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Conference Report

Cryptosporidium: From Molecules To Disease

7-12 October 2001, Fremantle, Western Australia.

The conference, held in the port city of Fremantle near Perth, Western Australia, was attended by about 80 delegates from 10 countries. This event marked the follow up to the *Cryptosporidium in Water* conference held in Melbourne three years ago [(1)].

The conference was opened by Mr Gary Meinck of Water Corporation, representing the major sponsor, the Water Services Association of Australia. Other sponsors included the CRC for Water Quality and Treatment, GlaxoSmithKline, the American Water Works Association Research Foundation, Water Corporation, Murdoch University and the Australian Society for Microbiology. Mr Meinck highlighted the support of WSAA for research on *Cryptosporidium*, and more generally on water quality and health, through direct funding of research projects and also through its participation in the CRC for Water Quality and Treatment. Mr Meinck then handed over to the Chair of the organising committee, Dr Andrew Thompson of the Division of Veterinary and Biomedical Sciences at Murdoch University, who opened the scientific proceedings.

The conference sessions were organised into the following topics:

- Cryptosporidiosis - Aetiology, Infectivity and Pathogenesis
- Epidemiology and Species Differentiation
- Viability and Infection
- Cryptosporidium and the Environment
- Chemotherapy

The program for each day comprised a number of presentations providing a current perspective of the topic, followed by brief poster presentations on specific research projects. Several international

speakers were unable to attend, however they submitted electronic audiovisual presentations so that information from their most recent work was available to the conference. The proceedings closed with a synthesis session drawing together the major themes and conclusions. This report covers some aspects of the conference that are of particular relevance to the water industry. The Conference Proceedings will be published in 2002 [(2)].

Public Health - in developed nations, *Cryptosporidium parvum* is responsible for around 2% of gastroenteritis cases in the community, making it less common than other enteric pathogens such as *Salmonella* and *Campylobacter*. Public health concerns focus mainly on the potential for large outbreaks from sources such as drinking water and swimming pools.

While improved drug therapy for HIV infection has reduced the occurrence of severe *Cryptosporidium* infections in people with AIDS, this pathogen is now being recognised as an important cause of illness in severely immunocompromised children and others with primary or secondary immunodeficiency. In such hosts, the infection is often chronic and may spread from the intestine to other organ systems such as the respiratory tract, and become life threatening.

The importance of different infection sources for *Cryptosporidium* (eg drinking water, recreational water, food, person-to-person contact) is not known in most countries except in the case of recognised outbreaks where a source can sometimes be identified. However such outbreaks generally comprise a small proportion of all reported cases, and information on the sources of sporadic (non-outbreak) infections is needed.

A case-control epidemiological study to investigate sporadic cases is just beginning in the UK, and the results of two recently completed Australian studies were reported at the conference. The studies, carried out by the CRC for Water Quality and Treatment, examined risk factors for sporadic cryptosporidiosis in Melbourne and Adelaide. These cities were chosen as they represent opposite ends of the water quality and treatment spectrum for Australian cities; Melbourne has a highly protected surface water supply that is chlorinated but not filtered, Adelaide has poor quality surface water sources with full conventional alum treatment, filtration and chlorination. A range of potential risk factors for *Cryptosporidium* infection were investigated including drinking water, recreational water, selected foods, contact with animals, contact with sick people or with children, and overseas travel. Drinking tap water was not significantly associated with sporadic cryptosporidoisis in either city. The major risk factors identified were swimming in public pools and person-to-person contact.

Genotyping of *Cryptosporidium* - a range of methods have been developed to differentiate the two major genotypes of *C. parvum* and to distinguish between isolates within genotypes. Most published genotyping data comes from the UK, and confirms that the majority of human infections are attributable to genotype 1 or H (which appears restricted to humans) and genotype 2 or C (which readily infects humans, cattle, sheep and a number of other mammals).

A minority of human infections are attributable to other genotypes/species which appear similar to *Cryptosporidium* usually found in cats or dogs, or to *C. meleagridis* found in turkeys. These rare genotypes seem to constitute about 2% of *Cryptosporidium* infections in immunocompetent people, and a higher percentage in immuno-compromised groups. However some detection and concentration methods are selective for the two most common genotypes and the frequency of infection by other types may be underestimated.

The UK has established a nation reference collection of *Cryptosporidium* isolates which contains samples from about 60% of reported cases. The archive holds records of the clinical history of the isolates, and stores the faecal specimen and extracted DNA from oocysts. Isolates are being initially typed by PCR/RFLP (polymerase chain reaction / restriction fragment length polymorphism), then by other techniques such as microsatellite characterisation.

In the UK, genotyping has been useful to determine the source of some outbreaks. For example, a drinking water-related outbreak associated with an old pipeline which ran under agricultural land had initially been attributed to ingress of animal manure into the pipeline, however genotyping showed the organism to be of genotype 1, indicating a human source. Further investigations showed that septic tank outflow from a farm was contaminating the water supply pipeline.

Interestingly, the recent Foot and Mouth Disease outbreak in the UK has been accompanied by a drop in the total number of human *Cryptosporidium* cases reported, particularly for genotype 2. The outbreak resulted in restrictions in animal movement and public recreational access to the countryside, and it has been speculated that the reduction in *Cryptosporidium* cases is evidence that contact with farm animals is normally a major route of infection for the human population. Nevertheless, speakers emphasised that genotype 2 was transmissible between humans, and infection with this genotype did not necessarily signify an animal source.

A number of presentations were made on techniques for distinguishing isolates within the major genotypes. Some techniques are able to subdivide the major genotypes into a few subtypes, while others appear to discriminate down to the level of individual strains (eg - a common pattern in an individual cattle herd over time). Such markers may have an important role in elucidating routes of transmission and sources of outbreaks, but considerable work is needed to characterise the range of variations and temporal stability of each molecular marker system before their meaning can be reliably interpreted.

Taxonomy - there was discussion of the current taxonomy of *Cryptosporidium* and whether revisions to present species definitions were warranted or useful. It was broadly agreed there were sufficient grounds to propose establishment of a separate species for *C. parvum* genotype 1, given the number of genetic differences and demonstrable distinction in host range for this type. *Cryptosporidium hominis* was proposed as the species name.

Volunteer studies - human volunteer studies of the Moredun isolate have been carried out, the fourth genotype 2 isolate to be tested. This strain has an ID 50 (dose of oocysts required to produce infection in 50% of subjects) of approximately 300, placing it in the middle of the range of isolates tested to date. Comparison of clinical symptoms showed a more rapid onset of diarrhoeal symptoms, and more severe and prolonged symptoms than for other isolates. These observations once again emphasise that the infection process and the development and severity of illness among infected people are independent steps in disease causation. Work has also commenced on a volunteer study with a genotype 1 isolate but results are not yet available.

With respect to infection studies in both humans and animals, a number of speakers noted that chronic subclinical infections of *Cryptosporidium* may occur in some individuals, and that a range of environmental stresses may induce detectable shedding of oocysts. Therefore it was important in infection studies that the genetic characteristics of the shed oocysts were determined to check that they were from the inoculated strain and not from overgrowth of an unsuspected intrinsic infection.

NATA accreditation for pathogenic protozoa testing - an update was presented on the Australian laboratory accreditation program for detection of pathogenic protozoa in water developed by NATA in collaboration with WSAA. This program was different from most others in the water testing field because of the small number of laboratories involved, and the need to allow for the existence of a variety of methods. The program was developed by a working group of experts from Australia, the US and the UK. The major features of the program are:

- recognition of the spectrum of methods available
- specification of the qualifications of the supervisor and analyst
- audit of the process via a detailed checklist
- specified levels of quality control (QC)
- participation and satisfactory performance in an ongoing proficiency testing program
- transparency of reporting for sample results and QC results
- effective management of resources and capacity to ensure QC failure does not occur at times of peak workload

Achievement of NATA accreditation requires compliance with a 30-point checklist and perfect scores on two rounds of the proficiency testing program. Eight laboratories in Australia and three in New Zealand have been taking part in testing. To date, four laboratories have been accredited and four are working towards accreditation.

The results of the 6 rounds of proficiency testing conducted in 2000/2001 were also described. In each test round, laboratories were sent 5 x 10 litre samples of water spiked with 1-300 *Giardia* cysts or *Cryptosporidium* oocysts, or confounding organisms (algae or other protozoa resembling *Giardia* or *Cryptosporidium*). The spike consisted of gamma-irradiated or heat treated protozoa (to avoid infection risks), counted by flow cytometry. The water matrix

consisted of either tap water, reverse osmosis or distilled water, with QCMUD (concentrated filter backwash material free of protozoa) added to some samples to simulate poor quality raw water.

