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Great Lakes Water Quality Board. Committee for the Assessment of Human Health Effects of Great Lakes Water Quality

International Joint Commission Water Quality Board and Science Advisory Board's
Committee for the Assessment of Human Health Effects of Great Lakes Water Quality

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DISCLAIMER

This report to the Chairpersons of the Science Advisory Board, and the Water Quality Board was carried out as part of the activities of the Committee for the Assessment of Human Health Effects of Great Lakes Water Quality. While the Commission supported this work, the specific conclusions and recommendations do not necessarily represent the views of the International Joint Commission, the Science Advisory Board, the Water Quality Board or their committees.

The Workshop on The Role of Epidemiology in Assessing the Effects of Great Lakes Water Quality on Human Health was held in 1988. Since that time, there has been a substantial evolution in the thinking about the risks posed by chemicals. An extensive review of the effects of chemicals on fish and wildlife has focused attention on reproductive, developmental and metabolic processes rather than on cancer and birth defects. This shift in orientation was a significant outcome of workshops sponsored by the Council of Great Lakes Research Managers and the Health Committee of the International Joint Commission (IJC) and by the Fourth Biennial Meeting of the IJC, held in Hamilton, Ontario on October 11-14, 1989. In the limited time available at the 1988 workshop, whose focus was traditional health outcome measures, the participants were not able to include in depth discussions on a number of these topics. Despite this limitation, these proceedings are a valuable record of the methodologies presented and of the information collected from participants.

The findings presented at the Biennial Meeting re-emphasize the need for agencies to undertake and sustain long-term epidemiological studies of highly exposed groups such as fish-eaters in the Great Lakes basin. Collaborative studies should be designed and funded to investigate the subtle effects of exposure on embryonic, fetal and post-natal development, not only in relation to structural anomalies, but also in relation to functional anomalies in behavioural and psychomotor development.

Katharine Davies Harold E.B. Humphrey

Health Committee

Criteria for Study Initiation

Regulatory agencies would benefit from developing explicit decision algorithms for deciding whether to proceed with environmental epidemiological studies. Some agencies have already developed procedures for this purpose, but consistency is lacking.

Funding

Epidemiological research into the potential health impacts of chemical contaminants in the Great Lakes is meager; there should be an infusion of public and private sector research funds to stimulate such studies. The Canadian Department of National Health and Welfare and the United States Environmental Protection Agency should take the lead in this regard.

2.0 INTRODUCTION

Canada and the United States jointly benefit from one of North America's most important natural resources: the Great Lakes. As well as being a major transportation route and offering recreational benefits, they are sources of drinking water and edible fish. The Lakes also serve as a catchment basin for precipitation, and ground runoff and a point of discharge for treated (and untreated) waste water.

Because of the lakes' significance, the possibility that a deterioration in their water quality could cause adverse human health effects has led to concern among scientists, regulators and the public. This concern arises from the knowledge or the suspicion that unknown quantities of toxic substances have found, and could continue to find, their way into the Great Lakes.

The Committee for the Assessment of Human Health Effects of Great Lakes Water Quality (HHEC) of the International Joint Commission (IJC) provides information and advice on the possible health effects of Great Lakes contaminants to the Water Quality and Science Advisory Boards of the IJC and, through them, to the jurisdictions within the basin. Since 1978 the Canadian and American scientists on this Committee have, within the limitations of available resources, reviewed scientific literature that might inform their judgments. It has become clear that the bases for current associations between water quality and human disease are derived from toxicology, not epidemiology. That is, most of our ideas about hazards to people and appropriate control and surveillance procedures are based on extrapolations from animal data. While toxicology data are an essential component in the evaluation of the harmful effects of chemicals, the Committee was concerned about the paucity of epidemiological studies on water contamination and human health.

Using a two-stage consultative process, the HHEC therefore sought expert opinion on the role of epidemiology in assessing the human health effects of water quality.

The first stage consisted of asking seven recognized experts in epidemiology to submit papers on a number of relevant topics. Two papers were empirically based; each involved a census and evaluation of Canadian or American data sources, that might be useful to epidemiologists studying health effects in the Great Lakes basin. The other five papers were speculative in nature; each addressed the potential benefits of various epidemiological strategies for studying from somewhat different perspectives the effects of water quality on human health. The seven papers are published in Volume II of this report.

The second stage of the consultative process was a workshop based on the papers developed in stage one. The workshop was attended by twenty-three participants (listed in Appendix 7.1), who examined the role of epidemiology in assessing the effects of Great Lakes water quality on human health. The participants brought to the discussions the expertise and experience gained from academic studies of epidemiology and biostatistics, from public health agencies at the federal, state and provincial levels, and from federal research agencies.

3.0 WORKSHOP ORGANIZATION

The specific questions and working papers to be addressed at the Workshop were circulated in advance to all participants. These questions appear here in summary form (for full text of questions, see Volume II).

1. Given the currently available sources of data on water quality and human health in the Great Lakes basin, what kinds of epidemiological studies can usefully be carried out?

2. What new data bases, or what modifications in existing data bases on water/fish quality and on human health could be recommended to improve the opportunity for, and the quality of, epidemiological studies?

3. What is the role of epidemiology in addressing the concern of a community that its water supply may be harming its citizens?

4. What criteria could local agencies use in deciding whether to proceed with a proposed or requested epidemiological study?

5. What sources of funding are available for epidemiological research into the health effects of water quality in the Great Lakes basin? Are these sources adequate?

The workshop opened with wide-ranging discussions to outline important issues; then five working groups were formed to draft a consensus response to each question and present the response at a plenary session. The working groups' conclusions are summarized in Section 4.1.

In addition to these general discussions, two other approaches were developed to summarize and rank proposed studies. Because the answer to Question 1 depended on the types of exposure variables and disease endpoints under consideration, a disease/exposure matrix (see Table I) was devised to structure the discussion. Each exposure/disease pair was assigned a score reflecting the potential value of studies based on aggregate or individual data. These scores were averaged across workshop participants, who also wrote brief descriptions of the study which they thought would be most feasible. The outcome of these endeavours is described in Section 4.2.

4.0 WORKSHOP RESULTS

4.1 Consensus Responses to Workshop Questions

4.1.1 Study Strategies

4.1.1.1 Studies Based on Aggregate Data

In studies based on aggregate data, the unit of observation is a defined population and the health effects are described in terms of incidence or prevalence rates within that group. Exposure levels are determined by measuring the contaminants in a medium to which the same population is exposed, e.g. chlorinated *versus* non-chlorinated drinking water. The working papers prepared by Walters and by Robertson and Donner (see Volume II) discuss the methodology and limitations of these studies.

Studies based on aggregate data are relatively inexpensive, compared with studies based on individual data, and the former can usually be designed, implemented and completed in a relatively short time. Participants felt that local authorities, in accomplishing their health surveillance responsibilities, should actively and continually pursue studies based on aggregate data within and between their jurisdictions. Carrying out such studies would provide early warning of problems and would also allow for the rapid provisional evaluation of hypotheses raised in other ways.

