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ANENCEPHALUS, DRINKING WATER, GEOMAGNETISM AND COSMIC RADIATION[1]

VICTOR E. ARCHER

Archer, V. E. (Division of Surveillance, Hazard Evaluation and Field Studies, National Institute for Occupational Safety and Health, Salt Lake City, UT 84101). Anencephalus, drinking water, geomagnetism and cosmic radiation. *Am J Epidemiol* 109:88–97, 1979.

The mortality rates from anencephalus from 1950–1969 in Canadian cities are shown to be strongly correlated with city growth rate and with horizontal geomagnetic flux, which is directly related to the intensity of cosmic radiation. They are also shown to have some association with the magnesium content of drinking water. Prior work with these data which showed associations with magnesium in drinking water, mean income, latitude and longitude was found to be inadequate because it dismissed the observed geographic associations as having little biological meaning, and because the important variables of geomagnetism and city growth rate were overlooked.

anencephalus; cosmic radiation; magnesium; magnetics; mortality; water supply

Three important factors were not adequately considered in a recent report by Elwood (1) who was seeking environmental factors in anencephalus: 1) The two strongest correlations (between rate of anencephalus and both latitude and longitude) were dismissed as "having no biological meaning", and "not of major concern"; 2) it was assumed that most anencephalus represents a nongenetic environmental developmental defect; and 3) there was no attempt to seek a correlation between city growth rate and anencephalus, magnesium level in water, or other factors. Not giving sufficient consideration to these factors caused the author to overlook what are probably the most important determinants of congenital anomaly rates, and might have led to misleading conclusions. I shall attempt to correct that situation.

Wesley (2) reported a strong correlation between horizontal geomagnetic flux and neonatal deaths due to congenital anomalies. In Canada, both longitude and latitude bear a strong relationship to horizontal geomagnetic flux (3), which probably explains the strong correlations that Elwood found between those geographic parameters and anencephalus. Horizontal geomagnetic flux has long been known to have a strong influence on where incoming charged cosmic particles strike the earth's atmosphere (4). High flux tends to divert the particles to areas of low flux. Areas of low flux therefore receive the most intensive bombardment from cosmic radiation. Since ionizing radiation is a known teratogen, mutagen, and carcinogen, the different intensity of cosmic radiation over the earth has been

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Abbreviations: γ, gamma, a unit of magnetic flux; N.B., New Brunswick; PPM, parts per million.

[1] A reply by Dr. J. M. Elwood appears in the Letters section of this issue.

From the National Institute for Occupational Safety and Health, Center for Disease Control, Public Health Service, U.S. Department of Health Education and Welfare.

Send reprint requests to Room 433, U.S. Post Office and Courthouse Building, 350 So. Main Street, Salt Lake City, UT 84101.

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postulated to account for much of the geographic differences in congenital anomalies and cancer rates (2, 5, 6). In addition, Gentry (7) found an association between congenital anomalies and estimated background radiation in New York state. Unfortunately, suitable measurements of cosmic or background radiation in Canadian cities have not been made, so we must use geomagnetism as a substitute.

If it is true that most (or many) congenital anomalies are the result of background radiation (including cosmic), then it is quite likely that rates of anencephalus (and probably other anomalies) represent accumulated damage to germ plasm, as well as the effects of current exposures to teratogens. One would therefore expect rates of anencephalus among recent migrants to an area to more nearly reflect the background radiation of the place (or places) where they had lived than of the current residential area. Even if most mutations for anencephalus were dominant lethals (anencephalus is lethal), one would expect that one or more generations would pass before the anencephalus rates of migrants would reflect that of their new environment. Observations on immigrants to Boston from Ireland (8) support this view. (In Ireland the rate of anencephalus and spina bifida was 8.7/1000. Babies in Boston born of mothers who came from Ireland had a rate of 4.9/1000. Babies with parents of Irish ancestry, most of whom were not born in Ireland, had a rate of 3.1/1000.) It is for this reason that it appeared to be necessary to examine the growth rates of the Canadian cities used in Elwood's analysis. To ignore city growth rates is to assume that anencephalus is due to current teratogenic exposures with little or no genetic component.