Laboratories are deemed to have "satisfactory" performance if they report between 10 and 110% recovery of spiked samples and no false positives in two consecutive testing rounds. Less than 10% recovery or false positive/negative results in one of two consecutive rounds is a "questionable" rating. If less than 10% recovery or false positive/negative result on two consecutive rounds are reported, the laboratory receives an "unsatisfactory" rating and suspension of NATA accreditation.

Over the 6 rounds of testing there was a general improvement in recovery rates for cysts and oocysts with *Giardia* recoveries averaging 40% and *Cryptosporidium* 30%, although recoveries were lower when QCMUD was present in samples. Some laboratories had less consistent performance than others, and these also tended to rate lower on assessor reports against the laboratory checklist. Accredited laboratories sometimes reported a poor result in a subsequent round of proficiency testing. While the amount of data is limited, it appears that the proficiency testing program is promoting improved accuracy and consistency in laboratory results.

Water treatment - continuing research on UV treatment with different *Cryptosporidium* isolates has confirmed a high degree of oocyst inactivation as determined by animal infection experiments. However two speakers noted that occasionally a batch of UV-treated oocysts would show unexpectedly high infectivity, suggesting the possibility of either UV resistance or recovery from damage. The reasons for this are unknown.
Australian work on the Miox system (mixed oxidants) has failed to demonstrate a reduction in infectivity as previously published by US workers. It is understood that the US researchers have not been able to replicate their original results, and therefore the Miox system may not reliably produce appreciable amounts of ozone (to which the killing effect was attributed).

Animal sources of oocysts - virtually all animal species ever tested have been reported to carry some variety of *Cryptosporidium*, however *C. parvum* genotypes 1 and 2 are undoubtedly the main causes of human infection. More genotyping data on human infections is needed to determine whether other genotypes (eg the marsupial genotype found in many Australian native animals) can readily infect people.

In considering the impact of different animal species in the catchment, behavioural factors are likely to be important for waterborne risks; most wild animals are cautious of predators in the vicinity of water sources and seldom remain longer than necessary to drink, in contrast domestic animals will remain longer and are more likely to defecate in or near the water. The consistency of faecal material may also be relevant; faeces which are relatively dry (eg from kangaroos) are less likely to be washed into water courses than faeces of soft consistency (eg from cattle).

In Canada a number of incidents have occurred where high numbers of oocysts were detected in water supplies without apparent impact on human health. One suggested explanation is that the spring snow thaw releases large faecal deposits from migratory birds, contaminating water supplies with oocysts which are not infectious for humans.

Detection methods - the technical difficulties inherent in measuring low numbers of *Cryptosporidium* oocysts and the lack of quality control descriptions in most published work were highlighted. While it is now accepted practice to use low doses (around 100 oocysts) for spiking controls, there is little appreciation of the critical effect of measuring the spiked dose accurately. Errors in spike measurement can greatly affect the calculated recovery rate as this is denominator from which the recovery is calculated.

Both haemocytometers and well slides tend to produce fewer oocysts in the spike than intended and have wide variability, leading to overestimation of recovery rates. Only flow cytometry can produce accurate spikes with a low range of variation. Considerable variations in recovery rates are observed between repeat samples even with experienced analysts and laboratories, and this is further compounded by matrix effects in natural water samples.

Given the many sources of error in calculation of recovery rates, imposition of water quality regulations and treatment requirements on the basis of scant numerical data is of dubious scientific validity and may be open to legal challenge. The use

of internal controls of labelled oocysts such as ColorSeed™ was advocated as the best means to measure recovery rates, account for matrix effects and provide comparability of results, while also reducing the need for external QA schemes.

Cell culture for viability testing - cell culture-PCR (CC-PCR) in human cell lines is seen as a desirable alternative to animal testing due to the lack of a suitable animal model for genotype 1 strains, and the logistical and ethical difficulties of animal experimentation. Work carried out in a number of independent laboratories supports the correlation between infectivity of genotype 2 oocysts in mice tests and infectivity in CC-PCR. Studies on UV-treated and ozone-treated oocysts have shown that the decline in viability in the CC-PCR system parallels that observed in mice, supporting the validity of the CC-PCR test system. Equivalent work on genotype 1 has not been performed because of the difficulty in obtaining large quantities of oocysts.

An international collaborative effort to develop a proficiency testing program for cell culture has been undertaken by a consortium of organisations including EPA and AWWARF (US), DWI and UKWIR (UK), WSAA (Australia) and KIWA (Netherlands). The aim is to develop a standardised method with known reproducibility between laboratories and well characterised limitations. The second stage will involve use of this method to assess UV inactivation of oocysts under realistic water treatment conditions. The response to the invited tender process for testing laboratories to take part in the program has been low, and the advisory group will review the process before deciding on further action. Comments from conference delegates indicated that no Australian laboratories had been invited to tender although some have cell culture capability, and most were unaware that the tender was occurring. The terms of the tender were also felt to have been too restrictive, particularly in requirements for laboratories to be already undertaking a large number of *Cryptosporidium* tests on a regular basis. This was not a realistic expectation except in countries where testing was mandatory.

(1) See Health Stream Issue 12 for a report on the 1998 Cryptosporidium Conference.

(2) The 2001 conference proceedings will be published by Elsevier.

Disinfection Byproducts and Health Effects Seminar

29 October 2001, Melbourne.

The seminar was opened by Professor John McNeil, Program Group Leader of the Health and Aesthetics Program of the CRC for Water Quality and Treatment. After welcoming the delegates, he noted that the seminar and subsequent 2-day workshop were part of the research program development process undertaken by the CRC following the renewal of federal government funding support to the Centre until 2008. The seminar was co-sponsored by the Water Services Association of Australia.

Professor McNeil outlined the historical significance of drinking water chlorination as a major advance in public health, leading to a substantial reduction in deaths and illnesses from waterborne pathogens. The discovery of disinfection byproducts during the 1970s led to concerns over the potential health effects of these chemicals, and stimulated investigations of their chemical and biological properties. This seminar would summarise current knowledge on DBPs and recent developments in research.

The first speaker, Professor Steve Hrudey (Dept. of Public Health Sciences, University of Alberta), noted that DBPs were first described at a time when public concerns had already been raised by the detection of trace amounts of industrial chemical pollutants in water supplies. While DBPs had undoubted been present since the introduction of water chlorination, their existence was not suspected because analytical methods involved chloroform extraction, thus masking the presence of trihalomethanes (THMs).

DBP research initially focused on THMs and has largely followed the pattern of identifying contaminants by analytical advances then looking for health effects that might be associated with them. The availability of analytical techniques for volatile compounds has led to a concentration of efforts on DBPs of this nature, and there has been a strong tendency to focus on chlorine-containing DBPs as posing a potential health risk. However the chlorination process produces a large range of byproducts, many of which do not contain chlorine, and there is no scientific justification to assume that the presence of chlorine (or other halogen) in a DBP molecule is a necessary requirement to produce adverse health effects.

Professor Hrudey outlined the properties of the known classes of DBPs, the influence of water parameters on their formation, and effectiveness of water treatment processes on DBP reduction. While several hundred DBPs have been identified, many more remain unknown. Mass balance calculations indicate that the known halogenated DBPs comprise less than half the total halogenated organic material in chlorinated water. The amount of unidentified non-halogenated DBPs cannot be estimated as no mass balance calculation can be performed. Major gaps in knowledge exist about the properties of the more water soluble, non-volatile and heat labile components of the DBP mixture. The odours associated with chlorinated water (and often attributed to free chlorine levels) may in many instances be due to DBPs. Human exposure to DBPs in drinking water may occur by ingestion, inhalation or dermal absorption. The relative importance of these three routes for a given DBP will depend on its hydrophilic or lipophilic properties, volatility and thermal stability. For most DBPs, little information of this nature is available to aid exposure assessment.

Efforts to reduce DBP exposure in order to reduce the risk of potential adverse health effects have focused on regulation of THM levels. However, as different classes of DBPs may be formed from different organic precursors, and formation is also dependent on temperature, pH and other variables, a reduction in THMs may not be accompanied by a reduction in all other classes of DBPs. The DBPs formed by chlorination have been most extensively studied, but all chemical disinfection process must by their nature form DBPs of some kind. Professor Hrudey noted that UV irradiation is also likely to produce some byproducts as it has the capacity to induce chemical changes in biological materials such as DNA and RNA molecules.