There are many limitations to studies based on aggregate data. They generally make use of routinely collected data, and the quality and detail of such data are important determinants of a study's value. It is often impossible to control for important confounding factors (smoking, other chemical exposures, socioeconomic status). Participants emphasized the importance of trying to collect information on confounders at the aggregate level and of seeking situations in which the problem might be minimized, such as studies before and after a change in contaminant exposure. While supporting the conduct of this type of study, participants emphasized the need for caution in assessing the results. Studies based on aggregate data can support a hypothesis, but do not rigorously test one. The supportive evidence is usually weak and requires independent corroboration.

Studies based on aggregate data on water quality and health are generally more feasible than studies based on individuals because data routinely collected for other purposes can be used. However, the validity of the associations in studies based on aggregate data is more questionable than associations identified based on individual data. Consequently, participants supported the methodological investigation of studies based on aggregate data. One example of such an approach would be for an investigator with epidemiological information on individuals to aggregate the data in different ways and describe the impact that each method had on the exposure/disease associations. The participants recommended that several such methodological investigations be undertaken.

A number of methodological issues were considered of sufficient importance for participants recommend that they receive further study. These issues included:

- the variation of exposure within and between population subunits in the analysis, e.g. differences in water quality within and between water distribution systems

- the degree of spatial auto-correlation in exposure and outcome measures over population subunits and the impact which this phenomenon may have on methods of statistical analysis

- the consideration of problems caused by transient populations, especially in the study of delayed effects. Identifying areas with low population migration rates would aid the selection of localities for studies based on aggregate data

4.1.1.2 Studies Based on Individual Data

These studies make the individual, rather than the population, the unit of observation. Because it is possible to analyze the effects of exposure, potential confounding variables and a variety of outcomes for each individual, these studies can be much more powerful and persuasive than those based on aggregate data. Research on individuals can take many forms, but the two main types are cohort studies, in which subjects are defined on the basis of exposure status and are followed to determine health outcomes, and case-control studies, in which subjects are defined on the basis of some health outcome and followed to determine their past exposure. Methods and limitations of epidemiological studies based on individual data are discussed in detail in working papers by Arbuckle, by Kanarek and by Neutel (see Volume II).

Studies based on individuals are most appropriate when the factor under study varies within the population. This phenomenon is a limitation in the study of air, water and food contaminants, since these exposures may be relatively uniform for an entire local population. Nevertheless, participants agreed that imaginative investigators might find circumstances in which cohort or case-control studies on air, water or food quality could usefully be carried out. Surveys to identify communities that might satisfy the requirement for intra-area variability in exposure would aid in the design of epidemiological studies.

Currently, exposures are estimated by measuring a small number of chemicals in environmental media and biological tissues at infrequent intervals. Participants noted that determining the total biological activity of an environmental medium (air, water, food) or the response of a tissue might overcome this limitation and provide a more relevant measure of both exposure and potential harm. They also agreed upon the need to develop and validate assays for environmental media that are indicative of biological activity (mutagenic activity of water or effluents) and assays for exposure of tissues to contaminants (DNA adducts, cell transformations).

Studies based on individuals would be strengthened if the effects of current exposures to potentially toxic agents in water and fish could be followed through biological markers of exposure and effect. These markers should be calibrated in exposed and unexposed populations, so that their normal variability could be understood and interpreted.

One of the most promising topics for investigation is the study of human populations who eat fish, because fish tend to bioconcentrate many contaminants of concern. Highly exposed populations can be defined through questionnaires attached to fishing licences or through censuses of regional consumption patterns. These populations can then be profitably followed through tumour and birth defect registries as well as mortality registers. Follow-up of established and proposed Great Lakes fish-consuming cohorts, monitoring changes in both health and body burden, may detect health effects in the more sensitive offspring, e.g. infants. Also recommended were case-control studies focussing on fish consumption as an exposure variable.

The working group discussed several methodological problems relating to exposure estimation that could themselves be useful topics of investigation:

- A study of differential recall of water consumption by cases and controls. This procedure might vary according to the type of disease studied.

- Investigation of methods for estimating past exposure to environmental contaminants. Historical data may be unavailable or lacking, and current levels may not reflect past exposure.

- Development of a list of contaminants known to have more than one toxicological outcome. Some chemicals, for example, may act as carcinogens, mutagens and teratogens.

4.1.2 Data Bases

State-wide or province-wide registries of vital records (death or birth certificates) are required by statute and are fairly uniform; registries of tumours and congenital malformations are not. In the working group's view, tumour and congenital malformation registries should be available in all jurisdictions because they increase the range of potential studies. Identifying cases efficiently and promptly can be of crucial importance for case-control studies. Recommendations for developing cancer registries have already been provided in the "Proceedings of the Workshop on the Compatibility of Great Lakes Basin Cancer Registries" in March 1981. Copies of this report may be obtained from the International Joint Commission, Information Services, 100 Ouellette Avenue, Windsor, Ontario, Canada N9A 6T3.

One of the most serious obstacles to conducting a study across different jurisdictions is that several institutional review boards must clear the proposal for data access and funding. Participants recommended that these institutions harmonize the procedures for access to information and standardize the contents of their data files. Although it may be difficult to standardize procedures used in private institutions, public-sector institutions should move in this direction.

This harmonization effort could extend to the collection, measurement and recording of water quality parameters. Because the measurement of these parameters is limited by the available technology (gas chromatography, atomic absorption/emission or x-ray fluorescence), the working group recommended that jurisdictions develop chemical screening procedures which guarantee that major classes of contaminants, such as total organic halogens, are not missed. Major unidentified peaks in chromatographs should at least be noted.

All agencies involved in contaminant monitoring should collectively conduct a periodic review to decide which parameters to measure for human health purposes, which to add or delete, and whether spot or intensive surveillance of specific chemicals is needed. Important issues for consensus include sampling strategies, geographic units and changes in analytical methodologies. Monitoring agencies should consult with health researchers to ensure that the data collected will be useful for epidemiological purposes. Details on monitoring and surveillance strategies have also been provided in "Proceedings of the Roundtable on the Surveillance and Monitoring Requirements for Assessing Human Health Hazards of Contaminants in the Great Lakes Basin Ecosystem," 1982, available on loan from the library of the International Joint Commission.

Data bases should incorporate high standards of quality assurance and quality control. The procedures for quality assurance and control should be clearly documented. This task will facilitate use by investigators not associated with the data-collecting agency and will increase confidence in the conclusions derived.

Contract laboratories can add significantly to the data bases collected by a jurisdiction's official laboratory. In such cases, the official laboratory should function as a reference centre, ensuring that the contractors are properly accredited and use approved sampling procedures and quality assurance protocols. The reference laboratory should also analyze a set proportion of duplicate samples from the contractor. The cost of quality assurance to the official laboratory should be estimated at between ten and twenty percent of the contract amount.

Whenever possible, and within legal constraints on protection of privacy, a standardized type of unique identifier should be attached to specific sampling units.

Data bases on fish and water contaminants can aid the study of human health effects if the data can be used to estimate individual exposure. For example, it would be helpful if agencies analyzed treated water at the household, rather than the plant level. Participants recognized, however, that household water sampling requires considerable forethought and research in order to

set goals and develop sampling rules that will provide useful data. In a similar vein, the group noted that fish samples used for analysis should reflect the portions that people actually consume. The proprietors of such data bases should be encouraged to make them available for epidemiological research.

