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DBPs And Birth Defects

In recent weeks some Australian newsletters have carried articles about two newly published studies reporting associations between maternal exposure to disinfection byproducts (DBPs) during pregnancy and the risk of some birth defects. One study was conducted in Perth, Western Australia (1) and the other in Taiwan (2). Both studies were based on analysis of birth registry data with exposure to DBPs in tap water inferred on the basis of the residential address of the mother at the time of delivery.

Birth defects are defined as abnormalities affecting the structure, function or body metabolism which are present at birth. Such defects are diagnosed in about 2-3% of newborn infants, and may range in severity from fatal or life-threatening through to relatively mild and easily treated conditions. In developed nations, birth defects are responsible for about 20% of deaths in newborn babies. Major structural defects are usually recognised at or soon after birth, but the rate of diagnosed defects continues to increase as infants grow and develop, and more abnormalities become apparent. By one year of age, the rate of diagnosed defects increases to about 6%, and by age five the rate reaches about 10%.

Given the relatively low rate of occurrence of birth defects, it is not considered feasible to undertake prospective epidemiological studies as it would be necessary to recruit around 30 pregnant women for every expected case of adverse outcome that would be apparent at birth. Thus in order to investigate risk factors for birth defects, only retrospective designs such as cross-sectional studies or case-control studies can be undertaken.

Western Australian Study This cross-sectional study examined birth defects for deliveries occurring over a five year period from 2000 to 2004 in a study area which spanned the northern suburbs of the city of Perth. Water sampling was conducted at 47 locations over a different time period (April 2005 to March 2006), with six samples collected from each site during this interval. Samples were analysed for the four individual trihalomethanes (THMs). The numbers of total births and birth defects for women residing in the postcodes corresponding to the study area were obtained from state registries. The coverage of these registries includes birth defects in live births and stillbirths and pregnancies terminated due to foetal abnormalities. The available information included postcode of maternal residence at the time of delivery, maternal age, and socioeconomic status, however the date of birth was not available for birth defects cases due to privacy constraints. The birth defects data was obtained in 2007 and thus included any birth defects registered since birth until that time. Pregnancy terminations were excluded from the study. The study examined all birth defects combined, and the seven most common categories of birth defects as classified under the British Paediatric Association International Classification of Diseases 9th Revision (ICD-9).

Total THM (TTHM) exposures were estimated by averaging the measurements for the six samples at each collection site. Postcodes were aggregated into areas approximately corresponding to water supply areas, and each of the resulting eight areas was assigned as having low (less than 60 microgram/L), medium (between 60 and 130 microgram/L) or high average TTHMs (130 micrograms/L or above). Women were assigned a TTHM exposure level according to their postcode of residence at the time of delivery. Associations between DBP exposure and birth defects were examined using binomial logistic regression models. Estimates were adjusted for maternal age at the individual level and socioeconomic status at the postcode level.

A total of 20,870 live births were included in the study, with birth defects being recorded in 1,097 individuals. Comparison of maternal demographic characteristics between the three TTHM exposure

levels showed the average maternal age to be slightly lower in the low TTHM area. A much wider range in socioeconomic status existed within the high TTHM area than within the low or medium TTHM areas. The high TTHM area contributed 63% of total births in the study, with the low TTHM area contributing 14% and the medium TTHM area 23%. The outcome analysis (summarised in the following table) showed a significantly increased Odds Ratio for any birth defect (combined category) when women living in high TTHM areas were compared with those living in low TTHM areas (OR=1.22, 95% CI 1.01-1.48). When the seven different categories of common birth defects were examined, a statistically significant increase was seen for cardiovascular defects (OR=1.62, 95% CI 1.04-2.51).

Summary of adjusted Odds Ratios and 95% CIs for association of TTHM exposure and birth defects for the Western Australian study (1)

	TTHM exposure (microgram/L)		
	Low less than 60	Med 60 to 130	High 130 and above
Any birth defect	1.00	0.98 0.75-1.28	1.22 1.01-1.48
Number	134	235	728
Cardiovascular	1.00	1.00 0.55-1.81	1.62 1.04-2.51
Number	24	55	181
Musculo-skeletal	1.00	1.05 0.60-1.83	1.48 0.99-1.21
Number	29	53	200
Gastro-intestinal	1.00	1.27 0.55-2.96	1.20 0.63-2.30
Number	11	24	66
Urogenital	1.00	1.09 0.68-1.77	1.40 0.98-1.99
Number	40	76	235
Nervous system	1.00	1.78 0.55-5.80	1.08 0.41-2.85
Number	6	15	38
Respiratory system	1.00	1.06 0.13-8.87	0.88 0.18-4.18
Number	2	3	12
Integument	1.00	0.91 0.36-2.33	0.95 0.49-1.83
Number	13	15	8

The authors comment that the TTHM levels examined in this study are higher than those seen most other published studies on this topic. The Australian Drinking Water Guidelines currently specify a guideline value of 250 micrograms/L for total THMs with no guideline values set for the individual compounds. A number of other countries have set lower guideline or standard values, while the World Health Organisation has set separate guideline values for the four individual THMs and recommended a fractionation approach for calculating TTHM limits. TTHM values recorded in the sampling program for this study ranged from a minimum of 36 micrograms/L in the low TTHM area to a maximum of 190 micrograms/L in the high TTHM area. In contrast to most disinfected drinking water supplies where chloroform is the dominant THM, the brominated forms are more abundant in waters in Perth due to the high bromine content of local groundwaters. Shallow groundwaters in Perth also contain high levels of organic matter due to the porous nature of the soils.

Taiwanese Study This was a cross-sectional study of births occurring during the three year period 2001-2003. The study area was restricted to five water supply regions which were stated to have only one type of water treatment plant and to use chlorination for disinfection. The number of water treatment plants included in the study is not given, although it is stated that 90% of the Taiwanese population is supplied with disinfected water from 200 treatment plants, while the remaining 10% use private wells. A total of 396,049 infants were included in the study population, representing 55% of all babies born in Taiwan during the study period. Birth records and information on birth defects was obtained from a national registry. This registry records information only on defects diagnosed up to 7 days after birth, and does not record defects present in foetuses lost before 20 weeks of gestational age due to spontaneous or induced abortion.

The study assessed the eleven most common categories of birth defects including two types of defects affecting the brain (anencephalus, hydrocephalus), three types of heart defect (ventricular septal defects, atrial septal defects,

Tetralogy of Fallot), three types of defect of the renal and urinary tract (renal agenesis and dysgenesis, obstructive urinary tract defects, hypospadias), cleft palate, cleft lip and chromosomal defects. The registry also contained information on the infant's sex, maternal age category, whether the birth was single or multiple, and several conditions relevant to the mother's health (eg diabetes mellitus, anaemia, cardiac disease). The population density for each municipality was used as a measure of urbanisation.

Exposure of the mothers to DBPs during pregnancy was estimated from water company records of total trihalomethane (TTHM) measurements for each water treatment plant. Such measurements were required at least four times per year at each plant under water quality regulations. Exposure for each woman over the whole pregnancy was estimated using a weighted average of TTHM measurements for the relevant time period for the water treatment plant(s) supplying the mother's place of residence. TTHM exposure for each pregnancy was classified into four categories; 0-4 micrograms/L (reference category), 5-9 micrograms/L, 10-19 micrograms /L and 20 or more micrograms/L. The prevalence of each type of birth defect and all defects combined was calculated and logistic regression was used to generate Odds Ratios.

There were no significant differences between women in the four exposure categories in terms of maternal age categories, ratio of male to female infants, prevalence of maternal diabetes or single vs multiple births. Population density was lower in the highest TTHM exposure category compared to the reference category suggesting a less urbanised population. There were no significant differences in these characteristics between the included and excluded populations.

A total of 2,148 births (0.5%) with one or more of the selected categories of birth defects were reported from the 369,049 births included in the study. In the final statistical analysis Odds Ratios were calculated with adjustment for maternal age, single or multiple birth and population density. The adjusted Odds Ratios are summarised in the following table.

