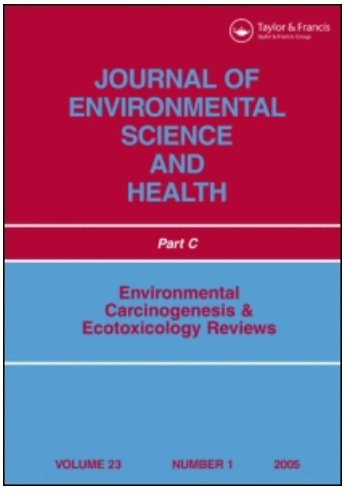

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Index of Congenital Minamata Disease in Canadian Areas of Concern in the Great Lakes: An Eco-Social Epidemiological Approach

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Cerebral palsy is one of the symptoms of congenital Minamata disease associated with exposure to methyl mercury. Cerebral palsy hospitalization rates for 17 Canadian Areas of Concern have been used as a health index in evaluating the effectiveness of the United States and Canadian governments in implementing their Great Lakes Water Quality Agreement. Elevated rates in males in several locations was associated with historic uses of mercury and with natural sources indicating that the governments have failed to protect human health from exposures to this persistent toxic substance. Advances in epidemiological theory indicate that the reasons for this failure cannot be explained solely in scientific and technical frames but that the social, economic, and political contexts of the two nations need to be examined.

Key Words: Minamata disease; Great Lakes; eco-social approach

BILATERAL CONTEXT AND DEVELOPMENT OF A MANDATE

In environmental toxicology, we are faced with an inconvenient conundrum. To maintain relevance on the one hand, we must become aware of effects that are actually occurring as a result of exposures to toxic chemicals. On the other hand, observations of effects imply injury, injury implies liability,

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and liability implies legal processes, punitive damages, and costly remedial engineering. Epidemiologists undertake the processes of becoming aware of chemically induced effects in human populations and epizootiologists perform similar functions for fish and wildlife populations. During the past century, the Great Lakes became seriously polluted with a variety of organic and inorganic persistent toxic substances. Since the 1950s, field biologists undertaking epizootiological research have documented the effects of organochlorine compounds on wildlife in the Great Lakes basin (1, 2). Similarly, since the 1980s, epidemiologists have compiled a comprehensive case describing the effects of organochlorine compounds, particularly polychlorinated biphenyls, on human health and specifically on neurodevelopmental processes in infants in Great Lakes communities (3–9).

The 1960s were characterized by the coalescence of a variety of protests to form powerful new social movements that included environmental and health activists (10). In response, the United States and Canadian governments enacted several reform measures including new or revised legislation, such as the U.S. Federal Water Pollution Control Act, and new institutions, such as formation of the U.S. Environmental Protection Agency and, in Canada, establishment of the Department of Environment. On a bilateral basis, the two countries negotiated and signed the Great Lakes Water Quality Agreement, based on advice of the International Joint Commission (11) concerning injury to health and property from pollution of the boundary waters, in contravention of Article IV of the 1909 Boundary Waters Treaty.

In addition to the concerns about organochlorine compounds, the International Joint Commission (11) drew the attention of the governments to the dangers posed by mercury. In the late 1960s, Norvald Fimreite (12) had investigated the occurrence of mercury in the Canadian environment from industrial and agricultural sources. The process of biomethylation of mercury had newly been documented (13) and the potential for human exposures from consumption of contaminated fish and wildlife was established (14). The effects of methylmercury on human health, particularly on infant mortality and development, had been reported from the outbreaks in the 1950s of poisonings at Minamata and Niigata in Japan [14, 15 cited in 12, 16]. These concerns were critical in the decisions of the two governments to negotiate the 1972 Great Lakes Water Quality Agreement (17).

While the priority for the 1972 Great Lakes Water Quality Agreement was on eutrophication, research on the teratogenic effects of organochlorine compounds on wildlife (18) and accumulations in humans from consumption of Great Lakes fish (19) resulted in reorientation toward a priority on persistent toxic substances during the 1978 renegotiation (17). The newly stated purpose of this bilateral instrument followed the wording of the intent of the 1977 United States Clean Water Act "to maintain and restore the chemical, physical and biological integrity of the nation's waters" and applied this

intent to "the Great Lakes Basin Ecosystem." From the start, the addition of the word "Ecosystem" was to prove ambiguous and problematic for defining the boundaries of the Agreement and the implications are examined later in this paper under the heading "Diversionary Reframing." In addition, the new purpose contained a new policy that "the discharges of any and all persistent toxic substances be virtually eliminated." In the 1987 Protocol Amending the 1978 Great Lakes Water Quality Agreement, provision was made for designating Areas of Concern for locations that frequently did not meet water quality objectives (see Figure 1) and for preparation of Remedial Action Plans and Lakewide Management Plans for Critical Pollutants (17). Mercury was included as a Critical Pollutant though there was no epidemiological research to determine whether any communities around the Great Lakes exhibited signs of mercury poisoning, even though some First Nation communities were as highly exposed as at Minamata (20).

The purpose of this paper is to evaluate the factors in the effectiveness of implementation of the Great Lakes Water Quality Agreement. Because evidence of mercury contamination of the Great Lakes was a major reason for negotiating the Great Lakes Water Quality Agreement, a health endpoint linked to mercury exposure has been used as an index to evaluate effectiveness.

CRISIS IN EPIDEMIOLOGY

Since the 1980s, there has been a growing recognition of a crisis in epidemiology. After the advent of antibiotics in the 1940s and the control of illnesses caused by germs, epidemiologists turned to multivariate techniques to identify risk factors for chronic illnesses in individuals (21–24). The subsequent successes, however, had been made with little reference to diseases in populations or to the advances in the biological sciences. Epidemiology tended to be an academic subject and removed from consideration of the social, economic, and political determinants of health. Epidemiologists have proposed the development of a new "eco-epidemiological era" (24) and an "ecosocial framework" (22) not only to reconnect epidemiology with public health and to link it to molecular epidemiology but also to place their science within social, economic, political, and cultural contexts (25, 26). A second thread of the debate has concerned the nature of causation, and epidemiologists have extensively reviewed and revised the categories of evidence that contribute to or detract from a relationship between a disease and its putative cause or causes (27–29). These are important not only in reducing the scientific uncertainties in developing indicators for evaluation of the effectiveness of implementation but also in understanding the changing social, economic, and political contexts of the past 35 years since the signing of the first Great Lakes Water Quality Agreement in 1972.