4.1.3 Role of Epidemiological Evidence

Public health officials should always be well briefed on the current health status of the communities they serve. For this purpose, they must have periodically updated statistics on local mortality and morbidity rates, which have been analyzed and evaluated against rates in other places and at other times.

When public concern does arise it should be swiftly and credibly addressed. Public concern may take the form of a perceived threat from a pollutant, or an apparent excess of disease occurrence (disease clusters). In either case, the first response of health officials must be to verify the data on which the concern is based, e.g. are people being increasingly exposed to an identified toxic substance or have the disease events been correctly enumerated and diagnosed? If, for example, cancer rates are indeed excessive, the next step is to judge whether the excess is due to chance fluctuation, whether it can be explained on the basis of previously recognized risk factors, or whether the cause is unknown. At this point, authorities must decide whether the situation needs immediate action and/or whether it warrants diversion of any resources to conduct further studies. Monitoring may be needed to determine if the excess is ongoing or transient. (This task may take a long time if the disease in question is normally rare.) Subsequently, the search for an explanation may take different directions, depending on whether or not exposure to the agent of concern is continuing.

If public concern persists and there is a scientific basis for this concern, then local authorities, in consultation with qualified epidemiologists, should evaluate the feasibility of conducting a study in the area.

4.1.4 Study Criteria

Participants discussed the type of decision mechanism and criteria that should be applied in developing the priorities for studies suggested by routine surveillance, physicians reports or community concerns. It was argued that an explicit set of decision rules could help managers determine whether a problem merits investigation and establish priorities for limited resources. Such decisions require expertise in the areas of epidemiology, environmental health and public administration, and entail considerations of the public health relevance, scientific significance and methodological adequacy of the proposed study.

There are serious methodological difficulties in evaluating the possible association of disease clusters and environmental exposures. By the very nature of statistical phenomena, occasional disease clusters will occur in certain communities. This phenomenon leads to false positive observations. Conversely, local populations are often small, so that only a few cases of some rare disease may be produced by even a severe toxic exposure. In such a situation any study carried out would probably have too little statistical power to detect the hazard. This phenomenon leads to falsely negative conclusions.

These difficulties are compounded by the fact that few jurisdictions have the quantity and quality of professional epidemiological resources to tackle all the study situations that might arise.

To partly offset this shortage of professional resources the State of Michigan's Toxic Substance Control Commission in Lansing has developed a means by which residents can help with the investigation of environmental health problems. Outlined in the "Citizen's Guide for

Community Health Studies," this program involves citizens in collecting preliminary health and exposure information. The approach enables authorities to more quickly and fully assess the need for further study.

The working group discussed a decision algorithm developed by the California Department of Health Services, which presents a system for rating proposed environmental epidemiological studies (see R. Neutra et al. 1988, Arch. of Env. Health 43(2):94-99). The studies are rated on the basis of public health significance, scientific significance, degree of public concern, contribution to program balance, ability to provide a definitive answer and likelihood of finding a problem that can be remedied. The total score from the rating system, the total cost and the cost per score point can be used to assess projects under consideration.

4.1.5 Sources of Funding

Few resources are currently available for research related to water quality and human health. Participants strongly urged the jurisdictions on both sides of the border to develop strategies for encouraging high-quality environmental epidemiological studies in the Great Lakes basin. These strategies should involve the establishment of research priorities, the allocation of sufficient funds, and announcements of their availability to the epidemiological research community.

The resurgence of funding within the United States Environmental Protection Agency (U.S. EPA) for environmental epidemiological research was noted with enthusiasm, though the limited scope was criticized. It was suggested that the U.S. EPA should consider expanding its Centers for Excellence Program to include a Great Lakes Centre for Environmental Epidemiology that would focus on Great Lakes problems. This Centre could be the stimulus for an International Centre jointly administered and funded by Canada and the United States. Such an arrangement would be consistent with the objectives of the recently signed revised protocol to the 1978 Great Lakes Water Quality Agreement.

There are many governmental and private agencies that might actively encourage research into the links between water quality and human health, the working group noted. Prominent among such American agencies are the Environmental Protection Agency; the National Institute for Environmental Health Sciences; the National Heart, Lung and Blood Institute; the National Cancer Institute; the American Cancer Society and the state health departments. In Canada, the main agencies funding such work should be the Department of National Health and Welfare, the National Health Research and Development Program, the Medical Research Council, the Ontario Ministry of Health, the Ontario Ministry of the Environment and the National Cancer Institute of Canada. The group recommended that private organizations, including consortia with industries, be encouraged to fund environmental epidemiological research.

4.2 Development of Proposed Studies

4.2.1 Matrix

In order to elicit opinions on the value of different types of epidemiological study, workshop participants were presented with a matrix (Table I) composed of the following three dimensions: type of exposure variable (hard/soft water, volatile organic compounds, metals, etc.), type of disease outcome (cardiovascular, cancer, malformations, etc.), and type of study design (ecologic, case-control, cohort, etc.). Each cell of the matrix therefore represented a class of studies and used a given method to address a given problem, for example, a case-control study to determine the association between cardiovascular disease and exposure to trihalomethanes in drinking water.

The participants were asked to rate each cell of the matrix on three scales:

- Would the study contribute substantially to present knowledge?
- Is the hypothesis under study biologically plausible?
- Is such a study feasible?

The possible scores in relation to each question were 0, 1, 2 or 3; where 0 indicated no opinion, and 1 to 3 indicated increasing estimates of the potential value and feasibility of the study. A zero was treated as a missing value when the means were computed for each cell.

The mean values for each cell are shown in Tables IIa and IIb. Cancer had the highest rating as a disease endpoint for almost every exposure, closely followed by congenital anomalies. The exposure parameters with the highest ratings were fish consumption and organic pesticides. The following intersections of disease and exposure rated highly: nitrates with congenital anomalies or childhood disease, and trihalomethanes or total volatile organics with cancer. In general, the cells representing studies based on individual data (IIa) scored higher than the corresponding cells representing studies based on aggregate data (IIb). Note that a high rating does not infer a high probability of a cause-effect relationship, simply that many epidemiologists believe that this relationship or research design should be investigated.

4.2.2 Proposed Studies

Participants were asked to briefly outline those studies to which they would attach the highest priority. Forty-five outlines were submitted; they appear in full in Appendix 7.2, and are summarized in Table III. The proposals outlined in Appendix 7.2 may aid jurisdictions and granting agencies in establishing priorities as well as assisting in the development of useful epidemiological studies.

The exposure parameter and disease endpoints most often proposed for study were fish consumption and cancer, respectively. One-third of the proposed studies are based on aggregate data while two-thirds (individual studies and fish-eater studies) are based on individual data.

