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Type of Disinfectant in Drinking Water and Patterns of Mortality in Massachusetts

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Chlorination has been the major strategy for disinfection of drinking water in the United States. Concern about the potential health effects of the reaction by-products of chlorine has prompted use of alternative strategies. One such method is chloramination, a treatment process that does not appear to have carcinogenic by-products, but may have less potent biocidal activity than chlorination.

We examined the patterns of mortality of residents in Massachusetts who died between 1969 and 1983 and lived in communities using drinking water that was disinfected either by chlorine or chloramine. Comparison of type of disinfectant among 51,645 cases of deaths due to selected cancer sites and 214,988 controls who died from cardiovascular, cerebrovascular, or pulmonary disease, or from lymphatic cancer showed small variation in the patterns of mortality. Bladder cancer was moderately associated with residence at death in a chlorinated community (mortality odds ratio = 1.7, 95% confidence interval = 1.3–2.2) in a logistic regression analysis using controls who died from lymphatic cancer. A slight excess of deaths from pneumonia and influenza was observed in communities whose residents drank chloraminated water compared to residents from chlorinated communities, as well as to all Massachusetts residents (standardized mortality ratio = 118, 95% confidence interval = 116–120 for chloraminated communities, and standardized mortality ratio = 98, 95% confidence interval = 95–100 for chlorinated communities).

These results are intended to be preliminary and crude descriptions of the relationship under study. The serious potential for misclassification of exposure status and errors in death certificate classification of cause of death affect the interpretability of the overall evidence that patterns of mortality are similar according to disinfectant in drinking water.

Introduction

Chlorination has been the major strategy for disinfection of drinking water in the United States. Studies have demonstrated that organic material can react with chlorine to produce chloroform and trihalomethanes (*1,2*). Chloroform has been identified as a carcinogen in laboratory animals (*3*), and several epidemiologic studies have suggested that this by-product may be a human carcinogen (*4–6*).

The addition of ammonia to chlorine to form chloramine is an alternative source of disinfectant that is less likely to produce carcinogens in drinking water. Chloramines, however, may not be as effective as chlorine in eliminating waterborne pathogens. Epidemiologic data that can clarify the potential health risks of chloramination are not available. The purpose of this study is to describe the patterns of cause of death among residents in communities using drinking water treated with two distinct types of disinfectant: chlorine and chloramine.

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Methods

Cancer Mortality Study

Study Population. Any residents of Massachusetts who were at least 45 years old at death and died during the years 1969–1983 were eligible for this study. Selected from this group were those whose last residence before death was in a community that provided drinking water treated with chloramine or chlorine.

Outcome. The outcome of interest was the incidence of primary cancer in organ sites judged to be potential targets for carcinogens in drinking water: bladder, colon, kidney, pancreas, rectum, and stomach. Lung and female breast cancer cases were also of interest because these sites have been reported to be associated with chlorinated drinking water in previous studies (*7–10*). Operationally, the outcome of interest was the presence of any of the ICDA codes listed in Table 1 on the death certificate as the primary cause of death. All cases were identified from computerized death tapes maintained since 1969 by the Massachusetts Department of Public Health, Division of Health Statistics. A total of 51,645 deaths attributed to these cancers were identified from records limited to residents of the communities of interest.

Table 1.

	ICDA 8th Edition	ICDA 9th Edition
Bladder	188	188
Colon	153.0–153.9	153.0–153.9
Kidney	189.0–189.2	189.0–189.2
Rectum	154.0–154.2	154.0–154.3
Stomach	151.0–151.9	151.0–151.9
Breast	174	174
Pancreas	157.0–157.9	157.0–157.9
Lung	162.1	162.2–162.9

Selection of controls was governed by two principles: (1) the primary cause of death was not known to be associated with type of disinfectant in drinking water; (2) the primary cause of death was known to be associated with smoking in the event that the case group comprised cancers associated with smoking.