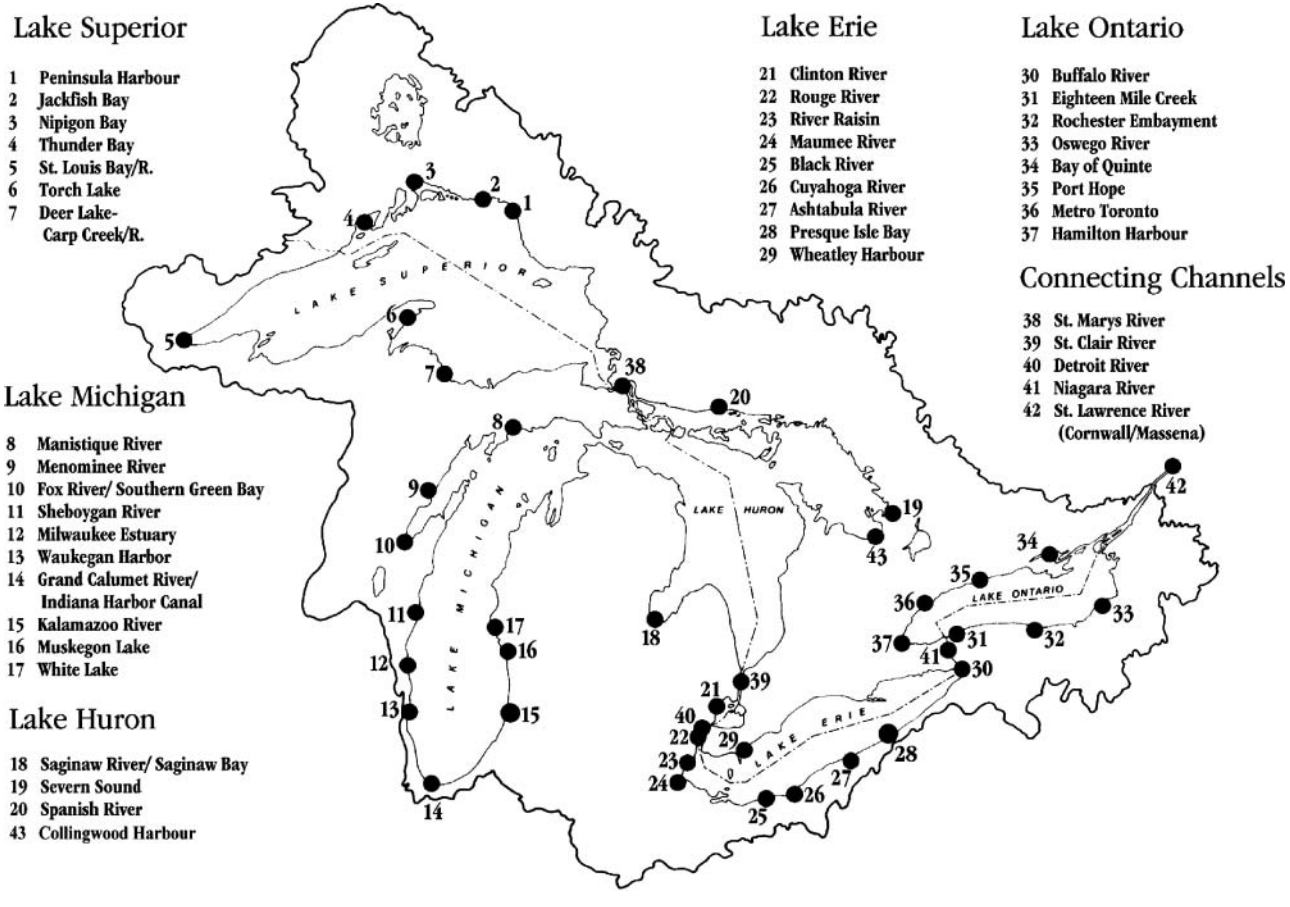

Figure 1: Areas of Concern in the Great Lakes Basin

MINAMATA DISEASE AS A CONTESTED ILLNESS

Detection of the health effects from pollution with methyl mercury poses particular problems for epidemiologists (30). At Minamata, Japan, about 100 tonnes of mercury was released into Minamata Bay (31) and contaminated the fish and shellfish consumed by the local fishermen and residents. One of the largest uses of mercury in the Great Lakes basin was in the chloralkali industrial sector for the production of chlorine, and reported releases (Table 1) documented several locations where mercury was discharged in similar or larger quantities than those at Minamata (32), indicating the potential for outbreaks of Minamata disease in communities in the Great Lakes basin. Mercury is one of the risks of modernity in that the contamination is essentially imperceptible except through the "sensory organs" of science (33). Methyl mercury poisoning can be regarded as a contested illness (34) in that it is difficult not only to diagnose because of the ambiguous signs and symptoms, but also to link it causally to pathways and sources of exposures. After 30 years of monitoring mercury levels in the hair of members of native communities across Canada, Health Canada (35) concluded that there were "no provable direct clinical effects." There is a lack of a pathognomonic endpoint for methyl mercury poisoning at any level of biological organization or in any species and there would seem to be a priority need for a biomarker of exposures, effects, and susceptibility (36).

In the late 1980s, Health Canada developed a Great Lakes Health Effects Program as part of the contribution of the Government of Canada to the implementation of the Great Lakes Water Quality Agreement. One of the projects was to compile health data and statistics, including rates of

Table 1: Ontario Mercury Cell Chlor-Alkali Plants: Operation Dates and Releases of Mercury in Tonnes[a] (After (43))

Location (Figure 1 Map Number)	Plant	Date Mercury Cells Opened	Date Mercury Cells Closed	Years in Operation	Operational Hg Release (Tonnes[b])
Thunder Bay (4)	Dow Chemical Canada Inc.	1966	1973	8	43.30
Peninsular Harbour (1)	American Can of Canada Ltd.	1952	1977	26	62.11
Sarnia (39)	Dow Chemical Canada Inc.	1948	1973	25	317.73
Sarnia (39)	Dow Chemical Canada Inc.	1970	1973	4	71.73
Hamilton (37)	Canadian Industries Ltd.	1965	1973	8	51.47
Cornwall (42)	ICI Ltd.	1935	1995	60	196.13

[a]After (32).
[b]Does not include mercury released in solids.

mortality, morbidity as hospitalization, and congenital anomalies for communities in the 17 Canadian Areas of Concern on the Canadian side of the Great Lakes for more than 70 health endpoints "that might be related to pollution" (37). The methods used included the following headings: Assigning Standard Geographic Codes; Selecting Health Outcomes; and Gathering and Analyzing Data (37, 38). Data were compiled separately for males and females and to ensure a sufficiently large sample size, data were aggregated for the 7 years from 1986–1992. One of the health endpoints selected by Health Canada was cerebral palsy because this condition was one of the diagnostic signs associated with congenital Minamata disease caused by prenatal and perinatal exposures to methyl mercury (39–42). Thus implicit in Health Canada's selection of cerebral palsy was the hypothesis that if the communities in the Canadian Areas of Concern were exposed to methyl mercury, the rates of morbidity as hospitalization for cerebral palsy would be expected to be elevated compared with the provincial rates for Ontario.

