

Sudden death from ischemic heart disease in Ontario and its correlation with water hardness and other factors

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Summary: It is possible that there is a systematic geographical variation in the proportion of deaths from ischemic heart disease that occur suddenly, and that this variation may be causally related to water hardness or some other environmental factor. Three indices of sudden death have been examined; each showed a correlation with water hardness that was of similar sign and magnitude. A detailed examination of 1686 deaths occurring in residents of two cities which differ widely in the hardness of their water supply confirmed that in deaths ascribed to heart disease the proportion of sudden deaths was higher (by 20-30%) in the northern (soft-water) city than in the southern (hard-water) city.

One of the most challenging yet least understood aspects of acute myocardial infarction is the large proportion of deaths that occur so soon after the onset of symptoms that the patient is dead before effective treatment can be instituted. The actual mechanism of death in these cases is uncertain, since by their nature they can rarely be studied until after the event, but it is likely that many are due to lethal arrhythmias such as ventricular fibrillation.

We have previously suggested¹ that there may be some geographic variation in the tendency to develop these arrhythmias and that this may account for some of the geographic variation that exists in overall ischemic heart disease (IHD) mortality. This suggestion was based on the observation that in 1967 the differences in IHD mortality between three regions of Ontario (defined on the basis of water hardness) were due almost entirely to differences in the proportions of deaths that were certified by coroners rather than by private physicians. We recognized that the frequency with which IHD deaths were referred to the coroner might be influenced by local usage and custom as well as by the suddenness of death, but the similarity in the coroner certification rates for non-IHD deaths in the three regions encouraged us to believe that local custom was relatively uniform throughout the province, and that the variation in coroners' rates reflected an increased incidence of "sudden" IHD deaths in the soft-water region.

The purpose of the present paper is to extend these earlier observations and to provide some additional evidence for the belief that (in Ontario at least) there is a systematic geographic variation in the frequency of sudden death from ischemic heart disease. Whether or not this variation is causally related to the composition of local water supplies remains uncertain, but we believe that further research in this area is well justified, since the identification of an easily alterable water component as one of the factors responsible could lead to some measure of control over the modern "epidemic" of fatal IHD.

To eliminate the possibility that urban-rural differences within the three regions of Ontario may have affected our previous results we have restricted the present analysis to 34 medium-sized Ontario towns and cities, and have expanded the period of observation from one year (1967) to three years (1965-67) to compensate for the smaller numbers involved.

In addition to classifying deaths by the status of the person signing the

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death certificate (coroner or non-coroner) we have made use of another item of information that is routinely coded from the death certificate in Ontario — the place of death, whether inside an institution or not. Although, as with coroners' deaths, factors other than the suddenness of death could conceivably influence the proportion of deaths occurring outside hospitals or other institutions (for instance, the presence of a large mental hospital in a town) we hoped that if there was a real geographic variation in the relative frequency of sudden death this would be reflected in a parallel variation in the proportion of "non-institutional" deaths.

A third index of sudden death that we have employed is the information on duration of illness that is requested (and in most cases provided) on Ontario death certificates. Unfortunately this information does not appear on the punch-card summary of death-certificate information which is routinely prepared at the office of the Registrar-General, so that it cannot be studied by mechanical sorting and tabulation, but must be determined by examination of the original death certificates. This is a time-consuming procedure, and for this reason we have analyzed deaths in this way for one year only (1967). Once again, while many extraneous factors could conceivably interfere with the validity of this index, we hoped that it might also reflect a true geographical variation in sudden death if such were present.

To assist in the evaluation of these three indices of sudden death we have made a detailed study of deaths occurring during a recent three-year period (1967-1969) in two Ontario cities, the water supplies of which are near the extremes of the water-hardness spectrum. All death certificates involving residents of Port Arthur (water hardness 47 parts per million) and Kitchener (water hardness 395 parts per million) during these years were examined and, where indicated, additional information on the circumstances of death was obtained from hospital and coroners' records and by enquiry from private physicians.

Initially it was hoped that it would be possible to analyze deaths in the two cities according to duration of symptoms, as was done in some earlier prospective studies such as those in Baltimore and Belfast.^{2,3} Unfortunately this was found to be impractical in the present (retrospective) study, since the available records often lacked specific information regarding the time of onset, and we were unwilling to involve the families or friends of the deceased in our investigation. However, as we collected our data it became evident that in both of the cities under study there was an almost universal preference for serious illness to be managed in hospital, and that in virtually every case where death occurred outside hospital, failure to admit to hospital had been due to lack of time, i.e. the final illness had been "sudden". We have therefore used the fact of admission to hospital to distinguish sudden from non-sudden deaths. We took the added precaution of analyzing separately those deaths occurring within a few hours of admission, to ensure that the differences found in the frequency of non-hospital deaths were not simply the result of differences in the availability of emergency and ambulance services in the two cities. Similarly, by using several diagnostic categories of varying specificity, we have attempted to eliminate the possibility that the observed difference between the two cities is the result of differences in diagnostic criteria and terminology.