Another factor which might have influenced the rates of anencephalus in Canadian cities is that, during much of the period under study (1950–1969), prenatal x-rays were common practise. Anencephalus would therefore have usually been diagnosed antenatally. Anticipating a difficult birth, as well as uncomfortable explanations to the family, many physicians might have been likely to refer the patient to the nearest medical center. Most of the cities in Elwood's tabulations appear to be large enough to have a medical center with specialists. The above factor is therefore more likely to have increased rather than to have decreased the rates among some of the cities, since Elwood's data were apparently assembled by city of birth, rather than by residence of parents. One city which had a much higher rate of anencephalus than the rest of its province was St. John, New Brunswick (N.B.). Its rate probably exhibits this "medical center" effect. In many other cities, a high growth rate may have obscured this effect.

Elwood's analysis (1) indicated that magnesium content of drinking water was a factor in rates of anencephalus. Magnesium content is usually related to water "hardness."

Methods

The horizontal geomagnetic flux for each of the 36 cities (plus N.B.) used by Elwood was estimated from an isometric contour map (3). The growth factor for each city (and N.B.) was obtained by dividing population data estimated for 1971 (9) by those for 1946 (10). Data on three suburbs of Montreal (Montreal-North, Jacques-Cartier and St. Michel) were incomplete. Their growth factor was estimated as 2.3. It may actually have been larger, but their growth was more likely a result of local population movement than of immigration, so it would be more appropriate to consider the growth rate of Montreal and its suburbs as a whole rather than each suburb individually, and Montreal's growth factor was only 1.3. However, since their rate of anencephalus was intermediate, it made little difference

to the analysis whether they were considered in the high growth or low growth group. City size was considered to be reflected by total births during the 1950–1969 period (1). Anencephalus rates and magnesium concentration in tap water are from Elwood (1).

The data were inspected to see if any city rates of anencephalus appeared to be unusually high because of the "medical center" effect. The only one that appeared to have a grossly inflated rate for this reason was St. John, N.B. It was the only city in the province large enough to be included by Elwood. The province of New Brunswick had a lower rate (11) which was consistent with that of similar areas. N.B. rates rather than those of St. John were therefore used for all correlations except those with magnesium, which might be dependent on a very local factor.

Most of the data mentioned above are given in table 1. Each of the above factors (city growth, geomagnetism, magnesium, city size, medical center effect) was screened for associations with anencephalus and with each other by a bipartite stratification. Further stratification was done of those exhibiting positive associations during the screening. Stratification was done so as to divide groups into nearly equal parts. Mean values with standard errors were obtained for results of the stratification analyses, and the "*t*" statistic was used to determine statistical significance of mean differences.

Results

Results of the screening tests are given in table 2. It may be noted that these data suggest an association of city growth factor, horizontal geomagnetic flux, and magnesium in tap water with rates of anencephalus. City size appears to have no direct association with deaths from anencephalus, but does have an indirect association through its relationships with horizontal geomagnetic flux and city growth factor. The association of magnesium in tap water with city growth factor appears to be just as strong as its association with anencephalus. These suggested associations merit further examination.

The analysis of rates of anencephalus with simultaneous stratifications for both city growth factor and horizontal geomagnetism is illustrated in figure 1. A surprisingly good separation of the associations of the two factors, yielding statistically significant differences was obtained. The curves indicate 1) a strong, possibly linear, relationship between low horizontal geomagnetic flux and high anencephalus rates when the city growth factor is low, and 2) consistently low rates of anencephalus when the city growth factor is high, regardless of horizontal geomagnetic flux. The higher that the rate of anencephalus would be under stable population conditions, the greater would be the reduction caused by high growth rates. An attempt to separate the associations of geomagnetism, growth rate and magnesium with anencephalus is given in figure 2. Only those cities with a low growth rate (factor less than 2.4) were used. Too few cities remained for a fully satisfactory analysis, but the data in figure 2 suggest that the lowest magnesium levels might have an influence on rates of anencephalus.