Regulation for THM levels in water supplies have been derived by different methods by different authorities. The US EPA has used the linearised low dose model which assumes a no-threshold mode of action for carcinogenesis, however toxicological evidence on the mode of action of chloroform indicates that a threshold model is more appropriate. The Australian Drinking Water Guidelines level for THMs is based on a No Observed Adverse Effect Level from animal studies, coupled with a safety factor of 100-fold.

In reviewing progress on the study of health effects, Professor Hrudey noted that available data on DBPs is almost entirely restricted to what drinking water regulations require to be monitored (generally only THMs). Retrospective epidemiology can only test causal hypotheses using available monitoring data for assessing exposure, however it is now clear that the DBPs being measured for regulatory purposes are not sufficiently toxic to account for the proposed health effects. The paradox remains that epidemiological studies with meaningful exposure assessment are needed to resolve the question of health effects, however the chemical(s) to which we must measure exposure have not yet been identified.

The second speaker, Ms Samantha Rizak (Dept. of Epidemiology and Preventive Medicine, Monash University), outlined the need to understand DBPs in water supply systems in order to improve exposure assessment and develop rational regulations. Concerns over possible effects of DBPs on reproduction have shifted the temporal scale of exposure assessment from the chronic exposures relevant to cancer risks to acute exposure windows and the potential effect of peak exposure levels.

The formation and evolution of DBPs in distribution systems is not well understood due to the complexity of chemical reactions which may occur. Factors influencing the formation of DBPs include water distribution and storage system hydraulics, pH, water temperature, the nature and concentration of NOM, and chlorine residual.

There are significant spatial and temporal variations in THM concentrations in the distribution system. Spatially, an increase in THM concentration of 3 to 4-fold with increasing residence time is typical. However there is wide variation across the distribution system and the increase is not always directly correlated with total residence time. Temporally, THM concentrations may vary significantly on an hourly, daily, or seasonal basis. THM levels are generally much higher in summer than in winter due to increases in both water temperature and precursor concentrations. Other important parameters influencing THM levels include pH (higher concentrations at higher pH) and persistence of chlorine residual. Similar trends have been reported for THMs formed by ozonation, and chloramination.

Haloacetic acids (HAAs) are generally the second predominant class of DBPs found in chlorinated drinking water, although their levels may sometimes exceed those of THMs. There is some evidence to suggest HAAs exhibit different spatial and temporal variations than THMs. The correlation between HAA levels and residence time is inconsistent, and it has been suggested that decreases in HAA concentration with increasing residence time seen in some systems are due to biological degradation and/or photo-degradation. HAA concentrations tend to increase with increasing temperature but seasonal differences are not as apparent as with THMs.

Haloacetonitriles, haloketones, chloropicrin and chloral hydrate are present at lower concentrations and there has been limited research on these classes of DBPs in the distribution system. Generally they have been reported to form rapidly upon chlorination but then level off or further degrade through distribution system, and have also been reported to diminish at high pH.

THMs are often used as a surrogate for other DBPs in estimating exposure, however in order for THMs to serve as a viable surrogate measure they must be correlated with these other DBPs after formation and must follow similar patterns of change in the distribution system. If correlations are poor this will lead to inaccurate exposure classification.

Examination of correlations between THM and HAA levels at the treatment plant and in the distribution system of two Canadian drinking water systems illustrated the importance of assessing the individual water supply system under study. For one system strong correlation was found between THM levels and HAA levels at both the treatment plant and the distribution system, however for the other system correlation was very poor. A study in the UK assessing correlations between total THM concentration and levels of individual THMs found that correlation ranged from high to extremely poor. These findings highlight the importance of site-specific analysis to understand the characteristics of the individual water supply system in order to accurately evaluate exposure to DBPs

Dr Martha Sinclair (Dept. of Epidemiology and Preventive Medicine, Monash University) provided a summary of epidemiological methods for assessing the health effects of DBPs then outlined the evidence relating to DBPs and cancer risks. A range of epidemiological study designs exist, and these differ in complexity, the rigour of their design, cost, and in the strength of evidence yielded by the study result. In assessing the findings it is important to consider the limitations intrinsic to the design, as well as the strengths and weaknesses of the individual study such as the accuracy of measurement for exposures and health outcomes. Epidemiological studies can provide evidence of association but can not prove a causative link between an exposure and disease. The issue of causation is a complex one, and a substantial and consistent body of scientific evidence is needed before a causal relationship can be established.

The study of health effects of DBPs has followed the usual pattern for environmental hazards; beginning with low cost hypothesis-generating ecological studies, then progressing to more complex analytical investigations with case-control and cohort studies. Early studies of cancer risk used cancer mortality as the outcome measure, however this may be a poor indicator of cancer incidence as mortality is influenced by availability of diagnosis and access to treatment. The results were variable, with some studies reporting associations between DBP exposure and mortality from bladder, colon or rectal cancer, while others did not.

Improvements in design were incorporated in later studies including the use of residential history to assess exposure to water sources, adjustment for confounders such as smoking, and use of cancer incidence instead of mortality statistics. Some studies also used THM levels recorded by water companies to assess exposure levels, rather than comparing types of water treatment (eg chlorinated vs unchlorinated supplies).

Despite improvements in methodology which should have provided more accurate exposure assessment, the results for colon and rectal cancer studies remain rather inconsistent. For bladder cancer, more consistently positive associations have been seen. However there have also been some contradictory or unexpected observations, and studies which have been able to assess dose-response relationships have shown inconsistent results.

While the epidemiological evidence seems to suggest an association between bladder cancer risks and DBP exposure, current toxicological data do not provide

support for this hypothesis. None of the DBPs characterised to date have been observed to produce bladder cancer in animal studies, and thus there is no known biological basis for increased risk for this type of cancer. For other cancers, animal studies have shown that exposure to high levels of some DBPs can cause colon or rectal cancers. However extrapolation of the cancer risk to the low levels of exposure seen with drinking water produces estimates very much lower (up to one million-fold less) than the cancer rates suggested by epidemiological studies.

Three possibilities need to be considered when assessing the continuing lack of clarity in the evidence for the association between DBP exposure and cancer risks.

1. That the observed associations are due to bias and confounding and they are not a real effect of water supply.

The comparisons made in non-randomised epidemiological studies assume that all important extraneous factors affecting disease outcome have been identified, measured and adequately adjusted for in the analysis, so that differences in DBP exposure levels are the most probable reason for any observed difference in health outcomes. However the possibility exists that residual confounding may still occur despite such efforts.

2. That the observed association represents a real effect of a water component other than DBPs.

In most epidemiological studies the water supplies being compared almost certainly differ in other components as well as DBP levels. If these other unmeasured components affect cancer risks, then an effect of DBP exposure may be erroneously inferred.

3. That the observed association represents a real effect of a DBP (or DBPs), but occurrence of this causative substance does not correlate well with the prevailing measures of DBP exposure.

Exposure assessment in epidemiological studies has been based on crude measures of water treatment type or THM levels, and water supplies classified as similar on this basis may in fact differ markedly in their DBP profiles. If the putative cancer-causing DBP(s) has a different occurrence pattern to THMs, then exposure classifications would be subject to considerable error, leading to inconsistent results in epidemiological studies.

On present evidence the existence of a causative link between DBPs in water supplies and elevated cancer risks remains unproven. However if such a link exists, it may represent a significant public health burden of avoidable disease and mortality. There is a need for further epidemiological research on this topic, but simple repetition of past methodology is unlikely to produce resolution of the issue.

Dr Mark Nieuwenhuijsen (Imperial College of Science, Technology and Medicine, London) provided an overview of studies on the reproductive effects of DBPs. This is a relatively recent area of concern with publications covering the last decade. A wide range of reproductive outcomes have been examined in relation to DBP exposure including congenital malformations (neural tube defects, cardiac defects, respiratory cleft, and urinary tract defects), spontaneous abortions, still birth, pre-term delivery and low birth weight.

