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Dementia in Newfoundland: identification of a geographical isolate?

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Abstract

***Study objective*—The aims were (1) to identify from death certificates regions with an increased incidence of dementia mortality; and (2) to determine whether a previously observed excess of patients with Alzheimer disease originating from a small area could be confirmed in a survey of death certificates.**

***Design*—The study identified all individuals dying with dementia, recorded on death certificates as an immediate, antecedent, underlying, or contributing cause of death. Rather than the usual residence, the birthplace of these individuals was used to determine regional differences in dementia mortality. A comparison was made of two areas to test the significance of a geographical isolate of persons. To test for a possible genetic component of the excess, an analysis was made of the frequencies of family names. To test for a possible environmental component an analysis was made of standard measurements of drinking water quality.**

***Setting*—The survey data were derived from all 1985 and 1986 deaths in the province of Newfoundland.**

***Measurements and main results*—Based on the current census population, the prevalence of dementia at death for 1985 and 1986 was 34 and 37/100 000. For both years there was a significant excess of persons originating from a small area (95% CI, 1·1–20·7%, and 2·5–20·4%). This excess could not be explained by differences in age, sex, ethnic origin, or by variation in mobility patterns. The study area has a high concentration of aluminium in the drinking water. An analysis of the family names gave inconclusive evidence of a clustering among the dementia cases.**

***Conclusions*—If all contributing causes of death are recorded and the birthplace of individuals is noted, mortality statistics can reveal regional differences in dementia rates. This shows the need to examine areas smaller than census districts to identify subpopulation variation in the prevalence of dementia. Environmental influences can vary substantially in areas relatively close together, as evidenced in measurements of drinking water chemistry. Genetic influences are more likely to be revealed from the birthplace of individuals, which may indicate a common ancestry.**

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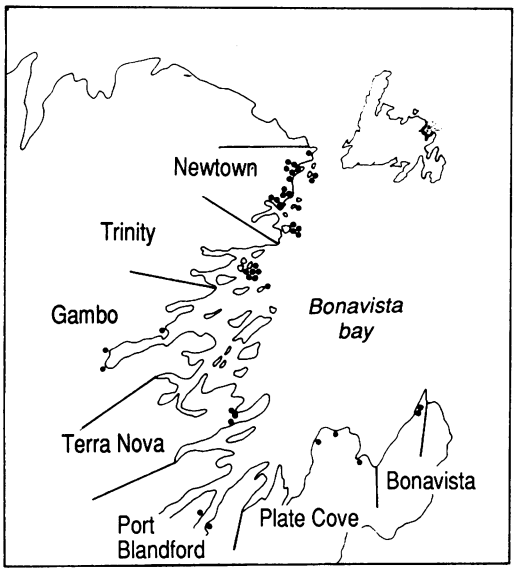
The reports in the 1950s of ALS-PD dementia with Alzheimer changes in the brains of the Chamorros on Guam[1] and of the Auyu and Jakai tribes of western New Guinea,[2] and subsequent endeavours to link the high incidence to abnormal deposition of calcium and aluminium in the central nervous system resulting from low environmental calcium and magnesium,[3] or to neurotoxins in the cycad seed,[4] remain landmarks in epidemiological studies of neurological diseases. Since then there have been few reports of areas in the world where an increased prevalence of a dementing illness can be attributed to environmental factors. Recently, a relationship between Alzheimer disease and aluminium in the drinking water has been reported in southern Norway,[5] in England and Wales,[6] and in the Gironde region of southwestern France.[7] These three reports differ in their identification of the dementia population; in England and Wales, cases were derived from computed tomography scan records, in France from elderly community residents, and in Norway from death certificates.

In Australia it was determined that the high rate of dementing disorders in certain states was an artifact of death certification practices.[8] A previous report of mortality data suggested that regions with a high incidence of dementia are correlated with areas containing long stay institutions.[9] This makes searching for clues of possible environmental causal agents of dementia difficult. In order to eliminate this latter distortion of geographical pattern, the birthplace of individuals, as stated on their death certificates, was used to identify areas with an increased incidence of dementia. A survey of all deaths in the province certified as due to dementia was conducted over a two year period in 1985 and 1986.

An epidemiological study of Alzheimer disease in Newfoundland revealed that, of nine patients enrolled in the study who were born in Bonavista Bay, eight came from a small area along the north shore of the Bay (Newtown, figure). Attempts were made to determine whether this observed excess of patients could be confirmed in a larger sample, such as in a survey of death certificates, and if so, whether the excess could be explained by a genetic isolate of people or by an environmental factor.