Discussion

Since the geomagnetic north pole (with its low horizontal flux and high cosmic ray flux) lies within the borders of Canada, it is to be expected that most immigrants to Canada will have come from areas with lower levels of cosmic radiation. If, as a result of this lower exposure (or for any other reason), immigrants have lower rates of anencephalus, then any given amount of immigration will have the greatest differential effect on rate of anencephalus in areas subject

TABLE 1

Rates of anencephalus (1950–1969) and other data used in correlations for 36 Canadian cities and New Brunswick (N.B.)

City	Rate of death from anencephalus/1000 total births*	Horizontal geomagnetic flux, $\gamma \times 10^3$	Magnesium in tap water, P.P.M.*	Population growth factor
Brantford	1.47	16.8	23.9	2.0
Burlington	0.97	16.6	8.6	3.1
Calgary	0.77	15.7	15.1	4.5
Dartmouth	0.80	17.3	0.5	2.1
Edmonton	0.93	13.8	10.4	4.7
Guelph	1.39	16.4	26.0	2.6
Halifax	1.23	17.3	0.6	1.7
Hamilton	1.41	16.7	8.3	1.8
Jacques-Cartier	1.32	15.6	7.5	2.3‡
Kingston	1.03	16.2	7.9	2.0
Kitchener	1.10	16.5	26.3	3.1
Montreal	1.51	15.6	7.6	1.3
Montreal-North	1.17	15.5	7.5	2.3‡
Niagara Falls	1.08	16.8	8.6	3.3
Oakville	0.74	16.5	8.3	4.3
Oshawa	1.17	16.3	8.4	3.2
Ottawa	1.55	15.4	2.2	2.0
Peterborough	1.60	16.1	3.1	2.3
Quebec	1.79	15.0	1.7	1.2
Regina	0.61	14.3	27.5	2.4
St. Catherines	1.24	16.7	8.6	3.6
St. John, N.B.	2.12†	16.6	0.7	1.3
St. John's, Nfld.	1.56	17.5	0.6	2.2
St. Laurent	0.90	15.6	7.5	2.9
St. Michel	1.37	15.5	7.7	2.3‡
Sarnia	1.54	16.9	6.7	3.1
Saskatoon	0.77	13.6	11.6	2.9
Sault Ste. Marie	1.46	14.6	3.0	5.1
Sherbrooke	1.69	15.8	2.8	2.2
Sudbury	1.28	14.7	5.0	2.8
Toronto	1.45	16.4	8.7	1.1
Trois-Rivières	2.04	15.2	0.7	1.3
Vancouver	0.79	18.4	0.2	1.5
Verdun	1.44	15.6	7.5	1.1
Windsor	1.11	17.4	7.8	1.9
Winnipeg	1.28	13.5	6.5	2.5
Province of N.B.	1.41	16.2	—	1.4

* Data from Elwood (1).

† Used only in magnesium correlations. N.B. rate was used for other correlations.

‡ Population data were incomplete on these three cities. Growth factor was estimated (see text).

to some additional factor (e.g., low horizontal geomagnetic flux) which leads to high rates in the stable population, but is not manifest in the immigrant population. As noted in figure 1, this is indeed the case. This finding is consistent with the mechanism of growth rate effects postulated above.

Elwood (1) noted a minor association between mean income of residents for each city and the rate of anencephalus. His income data were not reported, so

TABLE 2

Results of screening of four factors for possible correlation with rates of anencephalus for 1950–1969 period and each other for 36 Canadian cities

	City growth factor		Horizontal geomagnetic flux ($\gamma \times 10^3$)		Magnesium in tap water (P.P.M)		City size—total births 1950–1969	
	<2.4	≥2.4	<16.2	≥16.2	<7.6	≥7.6	<33,000	≥33,000
Anencephalus deaths per 1000 total births*	1.39±0.07	1.08±0.07	1.30±0.09	1.19±0.08	1.42±0.09	1.1±0.07	1.26±0.08	1.24±0.08
t-value	−3.2		−0.9		−2.8		−0.2	
Magnesium in tap water (P.P.M.)*	5.38±1.23	11.76±1.96	7.49±1.47	9.41±2.02			8.44±1.55	7.98±1.91
t-value	+2.8		+0.8				+0.2	
Horizontal geomagnetic flux ($\gamma \times 10^3$)*							16.12±0.17	15.79±0.34
t-value							−0.9	
City growth factor			2.56±0.27	2.44±0.21			2.72±0.23	2.29±0.24
t-value			−0.3				−1.3	

* Standard errors are indicated by ±.

