the null hypothesis that there was no association between an anencephalic outcome of pregnancy and month of birth and, secondly, that there was no difference between the observed distribution of anencephalics by season and that expected assuming an underlying harmonic variation in the monthly

TABLE IV
DISTRIBUTION OF ANENCEPHALICS BY SEX AND PARITY, 1961-66

Parity Group ¹	Percentage of Males and Year of Birth						1961-66
	1961	1962	1963	1964	1965	1966	
0	29.4	42.8	50.0	21.4	12.5	28.6	29.5
1+	31.0	19.3	15.0	20.0	36.0	23.1	24.3
All parities	30.7	23.7	25.0	20.5	30.3	24.2	25.8

¹Parity defined as number of previous live and stillbirths

TABLE V
DISTRIBUTION OF ANENCEPHALICS IN WINTER (OCTOBER TO MARCH) AND SUMMER
(APRIL TO SEPTEMBER), 1956-66

Season		1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1956-66
Summer	Total births	4,190	4,355	4,334	4,172	4,613	4,567	4,601	4,739	4,516	4,291	4,202	48,580
	Anencephalics	16	17	16	16	16	24	18	10	24	17	19	193
	Incidence	3.82	3.90	3.69	3.83	3.47	5.25	3.91	2.11	5.31	3.96	4.52	3.97
Winter	Total births	4,270	4,164	4,105	4,252	4,282	4,426	4,226	4,214	4,329	4,197	4,117	46,582
	Anencephalics	11	22	22	14	20	23	20	19	16	17	14	198
	Incidence	2.58	5.28	5.36	3.29	4.67	5.20	4.73	4.51	3.70	4.05	3.40	4.25
All year	Total births	8,460	8,519	8,439	8,424	8,895	8,993	8,827	8,953	8,845	8,488	8,319	95,162
	Anencephalics	27	39	38	30	36	47	38	29	40	34	33	391
	Incidence	3.19	4.58	4.50	3.56	4.05	5.23	4.30	3.24	4.52	4.01	3.97	4.11

distribution of all total births (Edwards, 1961a). At the 5% significance level and calculating the expected numbers from the observed monthly distribution of all total births, the null hypothesis was rejected ($\chi^2 = 25.78$; d.f. = 11; $0.01 > P > 0.001$). The observed trend by season also differed significantly from a harmonic distribution based on Edwards's test ($\chi^2 = 16.11$; d.f. = 2; $P < 0.001$), the ratio of highest to lowest incidence being 1.81. In Belfast the maximal number of anencephalics occurred in October and the minimum in February and March. When the two quinquennia, 1956-60 and 1961-65, were analysed separately, it was found that during the earlier period a minor peak in incidence occurred in March, and this was followed by a definite summer trough which continued until October. In the later quinquennium a noticeable increase in the total number of cases occurred—188 in 1961-65 compared with 170 in 1956-60—and the summer trough partially disappeared owing to the relative increase during May and June.

SCOTLAND

The analysis of the annual statistics of the Registrar General for Scotland (Leck and Record, 1966) showed not only significant seasonal variation in the incidence of anencephalic stillbirths but also that the monthly trends had changed around 1959. Before this date trends for the period 1939-58 showed a definite decrease between May and August, but during the more recent period 1959-63 this trough had been replaced by a rise in incidence from March with a plateau in the summer, no decrease occurring until the month of August. The high rates in the winter months then returned from the end of October and were evident until the end of February. In view of these findings two comparisons with the Belfast data were made, the first based on earlier anencephalic stillbirth trends in Scotland for 1956-60 (Fig. 6) and the second on the more recent period 1961-65 (Fig. 7). Owing to the aforementioned greater proportion of liveborn anencephalics in Belfast than in Scotland, incidence rates were

TABLE VI
DISTRIBUTION OF TOTAL BIRTHS AND ANENCEPHALICS (STILLBIRTHS PLUS INFANT DEATHS) AND
INCIDENCE PER 1,000 TOTAL BIRTHS BY MONTH OF BIRTH, BELFAST, 1956-66

