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Position Paper
Safe Drinking Water: A Public Health Challenge

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Abstract

Disinfection of drinking water through processes including filtration and chlorination was one of the major achievements of public health, beginning in the late 1800s and the early 1900s. Chloroform and other chlorination disinfection by-products (CBPs) in drinking water were first reported in 1974. Chloroform and several other CBPs are known to cause cancer in experimental animals, and there is growing epidemiologic evidence of a causal role for CBPs in human cancer, particularly for bladder cancer. It has been estimated that 14-16% of bladder cancers in Ontario may be attributable to drinking water containing relatively high levels of CBPs; the US Environmental Protection Agency has estimated the attributable risk to be 2-17%. These estimates are based on the assumption that the associations observed between bladder cancer and CBP exposure reflect a cause-effect relation. An expert working group (see Workshop Report in this issue) concluded that it was possible (60% of the group) to probable (40% of the group) that CBPs pose a significant cancer risk, particularly of bladder cancer. The group concluded that the risk of bladder and possibly other types of cancer is a moderately important public health problem. There is an urgent need to resolve this and to consider actions based on the body of evidence which, at a minimum, suggests that lowering of CBP levels would prevent a significant fraction of bladder cancers. In fact, given the widespread and prolonged exposure to CBPs and the epidemiologic evidence of associations with several cancer sites, future research may establish CBPs as the most important environmental carcinogens in terms of the number of attributable cancers per year.

Key words: cancer; chlorination; chlorine; disinfection by-products; epidemiology; ozonation; reproductive health; risk assessment; toxicology; trihalomethanes

Disinfection of Drinking Water: Historical Perspective

In the 19th century, major outbreaks of waterborne diseases were common in Canada, the United States and other developed nations. Beginning in the early years of the 20th century, the provision of chlorinated drinking water virtually eliminated typhoid fever, cholera and other waterborne diseases, representing one of the great achievements of public health.

Chlorine was discovered in 1774 by the Swedish chemist Karl Wilhelm Scheele and confirmed to be an element in 1810 by Sir Humphry Davy.[1] Use of chlorine as a disinfectant was first introduced by Semmelweis on the maternity ward of the Vienna General Hospital in 1846 to clean the hands of medical staff and prevent puerperal fever. In 1881 Koch showed that pure cultures of bacteria were destroyed by hypochlorites.[1]

The first continuous usage of chlorination in the US began in 1908 for the water supply to Jersey City, New Jersey, and at a site that served the Chicago Stockyards to control sickness in livestock caused by sewage-contaminated water.[1] In Canada, the earliest use of chlorination found by this author was in Peterborough, Ontario, in 1916.[2] Chlorination has been the main method of disinfecting drinking water in Canada, the United States and many other countries for several decades and has proven effective against most waterborne pathogens.

Health Effects of Chlorination Disinfection By-products

Chlorine's potent oxidizing power causes it to react with naturally occurring organic material in raw water to produce hundreds of chlorinated organic compounds, referred to generically as chlorination disinfection by-products (CBPs). One of the most commonly occurring groups of CBPs, the trihalomethanes (THMs), was first identified at higher concentrations in chlorinated drinking water than in natural raw water by Rook[3] and by Bellar et al.[4]

Raw drinking water supplies were found to have low background levels of mutagenic activity with relatively large increases in mutagenicity after chlorination.[5] The mutagenic activity of chlorinated water is caused mainly by reactions of chlorine with natural humic substances released by the breakdown of vegetation in the source waters.[6] Recently, the chlorinated hydroxyfuranones (e.g. MX) have been shown to be responsible for a major part of the mutagenic activity. Other CBPs, including brominated THMs and haloacetic acids, are also mutagenic. The concentration of THMs correlates strongly with the amount of organic precursors in raw water and, although imperfect, it can be a useful indicator of the level of total CBPs in treated water.