Summary of adjusted Odds Ratios and 95% CIs for association of TTHM exposure and birth defects for the Taiwan study (2)

	TTHM exposure (microgram/L)			
	0-4	5-9	10-19	20 +
Total births	181,985	55,950	82,797	396,049
Any birth defect	1.00	1.21 1.07-1.36	0.97 0.86-1.08	1.00 0.89-1.13
Number	978	368	421	381
Anencephalus	1.00	1.59 0.72-3.52	0.23 0.05-1.01	1.96 0.94-4.07
Number	19	9	2	13
Hydrocephalus	1.00	1.36 0.85-2.20	0.71 0.42-1.20	0.74 0.43-1.28
Number	58	24	19	17
Ventricular septal defects	1.00	0.74 0.31-1.80	0.65 0.29-1.43	1.81 0.98-3.35
Number	27	6	8	18
Atrial septal defects	1.00	2.15 0.70-6.60	0.53 0.11-2.49	1.33 0.39-4.58
Number	8	5	2	4
Tetralogy of Fallot	1.00	1.60 0.61-4.23	0.46 0.13-1.61	0.32 0.07-1.47
Number	13	6	3	2
Cleft lip w or w/o palate	1.00	1.15 0.84-1.56	1.20 0.91-1.55	0.98 0.73-1.32
Number	155	55	84	64
Cleft palate	1.00	0.94 0.53-1.68	1.17 0.74-1.86	1.56 1.00-2.41
Number	52	15	28	34
Renal agenesis or dysgenesis	1.00	1.33 0.71-2.48	0.92 0.48-1.75	1.27 0.69-2.33
Number	33	14	13	16
Obstructive urinary tract defects	1.00	1.65 0.77-3.56	1.24 0.57-2.67	1.44 0.66-3.14
Number	19	10	10	10
Hypospadias	1.00	0.59 0.28-1.26	0.76 0.41-1.38	0.47 0.21-1.04
Number	43	8	14	7
Chromosome anomalies	1.00	1.25 0.95-1.65	0.93 0.70-1.24	0.90 0.66-1.24
Number	174	72	67	51
Down syndrome	1.00	1.48 0.99-2.21	1.00 0.65-1.54	1.17 0.74-1.83
Number	73	36	30	27
Trisomy 13	1.00	1.56 0.28-8.55	3.36 0.94-12.0	1.12 0.20-6.29
Number	4	2	6	2
Trisomy 18	1.00	1.64 0.81-3.30	1.31 0.66-2.59	0.81 0.33-2.02
Number	23	12	13	6

In discussing the results, the authors highlight the increased adjusted Odds Ratios for anencephalus (OR=1.96, 95% CI 0.94-4.07), ventricular septal defects (OR=1.81, 95% CI 0.98-3.35) and cleft palate (OR=1.56, 95% CI 1.00-2.41) seen for comparison of the highest exposure group with the reference (lowest exposure) group. However, only the association with cleft palate reached borderline statistical significance at the $p=0.05$ level. This was also the only outcome which showed a consistent dose-response trend across the exposure categories. Both anencephalus and ventricular septal defects showed decreased risks in at least one of the intermediate exposure categories compared to the reference category.

The authors also carried out a meta-analysis of this study and five previous studies which have examined the relationship between DBP exposure and some of the seven most common categories of birth defects. These studies differed in their design (three cross-sectional, two case-control), exposure contrasts (high versus low TTHMs, high versus zero THMs, chlorine dioxide treated versus undisinfected water supplies), and index of exposure (THM measurements or high versus low colour). The number of studies addressing each type of defect ranged from two to four. This analysis resulted in a significantly elevated summary risk estimate for ventricular septal defects (OR=1.25 95%CI 1.08-1.46) based on three studies. For hydrocephalus and anencephalus, summary ORs were also significantly increased but the studies showed underlying heterogeneity. For atrial septal defects, cleft lip with/without cleft palate and for cleft palate, the meta-analysis showed consistent evidence of no effect.

Limitations of these studies Both studies used registries as a source of data on births and birth defects, and in both cases the coverage of pregnancies and accuracy of registries was said to be of high quality. However the exposure of pregnant women to TTHMs was simply inferred from their place of residence at the time of birth, and women were not interviewed to determine whether they resided there throughout their pregnancy, whether they drank tap water, or the extent of dermal or inhalational exposure to tap water (which may contribute substantially to exposure to volatile

DBPs). While the Western Australian study collected water samples from 47 different sites in the distribution system, these were not uniformly spread over the study area and may not have adequately reflected the variability in THM levels. In addition the water samples were taken in a different time period from the pregnancies and the lack of information on birth dates for birth defect cases prevented adjustment even for seasonal variations. From the methodology described in the paper it appears all pregnancies during the five year period in each of the eight geographic zones were assigned the same TTHM exposure level. The Taiwanese study recorded THM values during the same time period as the pregnancies but it appears the measurements were taken at water treatment plants and would not have accounted for changes in THM concentrations that may have occurred during travel through the distribution system. Exposure was averaged over the entire pregnancy rather than being restricted to the first trimester when congenital defects occur.

The database used in the Taiwanese study provided some information on maternal health status but both studies lacked important information on maternal smoking, alcohol consumption, and the use of vitamin supplements or medications. A number of medicinal drugs are known to cause birth defects including some drugs used to treat epilepsy, depression and bipolar disorder, anticoagulants, angiotensin converting enzyme inhibitors (used to treat high blood pressure) and isotretinoin (used to treat severe acne). In addition, a wide range of commonly used prescription and over-the-counter drugs including antibiotics, analgesics, and anti-inflammatories are believed to increase the risk of birth defects. Illegal drugs are also suspected to cause birth defects although this is difficult to verify given the association of illegal drug use with other risk factors such as alcohol, smoking, poor nutrition etc. While many pregnant women avoid medication use as much as possible during pregnancy, it is estimated that even in developed countries such as Australia at least one-third of pregnancies resulting in live births are un-planned, opening the possibility of inadvertent exposure in the first few weeks after conception but before the pregnancy is recognised. Significant structural birth defects in the major organ systems are most likely to arise during the first 60 days of pregnancy. Other known risk factors for birth defects

include maternal health conditions such as diabetes, maternal infections, genetic conditions and alcohol exposure in early pregnancy.

While both of these new studies reported increased risks of cardiac defects, a previous review of the weight of evidence on adverse reproductive and developmental effects found no evidence of association of cardiac anomalies with DBP exposure on the basis of eight epidemiological studies conducted prior to that time (3). This review also noted that animal toxicological studies of DBPs had shown adverse effects of fetuses only at levels that produced maternal toxicity, and that anatomical malformations had not been observed.

Overall, the findings of both of these new studies is limited by their cross-sectional design, inaccuracies in DBP exposure assessment and the lack of important information on other relevant maternal exposures which may affect the risk of birth defects. While it may be argued that lack of precision in assessing both DBP exposure and non-water risk factors is likely to be non-differential and thus result in a reduced Odds Ratio, the “ecological fallacy” is well known in field of epidemiology and it cannot be assumed that exposures assessed on the collective level will reflect individual exposures. Knowledge of the relationship (if any) between DBP exposures and birth defects is likely to be advanced only by studies of more analytical design which include detailed information on maternal exposures and health status at the individual level during the critical time window of early pregnancy.

(1) Chisholm K, Cook A, Bower C and Weinstein P (2008) Risk of birth defects in Australian communities with high brominated disinfection by-product levels. *Environmental Health Perspectives* doi:10.1289/ehp/10980

(2) Hwang BF, Jaakkola JJK, Guo HR (2008) Water disinfection by-products and the risk of specific birth defects: a population-based cross-sectional study in Taiwan. *Environmental Health* 7(23) doi:10.1186/1476-069X-7-23

(3) Tardiff, R. G., M. L. Carson, et al. (2006). Updated weight of evidence for an association between adverse reproductive and developmental effects and exposure to disinfection by-products. *Regulatory Toxicology & Pharmacology* 45(2): 185-205.