As some proposed studies did not fit into the matrix framework used at the workshop, they were placed in the 'other' category. There were a few proposals for 'before-after' studies; for example, research on communities that change their water supply (ground- *versus* surface-water source) and can thereby act as their own controls. Participants also suggested a range of methodological investigations that would improve our ability to carry out epidemiological studies and to interpret their findings. Suggestions included measuring the variability of immunological endpoints, assessing individual water consumption, evaluating the variation of chemical constituents between and within distribution systems, and developing a bioassay methodology to assess the toxicological potency of the total chemical mixture.

5.0 DISCUSSION

While Workshop participants were able to propose ideas for different types of epidemiological studies, there was not enough time to debate and reach consensus on specific proposals. Nevertheless, it was agreed that epidemiological studies are particularly suited for the discovery and quantification of adverse health effects of Great Lakes pollution.

Participants believed that there is a role for studies based on both aggregate and individual data. They pointed out that exploratory studies could often be undertaken using readily available aggregate data. Local and state/provincial authorities should be continually evaluating vital statistics and registry data. Research scientists should also have access to these same data bases to generate or test new hypotheses.

The usefulness of epidemiological studies of fish-consuming populations was discussed several times during the workshop. Fish-consumers tend to be exposed to higher levels of many waterborne pollutants due to the bioaccumulation of these pollutants in fish. The potential importance of such studies was also indicated by the high scores they attained in the matrix ranking exercise. Participants considered the expansion of ongoing fish-consuming cohort studies in the Great Lakes basin as well as the study of new fish-consuming cohorts to be very valuable.

Existing guidelines and standards for drinking water quality are based largely on extrapolations from the toxicological data obtained through animal studies of a single contaminant. Although it is expected that these guidelines for individual contaminants will protect humans, little is known about the validity of inter-species extrapolation and about the effects of combined exposure to the total contaminant load. Chemical surveillance of both raw and treated water employs laboratory procedures that screen for a large number of contaminants, but ignore many less well-known substances at lower concentrations. The current levels of health and water quality surveillance may not be sensitive enough to enable scientists to detect or predict the effects of these ultra-low-concentration exposures on human health.

There was clear consensus on the need for methodological investigations. For instance, not enough is known about the various sources of exposure to water pollutants. Many of the organic chemicals in drinking water are also found in other household sources; these chemicals may be more important in determining total population exposure than exposure *via* drinking water. The amount of water that people ingest from different sources (home *versus* work *versus* school) should be studied, as well as the relative importance of exposure through washing, showering and other domestic uses of water.

Workshop participants wanted to ensure that the urgent resource needs were brought to the attention of regulatory and funding agencies. Resources are needed now to improve existing population data bases, to develop more comprehensive ones and to support the conduct of good epidemiological studies within the basin. Because the public expects governments to use the epidemiological approach in predicting and investigating human health impacts of environmental contaminants, such studies are even more essential.

6.0 CONCLUSIONS

1. There is an urgent need for epidemiological studies of the possible health impact of human exposure to chemical contaminants in Great Lakes water and fish.

2. Ongoing surveillance of temporal and spatial patterns of human disease rates in the Great Lakes basin is needed to provide early warning of human health problems. This routine surveillance of morbidity and mortality statistics is primarily the responsibility of local and state/provincial authorities.

3. Because water quality appears to be similar within a given distribution system, and the water consumption of individuals is hard to quantify, it is often difficult to design valid studies based on individuals with exposures to contaminants in water. Participants concluded, however, that this endeavour was not futile and that the methodological difficulties could be overcome.

4. Epidemiological studies of fish-consuming populations in the Great Lakes basin would be particularly relevant. Populations that consume differing amounts and types of fish from the Great Lakes are identifiable, and are exposed to higher levels of chemical contaminants than are individuals exposed to the same chemicals through drinking water. Funding of existing prospective cohort studies and the study of new fish-consuming cohorts in the Great Lakes basin would be very valuable.

5. Since studies based on aggregate data are likely to play an important role in the study of the human health impacts of Great Lakes water quality because of the availability of these data bases (death certificates). It is important to investigate the methodological characteristics of such studies in order to assess their usefulness as health assessment tools.

6. The quality of data on mortality and some types of serious morbidity is reasonably uniform across jurisdictions, a condition which facilitates studies based on aggregate data. There should be greater standardization, however, in the collection and reporting of water quality parameters among jurisdictions. Furthermore, this information needs to be stored in an easily accessible form. These objectives can be achieved only through greater coordination among jurisdictions.

7. All jurisdictions should have tumour and congenital malformation registries; criteria for and methods of registration should be harmonized as much as possible.

8. The use of biological markers of exposure is a promising new approach that requires methodological validation and development.

9. Agencies concerned with the possible health effects of water and fish quality should use well-defined criteria in setting priorities for environmental epidemiological studies suggested by routine surveillance, physicians' reports or community concerns. Such criteria have already been developed in some jurisdictions: they include such basic elements as the biological plausibility of the exposure and health effects, the sample size available for investigation, the degree of public concern, and the public health impact. Use of carefully considered criteria would simplify and render more explicit the bases for decisions, as well as promoting the most efficient use of limited resources.

10. If epidemiology is to make its appropriate contribution to elucidating the health effects of water quality, qualified epidemiologists will have to be induced to work in this field. This state can be achieved by making available funds that are specifically allocated for this type of research. While many agencies are potential sources of funds, the leaders in this effort should be the United States Environmental Protection Agency and the Canadian Department of National Health and Welfare.

TABLE I
DISEASE EXPOSURE MATRIX

	HARD/SOFT WATER	GROUND/ SURFACE WATER	TOTAL VOLATILE ORGANIC COMPOUNDS	CHLORINATION AND OTHER DISINFECTANTS	CHLORINE RESIDUAL	TRIHALO-METHANES	ORGANO-CHLORINE PESTICIDES	NITRITES/ NITRATES	METALS	FISH CONSUMPTION	OTHER
CANCER											
CARDIOVASCULAR											
OTHER CHRONIC-NON-FATAL											
CONGENITAL ANOMALIES											
CHILDHOOD DISEASES AND LIMITATIONS											
ACUTE DISEASES (Chemical or infectious)											
OTHER											