Figure 2 shows that there are significantly elevated rates, particularly for males in certain locations (43) indicating the possibility that the United States and Canadian governments may have failed to implement the Great Lakes Water Quality Agreement effectively during the past 35 years. In Sarnia (St Clair River Area of Concern), the rate of male hospitalization for cerebral palsy is five times the provincial rate whereas the rate for females is five times lower than the provincial rate. These results suggested not only that there was some agent present in the Sarnia environment that was having a neurodevelopmental effect but also that males were differentially more susceptible than females to this environmental agent. Similar anomalously higher rates for males were found at Thunder Bay and Cornwall (St Lawrence River Area of Concern). All three locations had historic releases of mercury from chloralkali plants (43). The same pattern of elevated rates of hospitalization of males for cerebral palsy was found at Collingwood Harbour where there is no history of mercury releases. There are, however, high levels of natural geological mercury in the sediments of Georgian Bay from mineralization of sphalerite deposits in the dolomitic limestone of the Bruce Peninsular (44, 45).

REDUCTION OF UNCERTAINTY

These preliminary published observations, based on interpretation of health data and statistics compiled by Health Canada (37) indicate an association between elevated rates of hospitalization for cerebral palsy, particularly for males, in several locations and historic mercury use or natural geological mercury sources. This raises the possibility that there may have been previously undetected outbreaks of congenital Minamata disease at some of the Canadian Areas of Concern. The observations present us with an immediate conundrum.

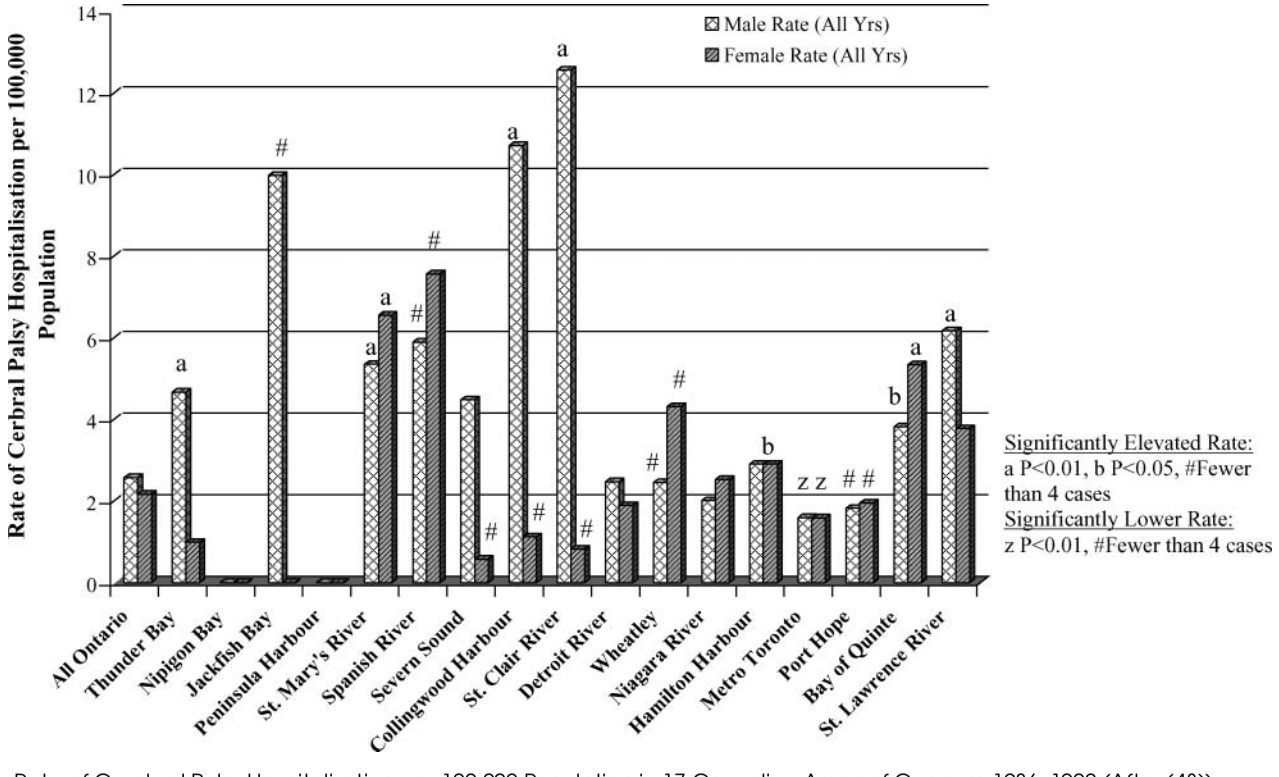

Figure 2: Rate of Cerebral Palsy Hospitalization per 100,000 Population in 17 Canadian Areas of Concern 1986–1992 (After (43)).

On the one hand, the authorities might act on the information and undertake further research, establish new regulations on mercury releases, improve fish advisories and implement costly remedial actions. On the other hand, the observations might be dismissed as "junk science" that should not be used to regulate risks (46). As with any contested illness associated with the risks of modernity, there is a need to reduce the uncertainties (33, 34). The method of reducing uncertainties that has been successfully used by Great Lakes epidemiologists and epizoologists for the past 20 years is based on modern concepts of causation (29, 47–49) including the following viewpoints: Probability; Consistency on Replication; Coherence; Specificity; Strength of Association; Temporality; and Performance on Prediction (for more detailed discussion see (2)).

PROBABILITY

Probability had been used "as a means of quantifying and excluding chance events" (50) and is one of the "criteria" more recently introduced for inferring a causal relationship (28). Intrinsic to the aspect of probability in judging whether there is a causal relationship, is the need to consider statistical power, particularly for small study areas. The data on hospitalisation for cerebral palsy (37) provided a sufficient number of cases for the statistical power to identify those Areas of Concern that might have communities exposed to elevated levels of methyl mercury. For example, the rates for males at Thunder Bay, Collingwood, Sarnia, and Cornwall were all statistically significantly elevated at the 99% probability level above the provincial rate (see Figure 2). Similarly, this was the probability level for the elevated rates for both males and females at St Mary's River, and the elevated hospitalisation rates for females at the Bay of Quinte. The decreased hospitalisation rates for males and females in Toronto compared with the provincial rate were, similarly, at the 99% level of probability, likely reflecting the availability of tertiary care facilities. There were Areas of Concern where the rates of morbidity as hospitalization for cerebral palsy were significantly different from the provincial rate at the 95% probability level, including elevated rates for females at Hamilton and males at the Bay of Quinte. The consideration of the probability viewpoint is important because it indicates that there is sufficient statistical power in the 17 Health Canada datasets to conclude that for the many locations where elevated hospitalisation rates for cerebral palsy were found there is a low probability that the deviations from the provincial rates arose by chance.