Operationally, the ICDA codes listed in Table 2, recorded on the death certificates as primary cause of death, were selected. A total of 214,988 controls were identified. The frequency of deaths, according to cause, is presented in Table 3.

Exposure Classification. The determinant under investigation was exposure to carcinogenic by-products of chlorine in drinking water. Operationally, a subject was considered to be exposed if residence at the time of death was in a community that treated its drinking water with chlorine. Nonexposure was defined as residence at the time of death in a community that treated its drinking water with chlorine and ammonia (chloramine). All Massachusetts communities using chloramine were selected. A subset of communities using chlorine

Table 2.

	ICDA 8th Edition	ICDA 9th Edition
Cardiovascular	390–398,402,404, 410–429	390–398,402, 404–429
Chronic obstructive lung	490–493	490–496
Cerebrovascular	430–438	430–438
Lymphatic cancer	200–207	200–208

Table 3. Frequency of deaths by cause among residents in 43 committees served by chlorinated and chloraminated drinking water (age at death at least 45 years).

Cause of death	No. of deaths
Cancer	
Bladder	2,311
Colon	10,517
Kidney	1,527
Rectum	2,700
Stomach	4,099
Breast (females only)	8,018
Pancreas	4,548
Lung	17,925
Lymphatic	6,297
Cardiovascular disease	166,433
Chronic obstructive pulmonary disease	6,709
Cerebrovascular disease	35,539

Table 4. Distribution of covariates of mortality according to type of drinking water disinfectant.

	Chlorine (23 towns)		Chloramine (20 towns)	
Covariate	No.	%	No.	%
Source of water				
Surface	23/23	100%	20/20	100%
Ground	0	—	0	—
Density (persons/sq. mile)[a]				
<5000	18/23	78%	5/20	25%
5000–9999	5/23	22%	9/20	45%
≥10,000	0/23	0%	6/20	30%
% below poverty level[a]				
<5%	6/23	26%	5/20	25%
5–9.9%	7/23	30%	12/20	60%
≥10%	10/23	44%	3/20	15%

[a] Source: 1970 and 1980 Census for Massachusetts (*13,14*).

only as the method of disinfectant was chosen according to identifiable characteristics of the chloramine communities that are associated with cancer mortality. The goal was to have comparability between the two types of community in the distribution of covariates of disinfectant in drinking water that may be independent risk factors for cancer mortality. These covariates were: (1) source of drinking water (surface water vs. groundwater); (2) density (people/square mile) of community, as reported in 1970 and 1980 U.S. Census data; (3) percentage of population below the poverty level, as reported in 1970 and 1980 U.S. Census data.

Data analysis. The mortality odds ratio was the parameter of interest, estimated as the odds of cancer among the exposed (chlorination) relative to the nonexposed (chloramination). This estimator approximates the observed-to-expected ratio if the control group comprises causes of death that are not associated with the exposure. Preference for this estimator relative to the proportionate mortality ratio is discussed by Miettinen and Wang (*11*). All estimates were adjusted for age at death, using the Mantel-Haenszel estimator, by pooling age strata (45–54, 55–64, 65–74, 75+ years). Sex-specific estimates were calculated for all cancers. The procedure used for interval estimation was test-based, two-sided 95% confidence intervals (*12*).

The characteristics of communities representing disinfectant exposure categories and associated characteristics are listed in Table 4. The distributions of density and the proportion of the population below poverty level were not comparable across categories of disinfectant. The chloraminated communities tended to have more people per square mile and fewer people below the poverty level than the chlorinated communities. The potential bias introduced by the imbalance of density and poverty between the two types of community was controlled by logistic regression analysis. For this analysis, the outcome of interest was bladder cancer mortality. A random sample of 1000 bladder cancer cases and 5000 controls comprising deaths due to heart and pulmonary disease, cerebrovascular disease, lymphoma, and lung cancer was selected from the original study population.