Although numerous CBPs have been identified in chlorinated drinking water, very few have been subjected to carcinogenicity bioassays. Chloroform induced significant increases in kidney tumours in male rats when administered in high concentrations in drinking water.[7] Chloroform also produced kidney tumours in male rats and liver tumours in male and female mice when administered by gavage in corn oil.[8] Unlike the brominated THMs, chloroform appears not to be carcinogenic through a direct DNA reactive mechanism, acting instead through regenerative cell proliferation, possibly with an exposure threshold.[9] In studies of the three other THMs, bromoform administered by corn oil gavage induced intestinal tumours in male and female rats; chlorodibromomethane by corn oil gavage produced liver tumours in both sexes of mice; and bromodichloromethane by corn oil gavage induced intestinal and kidney tumours in male and female rats, kidney tumours in male mice and liver tumours in female mice.[10-12]

After the THMs, the most commonly occurring group of CBPs in drinking water is the haloacetic acids (HAAs). Comparing published results from the two most studied HAAs, dichloroacetate in drinking water induced hepatic tumours in both rats and mice, but trichloroacetate induced hepatic tumours only in mice.[13-17] Both compounds appear to act as tumour promoters, but likely via different mechanisms: trichloroacetate has been shown to be a peroxisome proliferator, whereas dichloroacetate affects cell cycle kinetics.[18] While none of the brominated HAAs have been tested in carcinogenicity bioassays, preliminary screening tests have indicated a potential for the induction of liver tumours by bromochloroacetate, dibromoacetate and bromodichloroacetate; lung tumours by bromodichloroacetate; and colonic tumours by dibromoacetate.[18,19]

MX (3-chloro-4-(dichloromethyl)-5- hydroxy-2(5H)-furanone) is a CBP and is one of the most potent known mutagens as determined by the Ames assay.[20] MX is reported to occur at much lower concentrations than the THMs or HAAs, yet it appears to account for about one third of the mutagenicity of chlorinated drinking water.[21] DeMarini et al.[22] found that MX produced 50-70% hotspot 2-base deletions and 30-50% complex frameshifts; no other compound or mixture is known to induce such high frequencies of complex frameshifts. MX caused several types of cancer or benign tumours in rats, including thyroid, liver, adrenal gland, lung, pancreas, breast, lymphomas and leukemias.[23]

As noted in the following report, results of the epidemiologic studies of cancer have been most consistent in showing an association between exposure to THMs and bladder cancer. Conflicting results have been observed with respect to cancers of the colon and rectum. In 1996, King and Marrett[24] reported the results of a large population-based case-control study of bladder cancer conducted in Ontario. Persons exposed to chlorinated surface water for 35 or more years had an increased risk of bladder cancer compared with those exposed for less than 10 years (odds ratio = 1.41, confidence interval [CI] = 1.10-1.81)). Persons exposed to THM levels of at least 50 µg/L for 35 or more years had 1.63 times the risk of those exposed for less than 10 years (CI = 1.08-2.46). The authors concluded that the risk of bladder cancer increases with both duration and concentration of exposure to chlorination by-products, with population-attributable risks of about 14-16% for Ontario. Approximately 1150 persons in Ontario will be diagnosed with bladder cancer in 1998.[25] If CBPs do cause bladder cancer, then roughly 160-185 cases of bladder cancer per year in Ontario are attributable to such exposure.

There have been about 20 case-control and cohort epidemiologic studies of CBPs and cancer risk since 1978. The US Environmental Protection Agency (EPA) reviewed these studies[26] and identified 5 case-control studies (including the King and Marrett study) that met the criteria of being population-based, well designed and having adequate exposure assessment. The EPA concluded that, based on the entire cancer epidemiology database, bladder cancer studies provide better evidence than other types of cancer for an association between exposure to chlorinated surface water and cancer.

The EPA recognized that a causal relationship between chlorinated surface water and bladder cancer has not yet been demonstrated conclusively by epidemiologic studies, but concluded that the *assumption* of a potential causal relationship is supported by the weight of evidence from toxicology and epidemiology. Based on this assumption, the EPA estimated that the attributable risk of bladder cancer due to exposure to chlorinated water in the US is in the range of 2-17%; the annual number of bladder cancer cases attributable to such exposure was estimated to be in the 1100-9300 range. The EPA also stated that it believes that the overall evidence from available epidemiologic and toxicologic studies on chlorinated surface water continues to support a hazard concern and a prudent public health protective approach for regulation.[26]

The expert working group convened by the Laboratory Centre for Disease Control (see Workshop Report in this issue) observed that the few available epidemiologic studies of CBP exposure and pregnancy outcome indicated associations between exposure to THMs and spontaneous abortion, growth retardation and birth defects. However, these studies were weak in exposure assessment and control of potential confounders. When tested in rats, rabbits and mice, chloroform was not teratogenic, but both bromodichloromethane and chlorodibromomethane have shown evidence of fetotoxicity. Other CBPs have produced adverse effects on the testes and on sperm production in male rats and congenital heart defects in rats exposed in utero.