Legionella Outbreak At Car Wash

A car wash in Melbourne, Australia has been linked to an outbreak of Legionnaires' disease, an occurrence which appears to be the first of its kind reported worldwide. The outbreak has resulted in seven people being hospitalised, and led to rapid action by health authorities to manage this previously unsuspected source of public health risk.

Legionnaires' disease is a type of pneumonia caused by infection with bacteria of the genus *Legionella*. The majority of cases are caused by *Legionella pneumophila*, but several other species are also known to cause the illness. Onset of the disease can be up to 10 days after the initial contact with the bacteria. Those most at risk of infection are the elderly, smokers and those with pre-existing conditions affecting the immune system. The illness can be fatal. *Legionella* infection may also produce a less severe illness called Pontiac fever which is characterised by short-term flu-like symptoms. Legionellosis is a notifiable disease in Australia, with between 300 and 350 cases recorded annually in recent years. *Legionella* infections cannot be transmitted from person to person.

Legionella bacteria occur naturally in the environment, mainly in water and soil. These organisms are normally present in very low concentrations but can increase markedly in human-made aquatic environments with warm water (25 to 45°C), particularly if water is recirculated and a disinfectant residual is not maintained. *Legionella* bacteria may occasionally occur in disinfected tap water supplies, and may also persist in biofilms and inside amoeba which can provide some protection against chemical disinfection agents.

In order for the bacteria to cause an infection, they need to be inhaled in the form of particles which are small enough to reach the lower regions of the lung but large enough to contain at least one bacterial cell. The combination of warm water environments with processes that generate fine aerosols (1 to 3 microns in diameter) provides ideal conditions for *Legionella* outbreaks to occur. Until now, in Australia and other countries, outbreaks of Legionnaires' disease have

mainly been linked to aerosols generated by cooling towers. The infectious dose for *Legionella* has not been defined but water sources associated with outbreaks have generally been reported to contain concentrations of 10,000 to 100,000 colony forming units per litre or more.

The first case in the Melbourne car wash outbreak was notified to health authorities in late April, and by early May two more cases had been reported. All three victims lived in the western suburbs of Melbourne and investigations focused on potential exposures from cooling towers in this area. On 5 May an alert was issued by the Victorian Chief Health Officer to hospitals and General Practitioners in the area informing them of the outbreak and asking them to consider the possibility of Legionnaires' disease for patients presenting with flu-like or pneumonia symptoms. On 8 May health authorities announced that a further two cases had been identified, and that investigations were now concentrating on cooling towers in or near two local shopping areas. The cooling towers were being tested and then disinfected as a precautionary measure, but none had yet been found to be positive for *Legionella* bacteria. All cooling towers in the state of Victoria are required to be registered under legislation passed in 2001 following a major *Legionella* outbreak which resulted in 125 cases and four deaths. The registry permits rapid identification and testing of suspect towers whenever *Legionella* cases are reported.

According to media reports, the possibility of a link to a local car wash was announced on 9 May by a spokesman for the Department of Human who stated that the car wash owner had voluntarily closed the business as a precautionary measure until water test results had been obtained. On 20 May the Chief Health Officer announced that multiple water samples taken from the car wash had been confirmed to contain *Legionella* of the same species as the infected cases. Investigations had also established that water at the car wash was being heated to approximately 40°C and stored in a tank before being sent through the system to the outlets. This temperature provides an excellent condition for *Legionella* growth. The high pressure spray hoses used in this "do it yourself" car wash then created a

situation where customers were exposed to respirable-sized aerosols. Contrary to initial media reports, the facility did not recycle water on-site, but used only tap water for car washing. The car wash reopened several days later after disinfection procedures and further water testing had been carried out to ensure that the *Legionella* bacteria had been eliminated.

As a result of this incident, the Victorian Public Health Branch has consulted with the car wash industry to establish new guidelines to prevent further outbreaks (1). These guidelines emphasise the need for proper management of warm water systems in order to prevent the growth of *Legionella*. According to the Department of Human Services Victoria, discussions with the industry have indicated that the majority of car wash premises have at least some part of their process that involves the heating and storage of warm water. If such components are designed to supply water at temperatures between 30 and 60°C, then they would fall under the definition of a warm water system in the *Health (Legionella) Regulations 2001*. These regulations specify requirements for disinfection, maintenance, testing and record keeping for such systems. Other risk reduction measures which may be considered by car wash operators are the elimination of warm water storage, or raising water storage temperatures to 60°C or higher in order to kill any *Legionella* bacteria.

This outbreak closely follows two previous reports of *Legionella* cases associated with the use of high pressure spray devices. The first incident occurred in Auckland, New Zealand in early 2006 but was reported only recently (2). Four cases of Legionellosis were identified in a small coastal suburb. Epidemiological and environmental investigations suggested exposure to aerosols from a high pressure “water blaster” used to clean boats was the likely infection source for at least two of the cases. The water blaster was supplied with chlorinated bore water but the water supply may have been contaminated with soil during repair of a mains leak. Overnight storage of water in a reservoir tank and 30 metre hose during the summer season may have provided warm conditions permitting *Legionella* to grow. The second incident in mid-2007

involved two workers at a bus depot in Troy, New York. *Legionella* infections in a mechanic and a bus driver were attributed to spray exposure from bus washing equipment. Media reports of this incident suggest that water was being recycled on-site, and that high pressure spray devices were being used. An outbreak of Pontiac fever affecting 15 workers at a US factory has also been attributed to using high pressure spray devices to wash equipment, in combination with a water source containing high levels of *Legionella* bacteria.

These outbreaks highlight the potential for changing water use practices to give rise to situations which may generate new public health risks. High pressure spray devices are becoming more common in Australia in both domestic and industrial settings as water shortages worsen across the country. Characterisation of the aerosols produced by such devices suggests they may increase exposure to respirable aerosols compared to conventional trigger nozzles (3). The “do it yourself” style of car wash using such high pressure sprays is also becoming more common in comparison to the traditional “drive through” style. Water restrictions in Victoria currently ban the use of tap water for washing cars at home except for cleaning of windows and lights, and spot cleaning of corrosive substances, however use of water-efficient commercial car washes is permitted.

These trends are resulting in increasing numbers of people being exposed to water aerosols in the respirable size range and, as illustrated by this outbreak, there is the potential for public health risks to arise if relevant water quality issues are not adequately assessed and managed.

(1) www.health.vic.gov.au/environment/legionella/car_washes.htm

(2) A Legionnaires’ disease outbreak: A water blaster and roof-collected rainwater systems. Simmons G *et al.* *Water Research* **42** (2008) p1449 - 1458.

(3) A Series of Exposure Experiments – Recycled Water and Alternative Water Sources: Part A Aerosol-sizing and Endotoxin Experiments. Research Report 45. CRC for Water Quality and Treatment.

www.waterquality.crc.org.au/publication_occpr_resrpts.htm

Safer Water, Better Health

The World Health Organisation has issued a new report summarising knowledge about the disease burden caused by unsafe water and poor sanitation, the effectiveness, costs and impacts of interventions, and implications for financing. The report draws together the findings of several other WHO reports and reviews on these issues, and summarises the estimated burden of deaths and disability from water and sanitation related diseases in member countries.

Overall it is estimated that about 10% of the total burden of disease and 6.3% of all deaths worldwide could be prevented by improvements in drinking water, sanitation, hygiene and water resource management. Major contributors to the disease burden include:

- diarrhoeal diseases transmitted by contaminated drinking water, lack of sanitation and poor hygiene
- malnutrition associated with repeated diarrhoeal illness or intestinal nematode infection
- water and hygiene-related diseases including lymphatic filariasis, trachoma, schistosomiasis, malaria, dengue fever and Japanese encephalitis
- drownings, including flood-related events

Diarrhoeal illnesses were the largest single contributor, making up over 4% of the total global burden of DALYS (disability adjusted life years), or 39% of the water/sanitation/hygiene DALY burden. The consequences of malnutrition and malaria were the next most important contributors to the disease burden. The impacts of a number of water and hygiene-related diseases could not be estimated, including legionellosis, leptospirosis, conjunctivitis and otitis, physical injuries such as falls, and the adverse effects of exposure to excessive amounts of fluoride, arsenic, lead or nitrate in drinking water. The report also includes an Appendix detailing the country by country breakdown of figures for estimated deaths and DALYS lost under each of the major categories of disease.