Methods

Since the original observation of an unexpected excess was in persons born in the early 1900s, the sample should also identify persons who were born in this time period. It was felt that



Geographical distribution of birth places for deaths coded as dementia within Bonavista Bay.

individuals who died in 1985 and 1986 would be representative of this age group.

In order to determine any variation in the distribution of dementia in the province, all 1985 and 1986 death certificates registered at the Vital Statistics division of the provincial Department of Health were individually scanned for causes of death that could be attributed to dementia. Dementia was defined by one of five possible categories, Alzheimer disease, chronic/organic brain syndrome, dementia, senile dementia/senile confusion, or senility.

For each individual thus identified, the age, sex, place of birth, and place of death were recorded. All dementia codings listed on the certificate as an immediate, antecedent, underlying, or contributing cause of death were recorded.

None of the index patients from the original cluster of cases had died in 1985 or 1986, thus excluding them from this second study.

Age adjusted mortality rates for deaths with a dementia were calculated using the direct method and the 1986 Newfoundland population as the standard.

To determine whether the original observation of dementia within Bonavista Bay could be confirmed, all 1985 and 1986 deaths of individuals born in Bonavista Bay and having a dementing illness recorded on their death certificates were compared with all 1986 deaths of individuals born within the Bay, surviving beyond age 70 years, and not having a dementing illness recorded on their death certificates. Depending on where they were born, this group was divided into two geographical areas separating the north shore (Newtown and Trinity, figure) from the remainder of the Bay. The boundary between these two areas was determined from the original observation that this area might have an increased prevalence of dementia. The significance of the geographical isolate of persons originating from the north shore, determined in relation to those from the remainder of the Bay, was calculated as the difference between the two proportions with appropriate confidence intervals.[10] The Fleiss correction factor was used for proportions smaller than 0·1.[11]

To test for a possible genetic component of the increased incidence of dementia on the north shore, the frequencies of the last names of individuals' parents, which were available from the death certificates, were compared. Fewer last names would indicate that the group was more closely related. The last names of the parents of individuals dying with a dementia in 1985 and 1986 were compared with the last names of the parents of those born in the same area, who died in 1986 without a dementia and were over age 70 years.

To test for a possible environmental factor, a detailed analysis of untreated drinking water samples collected in June and October of 1986 from six communities in Bonavista Bay (figure) was available from Environment Canada.[12] These six communities coincide with the six census subdivisions within the Bay (one subdivision, Terra Nova, was not sampled). Comparison was based on standard measurements of water quality, including pH, water colour, and aluminium. The data for duplicate water samples for the two months were averaged.

Results

DEMENTIA IN THE NEWFOUNDLAND POPULATION

The distribution of the five dementia codings for the 191 deaths identified from 3656 1985 Newfoundland death certificates and for the 208 deaths from 3582 1986 death certificates is found in table I. The most frequent coding on the death certificates in 1985 was chronic/organic brain syndrome (26·7%); in 1986, Alzheimer disease was recorded most often (25·5%).

Based on the 1986 census population, the prevalence of dementia at death for 1985 was 34/100 000 population; for 1986, 37/100 000.

The geographic distribution of the birthplaces of individuals who died with a dementing illness in 1985 and 1986 is shown in table II. Two regions, census divisions 03 and 07, have high dementia mortality rates for both years (mean standardised rates, 56·5 and 54·4/100 000 population, for the two areas). Census division 03 is a relatively isolated region on the south west coast of the island; census division 07 includes Bonavista Bay and the north shore of Trinity Bay.

DEMENTIA IN THE BONAVISTA BAY POPULATION

The birthplaces of those who died in 1985 or 1986 with a dementia were compared with those of persons over age 70 years, who died in 1986 without a dementia. There was a statistically significant excess of persons with dementia from the north shore of Bonavista Bay (table III). For 1985, the 15 dementia deaths from the north shore represented 17·2% of all deaths of persons originating from that area, while the nine dementia deaths from the central and southern areas of the Bay represented 6.3% of deaths from that region (95% confidence interval, 1·1% to 20·7%). Similarly in 1986, the 12 dementia deaths from the north shore (14·3%) and the four dementia deaths from the other areas of the Bay (2·9%) also differed significantly from non-dementia deaths (95% confidence interval, 2·5% to 20·4%).