Table 5. Age-adjusted estimates of effect of chlorination relative to chloramination in drinking water on cancer mortality.

	All controls[a]		Lymphoma controls		Lung cancer controls	
Cancer site	Mortality odds ratio	95% confidence interval	Mortality odds ratio	95% confidence interval	Mortality odds ratio	95% confidence interval
Total						
Bladder	1.05	(0.97–1.14)	1.17	(1.06–1.29)	1.15	(1.06–1.26)
Colon	0.89	(0.86–0.93)	0.98	(0.92–1.05)		
Kidney	1.00	(0.90–1.11)	1.09	(0.97–1.22)		
Rectum	0.96	(0.89–1.04)	1.05	(0.96–1.15)		
Stomach	0.97	(0.91–1.03)	1.07	(0.99–1.16)		
Pancreas	0.94	(0.89–1.00)	1.03	(0.96–1.11)		
Lung	0.94	(0.91–0.97)				
Male						
Bladder	1.04	(0.94–1.16)	1.16	(1.03–1.32)	1.13	(1.01–1.26)
Colon	0.85	(0.80–0.90)	0.93	(0.85–1.02)		
Kidney	0.98	(0.86–1.12)	1.05	(0.91–1.22)		
Rectum	0.98	(0.88–1.09)	1.07	(0.94–1.21)		
Stomach	0.95	(0.87–1.03)	1.03	(0.92–1.14)		
Pancreas	0.92	(0.85–1.01)	1.00	(0.90–1.12)		
Lung	0.91	(0.86–0.96)				
Female						
Bladder	1.05	(0.92–1.21)	1.18	(1.01–1.37)	1.22	(1.05–1.43)
Colon	0.92	(0.87–0.97)	1.02	(0.94–1.11)		
Kidney	1.02	(0.87–1.20)	1.13	(0.95–1.34)		
Rectum	0.94	(0.84–1.05)	1.04	(0.91–1.18)		
Stomach	1.01	(0.92–1.10)	1.12	(1.00–1.26)		
Pancreas	0.96	(0.89–1.05)	1.06	(0.96–1.18)		
Breast	0.89	(0.85–0.93)	0.97	(0.89–1.05)		
Lung	0.95	(0.91–0.98)				

[a] Deaths due to heart, pulmonary, cerebrovascular disease, and lymphatic cancers.

Massachusetts Mortality Study

An alternative approach to data analysis was to estimate standardized mortality ratios, according to disinfectant type. The expected number of deaths was derived from age- and cause-specific deaths for all residents of Massachusetts who died during the study period (1969–1983) and who were at least 45 years old at the time of death. U.S. Census data on the number of Massachusetts residents in 1970 and 1980 supplied the estimate of the population at risk during 1969–1978 (for ICDA-8) and 1979–1983 (for ICDA-9), respectively. Expected rates were estimated separately for the chlorine and chloramine communities. Because these two age distributions were comparable, the Standardized Mortality Ratios (SMRs) across categories of disinfectant can be compared without the effect of confounding by age.

Results

Case-Control Study

The age-adjusted associations for chlorinated relative to chloraminated drinking water are shown in Table 5. In general, type of disinfectant was not associated with cancer mortality, with the exception of bladder cancer, which showed a small excess occurrence among residents of communities using chlorine as a disinfectant. Smoking is a known risk factor for bladder cancer. To evaluate if the chlorine association reflected more smokers among the bladder cancer cases than the control subjects, a special control group was enrolled. This control group consisted of lung cancer cases, because lung cancer is strongly associated with smoking. A similar association for bladder cancer and chlorinated drinking water was observed when using lung cancer controls, with a slightly higher excess of bladder cancer deaths among females relative to males.