Safer Water, Better Health, WHO,
ISBN 978 92 4 159643 5
www.who.int/quantifying_ehimpacts/publications/saferwater/en/index.html

Potable Recycling Guidelines Released

The Australian Guidelines for Water Recycling: Managing Health and Environmental Risks (Phase 2): Augmentation of Drinking Water Supplies were officially released on 8 May following final endorsement at the April meeting of the Environment Protection and Heritage Council (EPHC). This was the final stage of a 6-step approval process involving the EPHC, the National Health and Medical Research Council and the Natural Resource Management Ministerial Council.

Development of the Phase 2 Guidelines commenced in late 2006 following completion of the Phase 1 Guidelines covering non-potable uses of recycled water. The guidelines describe a risk management approach based in the 12-element framework developed for the Australian Drinking Water Guidelines. Significant changes introduced into the *Augmentation of Drinking Water Supplies* module as a result of the public consultation process in 2007 included the addition of a further 10-fold safety factor for pharmaceuticals, more guidance on monitoring (for validation, operational process control, and verification of water quality), and additional information on chemical hazards, trade waste controls, staff training and regulation of health-based targets.

Australia's first planned indirect potable reuse scheme is expected to be operational by early 2009 when purified recycled water from the Queensland Western Corridor Recycled Water Pipeline Project will be pumped into Wivenhoe Dam. This 1.16 million megalitre dam serves the city of Brisbane and surrounding areas. The project is said to be the third largest advanced water treatment project in the world and will have the capacity to produce over 230 megalitres of purified recycled water per day from three advanced water treatment plants. In addition to supplementing the drinking water supply in Wivenhoe Dam, the scheme will supply water to power stations, industrial users and agriculture in South East Queensland.

http://www.ephc.gov.au/ephc/water_recycling.html
<http://www.westerncorridor.com.au/>

News Items

CRC for Water Quality and Treatment Ends

On 30 June 2008 the Cooperative Research Centre for Water Quality and Treatment completed its term of operation under the Commonwealth Agreement. During its 13 years of operation the CRC undertook a broad portfolio of research and educational activities addressing issues relating to water quality management and health risk reduction, from catchment and reservoir management and water treatment to the distribution of drinking water to consumers' taps.

The CRC web page will be maintained until 30 June 2009 and will continue to be updated as Research Reports and other outputs from the CRC research program are completed and published.

The CRC has been succeeded by Water Quality Research Australia Limited (WQRA), a national not-for-profit scientific research institution. WQRA will develop and undertake a program of research and education to build on the achievements of the CRC.
<http://www.waterquality.org.au/>

What will happen to Health Stream?

The CRC has provided interim funding to continue production of Health Stream until the end of 2008. A decision on future production of this newsletter will then be made by WQRA.

Crypto Triggers Boil Water Alert In UK

The Anglian Water company in the UK has issued a boil water notice for 250,000 customers following detection of *Cryptosporidium* oocysts in the water supply. The notice was issued on 25 June for areas served by the Pitsford Water Treatment Works. This plant draws its water from a surface reservoir which is open to the public for recreational uses including fishing, sailing and windsurfing. According to a statement issued by Anglian Water, the contamination was discovered in routine samples taken from the plant. Some newspaper reports have suggested that an increase in turbidity also occurred, suggesting the possibility of a failure in filtration processes at the water treatment plant.

In a statement issued on 30 June, the Health Protection Agency stated that there had been no apparent increase in the number of cases of *Cryptosporidium* infection reported in the area. Anglian Water is still investigating the cause of the contamination, and is working to install UV treatment on the water supply to provide additional protection against *Cryptosporidium*.

Low Energy Desalination Process Wins Grant

A team from Siemens Water Technologies has won a grant from the Singapore Environment and Water Industry Development Council (EWI) for developing a new, more energy efficient method of desalination. The SGD \$4 million grant, to be used for further development of the process, was announced during World Water Week in Singapore in late June. The new process is reported to use electro dialysis, ion exchange softening, and a final desalting step using a novel continuous electrodeionization process to drive salt separation with minimum energy demand. The grant was offered last year by EWI for any research group that could demonstrate production of one cubic metre of purified drinking water from seawater using less than 1.5 kilowatt-hours of power. Current best available technologies use about twice this amount of power, and many older plants use more energy.

Alamosa Salmonella Outbreak Ends

The town of Alamosa, Colorado is returning to normal following the waterborne *Salmonella* outbreak that began in March (Reported in Health Stream Issue 49). Over 400 people are believed to have become ill as a result of contamination of the undisinfected groundwater supply. According to media reports at least 18 people were hospitalised and one death has been linked to the outbreak. The entire distribution system of the town was hyperchlorinated and flushed before restrictions on water use were progressively lifted from early April, and the water was declared safe to drink on 11 April. Despite an intensive investigation, the source of the contamination has not been identified. The water supply is now being chlorinated using a temporary disinfection facility and plans have been made to incorporate disinfection in a permanent treatment plant which was already under construction in order to reduce arsenic levels in the water supply.

Circulation Report – Issue 50 June 2008

Circulation for the print version of this issue is 2718 copies, with readers in 64 countries.

In addition, 1651 readers are registered for email notification of new issues.



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From the Literature

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Antimony leaching from polyethylene terephthalate (PET) plastic used for bottled drinking water. Westerhoff P, Prapaipong P, Shock E and Hillaireau A (2008) *Water Research*, **42**: 551-556.

Is Colon Cancer Mortality Related to Arsenic Exposure? Yang C-Y, Chang C-C, Ho S-C and Chiu H-F (2008) *Journal of Toxicology & Environmental Health, Part A*, **71**(8); 533-38.

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Disinfection by-product formation and mitigation strategies in point-of-use chlorination of turbid and non-turbid waters in western Kenya. Lantagne DS, Blount BC, Cardinali F and Quick R. (2008) *Journal of Water & Health*, **6**(1); 67-82.

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Characterisation of potential virulence markers in Pseudomonas aeruginosa isolated from drinking water. da Silva MEZ, Filho IC, Endo EH et al. (2008) *Antonie van Leeuwenhoek*, **93**(4); 323-34.

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A systematic review of analytical observational studies investigating the association between cardiovascular disease and drinking water hardness. Catling LA, Abubaker I, Lake IR, Swift L and Hunter PR (2008) *Journal of Water & Health*, **6**(4); 433-442.

Microbial groundwater quality and its health implications for a border-strip irrigated dairy farm catchment, South Island, New Zealand. Close M, Dann R, Ball A, et al.. (2008) *Journal of Water & Health*, **6**(1); 83-98.

Arsenic**Arsenic in drinking-water and risk for cancer in Denmark.**

Baastrop, R., Sorensen, M., Balstrom, T., Frederiksen, K., Larsen, C.L., Tjonneland, A., Overvad, K. and Raaschou-Nielsen, O. (2008) *Environmental Health Perspectives*, **116**(2); 231-7.

High arsenic concentrations (up to several hundred micrograms per litre) in drinking water have been associated with various internal cancers and with skin cancer. The effects of exposure to low doses of arsenic have not been addressed in many studies and results have been inconsistent. This cohort study was conducted to determine if individual exposure to low levels of arsenic in drinking water in Denmark is associated with a risk of cancer.

This study was based on the prospective Danish cohort Diet, Cancer and Health study in which 57,053 persons were enrolled between 1993 and 1997 living in one of 23 municipalities in the Copenhagen or Aarhus area of Denmark. At enrolment information was collected on diet, beverages, smoking, education, medical conditions, occupations, reproductive factors, body mass index and skin reactions to sun. Cohort members were followed up for cancer incidence using the population-based Danish Cancer Registry from the time of enrolment until the date of first cancer diagnosis, emigration, death or 1st August 2003, whichever came first. Cancers of the lung, bladder and colorectum and non-melanoma and melanoma skin cancers were included. Residential histories of cohort members were traced between 1970 and 2003 by record linkage to the Central Population Registry. Arsenic concentrations in Danish drinking water were obtained and the average arsenic concentration for each water utility was calculated between 1987 and 2004. Geographic information systems were used to link addresses with water supply areas. For each cohort member two exposure measures were calculated, a time-weighted average exposure and a cumulated arsenic exposure.