CONSISTENCY ON REPLICATION

The Consistency on Replication viewpoint relates to the degree to which other scientists, working on other populations, in other locations, and at other

periods of time, have found the same relationship. The possibility that male infants might be more susceptible than females to the prenatal and perinatal effects of methyl mercury was first proposed by McKeown-Eyssen (51) working on children of Cree Indians in Northern Quebec. Retrospective reanalysis of the data on the Japanese (52) outbreak at Minamata from consumption of mercury contaminated fish and shellfish and on the data on the outbreaks in Iraq from consumption of bread made from grains treated with organomercurial compounds (53) yielded similar results concerning differential susceptibility of infant males. Male susceptibility was even indicated in some of the studies of neurological function in children prenatally exposed to much lower concentrations, including children of fish-eating communities in French Guiana close to gold mines (54), children of the Faeroe Islanders whose mothers ate pilot whales (55) and children of Seychelle Islanders whose mothers consumed seafood (56). While this is a powerful viewpoint indicating a general differential susceptibility of infant males to the neurodevelopmental effects of methyl mercury, there does not seem to be a specific reference to the differential susceptibility of males for cerebral palsy.

COHERENCE

The Coherence viewpoint requires that "the cause-and-effect interpretation of our data should not seriously conflict with the known facts of the natural history and biology of the disease" (48). The new facts that there are elevated rates of hospitalization for cerebral palsy, particularly in males, in Areas of Concern associated with high levels of industrial or natural mercury (43) accords with the known facts and theory of congenital Minamata disease, based on outbreaks of poisoning in Japan and Iraq (40, 53, 57). In addition to the epidemiological evidence of differential susceptibility of males to the neurodevelopmental effects of methyl mercury, theory is informed by the experimental evidence in rodents of differential alterations in dopamine associated with changes in locomotor activity (58, 59) and differential antimitotic effects of methyl mercury in the cerebella cortex of 2-day-old mice (60).

Risks of modernity have "tortuous paths of their deleterious effects" that are "*erratic and unpredictable*" [33 (emphasis in original)] and mercury fits this description. The complexity of the pathways, distribution, and transformations of mercury in the environment has been extensively reviewed (61–63). Specifically, in 2003, the International Joint Commission hosted a conference on An Ecosystem Approach to the Health Effects of Mercury in the Great Lakes Basin that addressed the multimedia complexity of mercury sources, pathways, and routes of exposures (64) and reported the neurodevelopmental effects indicated by the cerebral palsy hospitalization cases in Canadian Areas of Concern (43).

There are a variety of mechanisms of toxic action linking prenatal exposure to methyl mercury and injury to neurological development (65). At the

biological level of the individual human infant, microcephaly has been observed in both the Minamata and the Iraq poisoning episodes (66, 67). Among prenatally exposed infants, lesions were throughout the cerebral hemispheres and the cerebellum, with slight lesions to the brainstem (68). Neuropathological studies on two dead Minamata children who had been diagnosed with cerebral palsy revealed greatly reduced brain sizes compared to controls, with underdevelopment of several structures (41). At the microscopic level there was marked disorganisation of many cellular structures believed to be "characteristic features of fetal Minamata disease" (16) with an "abnormal pattern in the organization and a distorted alignment of neurons in the cerebral cortex" (69, 70). Anti-mitotic activity through dysfunction of the micro-tubular spindles (71) could account for disruption of neuronal cell division and migration. At the molecular level, methyl mercury is a potent inhibitor of micro-tubule assembly (72) mediated through methyl mercury binding to the free sulphydryl groups on the ends and on the surface of the microtubules.

A preliminary attempt to correlate cerebral palsy rates of hospitalisation with mercury levels in fish near the Areas of Concern was unsuccessful (73). If there is a dose-response relationship, it was not demonstrated by the approach used on this occasion.

SPECIFICITY

Specificity refers to the precision with which the occurrence of one variable will predict the occurrence of another (27). In terms of the specificity of causes of cerebral palsy, although intra-partum hypoxia can result in cerebral palsy, there are many other risk factors that account for most of the cases. In addition to the increased risks associated with very low birth weight, chorioamnionitis, low thyroid levels and ventilatory management of preterm infants, viral infections, intrauterine strokes, congenital anomalies, and metabolic disorders in term infants have been identified (74) together with autoimmune and coagulation defects, and trauma or a combination of these factors (75). There would therefore appear to be little specificity in the cause of cerebral palsy. Cerebral palsy is, however, known to be "associated with maternal exposures to concentrations of organic mercury exposure" and methyl mercury is the only chemical compound known to be associated with cerebral palsy (75), indicating a high level of specificity in this compound as the only known chemical risk factor. In terms of the specificity of effects, although cerebral palsy is one of the characteristic effects associated with Congenital Minamata disease, there are many other signs and symptoms associated with prenatal exposures to methyl mercury (39). While a specific pathognomonic marker of congenital Minamata disease would be comforting, the lack of such a marker does not seriously detract from the hypothesis.

STRENGTH OF ASSOCIATION

This viewpoint refers to the degree to which the supposed cause and outcome coincide in their distribution and the size of the effect produced by the presumptive cause. Several odds ratios have been calculated from the Health Canada data and from population census data for the Province of Ontario (76) to compare the proportion of hospitalization cases in males and females. The first factor was a comparison of the number of hospitalisation cases in males (884) versus females (723) in the Province of Ontario compared to the respective number of males (13,454,580) and females (13,842,280) in the population. The odds ratio was 1.26 (Confidence Intervals 1.14–1.39) and indicates that being male in the Province of Ontario is a significant risk factor for hospitalization for cerebral palsy.

The second factor compared the number of cases of hospitalisation of males (441) for cerebral palsy within the Areas of Concern (total males AOC population: 2,719,955) with the number of cases (443) in locations that were not Areas of Concern (total male population: 10,734,625). This yielded an odds ratio of 3.93 (Confidence Interval from 3.44–4.48). A similar calculation for females in the Areas of Concern gave an odds ratio of 3.99 (Confidence Interval 3.45–4.61). These odds ratios for males and females indicate that living in an Area of Concern is a significant risk factor for cerebral palsy hospitalization compared with the rest of the Province of Ontario.

The third factor examined the risks associated with the presence of mercury chloralkali plants. In Areas of Concern with historic chloralkali plants, the number of cases of cerebral palsy hospitalisation in males (141) in the total male population (670,885) was compared with the number of cases (300) in the total male population (2,049,070) in Areas of Concern without this historic association. This yielded an odds ratio of 1.44 (Confidence Intervals 1.18–1.75). The results of a similar analysis for females was not significant (OR = 0.81, CI 0.63–1.05).