ANALYSIS OF FAMILY NAMES

A list of the last names of the parents of the

1985–86 dementia cases from the north shore was compiled. Of 54 possible family names, there were 34 different names among the 49 that could be recorded from the death certificates (five were unknown). From the 72 1986 non-dementia controls from the same area, two groups of 49 parents' last names were selected consecutively by registration date. In the first group, 34 family names were identified; in the second group, 38 family names. This was identical to the finding in the dementia cases in one instance; in the other, there were more family names identified, indicating this group was less likely to be related than the dementia group.

ANALYSIS OF DRINKING WATER

The birthplaces within Bonavista Bay were divided according to one of seven census subdivisions to coincide with the communities where drinking water had been sampled (table IV; figure). In the Newtown area the high incidence of dementia (37·5% and 75·0% of dementia deaths in 1985 and 1986, respectively *v* 28·5% of 1986 non-dementia deaths) coincided with the lowest pH (5·2), the highest concentration of aluminium (0·165 mg/litre) and the highest water colour measurement (108). In the Port Blanford and Plate Cove areas the concentration of aluminium in the drinking water was also high, 0·125 and 0·128 mg/litre, respectively, but there was no corresponding increase in dementia deaths.

There are potentially several biases in the data that could explain the excess of persons originating from this section of Bonavista Bay.

AGE

The persons dying with a dementing illness who had been born on the north shore were no older than those originating from the rest of the Bay. For 1985, the mean age of those from the north shore, 82·5 years, was not significantly different from the mean age of those from the central and southern regions, 80·3 years (95% confidence interval, −4·0 to 8·43). For 1986, the individuals from the north shore were slightly younger, with a mean age of 84·3 years compared with those from the rest of the Bay (85·0 years).

SEX

There was no significant difference in the sex distribution of those dying with dementia when comparing the two areas of the Bay. Combining the two years, the difference in the proportion of females, 70·4% from the north shore and 53·8% from the rest of the Bay, was not significant (95% confidence interval, −21·2% to 54·4%).

ASCERTAINMENT

A comparison was made of where the individuals with a dementia had been living before they died, as stated in the address on the death certificate. For 1985 and 1986 taken together, 63% of those who had been born on the north shore had moved in later life to areas outside Bonavista Bay compared with 38·5% of those originating from the central and southern regions (95% confidence interval, −13·3% to 62·3%).

When the data were divided according to whether the patients had died in an acute care facility or in an intermediate/terminal care facility, more had originated from the north shore (37·0%) than from the other areas of the Bay (15·4%). The difference was not significant (95% confidence interval, −10·9% to 54·1%).

Table I Frequency distribution of codings for dementia from death certificates, 1985–86

Causes of death	1985 n	1985 (%)	1986 n	1986 (%)
Organic brain syndrome/chronic organic brain syndrome	51	(26·7)	44	(21·1)
Alzheimer disease	45	(23·6)	53	(25·5)
Senility	42	(22·0)	51	(24·5)
Senile dementia/senile confusion	32	(16·8)	35	(16·8)
Dementia	21	(11·0)	25	(12·0)
Total	191	(100·1)	208	(100·0)

Table II The geographic distribution of birthplaces for deaths coded for dementia, 1985–86. Numbers in brackets indicate age adjusted mortality rates per 100 000, standardised to the 1986 Newfoundland population.

Census division	Dementia cases 1985	Dementia cases 1986	Total population 1986
01	80 (29·4)	101 (37·2)	246 150
01A	34 (19·6)	43 (25·0)	164 750
01B	46 (46·0)	58 (58·5)	81 400
02	17 (57·3)	11 (37·3)	30 285
03	14 (63·1)	11 (49·9)	25 735
04	3 (13·4)	4 (17·7)	27 270
05	1 (2·4)	4 (9·6)	45 650
06	4 (10·7)	– –	40 715
07*	36 (60·2)	29 (48·6)	43 620
08	22 (38·6)	27 (47·1)	54 225
09	5 (25·3)	5 (24·4)	25 955
10	2 (26·0)	3 (39·0)	28 740
Subtotal	184 (32·4)	195 (34·3)	568 345
Non-residents	6	9	
Birthplace unknown	1	4	
Total	191 (33·6)	208 (36·6)	

* This census division includes Bonavista Bay.