Recently, a prospective study[27] that included concurrent trihalomethane sampling data showed that women who drank at least five glasses per day of cold tap water containing at least 75 µg/L total THMs had an adjusted odds ratio of 1.8 for spontaneous abortion (CI = 1.1-3.0). Of the four individual THMs, only high bromodichloromethane exposure (consumption of at least five glasses per day of cold tap water containing at least 18 µg/L of bromodichloromethane) was associated with spontaneous abortion, both alone (adjusted OR = 2.0, CI = 1.2-3.5) and after adjustment for the other trihalomethanes (adjusted OR = 3.0, CI = 1.4-6.6).

The expert group concluded that it was possible (60% of the group) to probable (40% of the group) that CBPs pose a significant cancer risk, particularly of bladder cancer. The group concluded that the risk of bladder and possibly other types of cancer is a moderately important public health problem.

They also determined that there was insufficient evidence to establish a causal relationship between CBPs and adverse reproductive outcomes in humans, but that confirmation of the available limited data could establish CBPs as an important health problem. Finally, the group concluded that there were not enough data available to conduct a quantitative risk/benefit/cost evaluation and recommended that developing health risk data be monitored to determine when such an evaluation would be possible.

To the extent that epidemiologic studies randomly misclassify individual exposures to CBPs, the resulting risk estimates may be lower than the true risks. It is likely that many of the epidemiologic studies published to date have misclassified individual exposures to chlorinated water or CBPs. To lessen the impacts of this type of misclassification, Lynch et al.[28] recommended that future epidemiologic studies of this type should quantify exposures more extensively.

Next Steps

In most areas of Canada, the provinces, territories and local governments are responsible for providing safe drinking water. The Federal-Provincial Subcommittee on Drinking Water (DWS) of the Committee on Environmental and Occupational Health establishes and publishes *Guidelines for Canadian Drinking Water Quality.*[29] Health Canada acts as the secretariat for DWS and provides health and safety advice with regard to drinking water health risks in Canada. In 1993, DWS lowered the Canadian drinking water guideline for THMs from a maximum level at any one time of 350 ug/L to a maximum annual average, based on at least quarterly measurements, of 100 ug/L and recommended that THM levels be reduced as much as possible whenever treatment plants are expanded or upgraded. The THM guideline was based on a combination of risk assessment and risk management considerations, as is the case for all drinking water guidelines.

The *Guidelines for Canadian Drinking Water Quality* have no legal weight per se; however, they are used by the provinces and territories to establish their own drinking water regulations. In the US, the EPA promulgates drinking water standards that are legally binding on water supplies throughout the US that serve more than 10,000 persons.

The supporting document for the THM drinking water guideline states that the preferred method for controlling disinfection by-products is precursor removal, i.e. use of methods such as flocculation and filtration to remove organic material prior to disinfection. For surface waters in particular, use of filtration and postchlorination greatly reduces CBP levels.

Other options for reducing CBPs include ozone, chloramine and charcoal filters. Ozone has been used for water treatment in Europe for over 90 years, particularly in France and Switzerland.[1] If a sufficient dose of ozone is applied, its use does not lead to the creation of mutagenic compounds in drinking water and can even eliminate the initial mutagenicity of the water.[30] Combined treatment of ozone and activated carbon also decreases the chlorine consumption of treated water and reduces the formation of CBPs. DeMarini et al.[22] compared water treated by different methods: chlorination, chloramination or ozonation alone and ozonation followed by chlorination or chloramination. Ozone alone produced the lowest levels of mutagenic activity in treated water, and chlorine alone, the highest levels. However, ozonation disinfection by-products include bromate, a genotoxic carcinogen. Also, the effectiveness of ozonation in reducing microbial and CBP risks varies with the characteristics of raw water (e.g. pH, temperature, particulate matter, bromide concentration) and ozonation alone does not give residual disinfective capacity in distribution systems.