Month of Birth	1956-66			1956-60			1961-65		
	Total Births	No. of Anencephalics	Incidence per 1,000 Total Births	Total Births	No. of Anencephalics	Incidence per 1,000 Total Births	Total Births	No. of Anencephalics	Incidence per 1,000 Total Births
January	8,166	27	3.31	3,757	10	2.66	3,709	12	3.23
February	7,294	25	3.43	3,248	8	2.46	3,395	15	4.42
March	8,405	25	2.97	3,886	17	4.37	3,767	7	1.86
April	8,511	27	3.17	3,919	15	3.83	3,929	9	2.29
May	8,503	33	3.88	3,835	13	3.39	3,928	16	4.07
June	8,036	29	3.61	3,581	12	3.35	3,745	15	4.00
July	7,903	33	4.17	3,454	14	4.05	3,774	12	3.18
August	7,682	31	4.03	3,341	13	3.89	3,640	16	4.39
September	7,945	39	4.91	3,534	14	3.96	3,698	24	6.49
October	7,635	50	6.55	3,409	19	5.57	3,559	28	7.87
November	7,429	44	5.92	3,319	20	6.03	3,430	21	6.12
December	7,653	28	3.66	3,454	15	4.43	3,532	13	3.68
Total	95,162	391	4.11	42,737	170	4.00	44,106	188	4.26

1956-66 data: $\chi^2 = 25.78$; d.f. = 11; $0.01 > P > 0.001$

FIG. 6. Incidence of anencephalus per 1,000 total births by month of birth in Belfast (stillbirths and infant deaths) and Scotland (stillbirths only), 1956-60.

FIG. 7. Incidence of anencephalus per 1,000 total births by month of birth in Belfast (stillbirths and infant deaths) and Scotland (stillbirths only), 1961-65.

FIG. 8. Incidence of anencephalus (stillbirths and infant deaths) per 1,000 total births by month of birth in Belfast and Birmingham, 1958-65.

FIG. 9. Incidence of anencephalus (stillbirths and infant deaths) per 1,000 total births by month of birth in Belfast and South Wales, 1956-62.

calculated using affected stillbirths and infant deaths as numerator in Belfast and stillbirths only in Scotland. Both analyses show that the seasonal variations in the two areas are similar but the winter peak is much more pronounced in Belfast. Comparing the earlier Scottish trends for 1956-60 and the later trends for 1961-65 with Belfast, there is less concordance in recent years regarding variations in

the summer months but the winter variations appear more similar.

BIRMINGHAM

The seasonal incidence of anencephalic stillbirths and infant deaths in Belfast, 1958-61, was compared with data from Birmingham (Fig. 8), the latter referring to the incidence per 1,000 total births

TABLE VII
COMMUNITY SURVEYS OF ANENCEPHALUS IN THE BRITISH ISLES

Area	Period of Observation	No. of Total Births	Incidence per 1,000 Total Births	Reference
Northern Ireland				
Belfast	1957	8,519	4.6	Stevenson and Warnock (1959)
Belfast	1950-66	147,825	3.9	Present series
Belfast	1961-66	52,425	4.2	Present series
Irish Republic				
Co. Galway	1958-60	5,367	3.9	Cahalane, Kennedy, McNicholl, and O'Dwyer (1965)
Cork City & Co.	1962-66	37,135	2.0	Spellman (1969)
Wales				
South Wales	1956-62	102,786	3.5	Laurence <i>et al</i> (1968a)
Scotland				
All	1939-45	655,892	2.5	Record and McKeown (1949)
Dundee	1950-59	33,596	3.3	Walker and Smith (1961)
England				
Northampton	1944-57	62,224	1.0	Pleydell (1960)
Hertfordshire	1952-55	3,081	2.5	McDonald (1961)
Exeter	1954-60	8,117	3.0	Ward and Irvine (1961)
Leicester	1953-62	46,312	2.3	Moss (1964)
Reading	1958-63	12,951	2.2	Griffin and Sorrie (1964)
Southampton	1958-62	14,907	1.9	Williamson (1965)
Birmingham	1950-59	190,236	2.4	Leck <i>et al</i> (1968)
Liverpool	1960-64	91,176	3.1	Smithells (1968)
Camden	1964-67	17,102	1.2	Jepson (1969)

adjusted for length of gestation during the period from April 1958 to March 1965 (Leck and Record, 1966). The incidence of anencephalus in each month was higher in Belfast and the maximal rate was in October, while in Birmingham relatively lower monthly rates occurred and the highest was in November. The analysis of Birmingham anencephalic births by season during various years between 1945 and 1956 (Edwards, 1961b) does not permit the calculation of monthly incidence rates, but the observed numbers show a similar trend to that in Fig. 8 except that the maximal number of cases occurred in December. Apart from these differences the seasonal trends in Belfast and Birmingham are very similar.

SOUTH WALES

Trends in South Wales for 1956-62 (Laurence *et al.*, 1968b) differ in having a peak incidence in March in contrast to November in Belfast, and also no overall winter excess, the winter/summer ratio being 0.98 (Fig. 9 and Table IX).