For bladder cancer only, logistic regression analyses were performed to control for the potential effects of differences in levels of density and poverty, as well as age at death and year of death, between communities treated with different types of disinfectant. The antilog of the coefficient for the indicator for type of disinfectant was slightly higher than the simple, age-adjusted odds ratio when the comparison group consisted of lymphatic cancers (logistic odds ratio = 1.7, 95% confidence interval = 1.3–2.2 vs. age-adjusted odds ratio = 1.2, 95% confidence interval = 1.1–1.3). When lung cancer controls were used to assess the association of bladder cancer and chlorination in a logistic analysis, an indirect method for control of confounding by smoking, the logistic odds ratio estimate was 1.3 (95% confidence interval = 1.0–1.7), suggesting that smoking does not explain all the excess mortality from bladder cancer.

Standardized Mortality Study

The results of the standardized mortality ratio analysis (the ratio of observed to expected deaths) were similar to the results from the previous analyses. Little difference was apparent between the patterns of cause of death in the Commonwealth of Massachusetts and those patterns among residents of communities, re-

Table 6. Standardized mortality ratios, 1969–1983, for residents of selected chlorinated drinking water communities compared with Massachusetts residents.[a]

	Male		Females		Total	
Cause of death	SMR	95% confidence interval	SMR	95% confidence interval	SMR	95% confidence interval
Cancer						
Bladder	104	(96–112)	107	(97–118)	105	(99–111)
Colon	99	(95–104)	99	(95–103)	99	(96–102)
Kidney	102	(92–112)	100	(89–112)	101	(94–109)
Rectum	103	(95–111)	98	(91–107)	101	(95–106)
Stomach	108	(101–114)	110	(103–118)	109	(104–114)
Breast	—	—	96	(93–100)	96	(93–100)
Pancreas	103	(97–110)	105	(99–112)	104	(100–109)
Lung	106	(104–109)	101	(97–105)	105	(103–107)
Lymphatic	101	(96–107)	99	(94–104)	100	(96–104)
Cardiovascular disease	106	(105–107)	103	(102–104)	104	(104–105)
Chronic obstructive pulmonary disease	107	(102–111)	101	(95–108)	105	(102–109)
Cerebrovascular disease	110	(108–113)	106	(104–108)	108	(106–109)
Pneumonia/influenza	100	(97–103)	96	(93–99)	98	(95–100)

[a] Expected rates derived from cause-specific deaths in Massachusetts, using 1970 census data for deaths coded from ICDA-8 and 1980 census data for deaths from ICDA-9.

Table 7. Standardized mortality ratios, 1969–1983, for residents of selected chloraminated (chlorine plus ammonia) drinking water communities compared with Massachusetts residents.[a]

	Male		Females		Total	
Cause of death	SMR	95% confidence interval	SMR	95% confidence interval	SMR	95% confidence interval
Cancer						
Bladder	91	(85–98)	96	(87–105)	93	(88–98)
Colon	106	(102–110)	101	(98–105)	103	(101–106)
Kidney	97	(88–106)	92	(82–103)	95	(88–102)
Rectum	97	(90–104)	99	(91–106)	98	(93–103)
Stomach	105	(99–111)	103	(96–110)	104	(100–109)
Breast	—	—	103	(100–106)	103	(100–106)
Pancreas	103	(98–110)	103	(97–108)	103	(99–107)
Lung	104	(101–106)	105	(101–109)	104	(102–106)
Lymphatic	102	(97–107)	103	(98–108)	102	(99–106)
Cardiovascular disease	101	(100–102)	101	(100–102)	101	(100–101)
Chronic obstructive pulmonary disease	88	(85–92)	89	(84–95)	88	(86–92)
Cerebrovascular disease	85	(83–87)	87	(86–89)	86	(85–88)
Pneumonia influenza	125	(121–128)	112	(109–115)	118	(116–120)

[a] See footnote in Table 4.

gardless of the type of disinfectant (Tables 6 and 7). One exception was the excess deaths from pneumonia and influenza in the chloraminated communities, particularly among males.