Material and methods

Correlation analysis

The 34 Ontario towns and cities included in this part of the study were those which had a population of 10,000 or more at the 1951 census and for which representative analyses of municipal water supply were available.⁴ Metropolitan Toronto was excluded, since in many respects it is unlike most other Ontario towns and cities and because of its large size (over two million population) it would have exerted an undue influence in the weighted calculations.

The data-processing section of the office of the Registrar-General of Ontario kindly supplied us with tabulations of the 10,118 deaths ascribed to ICD 420 (arteriosclerotic heart disease)⁵ during the years 1965-1967, classified by place of residence, sex, 10-year age groups between 35 and 74, by status of the person signing the death certificate (coroner or non-coroner), and by place of death (institutional or non-institutional).

In addition we were provided with a listing of the registration numbers of all death certificates coded to ICD 420 relating to residents of the 34 municipalities during 1967. These death certificates were then located and examined, and classified into two groups: (1) duration of final illness given as sudden, instantaneous, seconds, minutes (up to one hour), etc.; (2) duration given as hours, days, years, etc.

Of the 3150 certificates examined, 364 (11.6%) had no information on duration. These were omitted from the calculations.

Three indices of the frequency of sudden death were then obtained by calculating the percentage of coroners' deaths, non-institutional deaths, and "sudden or less than one hour" deaths for various combinations of sex and 10-year age groups.

Correlation coefficients and regression equations were calculated with the aid of the University of Toronto computer, using the percentage figures for each town, together with water hardness, latitude and a variety of geographic and socioeconomic indices.⁶ The dependent variables were the sudden-death percentages for each town, and since we were interested in the slope of the sudden-death regressions rather than in their absolute levels, these percentages were converted to logarithms before being used in the calculations. In each calculation the contribution of an individual municipality to the correlation coefficient or regression equation was "weighted" by the total number of deaths appearing (as the denominator) in the percentage calculation for that municipality.

Detailed comparison

Port Arthur, located in northwestern Ontario, had a population of 48,340 at the 1966 census, while Kitchener, located in southern Ontario, had a population of 93,255. Both cities have enjoyed a high standard of medical care for many years and each has two modern, well-equipped hospitals. Intensive-care units using continuous cardiac monitoring were in operation in all four hospitals before 1967.

During the three-year period 1967-1969 there were 1686 deaths ascribed to natural causes in residents of these cities aged between 35 and 74 years (719 in Port Arthur, 967 in Kitchener). The certificate of death was examined in all these cases, and pertinent information recorded. In 665 cases death was ascribed to conditions unrelated to the cardiovascular system and clinically unlikely to have been

confused with ischemic heart disease (e.g. malignant neoplasm, acute hemorrhage, sepsis, etc.). Doubtful cases were retained and allocated to "potential" IHD in the subsequent analysis. Of the remaining 1021 deaths, 162 occurred in patients who had been receiving chronic institutional care (nursing home, mental hospital, etc.) or had been confined to hospital for more than six weeks before death; these were excluded, leaving a study population of 859.

Additional information on the circumstances of death in the study population was obtained from a variety of sources. Hospital records provided information for a total of 527 patients who either died in hospital or were dead on arrival. Coroners' records were consulted in the 424 cases where the death certificate was signed by a coroner, and in a further 106 cases letters of enquiry were sent to the physician who had signed the death certificate. By combining all these sources of information it was possible to establish the "suddenness" of death in 399 of the 402 patients who died outside hospital.

Deaths in hospital were classified into three groups based on length of time elapsing after admission: less than two hours; more than two but less than 24 hours; and 24 hours or more. No attempt was made to identify unexpected sudden deaths occurring in patients who were already in hospital at the onset of their final acute episode.

Deaths for all durations of hospitalization were classified into four diagnostic categories according to the diagnosis appearing on the death certificate:

(1) Deaths coded to ICD 420* (arteriosclerotic heart disease) — myocardial infarction, coronary thrombosis, etc.