DISCUSSION

In earlier investigations in Northern Ireland, Stevenson (1959) demonstrated that this part of the United Kingdom has a high incidence of anencephalus, and in his survey of all Belfast births during one year (1957) an anencephalic rate of 4.6 was estimated (Stevenson and Warnock, 1959; British Medical Journal, 1967). It is now apparent that there was an abnormally high incidence in that particular year.

The present investigation shows that the incidence

of anencephalus in Belfast has been consistently above 3.00 during 1950-66. Estimates of incidence based on deliveries in teaching hospitals, a commonly used source of ascertainment, were demonstrated to be much too high compared with the true community figures. The community surveys conducted to date in the British Isles (Table VII) confirm differences in incidence, Belfast being the highest, although Dublin data (Coffey and Jessop, 1957; Elwood and Warnock, 1969) suggest that the incidence there may be almost as high.

Many hypotheses have been put forward to explain the epidemiology of anencephalus. A genetic basis has been favoured by the observed increased risk of recurrence in subsequent sibs (Carter and Fraser Roberts, 1967; Carter, David, and Laurence, 1968), but the high frequency of discordance in monozygotic twins (Record and McKeown, 1951) and the lack of fit of pedigree data to Mendelian ratios (Penrose, 1957; Yen and MacMahon, 1968; Carter, 1969) argue against any simple genetic explanation. Family studies along the lines suggested by Edwards (1960), Carter (1964), Vogel and Krüger (1967), and Nance (1969) are needed to determine the proportions of affected births to maternal and paternal relatives so that the hypotheses of polygenic, recessive or cytoplasmic inheritance may be tested.

There is evidence that anencephalus is associated with environmental factors (Giroud, 1960; Mellin, 1964; Wilson, 1964), some of which will now be considered. The geographical distribution of incidence within the British Isles suggests that anencephalus may be associated with low parental income,

hence this malformation should be more frequent in areas where poverty is more common. However, the rates in Bombay, 1.40 (Kolah, Master and Sangvhi, 1967), Sao Paulo, 0.55 (Stevenson *et al.*, 1966), and in reported series from the poorer countries of the world are lower than in many more prosperous countries.

Studies of immigrant communities in Israel (Halevi, 1967), Australia (Collmann and Stoller, 1968), Canada (Horowitz and McDonald, 1969), the United States (Alter, 1962; Cassidy, 1969; Milic, 1969), and England (Leck, 1969; Hobbs, 1969) have demonstrated differences in incidence between these populations compared with those in their countries of origin. Some comparisons are therefore made between Belfast and the survey of 305 anencephalics, 393 infants with spina bifida, and 1,041 control (live and still) births of 20 or more weeks' gestation which occurred in four large hospitals in Boston, Massachusetts (Naggan and MacMahon, 1967). Analysis by religion showed that the highest incidence of both malformations occurred in Roman Catholics (2.8 per 1,000). Protestants were next (2.0) and Jews last (0.7). For anencephalus only, the rates in the Boston-Irish were 1.22 if the mother and 1.43 if the father were of Irish origin. A large proportion of the Boston Catholics originated from Ireland. Thus the incidence in the Boston-Irish is significantly lower than any of the Belfast hospital figures, including that of 3.91 for the Mater, a Roman Catholic unit working outside the National Health Service (Table II); it is, however, higher than in offspring of Italian mothers (0.79) or Italian fathers (1.01) living in the same American city. This suggests that the manifestation of anencephalus is influenced by both environmental and genetic factors which may be delineated to some

extent on an ethnic basis. High rates in non-Caucasian populations have been reported from the Shatby Hospital in Alexandria, 3.79 (Abul-Einen and Toppozada, 1966), the Nowrozec Wadia Maternity Hospital in Bombay, 1.40 (Kolah *et al.*, 1967), and in Sikhs at the Government Medical College, Amritsar, 4.0 (Phillips, 1967); it is of interest that a high rate (6.5) also occurs in Sikhs resident in Singapore (Searle, 1959). Within the British Isles, however, the South Wales survey (Carter *et al.*, 1968) did not find significant differences between the birthplaces of parents, grandparents, and great-grandparents of the main series index patients and controls and no preponderance of parents of Irish origin was present.