TABLE IIa
DISEASE EXPOSURE MATRIX: Studies Based on Individual Data

	HARD/SOFT WATER			GROUND/ SURFACE WATER			TOTAL VOLATILE ORGANIC COMPOUNDS			CHLORINATION AND OTHER DISINFECTANTS			CHLORINE RESIDUAL			TRIHALO-METHANES			ORGANO-CHLORINE PESTICIDES			NITRITES/ NITRATES			METALS			FISH CONSUMPTION		
	[a]K	F	B	K	F	B	K	F	B	K	F	B	K	F	B	K	F	B	K	F	B	K	F	B	K	F	B	K	F	B
CANCER	1.5	1.6	1.2	1.8	2.2	2.1	2.1	2.0	2.4	1.7	2.2	2.4	1.8	1.9	1.9	2.1	2.2	2.4	2.4	1.8	2.6	2.0	1.9	2.2	1.8	1.8	1.9	2.6	2.5	2.7
	[b]S = 4.2			S = 5.8			S = 6.5			S = 6.0			S = 5.2			S = 6.4			S = 6.5			S = 5.8			S = 5.2			S = 7.5		
CARDIOVASCULAR	2.0	1.7	2.3	1.6	1.9	1.8	1.6	1.6	1.4	1.6	1.6	1.4	1.6	1.4	1.3	1.7	1.6	1.3	1.8	1.5	1.7	1.7	1.5	1.4	1.7	1.7	1.8	1.8	2.1	1.6
	[b]S = 6.0			S = 5.0			S = 4.2			S = 4.3			S = 3.8			S = 4.2			S = 4.7			S = 4.5			S = 5.0			S = 5.6		
OTHER CHRONIC-NON-FATAL	1.5	1.5	1.5	1.6	1.6	1.6	1.8	1.5	1.6	1.6	1.5	1.4	1.6	1.4	1.3	1.7	1.4	1.3	2.1	1.6	2.2	1.8	1.6	1.5	1.7	1.5	2.0	2.5	2.2	2.4
	S = 4.2			S = 4.5			S = 4.8			S = 4.5			S = 4.2			S = 4.2			S = 5.7			S = 4.8			S = 5.0			S = 7.2		
CONGENITAL ANOMALIES	1.5	1.9	1.4	1.6	2.0	1.8	1.9	1.8	2.0	2.0	2.0	1.8	1.8	1.7	1.6	2.1	1.8	1.8	2.2	1.7	2.2	2.0	2.1	2.1	2.1	1.7	2.2	2.5	2.5	2.6
	S = 4.8			S = 5.2			S = 5.6			S = 5.7			S = 4.8			S = 5.5			S = 6.0			S = 6.2			S = 5.8			S = 7.7		
CHILDHOOD DISEASES AND LIMITATIONS	1.5	1.5	1.3	1.8	1.5	1.5	1.8	1.7	1.5	1.7	1.7	1.4	1.7	1.6	1.4	1.8	1.5	1.5	2.0	1.7	2.1	2.2	1.9	2.0	2.1	1.9	2.1	2.5	2.3	2.4
	S = 4.0			S = 4.4			S = 4.8			S = 4.8			S = 4.4			S = 4.7			S = 5.8			S = 6.0			S = 5.8			S = 7.3		
ACUTE DISEASES (chemical and infectious)	1.3	1.2	1.0	1.3	1.2	1.1	1.3	1.4	1.2	1.3	1.5	1.0	1.3	1.3	1.1	1.3	1.3	1.1	1.4	1.3	1.5	1.8	1.6	1.5	1.5	1.3	1.4	1.3	1.3	1.6
	S = 3.2			S = 3.4			S = 3.8			S = 3.8			S = 3.5			S = 3.6			S = 4.1			S = 4.5			S = 4.0			S = 4.1		

[a] K = Knowledge (0-3)
B = Biological plausibility (0-3)
F = Feasibility (0-3)

[b] S = K + B + F

TABLE IIb
DISEASE EXPOSURE MATRIX: Studies Based on Aggregate Data

	HARD/SOFT WATER			GROUND/ SURFACE WATER			TOTAL VOLATILE ORGANIC COMPOUNDS			CHLORINATION AND OTHER DISINFECTANTS			CHLORINE RESIDUAL			TRIHALO-METHANES			ORGANO-CHLORINE PESTICIDES			NITRITES/ NITRATES			METALS			FISH CONSUMPTION		
	[a]K	F	B	K	F	B	K	F	B	K	F	B	K	F	B	K	F	B	K	F	B	K	F	B	K	F	B	K	F	B
CANCER	1.3	1.8	1.2	1.4	2.4	2.2	1.5	1.6	2.2	1.3	2.0	1.3	1.4	1.6	2.0	1.3	1.6	2.4	1.6	1.5	2.2	1.7	1.7	2.1	1.7	1.7	1.6	1.8	1.8	2.5
	[b]S = 4.1			S = 5.7			S = 5.4			S = 5.6			S = 4.8			S = 5.3			S = 5.4			S = 5.4			S = 4.3			S = 5.9		
CARDIOVASCULAR	1.5	2.0	2.4	1.3	2.0	1.9	1.2	1.6	1.3	1.1	1.8	1.5	1.2	1.5	1.2	1.2	1.6	1.2	1.5	1.3	1.4	1.2	1.5	1.3	1.2	1.4	1.7	1.4	1.4	1.5
	S = 5.8			S = 4.8			S = 3.8			S = 3.8			S = 3.4			S = 3.5			S = 3.8			S = 3.6			S = 4.1			S = 4.2		
OTHER CHRONIC-NON-FATAL	1.4	1.4	1.6	1.4	1.5	1.5	1.6	1.5	1.7	1.5	1.3	1.5	1.5	1.2	1.5	1.5	1.3	1.5	1.6	1.2	2.0	1.6	1.5	1.6	1.4	1.3	1.8	1.6	1.4	2.2
	S = 4.0			S = 4.2			S = 4.7			S = 4.2			S = 4.0			S = 4.0			S = 4.7			S = 4.5			S = 4.5			S = 5.2		
CONGENITAL ANOMALIES	1.5	1.9	1.3	1.5	2.0	1.8	1.7	1.6	1.9	1.6	1.8	1.7	1.6	1.6	1.6	1.8	1.6	1.7	1.7	1.4	2.0	1.4	1.7	2.0	1.5	1.6	1.8	1.6	1.6	2.4
	S = 4.7			S = 5.1			S = 5.1			S = 5.1			S = 4.6			S = 4.9			S = 5.1			S = 5.1			S = 5.0			S = 5.8		
CHILDHOOD DISEASES AND LIMITATIONS	1.2	1.5	1.3	1.5	1.5	1.6	1.4	1.3	1.6	1.3	1.5	1.5	1.2	1.2	1.5	1.3	1.1	1.5	1.5	1.2	2.0	1.7	1.5	2.0	1.4	1.3	1.8	1.6	1.4	2.3
	S = 3.9			S = 4.3			S = 4.3			S = 4.4			S = 3.6			S = 3.6			S = 4.9			S = 5.3			S = 4.4			S = 5.4		
ACUTE DISEASES (chemical and infectious)	1.3	1.1	1.0	1.3	1.1	1.1	1.2	1.2	1.2	1.1	1.3	1.0	1.1	1.1	1.1	1.1	1.1	1.0	1.2	1.2	1.4	1.3	1.3	1.3	1.3	1.3	1.5	1.1	1.1	1.5
	S = 3.2			S = 3.3			S = 3.5			S = 3.3			S = 3.0			S = 3.2			S = 3.7			S = 3.6			S = 3.8			S = 3.6		

[a] K = Knowledge (0-3)
B = Biological plausibility (0-3)
F = Feasibility (0-3)

