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The Epidemiology of Chemical Contaminants of Drinking Water

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Summary—A number of chemical contaminants have been identified in drinking water. These contaminants reach drinking water supplies from various sources, including municipal and industrial discharges, urban and rural run-off, natural geological formations, drinking water distribution materials and the drinking water treatment process. Chemical contaminants for which epidemiologic studies have reported associations include the following: aluminium, arsenic, disinfection by-products, fluoride, lead, pesticides and radon. Health effects reported have included various cancers, adverse reproductive outcomes, cardiovascular disease and neurological disease. In evaluating epidemiologic studies for risk assessment, considering whether the study design was qualitative (hypothesis generating) or quantitative (hypothesis testing) is important and whether sufficient epidemiologic data of a quantitative nature exists to determine the dose–response curve. Each of the chemical contaminants mentioned are summarized by study designs (qualitative and quantitative) and whether a dose–response curve based on epidemiologic data has been proposed. Environmental epidemiology studies are driven by environmental exposures of interest. For drinking water contaminants, the design of epidemiologic studies and their interpretation should consider the following exposure issues: the source of the contaminant; other sources of the contaminant; the route of exposure; the frequency, duration and magnitude of exposure; the ability to document an actual internal dose; and the ability to document the dose to the target organ. Health effects of concern have other risk factors that must be measured in the conduct of these studies. In evaluating epidemiologic studies, potential errors and biases that may occur must be considered given the very low magnitude of associations (less than 2.0 for either odds ratio or risk ratio). Given the issues, the next generation of drinking water epidemiologic studies should include a multidisciplinary team beyond traditional epidemiologists and statisticians. Study teams will require toxicologists, chemists, engineers and exposure assessors. Arsenic is briefly discussed as an example of the importance of susceptible populations. Disinfection by-products are discussed as an example of epidemiologic studies of mixtures. *Published by Elsevier Science Ltd.*

Keywords: drinking water; chemicals; epidemiology; arsenic; disinfection by-products.

Abbreviations: DBPs = disinfection by-products; RR = relative risk; THMs = trihalomethanes.

Introduction

The quest for high-quality water has been an objective of human society going back to prehistoric times. Early humans gathered in locations with readily accessible sources of water and if the water was believed to be of questionable quality, entire settlements would be abandoned. The first documented drinking water treatment can be found in Egyptian hieroglyphics, describing procedures to purify water. The basic principles were the same then as they are today; boiling, chemical treatment and filtration were recommended treatments. Although the importance of drinking water quality was known, the specific contaminants would not be identified for centuries to come.

The importance of clean water, clean air and safe working conditions spawned the public health era in the mid-1850s. From this concern grew the science of epidemiology, with the landmark investigation of a cholera outbreak by John Snow. *From that filtration treatment for improving drinking water quality paralleled studies establishing the link between disease and water quality*. The introduction of chlorine as a chemical disinfectant was an alternative for those communities that could not afford the expense of elaborate filtration plants. The introduction of chlorination of drinking water was followed by a remarkable reduction in cholera, dysentery and typhoid worldwide. Today, water treatment and specifically chlorination and/or filtration of drinking water has been haled as **the** major pub-

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lic health achievement of the 20th century. As the century progressed, the identification of water contaminants shifted from microbiological to chemical. As the public health infrastructure grew, outbreaks associated with chemical spills or leaks into potable water drew the attention of the scientific community. Concern with inorganic contaminants such as arsenic, lead, copper and sulfate began to be reported in the epidemiologic literature. In the mid-1970s, two events occurred that spurred the health concern of chemicals in water. The first was a reporting of chloroform in finished water treated by chlorine especially along the Mississippi River in the United States. The second was a series of mortality maps showing higher cancer mortality rates in those communities. In the following years, the number of chemical contaminants identified in drinking water has grown exponentially. However, for the hundreds of chemicals identified, very few have been studied or have documented proof of their health effects in humans via ingestion of contaminated water. Of the few for which a body of epidemiologic literature exists, the interpretation of the data is often confusing and controversial given the chemical of concern.