(2) "Other IHD" — cases in which the immediate cause of death appeared to have been ischemic heart disease and which would have been coded to ICD 420 but for the terminology used (e.g. myocardial ischemia — ICD 422, arteriosclerosis — ICD 450), or where an "underlying" disease was recorded (e.g. diabetes — ICD 260).

(3) "Potential IHD" — cases in which death was ascribed to a condition *other* than ischemic heart disease, but which might be confused with it clinically (e.g. pulmonary embolus, ruptured aortic aneurysm, rheumatic heart disease, etc.).

(4) Cerebrovascular — deaths ascribed to cerebral thrombosis, cerebral hemorrhage, cerebrovascular accident and stroke.

Results

Correlation analyses (34 towns and cities)

Coefficients of correlation relating each of the three indices of sudden-death frequency to a number of environmental and socio-economic variables are shown in Table I. Total water hardness and the major components of this hardness — calcium and magnesium — showed consistently negative correlation which approached or exceeded the 5% level of statistical significance. Latitude and latitude-dependent variables such as mean temperature and annual snowfall showed correlations which were less consistent but in some cases exceeded the 1% level of significance. Whether the correlations shown by water hardness were secondary to the latitude effect is uncertain,

*The eighth revision of the International Classification of Diseases came into use in Canada in 1969. Deaths which had previously been coded to ICD 420 (seventh revision) were then split between ICD 410 and 414. To avoid confusion, the numbering of the seventh revision has been retained in this study.

since water hardness and latitude are closely correlated, with a gradient of increasing water hardness as one moves south through the province. Similarly, water calcium and magnesium levels are closely correlated with each other and with total hardness, and their individual effects cannot be separated mathematically. Water pH, population size, mean annual income, and percentage of Canadian-born in the population showed variable and mostly weak correlations.

Subdividing the data by sex and by age group had little effect on the overall pattern of the correlations, although as the size of the groups was reduced there was, as might be expected, some decrease in the size of individual correlation coefficients.

Table I

The coefficients of correlation between three indices of sudden death and some of the environmental and socio-economic characteristics of 34 medium-sized Ontario towns and cities. Based on deaths ascribed to ICD 420 in persons aged 35 to 74 during 1965-1967

	Proportion of sudden deaths		
	Coroners' cases	Non-institutional	Certificate duration
Latitude	.66†	.25	.49†
Annual snowfall	.37*	.09	.56†
Mean temperature	— .58†	— .21	— .42*
Total population	.14	.14	0
% Canadian born	.38*	— .03	— .02
Mean income	.25	— .01	— .04
Water: pH	.21	.06	— .27
Total hardness	— .37*	— .33	— .33
Calcium	— .42*	— .31	— .32
Magnesium	— .31	— .35*	— .34*

* $P < .05$.
† $P < .01$.

Table II

Predicted percentages of sudden deaths (in deaths coded to ICD 420) among residents of Port Arthur and Kitchener, and the ratios of these percentages

	% of sudden deaths		
	Coroners' cases	Non-institutional	Certificate duration
By water hardness:			
Port Arthur (47 PPM)	41.4	46.5	50.8
Kitchener (395 PPM)	27.0	39.9	40.4
Ratio (PA/K)	1.53	1.17	1.26
By latitude:			
Port Arthur (48° 28'N)	67.7	48.8	62.0
Kitchener (43° 25'N)	32.5	43.7	45.1
Ratio (PA/K)	2.08	1.12	1.38

Predictions based on equations of the form:
Log percentage (coroner) = 1.6421 — .0005359 (hardness).

Regression equations were calculated for each of the three indices and were used to predict the proportion of sudden deaths to be expected in Port Arthur and Kitchener. Since each index involved a different definition of sudden death, and since the slopes of the regressions were of more interest than their absolute levels, the relative frequency of sudden death in the two cities was expressed in terms of the ratio of the proportions (Table II). For example, on the basis of the coroners' index, and using total water hardness as the independent variable, the anticipated proportion of sudden deaths in Port Arthur (hardness 47 p.p.m) was 41.4% compared to 27.0% in Kitchener (hardness 395 p.p.m), giving a ratio of 41.4/27.0, or 1.53.

Detailed comparison (Port Arthur and Kitchener)

Of the 859 deaths (out of the original 1686) selected for further study, some form of ischemic heart disease was given as the cause in 648. Of these, 553 had been coded to ICD 420 (arteriosclerotic heart disease), while 95 had been coded to other ICD rubrics. In addition, there were 77 "potential IHD" deaths (pulmonary embolus, etc.) and 134 deaths due to cerebrovascular disease (Table III).