Of the cohort members, 56,378 persons were included who filled in the questionnaire, reported daily intake of tap water and had not had a cancer

diagnosis before enrolment. The time-weighted arsenic exposure of the cohort members calculated from 41 years of age up to the date of enrolment varied between 0.05 and 25.3 micro g/L with a median concentration of 0.7 micro g/L. The results with no adjustment for enrolment area showed no significant association between exposure to arsenic and risk for any type of cancer except for non-melanoma skin cancer, for which higher arsenic exposure was associated with lower risk. The incidence rate ratio (IRR) for non-melanoma skin cancer was 0.88 (95% CI, 0.84-0.94) per micrograms per litre increase in time-weighted average exposure. A similar pattern was seen for cumulated arsenic exposure with an IRR of 0.95 (95% CI, 0.92-0.97) for a 5-mg increase in exposure. Results adjusted for enrolment area showed virtually no effect for non-melanoma skin cancer, an insignificant inverse risk associated with melanoma skin cancer and a significantly increased risk for breast cancer in association with time-weighted average exposure to arsenic (IRR = 1.05; 95% CI, 1.01-1.10).

There were no statistical significant associations found between arsenic concentrations in Danish drinking water and the risk for cancers of the lung, bladder, kidney, liver prostate or colorectum. An inverse association was found between arsenic concentrations and risk for skin cancers, which suggests that arsenic might have a protective effect at low concentrations. The results also indicated that arsenic in drinking water might slightly increase the risk of breast cancer. The findings here should be interpreted with caution as more studies are required to confirm the results.

Atrazine**Atrazine exposure and breast cancer incidence: An ecologic study of Missouri counties.**

Hunter, L.D., Gadbury, G.L. and Huang, Y.-W. (2008) *Toxicological and Environmental Chemistry*, **90**(2); 367-376.

The triazine herbicide atrazine is extensively used and in the United States, with approximately 3.4 million kg applied to cropland annually. Numerous studies have implicated atrazine as an endocrine

disrupting chemical (EDC) and some epidemiological studies have associated atrazine exposure with breast cancer incidence. An ecological study of breast cancer incidence from 1996 to 2002 was conducted in Missouri where atrazine has been detected in treated drinking water, particularly in the northern section of the state.

The main source of exposure to atrazine was considered to be via drinking water in this study. During the study period the number of water tests of the public water supplies for each of the 115 counties was highly variable and water suppliers were not static. As there were changes in populations served from public water sources and a lack of data from private water sources, the combined acreage of corn and sorghum in each county was also used as a surrogate measure of probable atrazine exposure. Combined breast cancer incidence rates for 1996-2002 for each county were obtained and reported as age-adjusted to the 2000 standard population for all stages of breast cancer and invasive breast cancer alone. Median income was used as an indicator of socioeconomic status and percentage black race to account for differing racial composition of the counties. High parity in each county was determined using the incidence of women (per 100) giving birth who already had 4 or more previous live births for the combined years 1996-2002.

There were 19 counties classified as having high atrazine exposure and 25 as having low atrazine exposure. The mean concentration of atrazine for all the highly exposed counties was 1.3 micro g /L, which is well below the USEPA maximum contaminant level of 3 micro g /L. Linear regression analyses were conducted using covariates of median income, % black race and incidence of high parity. Models were generated using the rate of all stages of breast cancer (localised and invasive) and for invasive cancer alone. In the final model, high-parity predictor was statistically significant in the model for all stages of breast cancer ($p=0.018$) but not in the model for invasive cancer ($p=0.077$). The atrazine indicator was not statistically significant in either regression equation ($p=0.167$ for all stages and $p=0.371$ for invasive breast cancer).

In this ecological study the difference in breast cancer rates between counties classified as high in atrazine exposure and those classified as low atrazine exposure was not statistically significant. This does not rule out the possibility that such an association exists, however the authors note that studies of women where atrazine exposure is documented at the individual level have also not shown a significant association with breast cancer risks.

Cytotoxic Drugs

Do cytotoxic chemotherapy drugs discharged into rivers pose a risk to the environment and human health? An overview and UK case study.

Johnson, A.C., Jurgens, M.D., Williams, R.J., Kummerer, K., Kortenkamp, A. and Sumpter, J.P. (2008) *Journal of Hydrology*, **348**(1-2); 167-175.

This paper presents a preliminary risk assessment on the discharge of cytotoxic drugs (used for cancer treatment) via sewage treatment plants to water courses in the UK. The UK is particularly at risk of exposure, especially around urbanised catchments in central England which are densely populated with small rivers providing limited dilution. Over 50 cytotoxic drugs are used routinely for chemotherapy in developed countries, and the demand for chemotherapy treatment continues to increase at around 10% per year. The majority of cytotoxic drugs are highly water soluble.

A water quality model was developed for 5-fluorouracil (5FU) and its pro-drug capecitabine (metabolised to 5FU in the body) in order to assess the likely sewage effluent concentrations in the UK. 5FU is probably the cytotoxic drug used in the highest quantities in the UK. Health and Safety Executive (HSE) data for 2003 suggests that approximately 1 tonne of 5FU and 1.7 tonnes of capecitabine is used per annum in the UK, giving a combined value of 2.7 tonnes/yr. From a UK population of around 59 million people in 2003, a typical consumption value of 5FU of 125 micro g/day/head was calculated. An excretion value of 10% was assumed and no losses during sewage treatment. A 200L/head dilution in the STP was assumed and a further tenfold dilution in the river.

Predicted effluent concentration for 5FU and capecitabine combined was 62 ng/L as 5FU. The GREAT-ER model was used with the 125 microg/d/head input load to predict concentrations of 5FU in the Aire and Calder catchment in North Yorkshire (UK). This model estimates the distribution of chemicals in surface waters. Using the STP loading model described above and assuming no removal in sewage treatment or in the river, river water concentrations in the urbanised reaches of this catchment were predicted to contain 5-50 ng/L of 5FU during low flow, 90th percentile conditions. Currently there is little information on the effectiveness of drinking water treatment processes to remove these compounds.

Cytotoxic drugs will probably cause the same types of genetic damage in fish and invertebrates that they do in mammals. However the concentrations that will cause significant effects is still unclear. There may be an additive effect of a mixture of low concentrations of cytotoxic drugs which needs to be considered. In terms of human exposure, the authors estimate that daily intake of 5FU from drinking water would be at least 100 million-fold lower than a therapeutic dose, or at least 300 times lower than a precautionary threshold of toxicological concern. Further research is required with particular focus on predicted no effect concentrations for freshwater aquatic organisms; measurements to identify water concentrations of a range of relevant cytotoxic drugs in receiving water and where appropriate drinking water abstraction points; and efficacy of current drinking water purification techniques to remove the important cytotoxic drugs from river water.

Disinfection byproducts

Chlorination disinfection by-products and risk of congenital anomalies in England and Wales.

Nieuwenhuijsen, M.J., Toledano, M.B., Bennett, J., et al.(2008) *Environmental Health Perspectives*, **116**(2); 216-22.

Studies examining disinfection by-products and potential adverse reproductive health effects including low birth weight, spontaneous abortion, stillbirth and congenital anomalies have reported

inconsistent results. Most of these studies have had a small sample size and therefore low statistical power. This study is the largest study of its kind to report the relationships between trihalomethane (THM) levels in the public water supply and risk of congenital anomalies across England and Wales. The study area included 12 water companies in the United Kingdom. Areas supplied by each company were divided into water supply zones, each zone covering a population of less than 50,000 people. THM concentrations were used as the marker for chlorine disinfection by-products. Water samples were routinely collected and analysed from each water zone using random samples from consumer's taps. Modelling was used to calculate the mean annual individual THM concentrations for each water zone and to assign an estimated water source type to each water zone which was dependant on THM levels in four samples taken within each zone.