The sex of a child is not generally listed as a risk factor in the incidence of cerebral palsy within a population (74, 75). Factor one indicates that there is a higher rate of hospitalization for males in Ontario. While it is possible that the rate might reflect different policies and practices in Ontario hospitals, it is also not inconsistent with the known differential susceptibility of males to disturbances of neurological development from prenatal and postnatal exposure to methyl mercury. The second factor indicates that cerebral palsy hospitalization tends to be associated with Areas of Concern around the Great Lakes. Larger cities in Ontario may have better facilities for treating children with cerebral palsy and these tend to be around the Great Lakes. Thus the possibility that children with cerebral palsy were brought to Areas of Concern cannot be excluded in this analysis. The third factor indicates an association with the historic use of mercury in chloralkali plants, although this result may be

influenced by the disproportionate size of Toronto which has never had a chloralkali plant.

TIME ORDER

Time Order or temporality refers to the necessity that the cause precedes the effect in time (28, 48). The dates of the onsets of the increases in cerebral palsy hospitalizations in males in the Canadian Areas of Concern are unknown. All that can be established is that the 7-year period 1986–1992 that Health Canada chose to compile the health data and statistics (Figure 1) was long after the introduction of mercury-based technologies into many of the Areas of Concern. For example, Table 1 contains information on the dates when the mercury chloralkali plants became operational. In Sarnia, one of the Dow Chemical of Canada plants started in 1948 and the second came on stream in 1970. It would therefore seem that within the limitations of the available data there are no temporal grounds for rejecting mercury as a putative factor in the elevated rate of male cerebral palsy hospitalisation in Sarnia (St Clair River Area of Concern) in the period 1986–1992. Similarly, the Thunder Bay mercury chloralkali plant operated from 1966 to 1973, the plant at Hamilton operated from 1965 to 1973 and the plant at Cornwall operated between 1935 and 1995.

The distribution of the industries that had used mercury has been presented in maps (12, 14) that indicate use as a slimicide in pulp and paper plants at Sault Ste Marie on the St Mary's River and at Napanee on the Bay of Quinte before 1970. Thus, for each of the communities in Canadian Areas of Concern with rates of hospitalization for cerebral palsy that were statistically significantly elevated, on the grounds of time order, the possibility that the populations could not potentially have been exposed to elevated concentrations of mercury can be rejected.

There are other Areas of Concern where the rates of hospitalisation for cerebral palsy were elevated but for which there were statistically insufficient numbers of cases to establish significance. These included: Jackfish Bay (males only); Severn Sound (males only); and Wheatley (males and females). Both Jackfish Bay and Severn Sound are locations with elevated geological levels of mercury. Wheatley is a small fishing harbour on the north shore of Lake Erie and was seriously affected economically by the closures of the commercial fisheries in the 1970s because of mercury. Thus, on temporal grounds, the possibility of exposures of the communities to locally elevated concentrations of mercury cannot be rejected for these Canadian Areas of Concern.

PERFORMANCE ON PREDICTION

The Performance on Prediction viewpoint relies on the testing of a deduction and requires that a hypothesis drawn from an observed association predicts a

previously unknown fact or consequence and must, in turn, be shown to lead to that consequence (28). The inclusion of cerebral palsy, in the Health Canada (37) study of over 70 health endpoints that might be associated with pollution was, in a sense, a prediction based on a hypothesis drawn from previously observed associations that prenatal exposure to methyl mercury may result in cerebral palsy. The apparent coincidence between locations with mercury releases from chloralkali plants and the morbidity as hospitalization incidence of infantile cerebral palsy affirms the prediction.

Based on the elevated mercury concentrations in the Kingston basin of Lake Ontario (45), elevated hospitalisation rates for male cerebral palsy would be expected in Kingston, Ontario. At this point, new predictions can be made that similar elevated rates of cerebral palsy hospitalisation for males will likely be found in communities on the United States side of the Great Lakes. These would be expected in the following locations: Port Edwards, Wisconsin from the Wyandotte Chemical Corporation plant; Saginaw and Bay City, Michigan, downstream from the General Electric Co. plant at Edmore, Michigan; Trenton, Michigan, downstream from the Wyandotte Chemical Corporation plant located close to the Detroit River, and at Ashtabula, Ohio from the Detrex Chemical plant (77).

SUMMARY AND CONCLUSIONS CONCERNING REDUCTION OF UNCERTAINTY

There are limitations to the methodology of using hospitalization data and uncertainties in these preliminary associations (2). The means chosen for "reducing uncertainty" (33) is the application of the Hill's "viewpoints" (48). In terms of probability, the Health Canada approach seems to have been successful in obtaining sufficient cases, even in small communities, for the detection of statistically significant differences in rates of hospitalization for cerebral palsy on a gender-specific basis. There is a consistency of these new findings in Great Lakes communities with other studies undertaken on other populations, by other scientists, at other locations and at other periods of time. The new facts cohere with the existing body of theory concerning the role of methyl mercury in relation to cerebral palsy pathogenesis and there are coherent pathways, sources, and routes of exposure of Great Lakes communities to methyl mercury. There are plausible mechanistic interpretations of toxic action on neurological development at different levels of biological organisation. There are, however, at this time no data that have shown a dose-response relationship between cerebral palsy hospitalization and mercury exposures in the 17 Canadian Areas of Concern. There are useful aspects of specificity in that methyl mercury is the only chemical risk factor linked to cerebral palsy and the only chemical risk factor associated with differential neurodevelopmental susceptibility on a gender basis. Analysis of odds ratios has demonstrated the strength

of association between Canadian communities in proximity to the Great Lakes and hospitalization for cerebral palsy in both males and females and an association between male hospitalization for cerebral palsy and the historic presence of chloralkali plants. There are no temporal grounds for believing that the communities with elevated rates of hospitalization for cerebral palsy were potentially unexposed prior to the study period (1986–1992). Finally, the implicit prediction of Health Canada that Areas of Concern with elevated mercury concentrations would have higher rates of cerebral palsy has been affirmed.

Despite the remaining uncertainties, all this extensive evidence would have to be ignored to believe that there was no causal relationship between the elevated rates of male hospitalization for cerebral palsy in several Canadian Areas of Concern and exposures to methyl mercury from historic and natural sources in the Great Lakes. The elevated rates of male cerebral palsy hospitalization indicate previously unidentified outbreaks of congenital Minamata disease in several Canadian Areas of Concern in the Great Lakes basin. In conclusion, this finding indicates that there continues to be injury to health from pollutants in the boundary waters and that the United States and Canadian governments have failed to effectively implement their Great Lakes Water Quality Agreement for one of the primary pollutants for which it was originally negotiated in 1972. The finding of this effect poses the inconvenient conundrum for the International Joint Commission and the United States and Canadian governments because, as pointed out in the introduction, the knowledge of the continuing injury connotes "liability, legal processes, punitive damages and costly remedial engineering."

