

# **SAFE DRINKING WATER IN THE TWENTY-FIRST CENTURY: PRIORITIES FOR PUBLIC HEALTH**

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## **Summary**

Advances in water and wastewater treatment in the twentieth century have transformed public health worldwide. However, as a number of World Health Organization and American Academy of Microbiology expert reports have clearly shown, we are still a long way from guaranteeing safe drinking water even in the most developed nations. This chapter attempts to identify major knowledge gaps and summarize at least some of the priorities for the future provision of safe drinking water. Obviously, the major benefits to human health are through basic hygiene and sanitation practices — still much needed areas for public health intervention in many parts of the world. However, this chapter will emphasize more research-oriented needs and priorities. These include the need for a better understanding of biofilms and their control, improvements in risk assessment methodologies, the emergence of new disease, the balance between pathogens and disinfection-by-products, and the future promise of rapidly developing technologies.

## **1. Introduction**

The concept of safe, cheap drinking water as an inalienable human right for everyone emerged in the more developed nations in the latter part of the twentieth century. Although the quality of our source waters, and their protection, is recognized as the single most efficient factor in determining consistently high quality drinking water, the technology now exists to take wastewater and recycle it to potable water quality. As cities have developed, both in the US and globally, both water distribution and waste

collection systems have become more complex and far more difficult to maintain. Thirty to forty percent leakage from water distribution systems appears to be a common estimate, whether talking to utility personnel in the USA, or in India. The fundamental difference is pressure. Many cities in the developing world are unable to supply more than one to two hours of water per day. Distribution systems therefore remain stagnant for long time periods each day, and are highly susceptible to contamination through back-siphonage, cross connections, and biofilm regrowth. In contrast, developed nation cities maintain pressure resulting in incredible wastage of treated, potable water, yet reduced risk to human health.

Now we have entered the twenty first century, what are the future priorities? While for many regions watershed protection is still problematic, filtration and disinfection technologies are constantly being improved. A typical multibarrier approach to provide safe drinking water is presented in Table 1.

S.No.	Description
1.	Watershed protection that minimizes anthropogenic and wildlife impacts on source water, including programs to reduce the impact of waterfowl, particularly near water intake sites.
2.	<p>A treatment system with sufficient capacity to maintain adequate pressure throughout the distribution system for 24 hours/day, and that minimizes opportunities for microbial colonization in the distribution system. This could include,</p> <ul style="list-style-type: none"> <li>• Coagulation-flocculation and sedimentation to remove colloids, associated microorganisms, debris and macroorganisms.</li> <li>• Preozonation to effectively kill microorganisms in source waters, reduce odor, taste and color, precursors for DBPs*, and reduce the amount of chlorine/ chloramine necessary to maintain a system residual.</li> <li>• Filtration to further remove particulates and microorganisms, including granular or biological activated carbon to remove AOC.</li> <li>• Chloramination to provide residual disinfection, minimize biofilm formation and reduce DBPs, with intermittent chlorination and system flushing.</li> </ul>
3.	A rigorous program to upgrade distribution system networks and prevent interconnections through leakage, backflushing, improper hydrant use, etc.

\*Disinfection byproducts are formed by ozonation of source waters, including aldehydes and brominated byproducts (discussed in Boorman et al, 1999). UV disinfection, used extensively in wastewater treatment, is rapidly gaining acceptance as an alternative to ozonation.

Table 1. A multibarrier approach to maximize microbiological quality of water

A technology can always be developed to clean contaminated source waters, albeit at a high cost. It is harder, however, to find a technological solution to deteriorating

distribution systems. Replacing pipelines is an extremely slow and disruptive process, and lining existing pipes may only provide temporary solutions. Lining materials that are currently in use, e.g., cement and epoxy linings, may be susceptible to deterioration, particularly in microbiologically active environments.

There are many alternatives proposed for provision of safe drinking water, including separate potable and non-potable supplies, point-of-use treatment devices and bottled water. None of these alternatives are without risk to the consumer and are invariably many-fold more expensive than municipal supplies. Of course, there is a strong argument that centrally supplied drinking water is dramatically undervalued, and more appropriate costing of this invaluable resource would help to address some of the problems briefly listed above.

In the foreseeable future, drinking water is likely to continue to be supplied through distribution networks. What, therefore, do we see as future priorities for public health?