Four hundred and fifty-seven of the deaths occurred after admission to hospital, and in a further 177 cases the patient reached hospital but was found to be dead on arrival. Of the remaining 225 deaths we were able to determine that "suddenness" of death was the reason for

Table III
Deaths among residents of Port Arthur and Kitchener, by 10-year age groups from 35 to 74, by sex and diagnostic category

		Port Arthur				Kitchener			
		35-44	45-54	55-64	65-74	35-44	45-54	55-64	64-74
ICD 420	M	11	36	55	92	13	42	66	102
	F	1	8	19	29	1	7	23	48
Other IHD	M	1	1	2	9	1	5	10	28
	F	1	3	1	4	—	—	5	24
Potential IHD	M	1	2	2	17	4	5	15	6
	F	—	—	3	1	2	6	8	5
Cerebrovascular	M	1	3	11	24	3	4	11	27
	F	3	1	4	11	2	6	8	15
Total	M	14	42	70	142	21	56	102	163
	F	5	12	27	45	5	19	44	92

Table IV
Duration of hospital admission (in hours) before death, among residents of Port Arthur and Kitchener aged 35 to 74, by sex and diagnostic category

		Port Arthur				Kitchener			
		0	< 2	2-24	> 24	0	< 2	2-24	> 24
ICD 420	M	136	14	11	33	119	10	25	68*
	F	40	1	4	12	38	6	8	26
Other IHD	M	1	—	1	11	25	1	2	16
	F	1	—	—	8	13	1	2	12
Potential IHD	M	—	—	4	18	10	—	4	16
	F	3	—	—	1	3	2	3	13
Cerebrovascular	M	3	1	9	26	3	—	4	38
	F	—	—	7	12	2	1	4	24
Total	M	140	15	25	88	157	11	35	138
	F	44	1	11	33	56	10	17	75

*Including two non-sudden deaths at home.

non-admission to hospital in 220, while in two cases the patient had elected to be treated at home, and in three cases we were unable to ascertain the reason for non-admission. In no instance was a shortage of hospital beds or a lack of hospital insurance reported as contributing to the occurrence of death outside hospital. (Virtually the entire population of the province was covered by prepaid hospital insurance during this period.)

The numbers of deaths in each city, classified by diagnostic category and duration of hospital admission, are given in Table IV. Two deaths of patients who chose to stay at home have been assigned to the over 24-hour hospital group, while the three cases with inadequate information have been omitted.

For all sex and age groups combined the proportion of deaths which occurred suddenly was substantially higher among the residents of Port Arthur than among those of Kitchener. Using the first diagnostic category (ICD 420) alone, the proportions were 70% and 52% respectively, giving a sudden death ratio of 1.35 for Port Arthur compared to Kitchener. Broadening the diagnostic criteria led to a reduction in the size of this ratio, but it never fell below 1.20. Thus, using a combination of the first two diagnostic categories (ICD 420 and other IHD) the Port Arthur percentage was 65, compared with 52 for Kitchener (ratio 1.25). Adding "potential IHD" gave percentage figures of 61 and 49, and a ratio of 1.24, while the addition of cerebrovascular deaths gave percentage figures of 52 and 43, and a ratio of 1.21.

Separating the deaths by age and sex (Fig. 1) showed that the higher frequency of sudden death in Port Arthur as compared to Kitchener was not confined to any one age group or sex. The female differential was at least as great as the male, and in both sexes it was more marked under the age of 65.

It is conceivable that the lower incidence of deaths outside hospital in Kitchener might have been due to more rapid transportation of seriously ill patients to hospital in that city than in Port Arthur. If this were so, one would expect a higher proportion of hospital deaths to have occurred shortly after admission in Kitchener as compared to Port Arthur, but the figures in Table II demonstrate that in fact the reverse was true. Of the 284 Kitchener deaths in hospital, 21 (7%) occurred within two hours of admission, while 73 (26%) occurred within 24 hours of admission. Among the 173 hospital deaths in Port Arthur, the corresponding figures were 26 (9%) and 53 (31%).

There are two ways in which the Port Arthur and Kitchener data can be used to assess the reliability of the indices of sudden deaths on which the correlation and regression studies were based: first, by comparing the observed ratio (1.35) of sudden deaths in ICD category 420 with that predicted by the regression equations; second, by comparing the observed ratio with that obtained by applying the coroner, non-institutional and certificate-duration definitions of sudden death to the Port Arthur and Kitchener certificates.