Information on congenital anomalies was obtained from the National Congenital Anomalies System, regional registries and the national terminations registry. There were 22,828 cases with congenital anomalies; 1,641 (7.2%) of these had a chromosomal defect; 2,249 (9.9%) were classified as having multiple (nonchromosomal) anomalies, and 18,938 (83.0%) were classified as having isolated anomalies only. A postcode to water-zone link was created using geographic information systems (GIS). Postcode of the maternal residence at the year of birth was used to identify the water zone of interest and assign the appropriate exposure status for each birth record. THM exposure was estimated for the first 93 days of pregnancy when birth defects occur in the developing foetus. The weighted average THM estimate associated with each birth record was categorised into one of three predefined exposure categories: concentrations of total THMs (TTHMs; less than 30, 30 to less than 60 and greater than or equal to 60 micro g/L), total brominated THMs (less than 10, 10 to less than 20, and greater than or equal to 20 micro g/L) and bromoform (less than 2, 2 to less than 4, and greater than 4 micro g/L).

After exclusions there were 2,605,226 births left for analysis, including live births, stillbirths and terminations. Analysis was conducted using fixed-

and random-effects models for broadly defined groups of anomalies as defined by ICD-9 or ICD-10 codes (cleft palate/lip, abdominal wall, major cardiac, neural tube, urinary and respiratory defects). The authors also defined a more restricted set of anomalies for analysis that were considered to be etiologically coherent and likely to have better ascertainment, and also analysed isolated and multiple anomalies. The data were adjusted for potential confounders including maternal age, socioeconomic status, year of birth and registry.

The mean TTHM concentrations ranged from 16.4 micro g/L in the low-exposure category to 72.2 micro g/L in the high-exposure category. Higher prevalence of each anomaly was found when the most deprived areas were compared to the most affluent areas. There was a U-shaped relationship found between prevalence of congenital anomalies and maternal age, except for neural tube defects (NTDs) where the prevalence decreased with increasing maternal age. There were no statistically significant trends across the three exposure categories for total THMs, total brominated THMs or bromoform for either the broadly defined or more restricted sets of anomalies. The only significant associations (p less than 0.05) for the broadly defined groups of anomalies was a reduced risk of abdominal wall defects in the high TTHM exposure category [odds ratio (OR) = 0.81; 95% confidence interval (CI), 0.68-0.95] and an excess risk of major cardiac defects in the medium (but not high) exposure category of total brominated THMs (OR = 1.12; 95% CI, 1.01-1.23).

When the restricted set of isolated anomalies was considered, statistically significant excess risks were seen for TTHM in the high-exposure category of ventricular septal defects (OR = 1.43; 95% CI, 1.00-2.04) and in the medium- (but not high) exposure category for congenital anomalies of the oesophagus (OR = 1.66; 95% CI 1.12-2.45). For bromoform, there was a significant excess in the high-exposure category for major cardiac defects (OR = 1.18; 95% CI, 1.00-1.39) and gastroschisis (OR = 1.38; 95% CI 1.00-1.92). There were no significant associations between TTHM exposure and any of the potential confounders. Analysis of cases with multiple

anomalies showed no significant association with THM concentrations, but the numbers were small.

The study found little evidence of a relationship between concentrations of THMs and a wide range of congenital anomalies. There were no statistically significant exposure-response trends seen across the exposure categories for any of the anomalies considered. The statistically significant excess risks found in this study may have been chance associations as there is still little or no toxicological evidence of reproductive or teratogenic effects of bromoforms or other DBPS. Also the concentrations of bromoform across the study regions were generally very low. The subset analysis of major cardiac defects, ventricular septal defects and gastroschisis may have increased the accuracy of the case definition and further study of these specific anomalies and bromoform exposure may be warranted.

Comment As noted by the authors the large sample size, carefully thought out case definitions and targeted exposure assessment in the first trimester gave strength to the study compared to other registry-based studies. However individual water exposures, many non-water risk factors, and mobility during pregnancy could not be assessed.

E. coli

E. coli as a public health indicator of drinking water quality.

Standridge, J. (2008) Journal / American Water Works Association, **100**(2); 65-75.

E. coli is one of the major bacterial inhabitants of the gut of healthy humans and other warm-blooded animals, and has long been used as an indicator of faecal material. Only certain variants of *E. coli* are capable of causing disease, the most significant of these is *E. coli* 0157 which has been responsible for several waterborne disease outbreaks. A dilemma for the public health community is the fact that *E. coli* has both pathogenic and harmless variants. Routine testing of water for *E. coli* is not designed nor intended to detect the pathogenic strains. Therefore the presence of *E. coli* detected as the result of

regulatory testing indicates faecal contamination but not imminent *E. coli* disease. Following such detections it is often incorrectly believed that the pathogenic strain has been detected and therefore action is required to deal with disease threats.

Most of the literature overwhelmingly supports the use of *E. coli* as the indicator of choice for protecting drinking water. This support for *E. coli* may in part be attributed to the inadequacies of total coliforms as ideal indicators. There has been international acceptance of *E. coli* as a drinking water indicator organism with Australia, the World Health Organization and the European Union all having undertaken comprehensive reviews in the past five years of the status of microbial drinking water indicators and concluding that total coliform testing should be abandoned and only *E. coli* should be used.

The US Department of Agriculture (USDA) and the US Food and Drug Administration (USFDA) have both promulgated rules that identify *E. coli* as the chosen indicator of faecal contamination. The US Environmental Protection Agency (USEPA) has conflicting statements in its rules on contamination testing. There are sections strongly promoting the value of *E. coli* testing along with sections strongly discounting its value. A negotiated rule-making process to amend the USEPA Total Coliform Rule (TCR) is now underway and one of the important debates will be whether to replace total coliform testing with *E. coli* testing for monitoring of public water systems.

One of the goals in choosing indicator organism for drinking water monitoring is that the indicator predicts not only the presence of faecal contamination but also the presence of other waterborne disease organisms. One of the reasons to continue total coliform testing is that it may indicate other nonfaecal microorganisms of potential health concern. As most nonfaecal pathogens found in water distribution systems come from biofilms and as coliforms can be associated with biofilms, it has been suggested that the presence of total coliforms may be a good indicator of nonfaecal pathogens. This premise requires careful consideration however. Coliforms may be present in a biofilm community

however they are not often the predominant organism. Biofilms may have few or no coliforms associated with them and therefore reliance on total coliform testing to detect biofilm occurrence would be risky in terms of public health and create a false sense of security. Specific testing for free-living pathogens of concern may be more appropriate.

E. coli generally fulfils the criteria for an ideal indicator for drinking water monitoring but it is not without flaws. If *E. coli* is used as the main indicator of drinking water quality then a commitment to educate the public to allay any concerns over the confusion of the indicator function and the rare occurrence of pathogenic strains is also needed.

Comment The issues discussed in this paper highlight the difficulty in trying to define any single microorganism as an "ideal" all-purpose indicator organism for drinking water. *E. coli* is an excellent indicator of recent faecal contamination in undisinfected water. Its presence in (supposedly) disinfected tap water indicates either disinfection failure or recontamination, however its absence does not guarantee absence of non-bacterial faecal pathogens (viruses and protozoa) nor absence of non-faecal pathogens.

Household Interventions

Difficulties in bringing point-of-use water treatment to scale in rural Guatemala.

Luby, S.P., Mendoza, C., Keswick, B.H., Chiller, T.M. and Hoekstra, R.M. (2008) American Journal of Tropical Medicine & Hygiene, **78**(3); 382-7.