Table III The geographical distribution of birthplaces within Bonavista Bay of persons with and without a dementia on death certificates, 1985–86.

Deaths	North shore n	Central and south shore n	Confidence intervals for proportions†
1986 non-dementia deaths >70 yrs	72	135	
1985 dementia deaths	15 (17·2%)	9 (6·3%)	1·1% to 20·7%
1986 dementia deaths	12 (14·3%)	4 (2·9%)	2·5% to 20·4%

† with Fleiss' correction.

Table IV Dementia and non-dementia deaths and drinking water analysis by geographical area within Bonavista Bay.

Geographical area	Dementia deaths 1985	Dementia deaths 1986	Non-dementia deaths 1986	Drinking water measurments pH	Al	Colour
Newtown	9 (37·5%)	11 (68·8%)	59 (28·5%)	5·2	0·165	108
Trinity	6 (25·0)	1 (6·3)	13 (6·3)	6·0	0·105	20
Gambo	2 (8·3)	1 (6·3)	8 (3·9)	6·6	0·022	5
Terra Nova	1 (4·2)	2 (12·5)	43 (20·8)	–	–	–
Port Blanford	1 (4·2)	1 (6·3)	26 (12·6)	5·9	0·125	80
Plate Cove	3 (12·5)	– –	22 (10·6)	5·9	0·128	26
Bonavista	2 (8·3)	– –	36 (17·4)	6·0	0·064	16
Total	24 (100·0)	16 (100·2)	207 (100·1)			

Al = aluminium (mg/litre)

Discussion

Prevalence studies of dementia are invariably carried out on samplings of the existing population.[13 14] Only rarely have mortality rates been analysed to describe geographic and time trends of dementia.[8 9 15] These studies caution against misinterpretation of certain aspects of the data.

The unreliability of death certificates in defining dementia mortality rates has been investigated. Dementia is not always recognised as a distinct disease process and listed on death certificates. This can often lead to an underestimation of mortality rates, as was found

in Newcastle where only 57% of patients registered with a dementia at a psychogeriatric clinic had a dementia stated on their death certificates.[9] Studies which use records of the underlying cause of death from death certificates may also underestimate mortality rates.[8] Dementia as a contributing cause of death can sometimes be omitted in selecting the underlying cause of death, defined by the World Health Organization guidelines as the disease which initiated the chain of events leading to death.[16] Changes in the diagnostic patterns of coding dementia, an increase in codings for Alzheimer disease and dementia, or a decrease in codings for senility can often distort mortality rates.[8 9]

In Australia, death certificates were found to be misleading in the investigation of regional differences in mortality from dementia.[8] The investigators found that whether a dementia was recorded as a cause of death was a function of the place of death rather than the place at birth. The unreliability of the place of residence on death certificates as an indicator of underlying geographical variation was supported by Martyn and Pippard[9] who found increased mortality rates for dementia around locations of large psychiatric hospitals in England and Wales, and by Jorm and colleagues[8] who found that the diagnostic practices of a single physician could influence dementia mortality rates.

The present study, in examining the immediate, antecedent, underlying, and contributing causes of death as stated on the death certificates, ensures a more complete ascertainment of possible dementia codings, thus minimising the limitations of the ascertainment process. In using the place of birth, not the place of death, to look for regional differences in mortality rates, this study is also less likely to be distorted by clusterings around long stay institutions.

Because ascertainment is complete, the mortality rates based on the 1986 census population (34 and 37/100 000) may be higher than those recorded from other countries. In Australia, the highest prevalence at death, 22/100 000, was recorded in northern Tasmania[8]; this may be attributed in part to data which coded only the underlying cause of death. In Norway, however, the mortality rates are higher than those recorded in Newfoundland, ranging from 35 to 50 deaths/100 000 population.[5] Their definition of dementia is similar to that in the present study in that any one of four causes of deaths listed was recorded.

The excess of dementia mortality from the north shore of Bonavista Bay could be influenced by several factors known to affect rates. The death records of persons originating from the north shore showed that they were no older than those from the rest of the Bay, indicating that an increase in the age at death did not contribute to an increase in the probability of developing a dementing illness. It has sometimes been suggested that women are at a greater risk for developing a dementia.[13] Although there were more women in the group from the north shore the difference was not significant. Possibly, if more persons originating from the north shore than from the rest of the Bay had moved to larger more specialised centres they would have an increased probability of having dementia diagnosed and recorded on their death certificates. However, there was no relative excess of outmigration of persons from the north shore, and no relative excess of persons dying in acute care hospitals. Therefore age, sex, and variation in mobility patterns do not explain the north shore excess in dementia mortality.