[b] S = K + B + F

TABLE III
DISEASE EXPOSURE MATRIX: Proposed Studies

	HARD/SOFT WATER	GROUND/ SURFACE WATER	TOTAL VOLATILE ORGANIC COMPOUNDS	CHLORINATION AND OTHER DISINFECTANTS	CHLORINE RESIDUAL	TRIHALO-METHANES	ORGANO-CHLORINE PESTICIDES	NITRITES/ NITRATES	METALS	FISH CONSUMPTION	O T H E R	
CANCER	-	Blue[a] 1, 2[b]	Blue 3, 4	Blue 9 White 10	-	-	-	Blue 14, 15	-	Blue 18, 19 White 20, 21, 22	White 33, 34	15[c]
CARDIOVASCULAR	-	-	Blue 5	-	-	-	-	-	-	-	-	1
OTHER CHRONIC NON-FATAL	-	-	-	-	-	-	-	-	-	Yellow 23, 24, 25	-	3
CONGENITAL ANOMALIES	-	-	White 6,7	-	Blue 12	Blue 16	-	-	-	Yellow 26, 27	White 35, 36	8
CHILDHOOD DISEASES AND LIMITATIONS	-	-	-	-	Blue 13	Blue 17	-	-	-	Yellow 28, 29	-	4
ACUTE DISEASES (chemical and infectious)	-	-	-	-	-	-	-	-	-	-	-	-
OTHER	-	-	White 8	-	-	White 11	-	-	-	Yellow 30, 31, 32	Blue 37, 38, 39 White 40, 41, 42 43, 44, 45	14
	-	2[c]	6	2	-	1	2	4	-	15	13	45[c]

a.

Cards	Type of Study	Total Number	
Yellow	Fish eaters	13	>30
Blue	Individual	17	
White	Aggregate	15	

b. Proposed Study Number - See Appendix B for specific

c. The total number of proposed studies are given at the end of each row or column.

7.0 APPENDICES

7.1 WORKSHOP PARTICIPANTS

PLANNING COMMITTEE

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Carl Shy	University of North Carolina, Chapel Hill, U.S.A
Steven Stellman	American Cancer Society, New York, U.S.A

7.2 PROPOSED STUDIES

The following are outlines of proposed epidemiological studies that the workshop attendees considered would be particularly useful for the study of the possible health effects of Great Lakes water. The attendees were requested to comment on: a) study design, b) hypothesis to test, c) relevance (scientific/public), d) exposure parameters, c) disease parameters, f) confounders, g) methods of analyses, h) sample size/statistical power, i) costs/time and j) other information.

1

a) Historical cohort
b) Type of water consumed influences mortality from cancer, cardiovascular disease, or chronic disease of other types
c) Public reassurance
d) Nutrition Canada Survey, and Canada Health Surveys regarding place of residence
e) Linked to mortality database
f) Diet, smoking, hypertension, serum cholesterol
g) Compare rates/person-year and detailed analysis using proportional hazard model
h) 105
i) Very small since linkages already done

2

a) Prospective cohort
b) Type of drinking water affects risk of chronic disease
d) Add question on residence and water type to census or social survey
e) Link to mortality and cancer incidence
f) Not many on census, more available on social survey
g) Rates/person-year, by major category; analyze by multivariate analysis using proportional hazard model

3

a) Cohort
b) Death rates: cancer and other causes. Are these disease rates equal for long-term Great Lakes residents (with specific levels of tap water contaminants) and similar subjects with lower exposure
c) Test specific dose response relationships with respect to cancer
d) Specific tap water constituents, sampled directly in the homes. No data available, collectable according to study by CC Hammond, PI, (Contract #4C2321-NANT)
e) Death certificate data. Great Lake residents selected from American Cancer Society (ACS) study, Cancer Prevention Study II of 1-2 million adults in the USA, 1982-1988
f) Smoking, diet, history of illness, occupation, many others already in database
g) Standard cohort analysis
h) 100,000 people in geographic area of interest. Person-years (approx.) 600,000. Ample power for most important causes of death
i) Proportional to number of samples desired. Approximately 18 months to collect and analyze water samples
j) ACS has invested $9 million to establish cohort. The United States Environmental Protection Agency or some other water quality monitoring agency can provide a few hundred thousand dollars for the analyses

4

a) Retrospective cohort and nested case-control study
b) Exposure to Lake St. Clair water increases the risk of bladder and/or gastro-intestinal cancer

c) High volume of chemical discharges form an upstream industrial/municipal complex may pose a cancer risk to water users
d) Exposed cohort = residence in a community of approximately 10,000 persons drawing its water supply from Lake St. Clair, exposure would be length of residence in community and average daily water intake. Non-exposed cohort = a similar community drawing water from Lake Huron with minimal exposure to industrial/municipal discharges
e) Identify exposed/non-exposed cohorts between 1945-1955, follow-up of vital statistics through 1985, identify all cancer deaths in the cohorts. Select incidence density controls, matched on birth year of and sex for all bladder and gastro-intestinal cancer cases
f) Interview-based data on smoking, alcohol, occupation, family history of cancer, diet and residential history
g) Mantel-Haenszel adjusted odds ratio and logistic regression analysis. Effect of cumulative Lake St. Clair water exposure (volume and time), adjusting for confounders
h) 10,000 persons/community, 2 communities, 30 year follow-up, 600,000 person-years of follow-up will yield >90% power to detect an odds ratio of 1.5 for bladder, colon cancer, or stomach cancer
i) 5 year study, $500,000/year, depending on intensity of chemical analyses of water samples and sampling for biochemical markers
j) Consider obtaining urine/blood for analysis of biochemical markers

5

a) Case-control
b) Volatile organic compounds cause sudden cardiac arrest
c) Acute
d) Short interview on shower usage or indoor swimming during the last 48 hours
e) Hospital emergency room, cardiac patients

6

a) Correlational
b) Are variations in trihalomethane (THM) concentrations in Ontario counties related to variations in congenital anomalies or low birthweight?
c) Hypothesis generating
d) Data from new Ontario Ministry of the Environment drinking water analysis file
e) Rates of adverse reproductive outcomes
f) Some socio-demographic factors can be taken into account
g) The usual socioeconomic and occupational variables
h) At least 15 data points
i) Quick, negligible cost

7

a,b) Surveillance of hot spots in terms of exposure and selected outcomes
c) Determine which areas are suitable for further study
d) Series of chemicals in drinking water for the smallest possible geographic area
e) Cancer, congenital malformations
f) Few, if any, can be measured
g) Descriptive only but with critical comments
i) Ongoing, possibly costly

8 Methodological investigations of studies based on individual data to see if the same data, analyzed on an aggregate basis will lead to the same conclusions

9

a) Cohort
b) High trihalomethane (THM) levels associated with bladder and colon cancer

c) Mortality due to chlorination of water supplies - cost to society
d) Chlorine levels added to water as surrogate for THM, Ottawa, Ontario - high exposure. Toronto, Ontario - low exposure
e) Cancer registry - bladder and colon cancer cases
f) Smoking, saccharin consumption, other water supplies and socioeconomic variables
g) Compare number of bladder cancers /100,000, adjust for age, sex, smoking, in Ottawa (high THM) *versus* Toronto (low THM)

10

a) Ecologic or Cohort with potential for nested case-control study
b) Chlorinated water leads to adverse health outcomes when compared with non-chlorinated water
c) Public concern over effects of chlorination, especially THM
d) Total chlorine residual, THM, Total Volatile Organic Compounds (TVOC), water intake, showering, etc. (Controls - untreated ground water or ozonated water)
e) Cancer, adverse reproductive outcomes, kidney, liver and lung disease
f) Alcohol, diet, occupation, airborne levels, etc.
h) Probably requires a large sample to detect increased RR of even 1.5
i) Very expensive
j) A powerful, well-conducted study is needed to show that there are no detectable effects and concern over water chlorination is over-rated