Point-of-use water treatment has been shown to be the most cost-effective approach to reduce the number of person who do not have access to safe water. A flocculant-disinfectant treatment combining precipitation, coagulation and flocculation with chlorination has been developed for household use in developing countries. Two health outcome efficacy studies of this flocculant-disinfectant were conducted in Guatemala between 2001 and 2003. The first study found that children in households assigned to receive the flocculant-disinfectant had 25-29% fewer days of diarrhoea even though the use of the product was

suboptimal. The second study used a modified form of the flocculant-disinfectant with a lower dose of chlorine to improve taste. Those in households receiving the intervention reported 39% fewer days of diarrhoea compared to control households. Three weeks after the end of the second health outcome efficacy study, an intensive marketing campaign for the flocculant-disinfectant was conducted in the region. A single sachet of the flocculant-disinfectant sufficient to treat 10 L of water retailed for US\$0.14. Six months later the study population was investigated to assess purchase and use of the flocculant-disinfectant.

There were 462 of the 514 households in the efficacy study who completed a follow-up evaluation. All except one household reported using the flocculant-disinfectant at least once and 388 (84%) reported that use of the flocculant-disinfectant improved the taste of their water. However only 66 households (14%) reported using the flocculant-disinfectant in the preceding week and only 34 (7%) had bought the flocculant-disinfectant more than six times. Only 22 households (5%) met the criteria for active repeat use (reported purchasing the product within the last 2 weeks, using it within the previous week and having at least one unopened sachet in the household observed) and only 7 households (1.5%) had detectable chlorine in their drinking water. Of the 22 households that met the criteria for active repeat use, only 4 (18%) had detectable chlorine in their drinking water at the study visit. The only characteristics that were associated with becoming an active repeat user were a stated belief that the household's drinking water was dirty and a belief that the household drinking water made the family ill. However households that became active repeat users had a similar proportion of child days of diarrhoea during the study period in their households compared with household that did not become active repeat users (2.9% versus 2.7%, $P=0.73$).

The flocculant-disinfectant is largely effective in treating drinking water however there are multiple barriers to moving from technical efficacy to public health effectiveness in populations lacking access to safe drinking water. If these interventions are going to contribute substantially to reduce the number of

people whose drinking water is contaminated, then future research efforts are required to assess and improve the effectiveness and sustainability of large-scale point of use water treatment interventions.

Micropollutants

Health risks of micropollutants - the need for a new approach.

Fawell, J.K. (2008) *Water Science & Technology*, **57**(2); 183-87.

There have been an increasing number of micropollutants detected in water as the analytical capability to measure substances at low concentrations has increased. However, simply identifying micropollutants does not provide information regarding the risk to either aquatic life or human health. There is a need to begin to develop new approaches for determining just how important the risks from micropollutants are and to establish the priorities for controlling micropollutants.

The process of risk assessment requires knowledge of the key toxic effects of a substances and the dose response to determine a safe or acceptable level of exposure and to compare this with the actual levels of exposure. However, it is difficult to obtain a suitable assessment of overall exposure which is compounded by the increasing number of substances being identified and the problems of taking an adequate range of samples. It can also be difficult to find adequate data on the toxicity and the dose response. There is also an essential requirement for high quality data and for the scientific contribution to be completely objective. Scientists need to embrace a multidisciplinary approach for the identification of hazards and subsequent risk assessment; this will result in improved design of studies.

In the toxicological community there has been considerable interest on how to prioritise substances for further examination and testing. A methodology that has emerged is the "threshold of toxicological concern" or TTC. This approach involves determining a dose below which there is reasonable evidence that there will be no appreciable risk of adverse health effects. This approach provides a

good basis for prioritisation with regard to potential toxins, and has been used for establishing priorities for testing and further study of contaminants in food. It has been suggested that this is a way of determining whether there is a need for more detailed analytical and toxicological data for chemicals that may potentially leach from materials used in contact with drinking water.

The TTC concept considers chemicals under three structural classes. Class I: substances with simple chemical structures and for which efficient modes of metabolism exist, suggesting a low order of toxicity; Class II: substances which possess structures that are less innocuous than class I but do not contain structural features suggesting toxicity; Class III: substances with chemical structures that permit no strong initial presumption of safety or may even suggest significant toxicity or have reactive functional groups. Using toxicity data for well characterised chemicals, the generic TTCs derived for human exposure are 1.8 mg/kg per person per day for class I, 0.54 mg/kg per person per day for class II and 0.09 mg/kg per person per day for class III. This approach is suitable for most chemicals but for some substances (eg high potency carcinogens) a more conservative approach has been recommended, with a proposed threshold for regulation of 1.5 microg/day. For pharmaceuticals, comparison of detected levels with a 100-fold or 1000-fold fraction of the usual daily dose level provides a pragmatic threshold for triggering investigation, although again particularly toxic drugs may need a special approach. When considering implications of micropollutants for drinking water supplies, the removal of substances by water treatment processes is also relevant.

Volatile Organic Compounds

Chemical contamination of potable water in ship tanks.

Oldenburg, M., Huesing, U.P., Kalkowski, M., Baur, X. and Schleich, K. (2007) *International Maritime Health*, **58**(1-4); 79-91.

An increasing rate of problems relating to unpleasant odours from drinking water in newly built ships has been observed by the German Port Health Authority.

A suspected cause of such problems is leaching of solvent-based tank coatings (intended to protect against corrosion) due to the non-observance of required specifications, especially the drying periods. This study was conducted to explore the frequency of drinking water contamination by chemicals in a selected sample of vessels and to assess the effect of specific interventions to reduce these concentrations. Drinking water samples were collected and analysed for 22 different volatile halogenated hydrocarbons. This paper reports tests performed on 21 vessels between 2004 and July 2007 due to aromatic odours of the potable water. Water samples were either taken from the tanks (70.6%) or the galley (29.4%) depending on the accessibility of the ships water supply system. Microbiological quality tests (not specified) were also undertaken.

The vessels analysed ranged from 2 to 24 months of age. Unpleasant odours were mostly perceived by crew members within a few weeks of initial operation and often increased in stays in warmer climatic zones. The microbiological quality of potable water samples complied with German guideline values for drinking water. The guideline values (GVs) of chemical substances in drinking water were exceeded on five ships: Ship no 1 - xylene 770 micro g/l (GV 500 micro g/l), ethyl benzene 590 micro g/l (GV 300 micro g/l), vinyl chloride 0.6 micro g/l (GV 0.5 micro g/l); Ship no 2 - xylene 510 micro g/l, ethyl benzene 400 micro g/l; Ship 3 - xylene 860 micro g/l; Ship 4 - xylene 540 micro g/l; Ship 5 - benzene 1.0 micro g/l (GV 1.0 micro g/l). The highest chemical concentrations in ship tanks were found within the first 12 months after initial operation. Most other chemicals investigated were below the respective detection limit in potable water. In most cases chemical levels were reduced by complete discharge and ventilation of the tanks for at least 14 days.

This study showed that an aromatic odour in water supplies on newly built ships represents a potential hazard to the health of those on board due to chemical solvents. It is recommended that suitable codes of practice in the application of coatings need to be observed by water tank producers. Public Health officers, ship masters and other people responsible for health and safety on board need to be

aware of the problem and initiate appropriate surveillance and control measures if required. The authors make specific recommendations about remedial measures based on their experiences.

Water Hardness

Hard drinking water does not protect against cardiovascular disease: new evidence from the British Regional Heart Study.

Morris, R.W., Walker, M., Lennon, L.T., Shaper, A.G. and Whincup, P.H. (2008) *European Journal of Cardiovascular Prevention and Rehabilitation*, **15**(2); 158-189.

Studies published from 1956 to 2004 have generally suggested a protective effect of hard drinking water, in particular high calcium and magnesium intake against cardiovascular disease (CVD). In Britain water hardness varies greatly, with harder water in the south and east of the country and softer water in the north and west. Regional variations in mortality from CVD have been observed in the United Kingdom for many decades and it was noted almost 50 years ago that CVD mortality rates were lowest where water was the hardest. The British Regional Heart Study (BRHS) is a cohort study of men in 24 British towns with a wide variation in water hardness levels. Participants have been followed up for coronary heart disease (CHD) and CVD over 25 years. This study offers the opportunity to examine the relationship between water hardness and CVD.