Sources of contaminants

A number of chemical contaminants have been identified in drinking water. The chemical contaminants for which epidemiologic studies have suggested a risk associated with their presence in potable water include: aluminum, arsenic, disinfection by-products (DBPs), fluoride, lead, nitrate, pesticides, radon and sulfate. The contaminants are of both inorganic and organic origin. The source of the contaminant can be from point and non-point sources of pollution, naturally occurring, come from the treatment process or through materials used in distribution systems. Naturally occurring contaminants are generally the result of leaching from geologic formations and are found primarily in groundwaters. Ranges of concentrations of these contaminants range from less than nanograms per litre to milligrams per litre. Point sources of drinking water contaminants include direct dumping of chemicals from domestic and industrial sewage. Other sources of pollution include run-off from land application of chemicals or leaching from buried solid waste landfills. Finally, mining practices or smelter operations can increase the concentrations of metals in source waters through the atmospheric deposition or improper handling of mining tailings.

The treatment process can be a significant source of chemical contaminants. Disinfectants themselves are not believed to be a significant health hazard at levels used to treat water for drinking. The disinfectants (primarily chlorine or chlorine based), because of their strong oxidizing properties, react with the other organic constituents in the water to form chlorinated or brominated compounds believed to be of major toxicological concern. Aluminium and fluoride are both added to the treatment process but are not believed to be of concern at the levels they are added to water for treatment. It is when they are present as the result of geological leaching that concern has been raised. Contaminants can occur because of the distribution system or materials that comprise the distribution system. As the result of corrosion or leaching of distribution materials, many of the materials can be found as chemical contaminants in potable water.

Health effects

As mentioned previously, concern with chemicals in drinking water started in outbreak situations where individuals became acutely ill. Chemical spills or leaks still occur causing acute like toxicity (primarily vomiting). In the United States, 75 outbreaks involving chemicals have been reported since 1971. As more chemicals could be found in potable water, studies began to appear in the literature linking health effects with occurrence of the contaminant of interest (Table 1). Cancer has been one of the more popular endpoints to study in relationship to effects associated with exposure to specific chemicals in water. Recent years have seen an interest in reproductive and developmental effects. Studies of cancer and reproductive effects have been aided by

Table 1. Health effects of chemical drinking water contaminants reported in epidemiologic literature

Chemical	Cancer	Developmental/ reproductive	Neurologic	Other
Aluminium			Alzheimer's	
Arsenic	Skin, internal	SAB	Peripheral	Cardiovascular, immunologic, dermatologic
DBPs	Bladder, colon, leukaemia	SAB, LBW, defects		
Fluoride	Osteosarcoma			Fluorosis
Lead	Internal[occ]		Intelligence behaviour	Haemoprotein, kidneys
Nitrate	Internal	SAB		
Pesticides	Leukaemia	LBW		
Radon	Lung			
Sulfate				Diarrhoea

OCC = occupational; SAB = spontaneous abortion; LBW = low birth weight.

the existence in many communities of databases of mortality or morbidity for these endpoints. The epidemiologic evidence in conjunction with toxicological data (human and animal) has been considered important in establishing causal relationships between the exposure and effects for arsenic, lead, nitrate and radon. The remaining chemicals in the table have considerable controversy in whether they are causally associated with a specific health endpoint and what is the relative source contribution of water.

Characteristics of drinking water epidemiologic studies

Four characteristics of the drinking water epidemiologic studies were used to review the drinking water epidemiologic literature. There are two basic types of epidemiologic studies. The first is experimental where the risk factors or exposures are controlled by the investigators. These are typically studies that evaluate drugs, medical devices or major public health interventions such as vaccinations. The second and more familiar type is observational epidemiology. This is what most people typically think of when they think of epidemiology. There are two basic categories of observational studies. The first is descriptive or **qualitative** studies, the objectives of which are to determine status and trends and to generate hypotheses. The original concerns about chlorination of drinking water causing cancer arose out of cancer maps that identified hot spots of cancer in the lower Mississippi valley. These studies often compare populations rather than a study population consisting of information on individuals. It is difficult to consider other risk factors in these types of studies and therefore they may be subject to bias and confounding.

The second type of observational study is the analytic and **quantitative** study. It is sometimes referred to as an aetiologic study. The objective of this study is to test hypotheses, suggest biological mechanisms and obtain dose–response information. The unit of observation is the individual, and issues of confounding and bias should be addressed in either the design or the analysis. There is great body of studies that have shown dose-related effects for environmental chemicals such as asbestos, radon, lead and waterborne microorganisms. The literature on nine contaminants listed in Table 2 has a mixture of both qualitative and quantitative studies.