Discussion

The findings presented in this report are preliminary and should be interpreted as merely descriptive, rather than quantitative, patterns of mortality in relation to type of disinfectant in drinking water. Considerable potential for error exists in the classification of exposure and disease status.

First, residence at the time of death is a poor measure of the history of exposure to a particular type of disinfectant in drinking water. The temporal sequence of exposure and disease may be illogical in the context of slow-growing cancers that were diagnosed many years before death. A corollary to this type of exposure misclassification is that the etiologically relevant period of exposure may have been decades before the onset of carcinogenesis. Second, the outcome of interest in this study was cancer incidence, not cancer mortality. The underlying cause of cancer death recorded on the death certificate may not have been the primary tumor. For example, the site of metastasis, rather than the primary site, may have been noted as the underlying cause of death. Similarly, deaths attributed to pneumonia and influenza may actually have been primarily caused by cancer or some other disease. These types of misclassification generally lead to dilution of the measure of association when the errors are unrelated to the relationship under study.

It is not surprising, therefore, that the patterns of causes of death did not vary to any appreciable extent according to type of disinfectant. There is some indication, however, that bladder cancer mortality was excessive among residents of chlorinated communities relative to residents of chloraminated communities. The data also showed a small increase in deaths from pneumonia and influenza among residents of communities using chloramine in their drinking water. The excess deaths associated with different disinfectant methods may have been caused by unidentified or uncontrolled confounding factors, such as smoking and occupational exposures. It would be of interest to clarify the reasons for the patterns of mortality observed in this study.

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REFERENCES

1. U.S. Environmental Protection Agency. Industrial Pollution of the Lower Mississippi River in Louisiana. Region VI, 1972.
2. Rook, J. J. Formation of haloforms during chlorination of natural waters. Water Treat. Exam. 23: 234–243 (1974).
3. Page, N. P., and Saffiotti, U. Report on Carcinogenesis Bioassay of Chloroform. National Cancer Institute, Bethesda, MD, 1976.
4. U.S. Environmental Protection Agency. A Report-assessment of Health Risk from Organics in Drinking Water. Ad Hoc Study Group to the Hazardous Materials Advisory Committee, Science Advisory Board, 1975.
5. Crump, K. S., and Guess, H. A. Drinking Water and Cancer: Review of Recent Findings and Assessment of Risks. Council on Environmental Quality, Washington, DC, 1980.
6. Cantor, K. P., Kopfler, F. C., Hoover, R. N., and Strasser, P. H. Cancer epidemiology as related to chemicals in drinking water. Toxicol. Environ. Chem. Rev. 4: 47–65 (1981).
7. Gottlieb, M. S., Car, J. K., and Clarkson, J. R. Drinking water and cancer in Louisiana. Am. J. Epidemiol. 116: 652–667 (1982).
8. Cantor, K. P., Hoover, R., Mason, R. J., and McCable, L. J. Associations of cancer mortality with halomethanes in drinking water. J. Natl. Cancer Inst. 61: 979–985 (1978).
9. Kanarek, M. S., and Young, T. B. Drinking water treatment and risk of cancer death in Wisconsin. Environ. Health Perspect: 46: 179–186 (1982).
10. Bean, J. A., Isaacson, P., Hausler, W. J., and Kohler, J. Drinking water and cancer incidence in Iowa. Am. J. Epidemiol. 116: 912–923 (1982).
11. Miettinen, O. S., and Wang, J.-D. An alternative to the proportionate mortality ratio. Am. J. Epidemiol. 114: 144–148 (1981).
12. Miettinen, O. S. Estimability and estimation in case-referent studies. Am. J. Epidemiol. 103: 226–235 (1976).
13. U.S. Department of Commerce, Bureau of the Census. Census of Population, Massachusetts, 1970.
14. U.S. Department of Commerce, Bureau of the Census. Census of Population, Massachusetts, 1980.