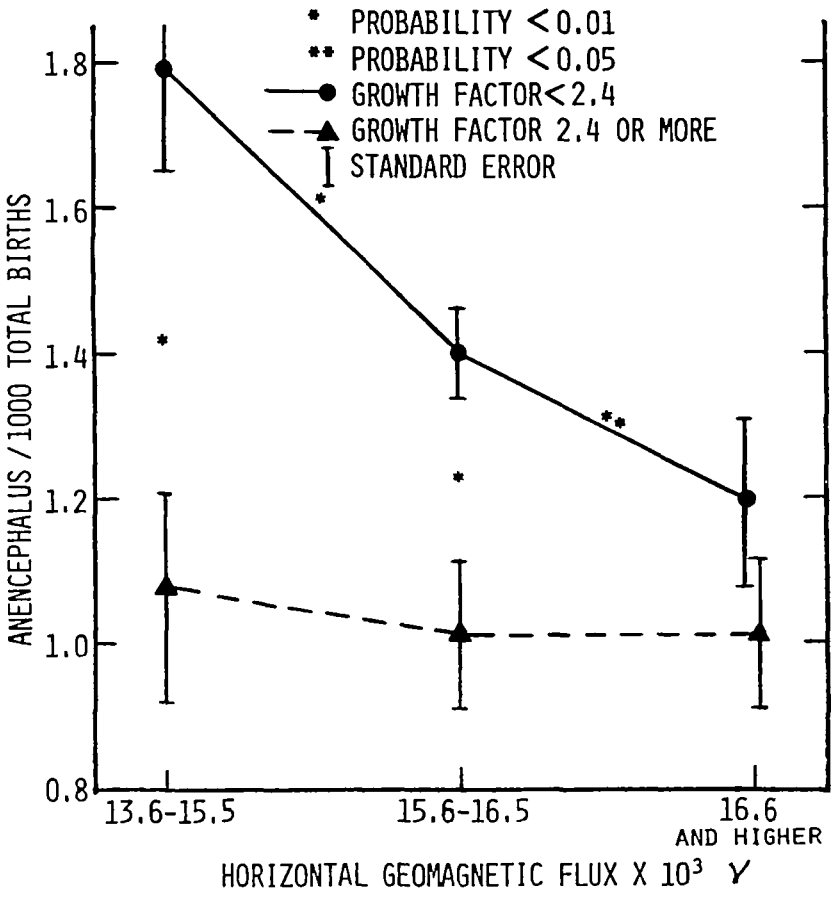

FIGURE 1. Rate of anencephalus as a function of horizontal geomagnetic flux in cities having high or low growth rates, 1960–1969, in 35 Canadian cities and N.B. (Based on relevant data from table 1.)

they were not reanalyzed, but it seems likely that an association between city growth rate and mean income would be present. In that case, part of the growth rate factor might be reflecting an association between mean income and anencephalus. The direction of such an association would be consistent with that reported by Elwood.

Since Elwood did not consider city growth rate as a factor; and since it was demonstrated above that city growth rate is strongly associated with magnesium content of tap water, it seems that he may have been dealing with a spurious association. The inconsistent findings in figure 2 with respect to magnesium in tap water are puzzling. The significantly high rate of anencephalus, associated with low magnesium, low growth rate, and low horizontal geomagnetism but not at high magnesium levels, suggests that there might be a threshold magnesium level below which there is an influence on congenital anomalies. However, some doubt is cast on this possibility by the fact that the mean level of magnesium in tap water is 2.1 parts per million (PPM) for the five cities having the highest rate of anencephalus in figure 2, versus 0.52 PPM for the five cities in the figure which have the lowest rate (low magnesium, low growth,