Exposure assessments in early studies were based on crude comparisons such as water source and type of treatment, while later studies have used routinely collected THM data with or without measures of personal water consumption or other water-related behaviours. A few studies have used water colour as a surrogate for DBP levels. When considering the studies done for each type of outcome there has been little consistency in methods, with different cutoff levels being used to classify DBP exposures, and the "high" levels of exposure in some studies have overlapped with "low" levels in others. Exposure assessments have generally not included estimates of individual water consumption and few studies have given any consideration to exposure via inhalation or dermal absorption.

Overall, there have been only a small number of good studies, and apparently inconsistent results. The small sample size and small number of cases in many studies has led to reduced statistical power, as has categorisation of outcomes leaving very small numbers of cases in each group. Only a limited number of confounders have been assessed, particularly for studies using routinely collected data from perinatal registries.

Case ascertainment for reproductive outcomes is not always straightforward, for example spontaneous abortion can not usually be measured from routinely collected health data, and failure to account for

elective pregnancy terminations will affect measured rates of congenital malformations. Grouping of congenital malformations into only a few major categories is inappropriate as these conditions are generally heterogeneous with respect to both phenotype and presumed cause.

Exposure assessment in reproductive studies has been limited mainly to THMs, and has not taken into account the considerable degree of temporal and spatial variability in THMs within water zones. Thus the exposure level assigned to each pregnancy may have substantial inaccuracy. Most studies have also not considered the possibility of residential mobility during pregnancy, nor exposure to water sources outside the home. Lack of individual data has also meant that use of private water supplies, bottled water or boiling of water before drinking have not been included in exposure assessment.

In summing up, Dr Nieuwenhuijsen concluded that current epidemiological evidence on reproductive outcomes and DBP exposure was generally inconsistent and inconclusive. There is a need for well designed analytical studies, with good case ascertainment, inclusion of relevant confounders, sufficient statistical power and in-depth exposure assessment. As a prerequisite for such studies, methods of exposure assessment need to be substantially improved. Efforts in this area need to address the spatial and temporal variability of DBPs in the distribution system, and the validity of using selected DBPs as surrogate measures of exposure to others. To determine individual exposures, better instruments are needed to assess water consumption and other water uses, and to identify the main determinants of exposure and uptake.

Dr Richard Bull (MoBull Consulting /Washington State University) noted that in considering future directions for DBP research, elevation of cancer risks has the greatest weight of evidence and the largest potential public health burden if a causal relationship with DBP exposure truly exists. However toxicological evidence indicates that the most prominent chlorinated by-products (chloroform, trichloroacetate, dichloroacetate) are not likely to be causal for these endpoints.

The almost exclusive focus of DBP research and regulation on halogenated products to the neglect of non-halogenated compounds can no longer be justified. The limitations of this approach have been demonstrated by the recent finding that levels of the potent non-halogenated carcinogen N-nitroso-dimethylamine (NDMA) may be higher in water supplies treated by chloramination than in those treated by chlorination. Other carcinogenic nitrosamine-like compounds may be formed if the source water contains secondary amines. It is open to speculation whether switching from chlorination to chloramination to achieve a reduction in THM levels may have the effect of increasing cancer risks by formation of nitrosamines rather than decreasing risks as is the intent.

While the major research focus to date has been on screening and identification of DBPs and potential risks, efficient resolution of the cancer issue requires a hypothesis-driven approach within a qualitative and quantitative framework. This new strategy needs to recognise that DBPs are complex mixtures, and that the properties of both the disinfectant and the source water (bromide concentration, pH, ammonia and total organic carbon) will determine the composition of the mixture formed. Rather than simply classifying DBP exposure in epidemiological studies as high or low, there is a need to consider how the components of the DBP mixture may relate to different health risks.

Toxicology can contribute to resolving health issues through characterization of exposure (in particular the use of pharmacokinetics to characterise exposure at the target organ), provision of evidence on health endpoints identified by epidemiology (such as defining the probable key events leading to cancer, or providing evidence of mechanisms of action from animal studies), and exploring the possible role of genetic susceptibility.

In closing, Dr Bull reiterated that the major question requiring resolution is whether the bladder cancer risk apparently associated with DBP exposure is real. Nitrosamine formation may provide biological plausibility for carcinogenesis, but as yet it is not known whether NDMA or other nitrosamines occur widely in drinking water supplies. The role of organic nitrogen precursors in DBP formation is worthy of further investigation. Ongoing research should build on what we know, with a more creative use of epidemiology and better characterization of differences in DBP profiles between systems.

Better focus is also needed in the use of toxicological tools, with more full characterization of modes of action. Issues of susceptibility also need to be addressed more broadly. Resolution of this issue needs careful, hypothesis-driven studies of mixtures and interactions on meaningful endpoints.

Dr Ken Froese (Dept. of Public Health Sciences, University of Alberta) provided an overview of the development of analytical methods for DBPs and described new developments in this field. DBP analysis techniques have been largely based on GC-MS (gas chromatography-mass spectroscopy) with a consequent emphasis on volatile and semi-volatile compounds.

There are a range of validated routine methods for DBP analysis, and these are largely adequate for regulatory monitoring purposes for a handful of well characterised target compounds, but mostly inadequate for identifying and characterising unknown compounds. Routine methods and monitoring programs based on regulatory requirements are also inadequate for exposure assessment for both epidemiological and toxicological studies. There is a need for the ability to analyse a broader range of DBPs using faster, more sensitive techniques.

Quantitative exposure assessment of DBPs faces several challenges:

- there are three major routes of exposure (ingestion, dermal absorption and inhalation)
- exposure sources are complex and varied (different water uses and locations of exposure)
- DBP profiles (relative ratios) are likely to change with different exposure routes
- potential confounders (eg sources of DBPs other than water) are not well characterised
- human pharmacokinetics are not characterised for the wealth of DBP compounds and mixtures which are known to exist
- little is known about the metabolites of DBPs

Given the difficulty of measuring exposure from multiple routes, efforts have been made to develop biomarkers which give an indication of the internal dose in the body. THMs in blood have a short persistence, and largely reflect inhalation and dermal exposure since ingested THMs are removed from the blood stream on the first pass through the liver. Haloacetic acids (HAAs) have also been investigated, and trichloroacetic acid (TCAA) has been found to be a promising biomarker of ingested dose. TCAA is non-volatile and polar, and does not appear to be significantly absorbed through the inhalation or dermal routes of exposure.

The use of biomarkers in large epidemiological studies poses a number of logistical problems. The use of HAA as a biomarker in a reproductive epidemiology study involving 2000 couples, with two biological samples per person and samples of home and workplace water is likely to require analysis of over 11,000 samples. It has been estimated that this would require funds of US $2 million and 2 years of analysis time using conventional GC-MS methods. A number of alternative analytical techniques are available, but these also require significant processing time or expense. Therefore, the limitations of current analytical methods are likely to preclude their use for individual exposure assessment in large scale epidemiological studies.

Dr Froese then described a recently developed analytical method called ESI-FAIMS-MS. This novel analytical technique combines direct injection electrospray ionization mass spectrometry with ion separation based on gas-phase ion mobility in an electric field. The technique is based on differences in ion mobility in low versus high electric fields, and was developed by Guevremont and co-workers at the Institute for National Measurement Standards, NRC, Ottawa. The ESI-FAIMS-MS technique offers the ability to rapidly separate and assay a wide array of compounds including DBPs, and to differentiate structural isomers. The technique does not require a derivatisation step and reduces sample preparation and analysis time to 5 minutes per sample. ESI-FAIMS-MS also has reduced background and sensitivity 10 to 1000-fold greater than direct ESI-MS techniques. The ESI-FAIMS-MS equipment is still in the prototype phase, but this new methodology appears to hold great promise for rapid and sensitive analysis of DBPs and other chemicals of environmental concern. The availability of such a method would make larger scale epidemiological studies on DBPs more feasible.

A full report on the DBP seminar and subsequent workshop will be available as a CRC Occasional Paper early in 2002.

Book Review

Water Quality: Guidelines, Standards and Health

Assessment of risk and risk management for water-related infectious disease. WHO Water Series, 2001.
ISBN 1 900222 28 0 (IWA Publishing)
ISBN 92 4 154533 X (World Health Organisation)

This publication comprises a series of expert reviews on the relationship between water quality and health, and a range of factors relevant to the development and implementation of effective, affordable and efficient water quality guidelines or standards suitable for local needs.

The book begins by summarising the World Health Organisation's harmonised approach to the management of infectious disease risks from drinking water, recreational water and wastewater use. Under this approach, WHO will implement a common framework for the assessment and management of microbiological health risks, and the development of guidelines in all three areas of water use.