Typically, when the lay person reads or hears about an epidemiology study, the type of study or even the specific study design is not mentioned. The focus is on the measurements of association and the accompanying statistics. The basic measurement of association in epidemiology is the risk. The risk is simply defined as the probability of disease given the exposure. Values of risk are between zero and one. Risk is a dimensionless number. The risk relationship between exposed versus unexposed is expressed as a ratio. Because these are ratios, the numerator is not a part of the denominator. These ratios are referred to as either risk ratios (RR) or odds ratios. In interpreting risk ratios, the magnitude of the ratio is important. If there is no difference between the exposed and unexposed then the ratio would be unity or one. If the risk is greater in the exposed then the ratio would be greater than one and if the exposure is protective the risk would be less than one. Traditionally, epidemiologists have considered a meaningful ratio to be at least two (a doubling of the risk). The coming of environmental epidemiology has changed that thinking since many environmental relationships are less than an RR of two. Unmeasured bias and confounding have less of an effect on the overall association with larger ratios. The majority of environmental contaminants reported in Table 2 have risk ratios less than five. The exceptions are lead and radon, where contaminant sources other than drinking water were evaluated (e.g. occupational exposures in radon).

For risk assessment purposes, the availability of dose–response data is important. These data allow for the selection of a specific level on which a policy or regulation will be based. Note in the table that both qualitative and quantitative studies can evaluate dose–response relationships, but because of the descriptive nature of qualitative studies it is not recommended that they be used for risk assessment. The final column in Table 2 is the occurrence levels of the contaminants evaluated in the study. With the exception of radon and sulfate, all the contaminants were reported in micrograms. Most chronic animal bioassays use milligram amounts in evaluating toxic effects. A major advantage of epidemiology is that real world exposures are studied. Therefore, epidemiologic studies have less uncertainty associated with use in risk assessment.

Why is epidemiology of chemicals in drinking water difficult?

Traditionally, epidemiology has been driven by the health effect of interest. The emergence of environmental epidemiology has focused the relationship on the exposure. Most environmental epidemiology studies are being driven by the exposure. This has complicated the study design, leading many people to describe environmental epidemiology as a black box. The environmental health paradigm (Sexton *et al*., 1992) is a good model of the complexity of the issues and therefore the difficulties epidemiologist face in conducting

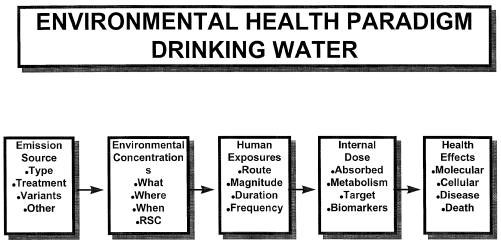

Fig. 1. Environmental health paradigm drinking water.

good epidemiology studies (Fig. 1). Each of the five areas of the environmental health paradigm can be a source of considerable variation. The emission source has four sub-categories. For drinking water, the type could be groundwater or surface water and the quality could be of high versus low quality. Studies of DBPs have compared groundwaters (low or no DBPs) to communities using surface water (high levels of DBPs). Exposure could vary based on low quality (high concentrations of organic carbon compounds or high concentrations of bromide) versus high-quality water (low organic compounds). The type of treatment used can affect the concentration of the chemical contaminant. Coagulation, type of disinfection, types of filtration and other treatments such as use of granular activated carbon need to be considered. Other variants that need to be considered are geography, mixtures and seasonal variation. Construction of an individual 20-year exposure history in a DBP cancer study could be very complex depending on how often that individual moved in a lifetime, the geographical areas in which they lived, the disinfectant used and the seasonal patterns of organic compounds in the water. Other issues that could affect the description of the source are the dynamics of the distribution system (e.g. DBPs increase with residence time in the system); private utility versus a publicly owned utility (depending on local laws, access to information may be curtailed in a private utility); water availability (areas where water is scarce may mean unusual consumption patterns in the study population); and economics (poor communities may have minimal treatment, minimal monitoring and therefore minimal information).

Environmental concentrations address the questions of what, where, when and how (relative source contribution). There may be many options in WHAT is measure. Historically, monitoring has obtained information on trihalomethanes (THMs). THMs may not be as prevalent as other DBPs such as haloacidic acids, or as representative as total organic carbon or total organic halide. Most monitoring programs include more than one sampling location. WHERE to measure options include the raw water, the plant effluent, the distribution system and the consumer's tap. For many chemicals this may not be an issue in that the concentration of the chemical of interest does not change depending on where it is measured. However, the dynamics of drinking water treatment and delivery can change the concentrations of a chemical such that the plant effluent concentration is not representative of the tap concentration (e.g. DBPs). WHEN to take a measurement is variable depending on the contaminant of interest. Very few monitoring programs monitor pesticides weekly. There are models that can give an hourly estimate of the DBPs at the tap depending on the flow and concentration of chlorine residual leaving the plant. The last question is HOW much of the chemical exposure is related to water relative to air, soil or food? In the US there is considerable controversy over the regulation of radon in water given that the majority of the exposure is air radon in the home. Lead is another chemical that could have other significant sources of exposure other than water.