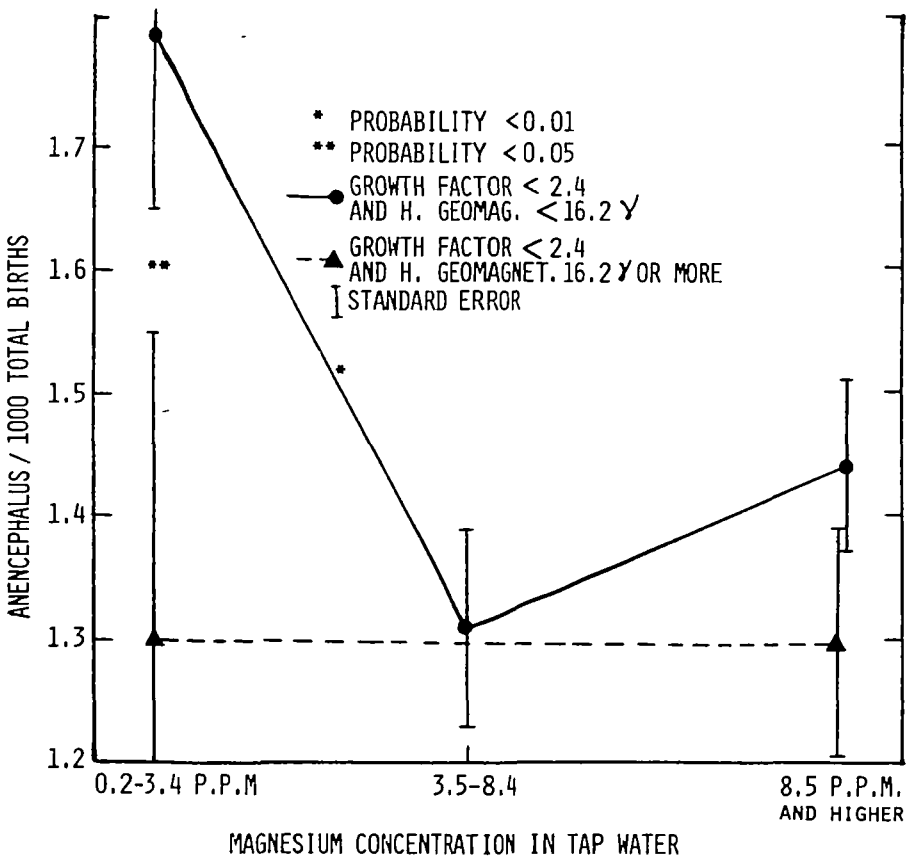

FIGURE 2. Rate of anencephalus as a function of magnesium concentration among cities having low growth rates, and high or low horizontal geomagnetic flux, 1960–1967, in 20 Canadian cities. (Based on relevant data from table 1.)

high horizontal geomagnetism). Apparently low magnesium by itself is not sufficient to cause anencephalus. Perhaps it has such an effect only in the presence of co-factors. I must agree with Elwood that it is unlikely that low magnesium content in drinking water has a direct causal effect on the rate of anencephalus.

Elwood noted that Vancouver held an anomalous position with respect to magnesium in water (1). However, it fits well with the geomagnetism-cosmic radiation model. It has the highest horizontal geomagnetic flux of any Canadian city in table 1 (18.4), and its rate of death from anencephalus is among the lowest (0.79/1000 total births).

There is a controversy in the literature as to whether congenital malformations (especially anencephalus and other neural tube defects) are the result of genetic factors or of environmental factors (12, 13). The argument involves findings with migrants (13–15), socioeconomic and temporal differences (13), ethnic factors (12, 16), and increased risk of neural tube defects among siblings (12). The hypothesis used here, and resultant data, tends to render that controversy moot. The present hypothe-

sis is that an environmental factor (background radiation) operates through a genetic mechanism. If most anencephalus represents a dominant lethal mutation, then it would be a genetic factor which is eliminated in the first generation. If most resulted from recessive mutations, then many generations might be required for substantial change after migration. The data on Irish immigrants noted above, and data which indicates that after a few generations in Hawaii, the rate of neural tube defects in Caucasoids and Oriental migrants moves away from the pattern observed in their country of origin and becomes quite similar (15), suggest either a continuous environmental factor or a quickly eliminated genetic factor which is dependent on an environmental agent. Dominant lethals might behave in this manner, and would also increase the risk of neural tube defects among siblings, as reported (12). Even if the above hypothesis is correct, one would not expect background radiation to cause all neural tube defects—other teratogens could add to the toll and confuse the epidemiologic picture. The genetic picture could be confused by newly-generated dominant mutations which would appear only in a small fraction of an individual's germ cells, by a mixture of dominant and recessive mutations for anencephalus or by polygenic mutations for some cases of anencephalus.

