Seasonal variation in anencephalus in Canada

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Elwood, J. M. (1975). *British Journal of Preventive and Social Medicine*, **29**, 22-26. **Seasonal variation in anencephalus in Canada.** A study of the monthly numbers of stillbirths and of deaths due to anencephalus in Canada from 1954 to 1962 showed a weak tendency to a winter excess of affected births. The seasonal trend was more marked in the Prairie provinces and in Quebec than elsewhere; the maximum rate of anencephalus occurrence was in October to December in the Prairies and in British Columbia, and in January to March in other regions.

Anencephalus is the most common fatal congenital abnormality in Canada. Large variations in incidence with time and between provinces have been described (Elwood, J. M., 1974). The Canadian experience is matched by the great variability in incidence reported in other studies, and these findings, taken with the evidence for hereditary transmission, have led most investigators to propose mixed genetic-environmental aetiological hypotheses.

Early studies (e.g., McKeown and Record, 1951) in the British Isles showed a winter excess of anencephalic births, suggesting the maximum action of a causative agent in spring and early summer. Later studies showed that this variation was not seen in all regions (Laurence, Carter, and David, 1968) and could show secular changes in one area (Leck, 1972).

In contrast to the British studies, no seasonal variation was seen in studies of anencephalus incidence in Rhode Island (MacMahon, Pugh, and Ingalls, 1953), Boston (Naggan, 1969), or Missouri (Silberg, Watson, and Martin, 1968). A small study of 33 cases in Charleston (Alter, 1963) showed a winter excess. Studies in Quebec (Horowitz and McDonald, 1969), Manitoba (Choi, Klaponiski, Ateah, and Nelson, 1972), and Halifax (Alter, 1963) showed no significant trends.

The present work presents data for Canada, 1954-62, showing a weak tendency to a winter excess of affected births.

METHODS

The population studied was all livebirths and stillbirths over 28 weeks' gestation from 1954 to

1962 in Canada, excluding the Northwest Territories and the Yukon. The numbers of deaths per month in each province recorded under the stillbirth code Y.38.0 'anencephalus' and the equivalent death code 750 'monstrosity' were obtained by special tabulations from Statistics Canada data, and rates are expressed as total deaths per thousand total births. It has been shown (Elwood, J. M., 1974) that Canadian mortality statistics give an estimate of the incidence of anencephalus with up to a 10-15% error; there seems no reason to suppose that this error would change with the month of birth.

RESULTS

During the period 1954-62 there were 5,100 deaths (stillbirths plus infant deaths) attributed to anencephalus in Canada, a rate of 1.21 per thousand total births. The monthly mortality rate, based on the monthly number of deaths and the number of births in the same month (Table 1), shows a variation from 1.37 per thousand in January to 1.01 in May. The departure from homogeneity is highly significant ($\chi^2 = 35.4$, $df = 11$, $P < 0.0005$).

The shorter mean gestation period of anencephalics (Record, 1961) means that the anencephalics born in one month may be more comparable in terms of conception date with other births one or two months later. Thus the analyses were repeated using a one- and two-month shift of denominator, with corrections for length of month. The January maximum and May minimum

TABLE I
MONTHLY NUMBERS OF DEATHS FROM ANENCEPHALUS, RATES PER 1,000 TOTAL BIRTHS, AND EXPECTED NUMBERS ASSUMING NO MONTHLY VARIATION IN MORTALITY RATE, CANADA 1954-62

Month	Total Births	Observed Deaths from Anencephalus	Rate per 1,000 Total Births	Expected Number of Deaths
Jan. ..	340,797	468	1.37	411
Feb. ..	318,319	399	1.25	384
Mar. ..	363,626	471	1.30	439
April ..	359,689	437	1.21	434
May ..	373,878	376	1.01	451
June ..	361,290	410	1.13	436
July ..	368,867	399	1.08	445
Aug. ..	358,531	472	1.32	433
Sept. ..	363,551	418	1.15	439
Oct. ..	352,173	448	1.27	425
Nov. ..	331,964	409	1.23	401
Dec. ..	336,894	397	1.18	407
Total ..	4,229,579	5,104	1.207	5,105