OTHER FAILURES OF THE GREAT LAKES WATER QUALITY AGREEMENT

In addition to the indications of congenital Minamata disease in several Canadian Areas of Concern, there are other indications of failures of the United States and Canadian governments to implement the Great Lakes Water Quality Agreement and to restore water quality (see (2) for detailed discussion). For example, although the concentrations of most organochlorine compounds have declined significantly since the catastrophic levels documented in the 1970s, the few epidemiological studies that are being undertaken indicate that effects are still occurring in human infants exposed prenatally from maternal consumption of Great Lakes fish (7–9).

Similarly, although bald eagles have re-established territories in many of the original sites, organochlorine levels are still so high that the fledged young are not viable and do not survive to enter the breeding population (78). Similarly, colonies of Caspian terns on the more contaminated United States side of the Great Lakes are maintained by recruits from Canadian colonies with lower levels of contamination with organochlorine compounds (79).

Similarly, there have been failures to use a precautionary approach to maintain water quality. In 1979, the known dangers of polybrominated biphenyls led to the proscription of all activities under the former Canadian Environmental Contaminants Act. The Canadian and United States governments, however, respectively failed to use the subsequent Canadian Environmental Protection Act and the Toxic Substances Control Act to prevent widespread contamination of the Great Lakes Basin Ecosystem with other closely related brominated flame retardants: the polybrominated diphenyl ethers (80).

The question that now arises is how did the United States and Canadian Governments fail to implement the Great Lakes Water Quality Agreement during the past 37 years? The answer is unlikely to be found in the scientific and technological aspects of pollution research, control, remediation, and prevention. Instead, the prescription of the epidemiologists for an eco-social approach (22, 24–26) might yield insights into the failure of the political will of the United States and Canadian governments (81).

METHODOLOGICAL FRAMEWORK FOR AN ECO-SOCIAL EPIDEMIOLOGICAL ANALYSIS

There does not seem to be a set methodology for implementing the advocated "eco-social" epidemiological analysis (22), but the following may provide some useful analytic frames (2, 82). Prior to the development of the Great Lakes Water Quality Agreement, the 1960s had been a period of growing awareness within the public and the scientific community of the dangers posed by the ubiquitous presence of radionuclides (83) and organochlorine pesticides (84) leading to *struggles* about their use. The anti-nuclear and environmental activists were important parts of the *new social movements* of the late 1960s and early 1970s that led to a period of social reform at the global level with new legislation and new institutions. But even as the far-reaching reforms were being formulated into legislation and began to be implemented, conservative elements were marshalling, particularly through the Trilateral Commission to contain "excessive" democracy (85) in order to protect capitalism (10, 86).

"There is an old saw in political science that difficult conditions become problems only when people come to see them as amenable to human action" (87). By the 1960s, there was a growing consensus that the conditions with respect to pollution of the boundary waters in the Great Lakes had become so serious that governments at all levels needed to act (10, 17). After the International Joint Commission (11) reported that there was "injury to health and property" from pollution of the boundary waters, the United States and Canadian federal governments responded by negotiating a Great Lakes Water Quality Agreement that was signed in 1972 at the beginning of the last decade of

the Keynesian consensus. The ascendancy of *neo-liberalism* during the 1980s in the United States under President Ronald Reagan and in Canada under Prime Minister Brian Mulroney has been extensively reviewed (88–90) and lead to retrenchment of government responsibilities and programs. Anomalously, Reagan extended his *laissez-faire* platform of *deregulation* beyond market economic policy to include social programmes such as environmental protection and occupational health and safety (90).

Snider (91, 92), in placing the tragedy of the deaths and hospitalizations caused by the bacterial contamination of drinking water at Walkerton, Ontario in sociological frames, noted that the establishment of the Commission of Inquiry, headed by Justice O' Connor, was a form of "*resistance*" against policies introduced by then Ontario Premier, Mike Harris, whose Conservative Government had been *captured* by neo-liberal ideology.

Because social change requires the communication of the perceived risks from scientists to the public and to policymakers, other analytic models may be needed from the *risk communication* literature (93). For example, the social processing of risk, through *amplification* and *attenuation* of the information, has been a significant area of research in the past two decades and may be important analytical tools for understanding the failure of the Great Lakes Water Quality Agreement (94–96). Of particular relevance in analysing the failure may be the processes of *diversionary reframing* as a mendacious means not only of risk message attenuation and avoidance of restoration costs but also of supporting other Great Lakes programs that were threatened by budget cuts and were unrelated to water quality (97, 98).

ECO-SOCIAL ANALYSIS OF THE FAILURE OF THE GREAT LAKES WATER QUALITY AGREEMENT

The negotiation of the Great Lakes Water Quality Agreement in 1972 represented recognition by the two federal governments of the deep seated resistance within the population, expressed through the coalesced new social movements, among other things to pollution of the boundary waters and to the associated injury to health and property. The continuing resistance within the population supported not only the renegotiation in 1978 with the reorientation towards persistent toxic substances but also the 1987 Protocol legitimating the preparation of Remedial Action Plans for designated Areas of Concern that failed to meet water quality standards as well as Lakewide Management Plans for Critical Pollutants.

The ascendancy of neo-liberal ideology in the late 1970s and early 1980s provided a resistance stimulus to reinvigorate the new social movement in the Great Lakes basin. Great Lakes United, Greenpeace, Pollution Probe, and the Lake Michigan Federation cooperated to organize grass roots movements

throughout the Great Lakes basin. The interests of these organizations coalesced with new science on endocrine disruptors (99), a new focus of the IJC science advisors on human health, particularly pollutant-induced effects on reproduction and development (100), and new work on causality (101). Representatives of this coalescence of interests made extensive interventions at the 1989 Biennial Meeting of the International Joint Commission. They were particularly effective in persuading Gordon Durnil (102), the then new U.S. Co-Chair of the IJC and his fellow commissioners to recommend that the United States and Canadian governments should implement their Great Lakes Water Quality Agreement, particularly the policy on the "virtual elimination" of discharges of persistent toxic substances (17, 103).