Information on emission source and environmental concentration is readily available for most chemical contaminants of concern. That is only a small part of the information needed to understand

Table 2. Characteristics of epidemiologic studies of chemical drinking water contaminants

Chemical	Qualitative	Quantitative	Risk Range	Dose–response	Occurrence μg/litre
Aluminium	X		1.0–5.0	X	1–3000
Arsenic	X	X	1.2 → 20	X	40–2000
DBPs	X	X	1.0–3.0		ND–200
Fluoride	X	X	0–3.6		200–4000
Lead	X	X	0–10***	X	ND–600
Nitrate	X	X	2–3.5	X	ND–27,000
Pesticides	X		0–1.7		1–25
Radon	X	X	1.5–15**	X	1–2000 pCi
Sulfate	X	X	0–2	X	1–770 mg*

*ND = not-detected, ** = includes occupational studies; *** includes studies evaluating sources other than drinking water.

human exposure to drinking water chemicals. Human exposure is the actual interface between environmental concentrations and the human body. Contact with the chemical via drinking water is not a simple event. Because we bathe in and drink water, the ROUTE of exposure could be inhalation or dermal absorption and ingestion. Risk assessments for trihalomethanes suggest an increased risk associated with inhalation rather than ingestion. The MAGNITUDE and DURATION need to be considered in evaluating exposure. Lastly, the FREQUENCY (single, constant, daily) needs to be part of the exposure matrix.

Epidemiology and risk assessment have begun to open that black box through the determination of an internal dose of an environmental contaminant. Information on internal dose can be modelled using pharmacokinetics modelling that takes into consideration absorbed dose (site and transport through the body), metabolism (site and toxicity of metabolic products), and target dose. If information on pharmacokinetics is not available biomarkers of internal dose, (exposure) can be incorporated into an epidemiologic study. The incorporation of biomarkers into environmental epidemiology can reduce a great deal of uncertainty associated with interpreting the results. However, very few biomarkers of exposure exist for most drinking water contaminants. A major success story for this is lead. Blood lead has been used successfully and many communities have regularly screening program for high-risk children. Blood lead is clearly a marker of internal dosimetry.

These four components of the paradigm comprise exposure. Given the complexity of defining an environmental exposure, understanding why exposure has been called the bane of epidemiology is easy. Errors associated with exposure include measurement and misclassification. As mentioned earlier, many environmental epidemiologic studies have small magnitudes of association. Errors in exposure could explain purported associations.

Traditionally epidemiology has evaluated overt disease or death as a health endpoint. As our knowledge of a disease endpoint grows, more sophisticated measures of organ system effects (respiratory or cardiovascular) to cellular (tumour assays) to molecular have or will be incorporated. These measures reduce the bias associated with ascertainment of disease but may raise issues from a risk management perspective as those effects may not necessarily be considered adverse.

Table 3. Examples of populations susceptible to effects associated with exposure to drinking water chemical contaminants

Chemical	Susceptible population
Aluminium	Dialysis patients
Arsenic	Genetic, nutritional
DBPs	Elderly men, pregnant women
Fluoride	Infants
Lead	Foetus, children
Nitrate	Pregnant women, infants
Pesticides	Unknown
Radon	Smokers
Sulfate	Infants

Susceptible populations

Increasingly, certain segments of the population are being identified as more at risk to the effects of chemical exposures than the general population. These *susceptible* populations can be categorized as susceptible because of demographics (age, sex, race, ethnicity), genetics (metabolic gene deficiencies or genes to increase health effects), and acquired traits (nutrition, underlying disease, smoking, alcohol, pregnancy). Table 3 describes some populations as susceptible to the chemical contaminant listed. In examining the DBP literature, both age and gender differences have been noted with differences in risk of DBP associated cancer. Very old men seem to show associations with bladder cancer consistently. A recent study from New Jersey suggested that women with poor nutrition and high DBP exposures had a higher number of neural tube defects. The literature on reproductive effects is growing, suggesting that pregnant women and their developing foetus may be more susceptible to effects associated with exposure to DBPs. To date, no genetic susceptibilities have been identified with an increase risk of effects associated with DBP exposure.