$$\chi^2 = 35.79; \quad df = 11; \quad P < 0.0005$$

TABLE II

QUARTERLY OBSERVED AND EXPECTED NUMBERS OF DEATHS FROM ANENCEPHALUS BY REGION, 1954-62

Region		Jan.-Mar.	April-June	July-Sept.	Oct.-Dec.	χ^2_3	P
Canada ..	Obs.	1,338	1,223	1,289	1,254	17.16	<0.001
	Exp.*	1,234	1,321	1,317	1,233		
Maritimes ..	Obs.	185	186	167	163	4.03	NS
	Exp.	167	179	182	173		
Quebec ..	Obs.	468	392	448	403	15.50	<0.005
	Exp.	416	455	437	402		
Ontario ..	Obs.	481	435	476	439	5.18	NS
	Exp.	444	464	473	450		
Prairies ..	Obs.	153	146	152	181	8.39	<0.05
	Exp.	153	164	164	152		
British Columbia	Obs.	51	64	46	68	6.55	NS
	Exp.	55	59	60	56		

*Expected numbers are based on the sum of annual expecteds to adjust for secular variation.

rates persisted, as did the degree of heterogeneity; for a one-month shift $\chi^2_{11} = 28.6$, $P < 0.005$ and

for a two-month shift $\chi^2_{11} = 41.5$, $P < 0.0005$.

Further tests to study the seasonal variation in the different regions of Canada compared observed and expected numbers of deaths in four calendar quarters (Table II). The seasonal variation is seen only in Quebec and the Prairies. In Quebec the greatest excess of observed over expected cases is seen in January-March, while in the Prairies it occurs in October-December. In Ontario and the Maritimes there is also an excess in January-March, suggesting that a similar variation to that seen in Quebec may be present which is not large enough to achieve significance. The ratio of observed to expected numbers of deaths in the winter months (October to March) is 1.07, 1.12, and 1.07 in Quebec, the Prairies, and British Columbia respectively, and is 1.03 in the Maritimes and in

Ontario. Analyses were also performed by Edwards' (1961) method using monthly numbers of deaths in each region after adjustment for varying monthly numbers of total births. The results were similar to those shown in all cases.

The sex distribution of anencephalus cases shows a female excess, but the distribution may show year to year trends (Rogers and Morris, 1971) and could conceivably vary with the season. Over the period 1954-62, the male proportion of anencephalics born in winter was 0.311 ± 0.009 and in summer 0.330 ± 0.009 . This difference is not significant.

DISCUSSION

The limitations of using Canadian mortality data as an estimate of anencephalus incidence have been discussed by Elwood, J. M. (1974). Comparison of the numbers of deaths recorded from anencephalus with the numbers observed from the same populations by incidence surveys using hospital

records in addition to mortality data showed that an underestimate of up to 10-15% occurred in some areas. This error is large compared to the seasonal variation reported, and thus the latter could be produced or minimized by seasonal variation in the degree of underreporting. However, similar trends towards a winter excess of affected births, although non-significant, have been reported in Canadian studies of incidence in Quebec (Horowitz and McDonald, 1969), Manitoba (Choi *et al.*, 1972), and Halifax (Alter, 1963), so it seems likely that the seasonal variation in mortality accurately reflects changes in incidence.

The present finding of a winter excess of anencephalic births in some but not all regions of Canada suggests similarities with the British experience. A winter excess of anencephalic births, suggesting a maximum conception rate in February to May, was shown in Birmingham (McKeown and Record, 1951), London (Carter and Evans, 1973), Scotland (Record, 1961), and Belfast (Elwood, J. H., 1970). However, no variation was seen in Liverpool (Smithells, Chinn, and Franklin, 1964), Southampton (Williamson, 1965), Edinburgh or Dundee (Elwood, J. H. and MacKenzie, 1971), and a summer excess was recorded in South Wales (Laurence *et al.*, 1968) and Aberdeen (Elwood, J. H. and MacKenzie, 1971). These differences may reflect changes in the seasonal pattern with time as well as place; thus in Birmingham a summer

excess was seen in 1955-60, but the winter excess occurred in 1965-69 (Leck and Record, 1966; Leck, 1972).