A relatively new concept outlined in the book is the use of the DALY (Disability-Adjusted Life Year) to estimate the effects of waterborne diseases and relate them to the health effects of other types of illness. The DALY is designed to be a common measure for examining diverse health outcomes and was used by WHO in its Global Burden of Disease project, first published in 1996.

The DALY is a means of measuring the impact of disease in terms of the gap between the current health state and the target of an ideal health state. The DALY value for a given disease is estimated from the number of years of life lost due to the disease, and the number of years lived with disability as a consequence of the disease. Disability is measured in three domains; the physical, the psychological and the social. This process results in an average "severity weight" being assigned to each condition, with a value of 0 representing no disability, and 1.00 representing death.

The applicability of the DALY to different types of disease outcomes permits the comparison of cancer risks from chronic exposure to chemicals in drinking water to the risks from acute exposure to microbial pathogens. This approach has already been used to compare the reduction in risk from *Cryptosporidium* infection due to ozonation of water supplies, to the increase in renal cell cancer from bromate formation as a consequence of ozone treatment. This case study indicated the DALY benefits from reducing the *Cryptosporidium* risk were more than ten-fold higher than the DALY burden from additional cancer cases.

The authors also call for health authorities to adopt a broader approach to the regulation of microbiological water quality. WHO guidelines for drinking water have always placed importance on the sanitary integrity of systems, coupled with the measurement of faecal indicator bacteria as a check for contamination. However most national regulations are founded primarily on measurement of indicator bacteria, with relatively little attention to system management aspects. This strategy may not be effective to protect public health, and tends to orient management considerations towards meeting the numerical regulatory limits rather than taking a more holistic, preventive approach.

The chapter on management strategies discusses the importance of considering the entire system and the multiple sources of microbial contamination which exist. For optimum public health protection a multibarrier, preventive approach is advocated, with management of hazards as close as possible to their source. The application of the HACCP (Hazard Analysis Critical Control Point) system to water supplies is outlined, and case studies for drinking water and recreational water are presented.

In addition to chapters on the scientific aspects of waterborne disease causation, measurement and prevention, the book includes useful discussions of the broader social, economic and political factors influencing the development of guidelines/standards. The concept of acceptable risk is discussed and various models for decision-making are described. While noting that choices in this area are necessarily based on location-specific values and priorities, the authors make a number of recommendations for a multi-disciplinary group process approach.

The role of public health is highlighted as providing a holistic viewpoint which allows waterborne disease risks to be placed in context with other influences on population health. Similarly the costs and benefits of interventions to reduce waterborne disease must be judged against other measures to improve public health and competing resource priorities.

News Items

US announces arsenic limit
The US governement announced on 1 November that the new standard for arsenic in drinking water would be set at 10ppb. The decision follows a review of the level proposed by the previous administration, and delivery of three new reports on different aspects of the proposed standard (reported in Health Stream Issue 23).

Bangladesh to sue over arsenic wells
It has been reported that a London law firm is preparing a group action suit on behalf of Bangladeshi villagers affected by arsenic contaminated tubewells built by the British Geological Survey. Many of the wells, dug in the 1980s and early 1990s, were contaminated by naturally occurring arsenic, exposing villagers to a range of health risks. According to a November 21 report in *Nature*, the law suit will contend that the BGS should have been aware of potential arsenic contamination of groundwater because of research in the nearby and geologically similar region of West Bengal, India during the 1980s.

Report on Battleford Crypto outbreak
Health Canada has released a report on the waterborne cryptosporidiosis outbreak in Battleford and North Battleford, Saskatchewan in April this year. It was estimated between 5800 and 7100 residents, and several hundred visitors, became ill during the outbreak. The outbreak was attributed to failure to reestablish correct operation of a solids contact unit at the surface water treatment plant after maintenance. As a result, particulate matter was not effectively removed, and finished water turbidity rose from 0.2 NTU to 0.4 to 1.0 NTU. Chlorination levels were normal and microbiological water quality (E. coli, coliforms) was in compliance with standards.

The towns are supplied by a mix of surface and groundwater, and the geographic distribution of cases matched the relative proportion of surface water in the system. The report mentions that preliminary genotyping results on clinical specimens suggest the contamination arose from human sewage rather than animal sources. It is also stated that *Cryptosporidium* oocysts were found in finished water samples during the investigation but no further details are given in this report.

From the Literature

Arsenic

A sustainable community-based arsenic mitigation pilot project in Bangladesh.
Anstiss R, Ahmed M, Islam S, Khan AW, Arewgoda M. Int J Environ Health Res (2001) **11**(3) p267-274

The town of Chapainawabganj in northwest Bangladesh was chosen as the location for a pilot arsenic mitigation project. Arsenic concentrations in and around the town have been found to be as high as 2.4 ppm with many samples above 0.05 ppm, the Bangladesh permissible limit. The results of the first 22 months of the pilot project are reported here.

The arsenic removal process was based on adsorption by ferric oxyhydroxide in a household water treatment system. Four families agreed to participate and use the systems for all drinking and cooking water. The untreated well water contained 0.932 ppm arsenic. During use the arsenic concentrations in the de-contaminated water increased as the ferric oxyhydroxide became more saturated until it was replaced in a 16-day cycle. Arsenic concentrations in treated water increased from 0.001 ppm on the first day of the cycle to 0.047 ppm on the 16thday.

There is anecdotal evidence of reduced gastrointestinal problems and skin effects in those consuming the de-contaminated water. The technical mechanism used here is flexible and can be scaled up or down for different water volumes, cycle lengths, and different tubewell arsenic concentrations and chemistries. An expansion of the project including a coordinated health monitoring program is planned.

Campylobacter

Thermophilic campylobacters in surface water: a potential risk of campylobacteriosis.
Rosef O, Rettedal G, Lageide L. Intern J Environ Health Res (2001) **11**(4) p321-327

Campylobacters are often found in water and water supplies and have been responsible for many outbreaks in countries including Norway. These organisms can remain dormant under unfavourable conditions and cannot be easily recovered on artificial media.

This study describes the occurrence of campylobacters in the Bø river in southeastern Norway which has a variety of environmental influences. Of the 60 samples taken, 32 were contaminated with campylobacters. 47 strains were isolated using an enrichment procedure and 28 were isolated by direct plating of a filter membrane. Of these 75 isolates, 33 belonged to *Campylobacter coli*, 26 to *Campylobacter jejuni* and 11 to *Campylobacter lari*; five strains were not culturable. In 19 of the positive samples more than one species was detected. All three species were detected in 3 samples. Isolation of *Campylobacter* did not correlate well with the occurrence of faecal coliforms. The high isolation rate of campylobacters from surface water and the fact that the virulence of strains isolated from the environment is not fully known indicates that precautions should be taken to avoid transmission of campylobacteriosis from untreated water sources.

Copper

Gastrointestinal Effects Associated with Soluble and Insoluble Copper in Drinking Water.
Pizarro F, Olivares M, Araya M, Gidi V, Uauy R. Environ Health Perspect (2001) **109**(9)n p949-52

Consuming drinking water or beverages with elevated copper concentrations can cause acute gastrointestinal symptoms such as epigastric pain, nausea, vomiting and diarrhoea. The aim of this study was to determine whether total copper or soluble copper concentration is associated with gastrointestinal signs and symptoms. Participants were women aged 18-55 years who worked at home and who were not pregnant or lactating.

Forty-five healthy women participated who lived in Santiago, Chile. All houses were similar and had copper piping systems. The study was conducted for 9 weeks and volunteers were randomised into three groups based on the sequence of soluble/insoluble copper they received. Subjects were blinded to copper concentrations they were receiving. The proportions of copper sulfate (soluble) to copper oxide (insoluble) subjects were given was 0:5, 1:4, 2:3, 3:2 and 5:0 (mg:mg/L). Subjects received flasks filled with a solution to add to their home drinking water each day, and recorded the amount of water ingested, and any symptoms experienced during the day. Once a week the copper concentration and pH of water prepared by the subjects in their homes was analysed for actual copper concentration. Blood samples were obtained 1 week before the beginning of the study and at the end of the protocol.

The copper content of tap water was <0.1 mg/L and therefore not considered a significant source of copper. Mean consumption of water was similar among the groups. Serum analysis showed copper levels, ceruloplasmin and activities of liver enzymes were within normal limits. There were 20 subjects who had gastrointestinal disturbances at least once during the study, 9 had diarrhoea and 11 reported abdominal pain, nausea or vomiting. There were no significant differences in the incidence of diarrhoea or other symptoms regardless of the ratio of copper sulfate to copper oxide.