## **2. Risk Assessment**

To begin with, we are still unable to characterize and quantify health risks associated with drinking water meeting World Health Organization Standards. It is likely that those risks are minimal to individuals with no predisposing factors (e.g., compromised immunity). However, on a global scale it could be argued that the susceptible individuals are as common as the non-susceptible. In developed nations we think about the very young, the elderly, the pregnant and those with diseases that directly, or through treatment, compromise immunity. Even in developed nations, the burgeoning field of environmental health has shown us that exposure to pollutants in air, food and water can affect susceptibility to disease. Likewise malnutrition, stress and socioeconomic status (e.g., inner city communities) render individuals more susceptible. In developing nations, the burden of diseases may be vast and malnutrition levels high. Rapid industrialization also exposes populations to uncontrolled pollution, leaded petrol is still accepted as the norm, and smoking, drug, alcohol abuse and prostitution are rampant.

However, although exposures appear to be vast, diseases may not be apparent due to multiple prior exposures resulting in population immunity. This then is the paradox. By all the above criteria, these populations are highly susceptible, yet immunity results in lower than expected incidence of many waterborne diseases. This immunity must come at some cost to the individual - which provides some validation to the Disability Adjusted Life Years (DALY) approach to estimate burden of disease, which could take into account the reduced quality of life (and lifespan) from exposure to multiple infectious agents (and toxins).

A study published in 2000 by Arie Havelaar and colleagues in the Netherlands used the DALY approach to compare the risks of disinfection byproducts vs. infectious disease. They conducted a hypothetical case study involving a drinking water system typical of the Netherlands. Their goal was to compare the reduction in risk of infection with *Cryptosporidium parvum* from ozonation of the water source, with the potential risk of cancer from ingestion of bromate (formed by reaction of ozone and bromine compounds

in source water). Net health benefits (in DALYs) were calculated based on published clinical, epidemiologic, and toxicological data on morbidity and mortality. Although bromate was produced in their model at concentrations exceeding US-EPA guidelines, they concluded that net benefits from ozonation outweighed risks by more than an order of magnitude, with a net benefit of approximately 1 DALY/million years. The DALY approach allowed the authors to consider life and health expectancy, including evaluation of the distribution of population susceptibilities. This approach provides a far more appropriate estimate of disease burden than can be obtained solely from annual mortality rates. Even so, considerable assumptions are made in 1) the exposure assessment; e.g., the median number of infectious *Cryptosporidium* oocysts, the median concentration of bromate, and the volume of water ingested; 2) in the hazard characterization; e.g., the shape of the dose response curves at low exposures, the applicability of rodent models to humans, and the distributions and models used to produce median parameter values and confidence intervals, 3) and in the risk characterization; e.g., assumptions made in calculating life years lost, years with disability and weightings for different population susceptibilities.

In 2001, Paul Gale from the WRc-NSF Ltd., UK, provided thoughtful analysis of the risk assessment process and has argued that distribution of pathogens, and in particular the protozoa, is extremely heterogeneous in drinking water. In other words, most consumers ingest zero *Cryptosporidium* oocysts and most water samples measure zero oocysts. However, a few individuals could consume a large number of oocysts. Gale argues that risk assessments based on median values obtained from spot sampling will underestimate risk as most samples are zero. Number of organisms present in a drinking water sample should be more accurately modeled as a distribution (in Gale's example for *Cryptosporidium*, a Poisson-log-normal distribution is used). Daily risks of infection are then calculated for this distribution using Monte Carlo simulation. However, Gale also reports that risks predicted by simple use of the arithmetic mean are very similar to those using Monte Carlo simulation. The arithmetic mean of pathogen density may be a better predictor of risk than the median value, as it provides a weighting to any positive samples based on the actual number of oocysts.

Gale also argues that spot sampling is inappropriate, as even during outbreak conditions most spot samples are zero, and that continuous monitoring, as is currently recommended in the UK for *Cryptosporidium*, is necessary. Similar arguments could be applied to pathogenic viruses and, in fact, to any pathogens with low infective doses and/or a tendency to adsorb to particles/biofilms contributing to a heterogeneous distribution. Gale has constructed a large number of risk assessments based on the arithmetic mean, rather than the median, including risk assessments for *Cryptosporidium parvum*, *Escherichia coli* O157, rotavirus and Bovine Spongiform Encephalitis (BSE; see later discussion).

Assumptions are also clearly present in estimating consumption of drinking water and it is argued that these too should be modeled on a distribution. The dose response relationship between number of pathogens ingested and infection is highly variable based on individual susceptibility (including immunity from prior exposures). Infectious doses measured in healthy volunteers may bear little relationship to the range of infectious doses in an average population.

Where else does uncertainty arise? For any pathogen, its presence in drinking water may not be enough to characterize risk. Organisms may lose their infectivity/virulence in the drinking water distribution system or after exposure to disinfection; or conversely, they may increase or change in virulence and in their ability to resist antibiotics.