From each of the 24 towns in the study a single general practice typical of the town's socio-demographic profile was chosen. A random sample of 400 men aged 40-59 years was taken from each age-sex register. Men were invited for a screening examination during 1978-1980 with 78% attending. At the time of screening, a single measure of water hardness, in calcium carbonate mmol/l equivalent was ascertained for each town. Information was also gathered regarding analytical results on water passing from various sources into the distribution system from relevant water authorities. Three drinking water samples (first draw, random daytime and flushed) were collected from a random sample of approximately 40 men selected from each town and

analysed for calcium and magnesium concentration as well as for water hardness. The mineral intake for each participant was based on calcium and magnesium tap water concentrations which were multiplied by a questionnaire estimate of tap water consumption (including consumption of water, tea and coffee at home and locally). Nurses visited each town between January 1978 and May 1980, and the height and weight of participants was measured and body mass index calculated. A serum sample was provided to measure nonfasting total cholesterol. A questionnaire was administered including questions on smoking habits, alcohol intake, physical activity and social class based on the longest held occupation.

All participants were followed up for major nonfatal and fatal CHD events (myocardial infarction including sudden cardiac death) and stroke through death registries and regular biennial review of general practice records throughout the follow-up period. Follow up for more than 25 years was available for mortality and until June 2004 for nonfatal episodes of CHD and stroke. There was data available for 7735 men on water hardness measures at the town level. There were 5796 men meeting the inclusion criteria for analysis of incidence of CHD or CVD. Of these, 998 experienced a major episode of CHD over the 25 years of follow-up (0.74 per 100 person-years); 564 of these episodes were fatal. There were 1371 episodes of CVD (major CHD or stroke). There were 721 men who were initially free of CHD who provided tap water samples. During follow-up of these men 126 events occurred (0.75 per 100 person-years).

Water hardness varied from 0.27 mmol/l in the town with the softest water to 5.28 mmol/l in the town with the hardest water. At the town level there was a weak inverse association between 25-year incidence of CVD and water hardness. However after adjustment for established cardiovascular risk factors there was no statistically significant association found for CVD. Statistical modelling was conducted using individual-level survival data and the hazard ratio (HR) for a two-fold increase in water hardness on 25-year incidence after adjustment for seven confounding variables. The relationships were found not to be statistically significant, especially for CHD

(HR 0.99, 95% CI, 0.94-1.04, $P=0.62$) and CVD (HR 0.96, 95% CI, 0.91-1.01, $P=0.083$). HRs were of similar magnitude for CHD mortality as for CHD incidence. No significant relationship was found for calcium intake with CHD incidence, CHD mortality and CVD incidence. A positive association was found for magnesium intake with incident CHD. After adjustment for confounding variables, the HR per two-fold increase was 1.10 (95% CI, 1.00-1.20), $P=0.045$. For CVD after adjustment the HR was 1.06 (95% CI, 0.99-1.14, $P=0.087$). No significant relationship was found for magnesium intake and CHD mortality. After subdividing magnesium intake by tertiles, the positive association did not display a dose-response relationship.

This long-term study does not provide evidence for an appreciable protective effect of any measure of water quality exposure at the individual level against CHD or CVD in general. The best estimate of CVD mortality reduction associated with a doubling of water hardness in this study was 4%. Therefore any protective effect is likely to be extremely small and of less importance to public health than the well-established cardiovascular risk factors such as high cholesterol and high blood pressure.

Water Treatment

Effect of pathogen concentrations on removal of *Cryptosporidium* and *Giardia* by conventional drinking water treatment.

Assavasilavasukul, P., Lau, B.L.T., Harrington, G.W., Hoffman, R.M. and Borchardt, M.A. (2008) *Water Research*, **42**(10-11); 2678-2690.

Previous studies have evaluated the removal of *Cryptosporidium* oocysts, *Giardia* cysts and other emerging waterborne pathogens during conventional drinking water treatment. However the spike concentrations used in these experiments were 6-8 orders of magnitude higher than those generally observed in natural waters. There is considerable uncertainty about pathogen removals that would be achieved under more realistic and much lower spiked pathogen concentrations as particle concentration may have significant impacts on particle separation kinetics. This study was conducted to compare the removal of *Cryptosporidium* oocysts and *Giardia*

cysts that were spiked at high initial pathogen concentrations and at more realistic concentrations and to describe removal as a function of spiked pathogen concentration. Also this study examined dependence of pathogen removal on other variables such as raw water quality (turbidity and temperature), alum dose and sampling method.

There were six experiments conducted from November 2004 to March 2007. The pilot plant received raw water from Lake Mendota in Madison, Wisconsin during all the experiments. *Cryptosporidium* and *Giardia* were not detected in the background raw water collected during any of the experiments. The pilot plant included two parallel treatment trains, one with a higher pathogen spike than the other. On each treatment train the raw water went through coagulation, flocculation and sedimentation. The raw water for each treatment train was spiked with a mixture of *Cryptosporidium parvum* oocyst and *Giardia lamblia* cysts. Initial pathogen concentrations ranged from 10^1 to 10^6 pathogens/L. There were a total of 9 locations sampled for each experiment. Two sampling methods were used (grab and continuous) for quantification of pathogens in the filter effluent.

To examine the effect of initial pathogen concentrations on log removal through conventional treatment, three grab sample results from each treatment train in the January 2005 experiment were used. Average *Cryptosporidium* oocyst log removals of 3.2 +/- 0.5 logs and 1.1 +/- 0.3 logs were achieved in the treatment trains with initial *Cryptosporidium* oocyst concentrations of 7.0×10^4 and 5.3×10^2 oocysts/L respectively. Average *Giardia* cyst log removals of 3.8 +/- 0.1 and 1.5 +/- 0.4 were achieved in treatment trains with initial *Giardia* cyst concentrations of 6.1×10^4 and 3.9×10^2 cysts/L respectively. At lower spike doses removal was about two orders of magnitude lower than at higher spike doses. The mean log removals in the train with the higher pathogen concentrations were significantly different at a 95% confidence levels from the mean log removals in the train with the lower pathogen concentrations (p -value = 0.03 and 0.01 for *Cryptosporidium* oocyst and *Giardia* cysts, respectively). The continuous sampling log removal

results for 30 h also showed lower pathogen removals at lower spike doses. For *Cryptosporidium* oocysts, conventional treatment was able to remove 2.6 logs and 2.2 logs when the respective spike doses were 7.0×10^4 and 5.3×10^2 oocysts/L. For *Giardia* cysts, conventional treatment was able to remove 4.3 logs and 3.1 logs when the respective spike doses were 6.1×10^4 and 3.9×10^2 cysts/L.

The initial oocyst concentration could explain 44% of the variance in the log removal data for *Cryptosporidium*. Multiple regression analysis was performed to assess whether any other explanatory variables were significant. For *Cryptosporidium*, log removal was associated with raw water turbidity (slope =0.5 and *p*-value less than 0.01) in addition to the initial oocyst concentration. Raw water turbidity and initial oocyst concentration explained 68% of the variance in log removal values, with higher log removal seen for higher raw water turbidity. For *Giardia*, multiple regression analysis showed that log cyst removal was a function of initial cyst concentration, raw water turbidity and sampling method. Raw water turbidity, sampling method and initial cyst concentration explained 73% of the variation in the log removal data whereas the initial cyst concentration explained 55% of the variation.

When grab sampling and continuous sampling were compared for determining *Cryptosporidium* removal, the mean log removal estimated for continuous sampling was 0.3-log higher than that calculated from grab sampling however the difference between grab and continuous sampling was not statistically significant with a *p*-value of 0.12. The mean log *Giardia* cyst removal calculated from continuous sampling was 0.6-log higher than that calculated from grab sampling. This difference was statistically significant with a *p*-value of less than 0.01.

Cryptosporidium oocyst log removal results were compared with *Giardia* cyst removal results based on continuous sampling from all six experiments. *Giardia* cysts were more readily removed than *Cryptosporidium* oocyst (*p*-value less than 0.01). The mean log *Giardia* cyst removal was 0.7 log higher than the mean log removal for *Cryptosporidium* oocysts. The higher level of *Giardia* cyst removal may be due to their larger size.

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