Cyanobacteria

Human Fatalities from Cyanobacteria: Chemical and Biological Evidence for Cyanotoxins.
Carmichael WW, Azevedo SMFO, An JS, Molica RJR, Jochimsen EM, Lau S, Rinehart KL, Shaw GR, Eaglesham GK. Environ Health Perspect (2001) **109**(7): p663-8

This study reports further information on the first documented cases of human fatalities due to cyanobacterial hepatotoxins occurring in a dialysis clinic in Caruaru, Brazil in 1996 (see Health Stream Issue 10). Up to 76 deaths were attributed to severe neurological symptoms or liver failure, after patients were exposed to contaminated water.

Two groups of cyanobacterial toxins were identified, the hepatotoxic cyclic peptide microcystins and the hepatotoxic alkaloid cylindrospermopsin. It was concluded that intravenous exposure to microcystins, in particular microcystin-YR, -LR and -AR was the major cause of the fatalities. It was estimated that 19.5 micrograms/L microcystin was in the water used in dialysis, this is 19.5 times the guideline level of 1 microgram/L proposed by the World Health Organisation for safe drinking water. The tragedy was attributed to inadequate maintenance of filtration equipment at the clinic, coupled with use of heavily toxin-contaminated water. The clinic used trucked water from the city's water treatment plant that had received only alum flocculation rather than full conventional treatment, and thus probably contained more algal cells and toxins than the tap water supply.

Comment: Intravenous exposure to cyanobacterial toxins via dialysis would have resulted in almost all the toxin entering the blood stream. In contrast, oral exposure results in a much lower uptake as some of the toxin is destroyed by stomach acid and absorption via the gut is poor.

Toxic cyanobacterial bloom problems in Australian waters: risks and impacts on human health.
Falconer IR. Phycologia (2001) **40**(3) p228-233

This paper reviews the major species of toxic cyanobacteria found in Australian waters and discusses the potential health impacts of exposure to these organisms and their toxins. The author also describes the basis of the World Health Organisation Guideline Values for safe cyanobacterial exposure levels for drinking water and recreational water.

Human deaths from oral consumption of cyanobacteria-contaminated water have not been unequivocally documented, however it is suspected that an unexplained outbreak of severe gastroenteritis in Brazil including a number of deaths may have been caused by cyanobacterial poisoning. Cyanobacterial toxins have been implicated in carcinogenesis and in tumour promotion although further evidence is needed to clarify these associations. In Australia there have been two reported instances of human injury resulting from toxic cyanobacterial contamination of drinking water reservoirs after treatment with copper sulphate which lyses the bloom but also liberates the toxins into water. Recreational exposure to cyanobacteria toxins is quite common with skin rashes, eye irritations and increases in gastrointestinal effects being reported.

Occurrence of microcystins in raw water sources and treated drinking water of Finnish waterworks.
Lahti K, Rapala J, Kivimaki AL, Kukkonen J, Niemela M, Sivonen K. Wat Sci Technol (2001) **43**(12) p225-228

The aim of this study was to determine the occurrence of microcystins in raw water sources and in treated drinking water of a number of Finnish surface water and bank filtration plants. Water samples were taken for microcystin and phytoplankton analysis from four bank filtration plants and from nine surface waterworks using different processes for water treatment. Microcystins were analysed by immunoassay and phytoplankton was identified and quantified.

The concentrations of microcystins in all raw water samples from bank filtration plants was reasonably low (maximum value 1.9 microgram/L as MC-LR equivalents). Microcystins were found in treated water less frequently and in low concentrations (the highest concentration was 0.1 microgram/L). Cyanobacteria were absent from bank filtered drinking water in most cases.

Microcystins were present in most of the surface water sources that were monitored in the summer of 1999. In treated drinking water, microcystins were only detected in 3 of 52 samples and concentrations were below 1 microgram/L. Cyanobacterial cells were rarely detected in treated waters. Bank filtration removed cyanobacteria and microcystins satisfactorily however the efficiency varied depending on the plant and circumstances. The surface waterworks efficiently removed microcystins.

Diabetes

Drinking water composition and childhood-onset Type 1 diabetes mellitus in Devon and Cornwall, England.
Zhao HX, Mold MD, Stenhouse EA, Bird SC, Wright DE, Demaine AG, Millward BA. Diabetic Med (2001) **18**(9) p709-717

It has been suggested that nitrate, mercury and arsenic in potable water may increase the risk of developing childhood-onset Type 1 diabetes mellitus and zinc may have a protective effect, however study results have been inconsistent. This study examined the relationship between zinc, magnesium and nitrate in drinking water and childhood-onset Type 1 diabetes mellitus using the Cornwall and Plymouth Children's Diabetes Register (CPCDR) and local water quality data.

The CPCDR includes all children aged 0-15 years who were diagnosed with Type 1 diabetes between 1 January 1975 and 31 December 1996. There were 517 children from the register for whom water quality data was known. The water company provided water quality data for nitrate, nitrite, copper, magnesium, zinc, iron, aluminium and calcium concentrations in the 40 water supply zones covered

by the study. Standardised incidence ratios (SIR) of Type 1 diabetes were calculated for each water supply zone using the UK 1991 census data. Analysis on thirds of the data set with SIR by x^2 tests for trend and Poisson regression analysis was undertaken.

The total child population in the study area was 157,000. In the whole study area between 1993-97, Ca and Fe showed an increasing trend and Al and Mn showed a decreasing trend. Mean copper concentrations showed a significant decrease with SIR (x^2 tests for trend = 6.58, d.f = 1, P =0.01), and a significantly decreased risk in the higher concentrations (middle and top thirds). Significant decreases were also found with an increase in magnesium concentration (x^2 tests for trend = 6.39, d.f = 1, P =0.01), and a significantly decreased risk in the top third.

The mean nitrate levels showed borderline significance of a decreased trend (x^2 tests for trend = 3.899 d.f = 1, P =0.01). Other variables examined showed no significant relation with the SIR of the disease. The data suggests a protective effect of increasing levels of zinc or magnesium, although dose-response trends were not consistent. A reduction in risk associated with high zinc levels has been previously reported. The study did not find an association between nitrate in drinking water and risk of diabetes, as reported in some previous studies.

Disinfection Byproducts

Weight of evidence for an association between adverse reproductive and developmental effects and exposure to disinfection by-products: A critical review.
Graves CG, Matanoski GM, Tardiff RG. Regul Toxicol Pharmacol (2001) **34**(2) p103-124

This paper reviews 13 studies on human reproductive and development effects of DBPs published since 1989, and a larger number of animal studies.

The review process indicated that the overall weight of evidence does not support an association with DBP exposure for the following reproductive or developmental outcomes: low birth weight, very low birth weight, preterm delivery, cesarean delivery, congenital anomalies by severity, spina bifida, cleft lip and palate, cardiac anomalies, gastrointestinal anomalies, genital anomalies, integument anomalies, musculoskeletal anomalies, chromosomal abnormalities and neonatal death.

Outcomes for which the weight of evidence was mixed, inconsistent or weak were the following: neonatal jaundice, all congenital anomalies/birth defects, all central nervous system anomalies, neural tube defects, respiratory anomalies, spontaneous abortion/miscarriages and stillbirth/fetal death.

Outcomes for which there was a suggestive positive association were: growth retardation including term low birth weight, intrauterine growth retardation or small for gestational age, small body length, cranial circumference and urinary tract defects.

The major limitation of the exposure assessment in the published epidemiological studies has been that exposure is based on residence rather than on individual exposure to DBPs at the appropriate time in pregnancy. Accurate measures of individual exposures are needed, taking account of variations in the water supply system, water consumption and exposure through dermal contact and inhalation.

Fluid Consumption

Fluid consumption related to climate among children in the United States.
Sohn W, Heller KE, Burt BA. J Public Health Dent (2001) **61**(2) p99-106

The recommended fluoride concentration in US public water systems ranges between 0.7-1.9 ppm and is based on the assumption that water intake is higher in warmer climates. This study assessed fluid consumption among US children relative to the local climate. The study population included 3,869 children aged 1-10 years who completed a 24-hour dietary interview during the National Health and Nutrition Examination Survey (NHANES III).