Our risk assessment approach examines individual organisms. We are in fact exposed to complex mixtures of both microbes and chemicals. Questions that arise from this are:

1. What are the synergistic effects (both in terms of infectious dose and disease outcome) of exposure to mixtures of pathogens, opportunistic pathogens and non-pathogenic microbes?
2. What are the synergistic effects of exposure to mixtures of microbes and chemicals? For example, could simultaneous exposure to high concentrations of a contaminant chemical and an infectious agent affect the pathogen's infectious dose? Certainly, there is an argument that long-term exposure to chemical contaminants may increase susceptibility to infection.
3. How is a pathogen's infectivity and exposure route altered by association with biofilms?
4. How is a pathogen's infectivity and exposure route altered by intracellular survival within protozoa? (For example, it has been argued that the disease outcome from exposure to *Legionella pneumophila* could be related to mode of transmission; within biofilms, within protozoa or free-living).

### 3. The Pathogens

Although a wide range of diseases are caused by waterborne pathogens (Table 2), the most common outcome, and the one that most frequently remains undiagnosed, is acute gastrointestinal infection (AGI).

	Infectious Dose <sup>b</sup>	Diseases	Comments
<i>Vibrio cholerae</i>	10 <sup>8</sup>	cholera	new toxigenic serogroups/AB resistance
<i>Salmonella</i> spp.	10 <sup>6-7</sup>	Salmonellosis, typhoid ( <i>S. typhae</i> )	AB resistance
<i>Shigella</i> spp.	10 <sup>2</sup>	shigellosis	AB resistance
toxigenic <i>E. coli</i>	10 <sup>2-9</sup>	diarrheal diseases	Major identified cause of diarrheal disease.
e.g., <i>E. coli</i> O157		hemolytic-uremic syndrome	Enteropathogenic, enterotoxigenic, and enterohemorrhagic strains identified – include multiple AB resistant strains
<i>Campylobacter</i> spp.	10 <sup>6</sup>	campylobacteriosis	AB resistance
<i>Leptospira</i> spp.	3	leptospirosis	increase with flooding events
<i>Francisella tularensis</i>	10	tularemia	significance in DW unknown
<i>Yersinia</i>	10 <sup>9</sup>	yersiniosis	significance in DW

<i>enterocolitica</i>			unknown
<i>Aeromonas</i> spp.	10 <sup>8</sup>	skin & respiratory infections	gastritis?
<i>Helicobacter pylori</i>	?	gastric ulcers/cancer	essentially, exposure route unknown
<i>Legionella pneumophila</i>	>10	legionellosis, pontiac fever	underestimated cause of pneumonia
<i>Mycobacterium avium</i>	?	disseminated infections	increasing in healthy populations
<i>Burkholdaria pseudomallei</i>	~10	melioidosis	mortality can be very high, widespread in some developing countries, associated with environmental exposure
<b>Protozoa</b>			
<i>Giardia lamblia</i>	1-10	giardiasis	underdiagnosed
<i>Cryptosporidium parvum</i>	1-30	cryptosporidiosis	underdiagnosed, extreme chlorine resistance
<i>Naegleria fowleri</i>	high?	primary amoebic meningo-encephalitis	disease very rare, yet exposures common
<i>Acanthamoeba</i> spp.	?	encephalitis + others	transmission of bacterial pathogens?
<i>Entamoeba histolytica</i>	10-100		high rates of infection and associated mortality
<i>Cyclospora cayentanensis</i>	?	cyclosporidiosis	most outbreaks associated with contaminated produce
<i>Isospora belli</i>	?		significance in DW unknown
The Microsporidia	?	microsporidiosis	maybe widespread
<i>Ballantidium coli</i>	25-100		significance in DW unknown
<i>Toxoplasma gondii</i>	?	toxoplasmosis	significance in DW unknown
<b>Viruses</b>			
	1-10	diarreal disease, meningitis, heart disease, liver disease, etc	incidence probably dramatically underestimated, many viruses may remain to be discovered

Including, Caliciviruses, Poliovirus, Coxsachievirus, Echovirus, Reovirus, Adenovirus, Hepatitis A, Hepatitis E, Rotavirus, Astrovirus, Coronavirus, and others

<sup>a</sup> Data compiled from WHO (1993), Hazen and Toranzos (1990) and Geldreich (1996);

<sup>b</sup> Infectious dose is number of infectious agents that produce infection (asymptomatic or symptomatic) in 50% tested volunteers and is therefore not useful for risk estimates for disease.