An alternative explanation of the lower incidence in the Boston-Irish is that these migrants may have been already at low risk even while resident in Ireland. Although migration is known to be selective (Adams, 1932; Isaac, 1947), this explanation is unlikely as the only substantial groups in Belfast having low rates are social classes 1 and II (Table VIII) who contri-

TABLE VIII
DISTRIBUTION OF ANENCEPHALUS BY SOCIAL CLASS, BELFAST, 1961-66

Social Class ¹	No. of Total Births	No. of Anencephalics	Incidence per 1,000 Total Births
I	1,253	2	1.60
II	3,184	6	1.88
III	26,903	114	4.24
IV	5,631	29	5.15
V	12,445	61	4.90
Unemployed	3,009	9	2.99
Total	52,425	221	4.21

¹General Register Office (London) classification 1966

TABLE IX
SEASONAL DISTRIBUTION OF ANENCEPHALUS IN SELECTED SERIES

Area and Period of Observation	Reference	Numbers and Season of Birth			Chi Square Value	Winter ¹ Summer Ratio
		Winter ¹	Summer	All Year		
Belfast 1956-66	Present series	200	191	391	0.20	1.05
Birmingham 1940-47	McKeown and Record (1951)	211	155	366	8.56	1.36
Scotland 1939-58	Record (1961)	2,749	2,290	5,039	41.80	1.20
Liverpool 1960-62	Smithells <i>et al.</i> (1964)	91	89	180	0.02	1.02
Southampton 1958-62	Williamson (1965)	15	12	27	0.32	1.25
South Wales 1956-62	Laurence <i>et al.</i> (1968b)	180	184	364	0.04	0.98
Rhode Island 1936-52 ²	MacMahon <i>et al.</i> (1953)	160	166	326	0.10	0.96
Boston 1930-65 ³	Naggan (1969)	139	166	305	2.38	0.84
Charleston, S.C. 1946-55	Alter (1962)	17	11	28	1.30	1.54
Israel 1959-60 ³	Halevi (1967)	33	22	55	2.22	1.50
France 1945-55 ³	Frézal, Kelley, Guillemot, and Lamy (1964)	142	146	288	0.04	0.97
Germany 1950-56	Tünte (1965)	189	149	338	4.72	1.27
Norway 1951-65	Westlund (1969)	71	88	159	1.80	0.81
Australia 1962-65 ³	Collman and Stoller (1968)	101	93	194	0.32	1.09

¹Winter defined as first plus last and summer as second plus third quarters of same year

²Hospital series; remainder community-based series

³Data relate to month of conception

At 5% significance level $\chi^2 = 3.84$ with one degree of freedom

bute around 10% of all births annually and probably migrate less than classes III, IV, and V. A social class gradient in anencephalus is present in Belfast, Boston, Scotland (Edwards, 1958), and Southampton (Williamson, 1965) but none was demonstrable in Birmingham (Record and McKeown, 1949) or in South Wales (Laurence *et al.*, 1968b). Finally, it appears that the significant seasonal variation in incidence present in Birmingham, Scotland, Germany (Table IX), and also Belfast (Table VI) has not yet been observed in the United States or in any other part of the world.

It is concluded that migration of Irish-born individuals from Ireland to Boston results in the incidence of anencephalus in their offspring declining within a time period of one or two generations. There is a change in the pattern of seasonal variation but the social class gradient persists, the Boston data by season (Naggan, 1969) showing a summer peak in April–June with a winter/summer ratio of 0.84 compared with the October peak and winter excess, ratio 1.05, in Belfast.

Many of the Boston–Irish may have originated from the Irish Republic where community studies of anencephalus have not yet been made. Because the findings may differ from those in Belfast these conclusions are made with reservation until further information is available. It is possible that nutritional differences, such as folic acid deficiency (Thiersch, 1952), could account for these changes although in recent years the general standard of living and health has improved in both the British Isles and the United States, while the long-term secular trends in the incidence of anencephalus show an increase in four British areas, but a decline in Birmingham, Boston, and New York State (Gittelsohn and Milham, 1962).

SUMMARY

An analysis was made of all livebirths and still births of 28 or more weeks' gestation (147,825) of which 584 were anencephalic stillbirths and infant deaths, delivered to residents of Belfast, Northern Ireland during 1950–66. The primary source of ascertainment was local authority records. The incidence of anencephalus in all births in the city was never below 3.00 and for 1961–66 it averaged 4.21 per 1,000 total births. This is the highest incidence yet reported from a community series.

In Belfast long-term secular variations in incidence from year to year were demonstrated and an overall increase in frequency, which was also observed in Dublin, Scotland, and South Wales, was found. In Birmingham, Boston, and New York State, on the other hand, incidence has declined.

A significant seasonal variation in the monthly

numbers of anencephalic births in Belfast was demonstrated for the period 1956–66. The maximal number occurred in October and there was a winter excess compared with summer. Trends by season resembled those found in Birmingham and Scotland.

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