On the basis of predicted values the most reliable of the three indices was certificate-duration, with predicted ratios of 1.38 (using latitude) and 1.26 (using water hardness), both of which were reasonably close to the observed ratio of 1.35. However, when the Port Arthur and Kitchener certificates were reclassified according to certificate-duration, an erroneously low value of 1.11 was obtained. This was due mainly to the relatively large

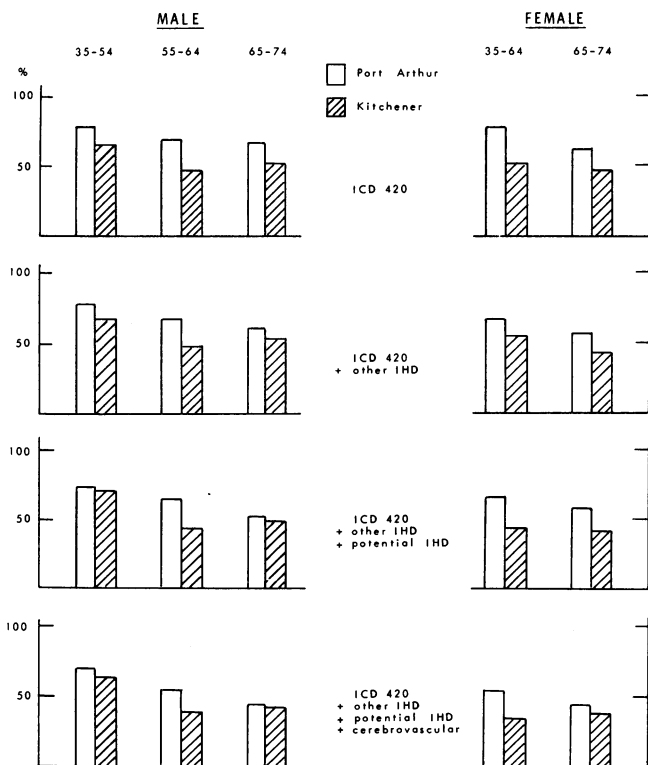


FIG. 1—Proportion of sudden deaths in Port Arthur and Kitchener by sex and age groups.

number of certificates in which a diagnosis such as “arteriosclerotic heart disease — years” was recorded, with no mention of the suddenness of the final episode.

Another potential source of error in the use of this index lies in the certificates on which no information concerning duration of illness has been provided. If these certificates are omitted (as was done in these calculations), one in effect assumes that they contain the same proportion of sudden deaths as do the other certificates. As it happens, in the present case this assumption was not seriously in error, since the proportion of sudden (non-hospital) deaths in the 50 certificates (9%) that had no information on duration was 70%, a figure that was reasonably close to the 60% shown by the rest of the certificates. However, it is evident that situations could arise in which this assumption would be unjustified and a large error could result, particularly if there were a large number of certificates lacking information on duration.

Contrary to what might otherwise have been expected (since the non-hospital definition of sudden death used in the detailed study was essentially “non-institutional”), the figures obtained with the non-institutional definition were even less satisfactory than those obtained with the certificate-duration index. Both the predicted ratios (1.12 using latitude and 1.17 using water hardness) were too low, but the recalculated ratio (1.80) was too high. The size of the latter was due almost entirely to the fact that out of 149 dead-on-arrival cases coded to ICD 420 in the two cities, no fewer than 95 had been misclassified as “institutional” deaths in the statistical abstract of the death certificate. The most common reason for this misclassification was that a hospital had been given as the “place of death” on the death certificate, and the qualifying letters “DOA” either had not been added or had been overlooked.

The coroners’ index exaggerated the difference in sudden-death frequency between the two cities, both in terms

of the predicted ratios (2.08 using latitude and 1.53 using water-hardness) and in terms of the Port Arthur and Kitchener certificates (ratio 1.66). The greater utilization of coroners in Port Arthur was apparent in all hospital-duration groups. Among deaths outside hospital the proportion of certificates signed by a coroner was 89% at Port Arthur and 71% at Kitchener. Among deaths occurring within 24 hours of admission the proportions were 61% and 24%, and among deaths with an in-hospital duration of more than 24 hours the proportions were 22% and 7%. Thus in spite of the earlier finding¹ that coroners’ rates for non-IHD deaths were relatively uniform across the province, there may well be some north-south variation in coroners’ rates in ischemic heart disease. If this were so, it would have the effect of exaggerating any underlying variation in sudden-death frequency, and could create an apparent gradient in the frequency of sudden-death where none existed.