11

a) Case-control
b) Model past exposures to THM using routinely collected water quality information
c) Exposure to THM is important in case-control epidemiological studies but is difficult to estimate
d) pH-Cl_2 residual (etc.) could be used to estimate past exposures if adequate models exist

12

a) Cohort
b) Exposure to Polychlorinated biphenyls/Hexachlorobenzene (PCB/HCB) increases risk of birth defects and pregnancy problems
d) PCB/HCB in follicular fluid of women attending a fertility clinic. See if there is any relationship to fish consumption
e) Pregnancy rate, birth defects, egg cell division
f) Bias due to women with pregnancy problems
g) Linear and logistic regression
h) 500 women
i) $100,000/2 years

13

a) Multicentre, prospective cohort study of pregnancy outcomes (blinded) with a nested case-control study
b) Are variations in pesticide residue levels in cord blood predictable from maternal dietary, occupational and residential history? Do elevated levels in cord blood predict developmental difficulties?
c) Identify exposures relevant to body burdens of the general population, useful for prognostic information
d) Maternal occupations, dietary recall, residence. Cohort divided on basis of top 2% *versus* bottom 2% cord blood levels found in the local population
e) Early (post-natal) mortality. Delayed development in first five years. Physical and mental test performance at age five
f) Socio-economic status, birth order, ethnicity
g) To include calculations of discriminant functions and relative risks
h) At least 20 pairs of infants/centre, aggregate of at least 100 pairs of infants from collaborative centres

i) $200,00; organization 1 year, 2 recruitment years, follow-up 5 years for a total of 8 years. One thousand cord and maternal bloods, one thousand follow-up interviews and tertiary examinations
j) Feasible and ethical to conduct with subjects and observers blind to blood status

14

a) Case-control
b) Effect of nitrates in water on the risk of stomach cancer
c) Important in areas of high water NO_3
d) NO_3 in water, individual measures
e) Stomach cancer

15

a) Case-control
b) Nitrates in water cause stomach cancer
c) Nitrate level, in water quality data bases
e) Stomach cancer on death certificate
f) Test hypothesis with and without controlling for nitrate in food
g) Standard
h) 1,000 stomach cancer deaths
i) $100,000, 1.5 years

16

a) Case-control
b) Risk of congenital anomalies associated with nitrate in water
c) Areas of high water NO_3 in Great Lakes basin, if they exist
d) No_3 in water - individual measurements
e) Adverse reproductive outcomes
f) Other risk factors for congenital anomalies and other sources of nitrates

17

a) Cohort
b) Are there subclinical effects in infants/children due to nitrate exposure below WHO/EPA limit
c) Scientific/public health concerns
d) NO_3 input from drinking water
e) Immunologic, O_2 -carrying capacity, subtle neurologic effects
h) Include 200 infants, with at least 100 consuming water with >5mg/L nitrate-nitrogen

18

a) Case-control
b) Does PCB, DDT, Dioxin body burden increase liver cancer rates?
c) Cancer registry - liver cancer cases
f) Cachexia
g) Typical case-control
h) Estimate expected effect using bioassay, assume all cancer is liver
i) 1,400 cases/year; prompt fat biopsy or serum sample (close to diagnosis) from patient or relative
j) If 3% lifetime risk is added to rare disease, odds ratio will be very high

19

a) Case-control
b) Is childhood cancer related to PCB, DDT or Dioxin body burden?
c) 3% added risk, pro-rated to first ten years of life
d) PCB, DDT, Dioxin body burdens
e) All childhood cancers
f) Cachexia

g) Typical case-control
h) Estimate effect using animal bioassay
i) Interviews and serum or fat biopsy of cases and controls (elective surgery)
j) A rare disease may show an increased odds ratio

20

a) Cohort with nested case-control
b) Does high intake of contaminated freshwater fish lead to developmental anomalies, adverse reproductive outcomes, or increased cancer rates?
c) Sport fishing is of major economic importance
d) Halogenated organics and alkylated metals in fish; consider human body burdens, pharmacodynamics, size of fish caught, fish consumption rates
e) Congenital anomalies, reduced reproductive capacity, fetal/infant development, liver disease, cancer incidence
f) Fishermen as a group may be reasonably homogeneous; confounders include diet, alcohol, smoking, occupation and others
h) Unknown. Ontario has probably 10,000 anglers, a portion are likely to fish frequently in Lake Ontario
i) Phased study over several years - follow cohort prospectively and retrospectively

21

a) Case-control
b) Is consumption of contaminated fish associated with a higher risk of cancer?
c) Exposure to contaminants in Great Lakes fish eaters would be about 5-10 times higher than exposures seen in the general population
d) Determine human body burdens of fish contaminants and see how well this figure matches fish consumption
e) Those cancer sites previously associated with that class of contaminants
f,j) Depends on preliminary evaluation of local conditions and available data

22

a) Cohort - retrospective and prospective
b) Is there an excess of cancer in licensed fishermen, whether sports or commercial?
d) Questionnaire on lifestyle, demographics, source of fish, consumption of fish and medical history. Annual follow-up. Fish sampled for chemical content
e) Mainly cancer, other endpoints would show up in a follow-up study
f) Usual lifestyle and demographic variables, especially smoking
g) Multivariate. Logistic regression, Cox-proportional hazard
i) Costs may be high (depends on data collection). Time span of study depends on sample size, but probably at least 5 years

23

a) Cohort
b) Do PCBs DDT, Dioxins (TCDD) and Dibenzofurans (TCDF) cause immunologic deficits in neonates/infants?
c) Exposure of fish-eating public to fat-soluble, bioaccumulating compounds and their effect on human offspring
d) Fish consumption and maternal blood/milk levels of DDE, PCB, TCDD, TCDF, or total level of fat-soluble compounds as an index of exposure
e) Measure of cell mediated immunity, t-cell stimulation test
f) Parity, socioeconomic status, alcohol consumption
i) Several years to include enough births in highly exposed cohort

24

a) Cohort
b) PCBs and other contaminants in fish have peri-natal and developmental effects on infants and neonates

d) Extent of consumption of sports and commercial fish from the Great Lakes
e) Exposure: biochemical markers of PCB/DDE, etc. in maternal/cord blood. Health endpoints: series of neurologic and other developmental tests
f) Smoking, alcohol consumption, occupation, etc.