Multiple regression analysis found that age, socioeconomic status, sex, race and ethnicity were significantly related to fluid intake. There was no significant association between amount of total fluid or plain water intake and mean daily maximum temperature, even after controlling for the other factors. This study suggests that the temperature related guidelines for fluoride in drinking water set in 1962 might need to be re-evaluated.

Gastroenteritis

Changes in the incidence of gastroenteritis and the implementation of public water treatment.
McConnell S, Horrocks M, Sinclair MI, Fairley CK. Intern J Environ Health Res (2001) **11**(4) p299-303

There is debate over whether endemic waterborne disease exists in the developed world. This study examined gastroenteritis rates before and after the introduction of water treatment in rural communities in Victoria and South Australia. Disease incidence was measured by the number of requests for analysis of gastroenteritis related faecal specimens. Communities were identified with populations of 1000 or more that had upgraded their surface water supply between December 1992 and December 1996. To control for changes in the provision of pathology services, data on common laboratory test (mid stream urine samples (MSU)) that would not be influenced by rates of gastroenteritis was collected. Three water quality parameters were assessed: the percentage of water samples with coliforms or *E. coli* detected, and turbidity. Seventeen systems were included in the study; ten systems had filtration added to existing disinfection, four had both disinfection and filtration added to no existing treatment, and three had disinfection alone added to no existing treatment.

There were no consistent trends among groups of communities with the same type of change in treatment. Changes in water quality parameters did not correlate with changes in gastroenteritis related faecal requests. The results suggest that any reduction in gastrointestinal disease from the introduction of water treatment was small as a percentage of all gastroenteritis. Water treatment still remains however an essential measure to protect the public from the risk of outbreaks of waterborne disease.

Indicator organisms

Advances in the bacteriology of the Coliform Group: Their suitability as markers of microbial water safety.
Leclerc H, Mossel DAA, Edberg SC, Struijk CB. Ann Rev Microbiol (2001) **55** p201-234

This paper reviews the historical development of coliform organisms as indicators of water contamination, the evolving definition of this group of bacteria as detection methods have changed over the year, and the characteristics of different subgroups. The suitability of different coliform groups as indicators of water contamination is critically examined and the authors discuss the distinction between "index organisms" (signifying the potential presence of pathogens) and indicator organisms (signifying process failure). They conclude that among the coliforms, *E. coli* holds a unique place as being almost completely limited to the intestinal tract of humans and warm blooded mammals. However this organism, and other coliforms can not serve as reliable markers for all types of enteric pathogen, and more work is needed to assess the suitability of additional markers for the effective monitoring of drinking water safety.

Mycobacterium

Bactericidal effect of chlorine on Mycobacterium paratuberculosis in drinking water.
Whan LB, Grant IR, Ball HJ, Scott R, Rowe MT. Letters Appl Microbiol (2001) **33**(3) p227-231

The bacterium *Mycobacterium paratuberculosis* is the cause of Johne's disease in cattle and other ruminants and may be associated with Crohn's disease in humans. Potential routes of transmission to humans include recreational water, drinking water and milk. The aim of this study was to determine whether this organism can survive standard water treatment processes. Two strains of *M. paratuberculosis* were used, a bovine strain and a human strain. These were subjected to chlorine concentrations of 0, 0.5, 1.0 and 2.0 micrograms ml^{-1} for 15 and 30 minutes.

The chlorine concentrations used did not entirely kill either strain of *M .paratuberculosis*, Log_{10} reductions in the range 1.32-2.82 were found. The largest Log_{10} reduction with the bovine strain was 2.83 and with the human strain it was 2.35. The combination of the highest chlorine concentration (2.0 microgram ml^{-1}) and the longest contact time (30 min) resulted in the greatest reduction in culturability.

Comment The issue of a causative link between M. paratuberculosis and Crohn's disease remains controversial, and there is some evidence that genetic susceptibility or immunosuppression may also be involved. The authors do not comment on the likely concentration of these bacteria in raw water sources.

Norwalk virus

Outbreak of Norwalk virus in a Caribbean island resort: application of molecular diagnostics to ascertain the vehicle of infection.
Brown CM, Cann JW, Simons G, Fankhauser RL, Thomas W, Parashar UD, Lewis MJ. Epidemiol Infect (2001) **126** (3) p425-432

An outbreak of gastroenteritis occurred at a large resort hotel in Bermuda in February 1998. The investigation included assessment of possible food and waterborne sources. Water from the hotel's potable water supply was tested for coliform bacteria and residual chlorine, but no food samples were available for analysis. Stool specimens from sick people were analysed for a range of bacteria, parasites and viruses. There were 448 people identified with at least one gastrointestinal symptom. Those who ate and/or drank at the hotel were significantly more likely to report gastroenteritis than those who didn't (OR=6.0, 95% CI = 2.4-15.1). The laboratory analysis found genogroup-II Norwalk-like virus (NLV) in 18 of 19 tested stool samples. NLV of the same genotype and DNA sequence was found in a 3L water sample. There were no bacterial or parasitic pathogens identified in faecal specimens.

The hotel's water supply was not chlorinated and the underground storage tank was vulnerable to surface runoff and overflow from nearby toilets. There were no service logs or engineering records for the water supply, and the tank had not been cleaned for at least 5 years. The authors note that regions where tourism is important should consider some food and water safety initiatives such as the regular inspection and monitoring of drinking water supplies and waste water systems, as well as active surveillance so outbreaks are detected and controlled early.

Outbreak Investigation

Waterborne disease outbreaks caused by distribution system deficiencies.
Craun GF, Calderon RL. J AWWA (2001) **93**(9) p64-75

In the United States from 1971 to 1998, there were 619 waterborne disease outbreaks reported in community water systems (CWSs) and noncommunity water systems (NCWSs), from both chemical and microbial causes. Of these, 113 outbreaks were caused by distribution system contamination, resulting in more than 21,000 cases of illness. Most of these cases of illness (81.7%) and almost all of the 498 hospitalisations occurred in CWSs, with 13 deaths recorded. The largest distribution system outbreak caused 5,000 illnesses. The causes of outbreaks included cross-connections, backsiphonage, contamination of storage tanks, mains breaks/repairs, and corrosion of household or commercial plumbing.

Since 1995, distribution system deficiencies were the cause of 45% of outbreaks in CWSs. Inadequate treatment of groundwater and surface water caused 20% and 15% of outbreaks respectively. In noncommunity water systems (NCWSs) outbreaks were mainly caused because of inadequate or no treatment of groundwater, although 14% of outbreaks reported since 1995 were caused by distribution system deficiencies. For both CWS and NCWSs surface water systems, significantly higher distribution system outbreak rates were reported compared with groundwater systems.

The authors note that not all waterborne disease outbreaks are recognised or investigated. It is estimated that only 10-30% of US waterborne disease outbreaks are reported. Outbreaks are more likely to be recognised and investigated in large CWSs and when they involve serious illness.

Improving waterborne disease outbreak investigations.
Craun GF, Frost FJ, Calderon RL, Hilborn ED, Fox KR, Reasoner DJ, Poole CL, Rexing DJ, Hubbs SA, Dufour AP. Int J Environ Health Res (2001) **11**(3) p229-43.

This article summarises the outcomes of a workshop held in December 1998. A significant percent of waterborne outbreaks do not have the etiological agent identified, and/or the water system deficiencies and sources of contamination are not determined. If public health authorities and water utilities are to prevent waterborne outbreaks, then this type of information is needed. A number of recommendations were made by the workshop participants to improve the recognition and investigation of waterborne outbreaks, including enhanced surveillance, pre-planning of investigation methodology, use of standardised methods and questionnaires, and better training of personnel.

Protozoa

Possible undetected outbreaks of cryptosporidiosis in areas of the North West of England supplied by an unfiltered surface water source.
Hunter P. Commun Dis Public Health (2001) **4**(2) p136-8

From 1991 to 1999 there were 22 outbreaks of *Cryptosporidium* infection in England and Wales associated with mains drinking water. From 1997-99 there were three outbreaks of cryptosporidiosis in the North West region of England. These outbreaks were linked to a chlorinated unfiltered supply drawn from a surface water reservoir in the English Lake district.

A retrospective analysis of laboratory reports was conducted in this region. Data from the PHLS Communicable Disease Surveillance Centre from laboratories in the North West Region of England was used in the analysis. Time series of weekly reported cases for the six implicated authorities involved in the three outbreaks and for the remaining unaffected authorities were analysed to estimate crude rates of reporting.