Discussion

The detailed examination of deaths among residents of Port Arthur and Kitchener demonstrates that each of the three indices of sudden death used in the correlation analyses is liable to serious error. It follows that none of the correlations obtained can be accepted as firm evidence of a real correlation between sudden death and either latitude or water hardness. None the less, the fact that all three indices show correlation of the same sign (positive with latitude and negative with water hardness) suggests that each may be reflecting — however crudely — an underlying gradient in the frequency of sudden death in the province.

Furthermore, there does seem to be a real difference in the frequency of sudden death among the residents of Port Arthur and Kitchener, which is presumably secondary either to a basic difference in their genetic structure or to one or more factors in the environment or “way of life”. Subdividing the deaths by country of origin did not reveal any unusual susceptibility to sudden death in one ethnic group as compared to another, so that it is unlikely that genetic differences were responsible for the differences observed. As for environment and way of life, there are a number of factors that could, theoretically, be affecting the frequency of sudden death in the two cities, but from a practical point of view there are relatively few that, if identified, could be easily changed. The composition of the local water supply is one such factor, and for this reason we believe that the relationship between water hardness and IHD mortality is worth pursuing, even though the relationship is still obscure and may eventually prove to be nothing more than a statistical artifact.

Comparative studies of the incidence of sudden death in communities outside Ontario would be helpful in establishing whether or not geographic variation in the incidence of sudden death was peculiar to this province, and whether the inverse correlation with water hardness was anything more than a coincidence. The only such published study of which we are aware is that of Peterson, Thompson and Nam⁷ in the state of Washington, which did in fact show a similar pattern to that in Ontario, with a higher frequency of sudden death in the soft-water area.

Several other studies of sudden death frequency have been reported from individual communities, but differences in the definition of sudden death and in the criteria used to select the cases to be studied make comparison difficult. However, it is of interest that in Baltimore,²

among persons aged 40 to 64, 67% of the deaths studied occurred outside hospital, while in Belfast,⁸ among persons of all ages, the figure was 66%. Both these figures are reasonably close to our findings in Port Arthur, where, among deaths classified to ICD 420 and "other IHD", the figures were 73% in persons aged 35 to 64 and 66% in persons aged 35 to 74. The corresponding figures for Kitchener were 57% and 53%, suggesting that the Kitchener rates were abnormally low, rather than the Port Arthur rates were abnormally high. Again, there is the tantalizing possibility that the frequency of sudden death in the cities mentioned may be related to water hardness, since, like Port Arthur, both Baltimore and Belfast have very soft water supplies (53 p.p.m. and 64 p.p.m. respectively).

We had originally hoped that the frequency of sudden death would prove useful as a more sensitive measure of the effect, if any, of the "water factor" in ischemic heart disease than the overall IHD death rate. However, the present lack of any reliable index of sudden death in routinely collected mortality data severely limits their usefulness in large-scale studies, and a new approach must be sought. One such approach, which we intend to pursue in future studies, is the investigation of serum and tissue electrolyte levels in victims of sudden and non-sudden death from ischemic heart disease. If these electrolyte levels are different from those found in normal persons, and if differences of similar magnitude can be found between persons living in hard and soft water areas, the probability that a real "water factor" exists would be greatly strengthened.

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Résumé

Les morts subites par cardiopathie ischémique en Ontario et leur corrélation avec la dureté de l'eau et d'autres

facteurs

Il est possible qu'il existe une variation géographique de la proportion de morts subites par cardiopathie ischémique et que cette variation ait une relation de cause à effet avec la dureté de l'eau ou avec quelque autre facteur mésologique. Nous avons étudié trois index de mort subite et avons passé en revue les cas impliquant le coroner, les décès survenant en dehors des hôpitaux et avons évalué la durée de la maladie terminale, telle qu'elle figure sur le certificate de décès. Même si on admet que chacun de ces index peut prêter à des erreurs considérables, il n'en demeure pas moins qu'on y trouvait une corrélation constante avec la dureté de l'eau, corrélation qui était toujours de même signe et de même ampleur. L'examen approfondi des dossiers de 1686 décès qui étaient survenus chez des résidents de deux villes, très différentes entre elles au point de vue de la dureté de l'eau potable, a permis de confirmer que, dans les cas de décès attribuables à une cardiopathie, la proportion de morts subites était beaucoup plus élevée (de 20 à 30% supérieure) dans la ville du nord où l'eau était douce que dans la ville du sud où l'eau était dure.

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