The success of this counter-hegemonic movement was, however, short lived, particularly after the International Joint Commission (104) overreached its credibility when it recommended that "the Parties, in consultation with industry and other affected interests, develop timetables to sunset the use of chlorine and chlorine-containing compounds as industrial feedstocks." The reaction was immediate and eventually lead to industry representatives influencing the White House of incoming President Clinton to appoint new U.S. commissioners "who were not as green as the current bunch" (102). The International Joint Commission thus became captured by the chemical industry after 1992 and the agenda on persistent toxic substances was quietly and skilfully sandbagged. In the mid-1990s, the situation was exacerbated by decisions of the international non-government organizations to transfer the resources from the virtual elimination priority in the Great Lakes to their European processes to influence the development of the REACH legislation (Registration, Evaluation and Authorization of Chemicals) by the European Union. The recent election of President Obama offers the United States an opportunity to appoint new U.S. commissioners who can refocus the International Joint Commission to undertake their designated duties that include critically reviewing the Parties' progress under the Great Lakes Water Quality Agreement.

ATTENUATION OF THE RISK MESSAGE

One of the central roles and responsibilities of the International Joint Commission under the Great Lakes Water Quality Agreement relates to risk communication through "tendering of advice and recommendations . . . on problems of and matters related to the boundary waters of the Great Lakes System. . . . " After the International Joint Commission was captured, it surreptitiously embarked on a process of attenuation of the risk message concerning the continuing injury to health characterized by systematic omissions from its reports of new health research. For example, in May 1997, health

authorities from the United States, Canada, and Quebec hosted a conference on Great Lakes/St Lawrence health effects research. The purpose was to present results of nearly a decade of research on the effects of pollution on human health. The research had been funded by the respective governments as part of their contributions to the implementation of the Great Lakes Water Quality Agreement. More than 18 months after publication of the papers (105), the International Joint Commission (106) sent its 10th report on Great Lakes water quality to the governments and purposely omitted all the new research. This indicates a deliberate dereliction of duty to advise governments of water quality problems at the boundary.

Similarly, in February 2003, the International Joint Commission hosted a conference on "An Ecosystem Approach to the Health Effects of Mercury in the Great Lakes Basin Ecosystem" and the papers were published in July 2004 (64). However, the information on the indications of congenital Minamata disease (43) was deliberately omitted from the subsequent report on water quality to the governments with reassurances that "Methyl mercury . . . has not been conclusively established as a teratogen" (107). The new information posed the conundrum of finding injury with its implied liability, legal processes, punitive damages, and costly remedial engineering. The process of silencing those involved in forensic research on the chemically induced injury to health and property is an effective means of attenuating the risk message. Evaluation by the new U.S. administration of the suitability of candidates for the new U.S. appointments to the International Joint Commission and its advisory boards should include qualifications for their abilities to evaluate new evidence of injury to health from trans-boundary pollution and a willingness to report it.

DIVERSIONARY REFRAMING

Another powerful means of attenuation of the risk message relates to diversionary reframing (97). The Great Lakes Water Quality Agreement is a minimalist bilateral instrument between two sovereign nations for maintaining and restoring water quality from pollution of the boundary waters (108). Based on the inclusion of the word "ecosystem" in Article II, there has been a widespread pattern of misrepresentation of the purpose as a broad, open-ended agreement for "transboundary problem-solving" using ecosystem management for restoration of ecosystem integrity for the entire Great Lakes basin (109–111). The new agenda now downplays the role of persistent toxic substances and privileges other "ecosystem stressors" such as the introduction of exotic species, wetland conservation, lake levels and water quantity, and climate change (see (2) for detailed discussion). Based on discourse analysis, there seem to be many beneficiaries of this unauthorized attempted transformation with a variety of motives (108).

For example, in the early 1970s, fisheries biologists formulated a post-modern approach to the extirpations of Great Lakes fish stocks (112). Instead of choosing between causal hypotheses (113), they invoked an analogy with physiological stress (114) and advocated consideration of the role of multiple stressors acting together at the ecosystem level (115). Based on the report of a joint committee of the National Research Council and the Royal Society of Canada (116) they have attempted four times over the past 25 years to superimpose this post-modern approach on to the Great Lakes Water Quality Agreement. Alternative causal stories lead to very different formulations of policy (87). The post-modern approach of the fisheries biologists led to policy recommendations for the Great Lakes Water Quality Agreement to "evolve" to include a wide array of Great Lakes programs (17, 109, 117). The multi-stressor assumptions underlying this ecosystemic formulation, however, have recently been challenged by a retrospective toxicological risk assessment that indicates that the lake-wide extinction of the indigenous lake trout population in Lake Ontario was caused by dioxin-like activity acting "alone" (118). Fisheries biologists have met this Kuhnian crisis with a Lakatosian "protective belt" around the "hard core" of multi-stressor assumptions (113). However reluctantly, fisheries biologists need to deconstruct all their science from the past century concerning the factors that caused the extirpations of stocks and extinctions of species and reconstruct it using techniques to achieve parsimony. "The interests reflected in one choice of classification rather than another may become structural, embodied in institutional routines, rather than voluntaristic" (119).

The use of the post-modern approach with its multi-causal assumptions in attempts to reframe the Great Lakes Water Quality Agreement have suited government managers of research programs for management of biological resources in the Great Lakes basin. Managers have tried to justify continuation of their research and management programs, threatened with closures following neo-liberal tenets of small government, by claiming the Great Lakes Water Quality Agreement as a broad mandate for "transboundary problem-solving" (109, 120). Similarly, with neo-liberal tenets of small government, laissez-faire economics, and deregulation, governments have endorsed diversionary reframing as a means of avoiding implementation of most of the costly remedial provisions of the Great Lakes Water Quality Agreement (cf. (121)). During this decade, the International Joint Commission has aligned itself with the position of the governments, avoided its role of critically analyzing the progress of the governments in implementing the Great Lakes Water Quality Agreement, and, in 2007, dispensed with the services of the team of forensic environmental toxicologists who through the Great Lakes Science Advisory Board had continued to make statements about the injury to health from exposures to persistent toxic substances from trans-boundary pollution. Similarly, the chemical manufacturing industries have implicitly supported the diversionary

reframing (122) to protect profitable chemical products and as a means to avoid undertaking costly remedial actions.

The 1972 Great Lakes Water Quality Agreement was a bilateral response of the United States and Canadian governments to the political outrage expressed in their respective nations through the new social movements of the 1960s. The 1978 renegotiation reoriented the priorities toward the new information on injury to health and property caused by persistent toxic substances. However, by the early 1980s, the superimposition of the political economic theory of neo-liberalism by President Ronald Reagan and Prime Minister Brian Mulroney effectively eclipsed the use of the Great Lakes Water Quality Agreement in protecting health and the environment from exposures to pollutants in the Great Lakes boundary waters. There is increasing evidence that the United States and Canadian governments (123) and the International Joint Commission (124) have embraced the proposal, initiated through the National Research Council of the United States and the Royal Society of Canada (116) to transform the purpose of the Great Lakes Water Quality Agreement into an instrument of ecosystem management.