To better define the category of dementia found listed on death certificates of individuals originating from the north shore area, the codings were checked to compare the north shore with the rest of the island. More (67%) from the clustering of north shore cases could be classified as Alzheimer or chronic/organic brain disease than from the rest of the island (47%). Although the difference is not significant (95% confidence interval, 0% to 40·4%), it may indicate that a single disease process is found in this area, distinct from the broad category of dementia.

The area in Bonavista Bay that appears to have a high prevalence of dementia is a 30 km strip of land along the north shore. The communities derive their drinking water from lakes that are fed mainly from peat bogs; this accounts for the low pH of the water (table IV). Metal ions, including aluminium, have an increased solubility in acidic water. In southern Norway a high prevalence of dementia mortality, in the absence of mortality from age related diseases of the circulatory system, has been correlated with an increase of aluminium in the drinking water from lakes receiving the greatest amount of acid rain.[5] In England and Wales dementia as defined from CT records was increased in areas with high concentrations of aluminium in the drinking water.[6] In France the risk of probable Alzheimer disease was increased significantly for residents living in areas with the highest levels of aluminium in the drinking water.[7] In Newfoundland the levels of aluminium in the drinking water from communities in Bonavista Bay does not exceed the guideline of 0·2 mg/litre established by the European Community directives.[6] Nevertheless, the highest aluminium concentration in the Bay is recorded in the area with the highest dementia mortality. Although aluminium has been the element most often cited as a causal agent with relation to Alzheimer disease, it is also possible that other environmental factors, as yet undefined, can produce a dementing process.

From the original study, seven of eight individuals from the north shore of Bonavista Bay had moved from the area at various times throughout their lives. Since the mobility pattern of the 1985 and 1986 cases remains unknown, it is difficult to assess any possible life time risk of exposure to an environmental agent such as aluminium in the drinking water.

There is no reason to suspect that the people who originally settled on the north shore of Bonavista Bay were of different genetic stock from those settling around the rest of the Bay. Initial settlement in the mid 1800s was by migration from the south west coast of England of individuals employed by the English fish merchants.[17] More particularly, Greenspond (Newton, figure) was settled by persons from

Poole in Dorset and Christchurch in West Hampshire; Bonavista was also settled by persons from Poole, with a small percentage (15%) from Ireland. Subsequently, settlement spread along the coast from these two well established communities to the central regions of the Bay. This section of the south west coast of England was not identified by Martyn and Pippard[9] as a region with high dementia mortality.

If the cluster of persons from the north shore with dementia were to represent a genetic entity, it follows that many of the parents of these individuals would have the same family name. A comparison of the last names of the parents of dementia cases with the last names of two groups of non-dementia controls from the same area gave inconclusive evidence of a clustering of family names. The parents in the dementia cases were as likely to be related as the parents in one set of controls, while they were more likely to be related when compared with the second set of controls.

Evidence for a genetic isolate of people comes from the family histories of the eight probands enrolled in the Newfoundland Alzheimer study (unpublished data). Six of these probands from the north shore had a first degree relative with "possible"[18] Alzheimer disease. Three probands had a single affected parent, while the other three had one, three, and five affected siblings. The shared environment and therefore an environmental causal agent of dementia must be considered in the families with multiple affected siblings. In no instance did the proband have an affected parent and sibling indicating a multigenerational dominantly inherited genetic disease. As is always the case in diseases with late onset of symptoms, parents or siblings may have died before manifesting the disease. Unfortunately, the families of the cases identified from death certificates cannot be approached to obtain family histories.

This study demonstrates that if all contributing causes of death, in addition to the underlying cause of death, are recorded, and the birthplaces of persons are noted, mortality statistics can reveal regional differences in dementia rates. Further, it shows the need to examine areas smaller than census districts to identify subpopulation variation in the prevalence of diseases such as dementia. If an environmental factor is suspected to be a cause of dementia, drinking water can be substantially different chemically in areas that are relatively close together. If a genetic factor is suspected, the identification of a related group of individuals with common ancestry, demonstrating a founder effect, is more likely to be identified from a group selected by birthplace. Further studies are being carried out to determine the exact nature of the genetic and environmental components of this isolate of persons.

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