Infants or the developing foetus have clearly been the most susceptible to lead exposures. It is believed that sulfates affect primarily infants and children. Aluminium is thought to be important to kidney dialysis patients. The arsenic literature has suggested there are differences in susceptibilities from population to population. The classic Taiwanese studies of the late 1960s (Tseng *et al.*, 1968) reported blackfoot disease and skin cancer associated with arsenic in drinking water. Other international populations at similar exposure levels have not reported blackfoot disease. A recent report suggested that there may be a difference in arsenic metabolic profiles and methylation genotypes. Personal habits such as smoking can increase susceptibility, as have been shown on studies of radon. Epidemiologic studies are the primary means by which susceptible populations are identified. However, susceptibility factors are often overlooked or are not considered in either the design, analysis or interpretation of epidemiologic studies. As methods for measuring internal dose or early biologic effect become available for use in epidemiologic studies, susceptible populations may be more readily identified and studied.

Table 4. Characteristics of recent epidemiologic studies on reproductive effects of disinfection by-products

Characteristic	Study by (author)			
	Bove *et al.*	Kanitz *et al.*	Savitz *et al.*	Waller *et al.*
Study design	qualitative	qualitative	quantitative	quantitative
Disinfectant	unknown	chlorine dioxide	chlorine	chlorine
Outcome*	BD, LBW	LBW	LBW, SAB, PMD	SAB
Exposure	population	population	individual	individual
Water consumption	not obtained	not obtained	obtained	obtained

*BD = birth defects; LBW = low birth weight; PMD = premature delivery; SAB = spontaneous abortions.

Mixtures, DBPS and reproductive effects

Water is not a pure mixture of hydrogen and oxygen. As the universal solvent, it carries many other chemicals. Epidemiologic studies of drinking water are, in reality, studies of exposures to mixtures. It is often assumed that the other chemicals in the water under study are of no health consequence. This has worked well for chemicals such as fluoride, lead, radon and sulfate, but it has not worked well for DBPs and the arsenic literature has suggested that other water contaminants may be important in understanding the effects of arsenic on humans. Because epidemiology studies primarily real world exposures, epidemiology does in fact study mixtures. Addressing the mixtures area is where there is a great need for greater communication and collaboration between epidemiologists and toxicologists. Epidemiologic studies of DBPs and bladder cancers may be more interpretable if we knew more about interactions between and among DBPs. The inconsistency of colon and rectal cancer studies may be explained by the differences in mixtures and therefore effects of DBPs.

Five recently published epidemiological studies (Table 4) of adverse reproductive and developmental outcomes have employed both qualitative and quantitative study designs. Adverse pregnancy outcomes were studied in women using water systems with various water sources and disinfectants, primarily chlorine. A number of adverse outcomes have been considered: stillbirths, neonatal deaths, miscarriage, low birth weight (<2500 g), preterm delivery (<37 weeks), intrauterine growth retardation (<5th percentile of weight for gestational age), small for gestational age or short body length (<36 cm), small cranial circumference (<50 cm), neonatal jaundice, and birth defects such as major cardiac defects, NTDs and oral clefts. Adverse reproductive effects in men and a couple's ability to conceive have not yet been studied. Water exposures compared include: municipal community water supplies versus private wells or bottled water; chlorinated versus chloraminated surface water supplies; chlorinated surface water versus unchlorinated groundwater; and surface water disinfected with chlorine versus chlorine dioxide or untreated groundwater. Most studies attempted to estimate a woman's exposure to THMs in water; two studies considered exposures to each of the four THM species. No studies, however, considered exposures to other DBPs, such as HAAs or brominated by-products as a group. Estimates of exposure to THMs in tap water were based on THM levels in the distribution system, either on an ecological or personal basis. Both water consumption and levels of THMs were considered in only two studies, and possible inhalation exposures were considered in only one study (Waller *et al.*, 1998). Water quality data to estimate exposures were obtained primarily from regulatory or other monitoring programs. No studies assessed water exposures at place of employment or away from home.

The results of epidemiological studies reported to date do not provide compelling evidence about the association of adverse outcomes of pregnancy and DBPs. Associations found in most studies may be due to one or more sources of bias or residual confounding from unidentified risk factors. Exposure misclassification due to poor estimates of exposure may also have biased results. If misclassification were non-differential, relative risks would be underestimated. If differential misclassification were present, relative risks could be either under- or overestimated.