Previous North American studies are summarized in Table III and these suggest that the seasonal variation seen in Canada is not constant throughout North America. However, the failure of some smaller studies to demonstrate a trend is inconclusive; to show a significant χ^2 at the 5% level on 1 df assuming a winter : summer ratio of observed cases of 1.1 : 1 as is present in Canada, a total of 1,500 cases must be included. The negative results from the large Quebec study may be due to secular change. In the present work the Quebec seasonal variation is much more marked in the period 1954-56 than in 1957-59 or 1960-62, and this first period was not included in the work of Horowitz and McDonald; also they were limited by incomplete reporting in 1956-60 (Elwood, J. M., 1974).

The factors responsible for the seasonal variation in Canada have more effect in Quebec and the Prairies than elsewhere. Assuming a mean gestation period of eight months and the action of a noxious factor at four weeks' gestation, the maximum action of such a factor would be in May-June in Quebec and in February-April in the Prairies.

In the British Isles the estimated conception dates of anencephalics have been shown to have a negative association with maximal air temperature

TABLE III
NORTH AMERICAN STUDIES OF SEASONAL TRENDS IN ANENCEPHALUS AND SPINA BIFIDA

Study	Place	Type	Time Period	No. of Cases	Period of Maximum Births	Significance of Trend	Winter Summer Ratio
MacMahon <i>et al.</i> (1953)	Rhode Island	H	1936-52	Anen 326	July-Dec.	$\chi^2_3 = 0.1$ $P > 0.9$	1.00 ¹
				SpB 426	Oct.-Mar.	$\chi^2_3 = 1.1$ $P > 0.8$	1.06 ¹
Alter (1963)	Halifax, N.S., Charleston, S.C.	H, C	1946-55	Anen 74	Sept.-Feb.	$\chi^2_1 = 0.98$ $P > 0.3$	1.24 ²
		H, C	1946-55	Anen 34	Sept.-Feb.	$\chi^2_1 = 6.8$ $P < 0.01$	2.67 ²
Naggon (1969)	Boston	H	1930-65	Anen 305	Apr.-June	$\chi^2_3 = 1.9$ $P > 0.6$	0.85 ¹
				SpB 393	July-Sept.		0.93 ¹
Silberg <i>et al.</i> (1968)	Missouri	B	1953-64	Anen 252	Apr.-Sept.	$\chi^2_3 = 3.9$ $P > 0.2$	0.84 ¹
				SpB 715	Oct.-Mar.	$\chi^2_3 = 7.2$ $P > 0.05$	1.15 ¹
Horowitz and McDonald (1969)	Quebec	H, C, B	1956-65	Anen 1,497	Dec.-June	NS (Edwards' test)	> 1.00 ³
				SpB 2,077	Dec.-June		
Choi <i>et al.</i> (1972)	Manitoba	H, C, B	1964-68	Anen 113	Mar.-Aug.	NS	> 1.00 ³
				SpB 93	Dec.-Feb.		

H = hospitals

C = stillbirth and infant death notifications

B = birth certificates

¹ratio of incidence rates

²ratio of number of cases

³insufficient data to calculate ratio

in Belfast and four Scottish cities (Elwood, J. H. and MacKenzie, 1971) and a positive association with hours of sunshine and daylight in Scotland (Record, 1961). In all regions of Canada maximum daily temperatures and sunshine hours are in July, and minima in January-February. Maximum rainfall is in October to December in the Maritime areas and in British Columbia, and in June to August elsewhere (Canada, Department of Transport, 1967). Thus there is no apparent association of the anencephalus risk period with these meteorological variables.

Most studies of an association with infectious diseases have been negative, although there are some reports of an increased risk after influenza during pregnancy (see review by Leck (1963)). In Canada, influenza is most common in January-February, as are notifiable diseases such as streptococcal sore throat and infectious hepatitis (Canada, Dominion Bureau of Statistics, 1954 *et seq.*).

Renwick (1972, 1973) has suggested that such a seasonal variation as this could be due to the maximum consumption of blight-damaged potatoes at the end of the winter, when stored potatoes are consumed, and that the lack of seasonal variation in previous North American studies may reflect less storage of potatoes than in Great Britain. Sufficiently detailed information on potato storage habits is not available to check this hypothesis, although it might be expected that such an effect would be more marked in the Maritimes than in the Prairies, as the former area has greater potato production, consumption, and blight prevalence (Elwood, J. M., 1973).

Thus this study shows that during the period 1956-62 a winter excess of anencephalic births occurred in Quebec and the Prairies. There was a smaller non-significant winter excess in other areas of Canada. This variation is similar to that reported in some areas of the British Isles.

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