The average crude rate of case reporting for the six authorities was 2.8 times higher than for the other health authorities in the region ie 3.97 cases/week per 1 million people compared to 1.41 ($p<0.0001$). In a single week the maximum rate of reporting for the six authorities was 35.2 compared to 7.01 for the others. The six authorities experienced major peaks in *Cryptosporidium* infection that were not observed in the rest of the region. These peaks may represent unrecognised outbreaks due to the unfiltered surface water source that was implicated in the three reported outbreaks.

The reasons these outbreaks were not recognised at the time is not obvious. The overall lower numbers of positive laboratory reports in the initial years of the study may be an explanation, or it may be that consultants and environmental health officers in affected areas accepted that a rise in incidence in spring was normal and therefore did not warrant investigation. The authors conclude that excess rates of cryptosporidiosis in the affected health authorities suggest that waterborne disease in the North west region may be more common than earlier thought.

Occurrence of Cryptosporidium oocysts and Giardia cysts in raw waters in Norway.
Robertson LJ, Gjerde B. Scand J Public Health (2001) **29**(3) p200-207

A total of 408 raw water samples were collected between June 1998 and November 1999 from 147 sites across Norway and analysed for *Cryptosporidium* and *Giardia*. Parasites were detected in 103 samples from 47 sites. *Cryptosporidium* oocysts were found in more sites and in more samples than *Giardia* cysts. Maximum concentrations of *Cryptosporidium* oocysts were 3.75/10 litres and *Giardia* cysts 2/10 litres.

There were no statistically significant associations between seasons and detection of protozoa in the water samples. Samples with turbidity of 2.0 NTU or more were significantly more likely to contain parasites, and there was also a correlation with animal numbers in the catchment.

Water treatment

Solar disinfection of drinking water protects against cholera in children under 6 years of age.
Conroy RM, Meegan ME, Joyce T, McGuigan K, Barnes J. Arch Dis Childhood (2001) **85** (4) p293-295

A cholera outbreak occurred in an area of Kenya between November 1997 and January 1998 where a field trial of solar disinfection of drinking water had recently been completed. The trial had involved all families with children under 6 years of age living in the Kajiado District. In the field trial, families were randomised into either solar disinfection or control conditions. In the solar disinfection group, drinking water for children under 6 was kept in plastic bottles on the roof. In the control group, children's drinking water was kept in plastic bottles indoors.

Households were visited within six weeks of the cholera outbreak and interviewed to determine whether illnesses meeting specific criteria to be diagnosed as cholera had occurred. Cases of cholera were found in 31 of 131 households. In the 67 households using solar disinfection there were 155 children under 6 years and there were 144 in the control group. Three cases of cholera were recorded in children in the solar disinfected group and 20 cases in the children in the control group, odds ratio 0.12

(95% CI 0.02 to 0.65, p=0.014). For children aged 6-15 and for adults there were no significant differences in cholera rates between the two groups.

These observations therefore support the value of solar disinfection, which is a low to no cost intervention method that can be utilised quickly by the community as a first line of defence.

Synergistic effect of solar radiation and solar heating to disinfect drinking water sources.
Rijal GK, Fujioka RS. Wat Sci Technol (2001) **43** (12) p155-162

This study evaluated the efficiency of two solar systems to disinfect drinking water. The Family Sol*Saver (FSP) system using a non-UV transmittable cover sheet so sunlight heats the water (System A) was compared with the modified FSP systems with a UV transmittable cover sheet where heat and direct solar radiation are used to treat the water (System B). The two systems were set up on the roof of a building at the University of Hawaii. Stream and diluted sewage water samples were tested in each system under sunny and partly sunny conditions. Disinfection efficiency of both systems was assessed by reduction of the natural populations of faecal coliform, *E. coli*, enterococci, *C. perfringens*, total heterotrophic bacteria, hydrogen sulphide producing bacteria and FRNA virus.

Under sunny and partly sunny conditions water was heated to the critical 60 degrees C in both systems and concentrations of faecal coliforms, *E.coli* and enterococci were inactivated to undetectable levels of <1 CFU/100mL within 3-5 hours of exposure to sunlight. System A showed a faster temperature increase but a lower inactivation rate than system B. A synergy between solar radiation and heat was suggested in system B. This synergistic effect was observed in water temperatures as low as 41-50 degrees C.

Under sunny conditions both systems were able to disinfect *C. perfringens* spores and FRNA virus. Inactivation of *C. perfringens* was enhanced by the synergistic effect of system B. When conditions were cloudy neither system could reduce levels of faecal indicator bacteria to <1 CFU/100mL reliably. Generally, the gram-negative enteric bacteria were reduced more rapidly than gram-positive enterococci.

Not just a drop in the bucket: Expanding access to point-of-use water treatment systems.
Mintz E, Bartram J, Lochery P, Wegelin M. Am J Public Health (2001) **91**(10) p1565-1570

There are approximately 1.1 billion people in the world who do not have access to safe water sources. This paper reviews two low-cost technologies, which can be used to improve drinking water quality in developing countries.

Boiling of water inactivates viral, parasitic and bacterial pathogens but is not sustainable economically and environmentally and there is the risk of scalding. A variety of point-of-use chemical agents for water treatment have been reviewed. Sodium hypochlorite seems to be the safest, most effective and least expensive, and has been demonstrated to reduce diarrhoeal illness by up to 85%. The limitations of this disinfectant are it is ineffective against parasites and viruses, and when water with large amounts of organic material is treated the efficiency is reduced and a disagreeable taste and odour may be produced.

Solar disinfection by means of ultraviolet radiation and/or increased temperature can be used to inactivate pathogens in water, using clear plastic soda bottles or bags made of polyethylene terephthalate which transmit ultraviolet A. These are inexpensive and widely available. Field trials in Kenya have shown that this method is an acceptable and effective way of to improve water quality with significant reductions in the incidence of diarrhoea in children. The limitations are that sufficient solar radiation and reasonably clear water are required, and treating large volumes is also a problem.

Water that has been disinfected can be contaminated during collection, transport and storage. By replacing unsafe water storage vessels with safer ones with tight-fitting lids and narrow mouths, rates of disease can be lowered. The introduction of a new vessel or disinfection processes must be accompanied by changes in behaviours. Improvements in the quality of drinking water provide far more benefit when coupled with improvements in hygiene and sanitation. Self-sustaining and decentralised approaches to providing safe drinking water reviewed here, target those most affected directly, enhance health and contribute to productivity and development.

Additional Articles

Position of the American Dietetic Association: The impact of fluoride on health.
Palmer CA, Anderson JJB. J Am Dietetic Assoc (2001) **10**(1) p126-132.

Aluminium as a risk factor in Alzheimer's disease, with emphasis on drinking water.
Flaten TP. Brain Res Bull (2001) **55**(2) **p**187-96.

Benefit-cost estimation for alternative drinking water maximum contaminant levels.
Gurian PL, Small L, Lockwood JR, Schervish MJ. Wat Resources Res (2001) **37**(8) p2213-26.

Is the water safe for my baby?
Balbus JM, Lang ME. Pediatr Clin North Am (2001) **48**(5) p1129-52.

The role of natural organic matter during formation of chlorination by-products: A review.
Nikolaou AD, Lekkas TD. Acta Hydrochim Hydrobiol (2001) **29**(2-3) p63-77.

Hemolytic-uremic syndrome and Escherichia coli O121 at a Lake in Connecticut 1999.
McCarthy, T. A., N. L. Barrett, et al. (2001). Pediatrics **108**(4): 991-2.

HACCP (Hazard Analysis and Critical Control Points) to guarantee safe water reuse and drinking water production - a case study.
Dewettinck T, Van Houtte E, Geenens D, Van Hege K, Verstraete W. Wat Sci Tech (2001) **43**(12) p31-8.

An examination of risk factors associated with beef cattle shedding pathogens of potential zoonotic concern.
Hoar BR, Atwill ER, Elmi C, Farver TB. Epidemiol Infect (2001) **127** (1) p147-155.

Participant Blinding and Gastrointestinal Illness in a Randomized Controlled Trial of a In-Home Drinking Water Intervention.
Colford, J. M., J. R. Rees, et al. (2002). Emerg Infect Dis **8**(1).

Genotyping Cyptosporidium parvum by single-strand conformation polymorphism analysis of ribosomal and heat shock gene regions.
Gasser, R. B., X. Zhu, et al. (2001). Electrophoresis **22**(3): 229-43.

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