Chlorine is still the most widely used disinfectant in Canada and the United States because of its low cost, ability to form a residual and effectiveness at low concentrations. The continued occurrence of waterborne disease outbreaks demonstrates that contamination of drinking water with pathogenic bacteria, viruses and parasites still poses a serious health risk. A single outbreak of Cryptosporidium in Milwaukee, Wisconsin, in 1993 resulted from a breakdown in filtration and led to an estimated 400,000 cases of acute gastroenteritis and 100 deaths.[31] Microbiologically contaminated drinking water is a special risk to children, the elderly and persons with compromised immune systems.

In November 1998, the EPA will promulgate a disinfectants/disinfection by-products rule originally proposed in 1994. The rule will reduce the maximum contaminant level (MCL) for total THMs from 100 to 80 µg/L and establish new MCLs for other by-products such as HAAs, bromate and chlorite.

The new rule will also establish enhanced coagulation requirements for precursor removal, which should help to reduce both the number of microbes and the level of CBP precursors. The EPA is also establishing an extensive national information collection effort on contaminant occurrence, CBP levels and microbiological contaminants.[32]

The EPA has requested $1.9 billion to help state, tribal and local jurisdictions construct the facilities required to comply with federal requirements. Infrastructure plans include installation of sensors for real-time monitoring of important distribution system quality indicators such as disinfectant residual, water pressure, flow direction, microbial densities and total organic halides.

A 1994 national survey[33] showed that 19.5% of households in Canada reported using a filter or purifier for their drinking water compared with 13.9% in 1991, while 21.9% of households purchased bottled drinking water in the month before survey compared with 16.1% of households in 1991. Similarly, in a 1997 survey, one third of US consumers used a home water treatment device other than bottled water, an increase from 27% in 1995.[34] The use of devices such as pour-through water pitchers with carbon filters grew more than any other type of water treatment device. These data are consistent with increasing public concern about the safety and quality of drinking water.

There is an urgent need for co-ordinated epidemiologic and toxicologic research to seek definitive evidence on the nature of the association between exposure to CBPs in drinking water and outcomes such as cancer, spontaneous abortion and related adverse reproductive outcome conditions. Future epidemiologic studies should focus on associations between diseases and high potency CBPs identified in animal bioassays, for example, brominated THMs and HAAs. The effects of CBPs and CBP metabolites could be examined in vitro with human bladder epithelial cells.

Biomarkers of susceptibility, exposure and outcome would strengthen epidemiologic studies of CBP exposures and disease risks. Biomarkers such as DNA adducts or specific types of mutations may eventually support the attribution of individual cancer cases to exposure to specific CBPs, leading to more accurate risk estimates and targeted, effective control measures. For example, MX reacts with DNA in vitro to form a unique adduct;[35] although the biologic significance of such adducts is unknown, they may prove to play an important role as biomarkers of specific exposures.

Despite the undisputed benefits of chlorination in controlling waterborne infectious diseases, the epidemiologic evidence now available clearly suggests that CBPs pose a cancer risk to humans, particularly a risk of bladder cancer. Given the wide and prolonged exposure of Canadians to this risk, public health authorities must decide if the available evidence warrants actions to at least reduce public exposure to CBPs while safer alternatives are sought. In his report of the Commission of Inquiry on the Blood System in Canada,[36] Justice Krever emphasized the importance of a valuable tenet in the philosophy of public health, namely, "action to reduce risk should not await scientific certainty."

In the process of public health risk assessment and risk management, scientific experts must be satisfied that the "weight of evidence" exceeds a certain threshold before they can reach consensus and recommend action. With this end in mind, Health Canada set up the Chlorination Disinfection By-product Task Group in July 1998. The new group has multi-stakeholder representation in order to plan and oversee a co-ordinated effort involving epidemiologic, toxicologic, water treatment and other types of expertise to estimate the risks from CBPs and to develop risk management recommendations.

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