25

a) Detection of sensitive biomarkers
b) Exposure results in biological damage
c) Categorizes subgroup at risks of developing a disease outcome
d) Total chemical contaminant body burden
e) Enzyme induction

26

a) Case-control
b) Contaminants in fish are associated with increased birth defects
c) Great Lakes fish-eaters consume 5-10 times the level of chemical contaminants present in other types of foods and these chemicals may have an effect upon their offspring
d) Determine body burden of fish contaminants in mothers, as well as recall of fish consumption
e) Standard birth defects which can be determined in 0-3 years
f,j) These depend on preliminary evaluation of local conditions and available data

27

a) Cohort with nested case-control
b) Does eating Great Lakes fish have deleterious effects on reproductive outcomes?
c) High exposure population - estimate upper limits for whole population
d) Fish consumption, residential history, occupational history
e) Periodic survey of fish eaters, periodic linkages to birth file, congenital anomalies file, cancer incidence, mortality and hospital morbidity data bases
h) Probably not less than a cohort of 5-10 thousand
i) Ongoing, not less than $60,000 a year

28

a) Cohort
b) PCBs from fish cause developmental effects on young children
d) Fetal and infant exposure to PCBs from fish eating
e) Behavioral and intelligence testing
h) 1300 women
i) $350,000 over 3-4 years

29

a) Multistage study - cross-sectional/cohort
d) Prenatal and postnatal exposure to chemical contaminants in fish
e) Non-specific illness in childhood or neurological and behavioral deficiencies

30

a) Panel study of immunological endpoints
b) Epidemiology and natural history of immunologic endpoints in exposed and non-exposed groups
c) Need to know the inherent variability and determinants of these parameters
d) PCB levels in serum
e) Lymphocyte, skin tests done every 3 months for 4 years in groups with low and high fish consumption
f) Determined by study
h) 100 people
i) 4 years/$1,000,000

31

a) Cohort
b) Does consumption of Great Lakes fish increase body chemical load, morbidity or mortality
d) Origin of fish eaten and quantity consumed, by questionnaire
f) Age, sex, personal habits and customs
g) Compare to population rates
h) Dependent on outcome
i) $100,000/year; 3-5 years

32

a) Prospective cohort
b) Great Lakes fish consumption has an adverse effect on reproductive outcomes or mortality
c) Public/scientific
d) Amount of fish consumed, location. Ontario sports fishing questionnaire
e) Birth defects - CCASS. Low birthweight - prematurity, vital statistics. Cause of death - vital statistics
f) Age
g) Logistic regression
h) 2,000 persons or more
i) Ontario Ministry of the Environment could request questionnaire to be filled out during licence registration. Computer costs for linkage

33

a) Cross-sectional
b) Asbestos in drinking water leads to cancer
c) Minneapolis-St. Paul *versus* Duluth for cancer incidence. Thirty-five years since start of exposure so latent period should be encompassed

34

a) Case-control of communities - for communities with routinely recorded data bases on cause of death, e.g. cancer, heart disease, etc.
b) Chemicals present in drinking water can affect cancer rates and other causes of mortality
d) Twenty sample homes in each town; measure any number of water parameters at the tap. Mean becomes the exposure data point for the city
e) Cancer and other mortality rates for the comparison cities
f) Socio-demographic variables for the cities as per census
g) Cases; 30 towns with highest incidence. For control; 30 towns with lowest incidence, matched on basis of some socio-demographic variables
i) 1 year analysis of tap water for 20 homes/town in 60 towns

35

a) Case-control of communities - for communities with congenital anomalies register
b) Chemicals present in drinking water can affect congenital anomaly rates
d) Twenty sample homes in each town; measure any number of water parameters at the tap. Mean becomes the exposure data point for the city
e) Congenital anomalies registry for cities as per census
h) Cases; 30 towns with highest incidence. Controls; 30 towns with lowest incidence, matched on basis of some socio-demographic variables
i) 1 year; analysis of tap water for 20 homes/town in 60 towns

36

a) Before/after, based on communities
b) Provision of water from Great Lakes is associated with changes in reproductive outcomes

c) Direct test of an association which is relevant to public concern regarding Great Lakes water
d) Provincial and local records at time of changeover from well water to Great Lakes surface water
e) Spontaneous abortion, stillbirth, congenital anomalies, low birthweight. Federal and provincial vital statistics
f) Not a major problem
g) Direct comparison of incidence rates
h) To be determined by a feasibility study
i) 2 years; $100,000

37

a) Cross-sectional survey
b) Regional and local variations in chemical contaminants/constituents of drinking water explain variations in measurable health effects
c) Identify small area effects; establish cohort for follow-up
d) Everything that could be reasonably afforded and that has reasonable biological plausibility
e) Cancer, reproduction, mortality

38

a) Investigation of water consumption habits
b) Identify relative and absolute amounts of water and other liquids consumed at home, work and elsewhere
c) Basic characteristics of population exposure, get dosage figures for toxins of concern

39

a) Method development - identify toxicological activity of water samples by bioassay methods
b) Purpose: provide epidemiologists with a tool to characterize the genotoxic, abortifacient or mutagenic potential of public water supplies
c) Apply principles of biological markers to characterize water supplies of varying toxic potential
d) Instead of obtaining information on the chemical species of water pollutants, the objective is to assay the bio-toxicological potency of the water supply
e) Case-control and cohort studies of carcinogenic and reproductive outcomes could be designed to study communities with high and low bio-toxicological potency of the water supply
j) This is a proposal for the method development, where results involve selecting communities for epidemiological research

40

a) Health effects are due to changes in the water supply
d) Study people who switched from wells to surface water, or *vice versa*. Also, places that change the quality of water, i.e. new reservoir, new well
e) Depends on what outcomes are relevant to changes in water quality

41

a) Exploratory analysis of available, routinely compiled or secondary source data
b) Early fetal mortality is reflected by lower proportion of males (among dizygotic twins) in surviving live born population
c) If verified, could provide useful endpoint for environmental health studies
d) Economic and climatic adversity/stress, low birthweight, vital statistics, congenital malformation registers
e) (Inferred) variation in all-causes fetal mortality
f) Maternal age, birth order, ethnicity

g) Comparison of observed proportions in male/multiple births with binomial expectations
h) As available/not predictable
i) Time: open ended (no observations reported in first two years). Data costs essentially nil, one research assistant with personal computer

42

a) Use data bases on known discharges into Great Lakes basin; characterize the potential of public drinking water supplies for exposure to certain pollutants
d) The output of this evaluation would be a two-dimensional matrix of pollutants by community, with an ordinal ranking of exposure potential for the cells
e) The matrix would be a means to target communities for analytic epidemiological studies

43

a) Validate water ingestion questionnaire data
b) Personal recall of amounts of water consumed is a valid estimator of the actual amount
d) Compare recall data with directly measured intake over a 2-3 day interval. Also consider assessing exposure to atomized volatile organics through domestic showering, washing, toilet flushing, etc.
e) This validation study could be incorporated into a case-control study of water quality and a chronic disease outcome

44

a) Methodological research
b) Do ecological studies of water quality and health yield the same conclusions as studies of individuals?
c) Scientific. If true, more faith can be placed in the conclusion derived from ecological studies
d) Data file(s) of individuals which can also be sorted into aggregate units, so that both forms of analyses can be conducted and compared

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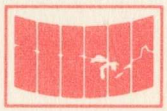
a) Before/after, water supply changes
b) Change in water supply did not affect the rate of deleterious reproductive outcomes in the communities
c) Design using community as its own control is more powerful than designs using comparisons among communities
d) Change in water supply
e) Reproductive outcomes (spontaneous abortions, low birthweight)



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