The hypothesis that anencephalus results from genetic damage largely accumulated during the parent's lifetime carries with it the implication that an increased incidence of anencephalus would occur with increased age of parents. Such an increase has been observed (17), although there was also an elevated incidence among births to mothers below age 20 years which would not be explained by the hypothesis. An increase in other birth anomalies with increased age of parents, such as Down's syndrome, have also been observed (18, 19).

There are a number of unanswered questions which cause one to have reservations about the present results. Among these are the following: Do the temporal variations in rates of neural tube malformations that have been noted correlate with solar activity cycles? How constant was the magnesium content of drinking water over the period of Elwood's observations? How good is city growth rate in Canada as an indicator of immigration from areas of higher horizontal geomagnetic flux? Would maternal age and socioeconomic factors (which could not be controlled) be included in the city growth factor (which was adequately controlled)? Since data in the present study has to be accumulated over a long period of time, would such accumulation tend to produce spurious results as a result of inconstant variables, or would it give superior results by averaging out the effects of otherwise confusing variables?

There is considerable skepticism that the very low doses associated with background radiation (especially cosmic radiation) are capable of influencing rates of congenital abnormalities. However, the efficiency of highly ionizing particles such as neutrons and protons (components of secondary cosmic radiation) for inducing chromosome damage is known to increase markedly at very low dose rates (20–23). In addition to the report of Wesley (2) noted above, there are a number of epidemiologic observations which suggest that small amounts of radiation may have effects on man: cancer of a number of sites is associated with horizontal geomagnetic flux on a worldwide basis (5, 6); genetic damage has been reported from diagnostic radiation (24); an increased incidence of Down's syndrome was found to be associated with residence in an area of high background radiation in India (25); a higher cancer rate was found to be as-

sociated with areas having higher background radiation in Yugoslavia (26); increased chromosome aberrations in human lymphocytes have been reported from exposure to very small amounts of alpha radiation from plutonium and radon daughters (27, 28); increased lung cancer rates have been noted among miners whose radon daughter exposure is little above background rates (29-31); excess cancer has been noted among mildly-exposed radiation workers (32) and after exposure to diagnostic radiation (33); ovarian doses of less than one rad are associated with Down's syndrome (34); and increased rates of congenital malformations were found in areas containing materials with higher than average radioactivity (35).

Some of the above observations are considered to be controversial, and there are a number of studies which have failed to find these types of associations. Three studies have found a correlation between high altitudes (which have higher cosmic radiation) and neonatal death rate or growth retardation (36–38), but not with background radiation (36). This effect was attributed to relative hypoxia. However, only 10 or 15 per cent of these deaths were the result of congenital malformations. If congenital malformations represented the only, or the major contribution to neonatal deaths by background radiation, then one would not expect these studies to find a relationship, since such deaths are only a small part of the total neonatal deaths. Several studies have sought but failed to find consistent correlations between background radiation or altitude and leukemia rates (39–44). There are two important reasons why these authors failed to find a correlation with background radiation: 1) those who looked only at altitude neglected the fact that cosmic radiation is also dependent on geomagnetic latitude, and 2) leukemia as an indicator of radiation effect was an unfortunate choice. Although leukemia can be caused by radiation, it appears that many human leukemias are caused by other agents, such as benzene or viruses. At any rate, cancer of several sites was found to correlate much better with horizontal geomagnetic flux than leukemia (6). Total cancer rates would also be a poor choice because such rates would be strongly affected by sites (e.g., lung and bladder) which are largely due to chemical carcinogens.

The studies noted above which reported associations between radiation and cancer or congenital anomalies are not negated by the studies which failed to find the association. The findings reported in this study of an association between horizontal geomagnetic flux and anencephalus are consistent with the positive studies noted above, and with the concept that background radiation has definite biological effects on man.

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