Arsenic

In the US, the current drinking water standard for arsenic must be revised and a new standard proposed by 2001. To reduce the standard from the current 50 μg/litre would be extremely expensive. The current risk assessment performed by the US Environmental Protection Agency in 1986 has three major areas of uncertainty: (1) the ***shape of the dose–response curve***; (2) cancer versus non-cancer ***health effects***; and (3) ***generalizability*** of Taiwanese data to US populations.

Shape of the dose–response curve

The fundamental issue in the risk assessment of arsenic remains the shape of the dose–response curve, particularly for the low levels of exposure that may occur in industrialized nations. Because arsenic may not be a direct-acting genotoxin, the

suitability of an assumption of linearity in the dose–response relationship has been questioned. Currently, there is no adequate animal model for arsenic carcinogenesis. Very few studies exist that have quantitative data below 200–300 μg/litre. Carefully designed and conducted epidemiological studies in human populations in which arsenic exposure is quantifiable may offer the best hope for elucidating the nature of the dose–response relation for arsenic.

Cancer and non-cancer health effects

International studies have shown that skin cancer (Ma *et al*., 1995; Tseng *et al*., 1968), internal cancers (Bates *et al*., 1992; Cuzick *et al*., 1992), cardiovascular (Engel and Smith, 1994), reproductive (Tabacova *et al*., 1994) and neurological (Kilburn, 1997) health effects are associated with arsenic exposure. To address some of the uncertainty about the types of health effects that may be incurred in exposed populations due in part to arsenic in drinking water, additional studies need to consider all potential health effects, not just cancer.

Generalizability

A study conducted in Taiwan raises questions of generalizability of these results to other countries and raise questions of the potential for a different level of susceptibility to drinking water arsenic in different populations. Although the Taiwanese studies appeared to achieve landmark results when they were originally published, work in other populations has since come to light. Results may be generalizable if two populations are very similar. Some portions of the diseased individuals in Taiwan were reported to have competing morbidity from blackfoot disease that is aetiologically linked to arsenic in drinking water. Given that blackfoot disease is not universally observed, a risk assessment based in part on individuals with multiple arsenic-related health conditions may not be applied to a population where the frequency of arsenic-related health outcomes has yet to be firmly established. Another problem with generalizing results from studies of the Taiwanese to other population is the large magnitude of the difference in exposure. Exposure levels in the Taiwanese studies fell mostly in excess of 300 μg/litre and ranged upwards of 1200 (g/litre for those with known exposures. These represent levels that have not been consistently documented in industrialized nations. Other issues about the generalizability of the Taiwan data are concerned with the overall health of the Taiwan population, the nutritional status of the Taiwanese (it is known that the Taiwanese consumed up to 80% of their total intake in rice and sweet potatoes), economic status (most represented by the Taiwan data were of lower economic status), and even the age structure of the populations. The selection of skin cancer aetiologically linked to arsenic exposure as a health outcome also raises issues of the appropriateness of these data applied to other populations. Arsenic-related skin cancer may not be common in other countries.

Recommendation for future drinking water epidemiologic studies

1. Epidemiologists and toxicologists need to work together to gain insight into the health effects of chemical drinking water contaminants. A recent ILSI/EPA workshop suggested that there may be other effects unrecognized associated with exposures to DBP mixtures. An ideal model of a health effects research program is the interplay between animal studies, human experimental studies and epidemiologic studies.
2. Better exposure estimates are needed for epidemiology studies. This could entail better understanding of water chemistry to the use of exposure markers of dose. Given the complexity of most drinking water chemical exposure assessment, this area will continue to be a major uncertainty in the interpretation of epidemiologic studies.
3. A multidisciplinary team needs to conduct these studies. Too often the epidemiologist does not consult the drinking water engineer or knows little about the water chemistry. Drinking water epidemiology has not been a popular area of endeavour because of the complexity in designing, conducting and interpreting the studies.

Summary

Epidemiologic data have been used successfully in risk assessments to help set drinking water standards. When a body of epidemiologic studies exists that are of a quantitative design, have minimal bias and confounding and contain dose–response data, then regulations can be based directly on the data with little extrapolation and minimal uncertainty. As knowledge of metabolism and mechanisms of chemicals in drinking water expand, new epidemiologic studies should incorporate that knowledge into their design.

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