In retrospect, it is important to understand the implications of the misguided political extrapolation of the tenets of neo-liberalism from market economics to environmental health issues. Professor Friedrich August von Hayek, writing in the mid-1940s, is generally regarded as the father of neo-liberalism designed to protect market competition from distortions by governments. However, decades before the modern critique of capitalism by the environmental health movement, he recognized the need for regulatory interventions "to prohibit the use of certain poisonous substances or to require special precautions in their use" and that this "is fully compatible with the preservation of competition" (125).

Reframing of the Great Lakes Water Quality Agreement has been surreptitiously embraced by parts of the environmental non-government organizations for more than 20 years (17). This has been repeatedly encouraged, during the past decade, by the International Joint Commission and the United States and Canadian governments, particularly through the State of the Lakes Ecosystem Conferences with open-ended agenda and an ambiguous relationship of the conference programs to the Great Lakes Water Quality Agreement. "Repetition is the best didactic means for working on the popular mentality" (126). The Great Lakes Water Quality Agreement has been extensively reviewed by the two governments through extensive public consultation. During the past 25 years, the implementation of neo-liberal tenets of small government, privatization of services, and deregulation have resulted in many constituencies in the Great Lakes basin seeking a vehicle through which to attempt to mobilize unresponsive governments. Even though these agenda are essentially unrelated to water quality, there is a network of policy analysts who have sought to use the review process to transform the Great Lakes Water Quality

Agreement into the multi-purpose vehicle for these constituencies (17, 127, 128). These policy analysts, however, have not undertaken their work in consultation with the various networks of scientists who have undertaken the forensic research on the injury to health and property from trans-boundary pollution. Their pluralistic interpretation of the purpose of the Great Lakes Water Quality Agreement has further contributed to obscuring the original minimalist intent of the 1909 Boundary Waters Treaty of maintaining and restoring water quality at the shared boundary of the Great Lakes to prevent injury to health. For example, when President Obama met with Prime Minister Harper in Ottawa on February 10, 2009 shortly after taking office, representatives of many environmental non-government organizations signed a letter to the organizers advocating that "The Great Lakes Water Quality Agreement is the most appropriate mechanism to articulate many of these binational goals, priorities and commitments."

SCIENTIFIC, TECHNICAL, AND POLITICAL IMPLICATIONS

Although PCBs and mercury were two of the substances that stimulated the negotiation and signing of the first Great Lakes Water Quality Agreement in 1972, the consequences of the continuing exposure of Great Lakes populations to these and other persistent toxic substances are still being elucidated, particularly in relation to reproduction and development. The theoretical and experimental advances in research on endocrine disruptors have contributed new insights into the effects of exposures of early life stages on subsequent developmental processes at concentrations several orders of magnitude below "safe" levels established by traditional toxicology. These include effects on the differentiation of the reproductive tract and on the developing endocrine, immune, and neurological systems as well as other effects such as a predisposition to development of cancer. The empirical part of this paper indicates the possibility that human populations in Great Lakes communities are being exposed to methyl mercury at concentrations that are resulting in neurodevelopmental effects in infants. Previous epidemiological studies of cohorts of infants have indicated that human developmental processes continue to be injured by exposures to persistent toxic substances at ambient concentrations, particularly to PCBs (3–9). Although concentrations of many persistent toxic substances have declined, concentrations of substitute compounds, such as polybrominated diphenyl ethers, are increasing (80). Of particular concern from these studies are the delayed effects of early life stage exposures on subsequent development and health not only in human populations as demonstrated in the infant cohort studies but also in fish and wildlife populations.

The new information on the suspected outbreaks on congenital Minamata disease in several Canadian Areas of Concern (43) indicates that the United

States and Canadian governments failed to implement the Great Lakes Water Quality Agreement to protect human health through restoration of Great Lakes water quality. President George W. Bush, following neo-conservative tenets of unilateralism, eschewed bilateral treaties and agreements, and the 2004–2008 review of the Great Lakes Water Quality Agreement offered an opportunity to dismantle a bilateral agreement on which domestic obligations for regulatory control of pollution of the boundary waters have been based for three decades. Despite his long record of rolling back the advances in environmental protection that had been made by Congress since the 1970s following the protests by the new social movements in the late 1960s and early 1970s (129), the Great Lakes Water Quality Agreement survived for the new administration of President Obama to address. In Canada, newly re-elected Prime Minister Stephen Harper has appointment Jim Prentice to replace environment antagonist John Baird as Minister of the Environment. Although Stephen Harper, as a modern economist, has impeccable neo-liberal credentials, he has realized from his third failure to obtain a parliamentary majority for the Conservative Party that among other things environment is important to Canadian voters. In their review and possible renegotiation, the United States and Canadian governments should maintain the purpose of the Great Lakes Water Quality Agreement as a minimalist agreement focused on maintaining and restoring water quality along the shared Great Lakes boundary waters between the United States and Canada, in fulfilment of their commitments, made 100-years-ago under the 1909 Boundary Waters Treaty, to prevent injury to health and property from trans-boundary pollution.

On June 13, 2009, Hilary Clinton as the new Secretary of State announced at the 100th Anniversary of the Boundary Waters Treaty that the Great Lakes Water Quality Agreement would be "updated" to address "new threats" including "new invasive species" and "new worrisome chemicals," both of which are already in the existing agreement. Fortunately, it seems that the new U.S. administration wants to address other "environmental threats" such as "climate change" and "the safety of coastal regions, the future of agriculture and health, and the stability of communities" through other "partnership" mechanisms (130). It seems that this fourth attempt to transform the Great Lakes Water Quality Agreement into a multi-stressor ecosystem agreement may again have failed.

SUMMARY AND CONCLUSIONS

Over the past century, there has been extensive injury to health from releases of persistent toxic substances to the Great Lakes. Environmental health researchers have developed forensic techniques to reduce the uncertainties about the diagnoses of this injury and of its putative cause or causes. The

situation became so serious by the mid-century and sustained expressions of outrage by new social movements so vociferous that in 1978 the United States and Canadian governments renegotiated the 1972 Great Lakes Water Quality Agreement specifically to address persistent toxic substances. Elevated hospitalization rates for male cerebral palsy indicate that there may be outbreaks of congenital Minamata disease in several of the Canadian Areas of Concern. In turn, this indicates that the two governments have failed to implement the Great Lakes Water Quality Agreement. The causes of the failure cannot be understood solely in scientific and technical terms, but the development of an eco-social epidemiological approach, using frames from risk communication, sociology, economics, and politics, has been useful in elucidating other factors. The failure of the United States and Canadian governments to implement the Great Lakes Water Quality Agreement would seem to preclude any justification for expanding the purview from its minimalist focus on trans-boundary water pollution into an unbounded agenda on ecosystem management of the entire Great Lakes basin.

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