Table 2. Pathogens in drinking water, their infectious doses, diseases and additional comments

AGI can be caused by viruses, bacteria, protozoa or symptoms similar to AGI may be caused by chemical contaminants. Increasingly, however, viruses are being suspected as major causative agents due in part to the difficulties inherent in both their specific diagnosis and measurement of the agents in drinking water. Of well over 100 known

viruses that can potentially be transmitted in drinking water, the Caliciviruses (primarily Norovirus) and Rotavirus are most commonly diagnosed. However, types of Poliovirus, Coxsachievirus, Echovirus, Reovirus, Adenovirus, HAV, Astrovirus, Coronavirus, and Hepatitis E have been implicated in waterborne outbreaks and there may be many further, as yet uncharacterized, groups of viruses that are responsible for AGI and other disease manifestations.

The bacteria include both true and opportunistic pathogens and are the usual list (included in Table 2).

Campylobacteriosis remains the most common form of bacterial dysentery, followed by pathogenic *E. coli*, salmonellosis and shigellosis. Under the umbrella of new pathogens, *Legionella pneumophila* and the non-tuberculous Mycobacteria occupy a unique niche in their ability to proliferate in hot water systems, their environmental ubiquity and their resistance to disinfection. In addition, they can apparently survive and in some cases proliferate within protozoan cells. As with the viruses, there are many unknowns. Water may or may not be a significant route for dissemination of *Helicobacter pylori* - the research community is divided. How much do the opportunistic pathogens, *Aeromonas* spp., *Pseudomonas* spp., *Klebsiella* spp., etc. contribute to morbidity and mortality through consumption of drinking water? Certainly they are a major cause of hospital-acquired infections with high associated mortality risks.

Aeromonads isolated from water, for example, contain a wide range of virulence and antibiotic resistance factors. They are known to cause a number of non-GI infections, including wound infections from exposure to water, but their true involvement in gastrointestinal disease would appear to be unknown. They can be isolated from patients with diarrheal disease, and a report published in 2000 by researchers working in Bangladesh, showed close associations between a number of *Aeromonas* enterotoxin genes and severe diarrhea. This research team was also able to demonstrate that a small number of children with diarrhea were only infected with *Aeromonas* spp., strongly suggesting that the aeromonads were the causative agent of the disease. Given the comparative ease of detection of virulence and antibiotic resistance genes in *Aeromonas* spp., and the ubiquity and ease of isolation of these opportunistic pathogens in drinking water, aeromonads should be a useful model organism to study changing virulence and antibiotic resistance patterns.

The protozoa receive most attention in the media due to the size of recent outbreaks - partially due to low infectious doses and high resistance to water treatment. *Cryptosporidium parvum* has attracted most attention, with *C. parvum* replacing *Giardia lamblia* as the most common cause of waterborne disease outbreaks in the UK, and second most common cause in the US. The protozoa that are currently receiving increased scrutiny are the *Cyclospora* and *Toxoplasma*, although a waterborne route of transmission is far from proven. It is likely we will also see increased scrutiny of the routes of exposure to microsporidia. Smaller than the other protozoans, the microsporidia group is recognized increasingly as one of the causative agents of both human and animal diseases. They are also more likely to penetrate filtration systems than the larger protozoa, hence it is reasonable to suspect a waterborne route of exposure. An interesting question is why are diseases caused by the pathogenic

amoebae not more prevalent? A risk assessment for *Naegleria fowleri* published in 2001 showed that many surface water bodies are positive for this pathogen, yet only a few cases of primary amoebic meningoencephalitis occur each year? In fact, seroprevalence studies indicate that infection may be fairly common, although disease is absent.

It would be remiss not to at least mention other potentially infectious agents; the fungi, prions and viroids. Most research is focused on the viruses, bacteria and protozoa in drinking water and very little information is available on these other infectious agents. A wide range of fungal species do, however, grow submerged in water or at the air-water interface. Fungi are readily isolated from drinking water, yet are seldom implicated in disease.

Studies published in 1999 indicated that fungal species of *Aspergillus*, *Cladosporium*, *Epicoccum*, *Penicillium* and *Trichoderma* are frequently isolated from treated drinking water. *Candida* yeasts are also occasionally isolated and apparently correlate with the indicator organisms, total and fecal coliforms. A number of fungi and yeasts isolated from treated drinking water are potential pathogens, or at least can produce toxic metabolites and readily spoil foods. However, more research is clearly necessary to establish a role, if it exists, for these microbes in transmission of human diseases through consumption of drinking water.

Of viroids and prions, to my knowledge no attempts have been made to look for these infectious agents in drinking water. Viroids, single stranded RNA, are thought to only cause plant diseases. Together with similar infectious agents known as satellite RNAs which are dependent upon a helper virus for replication, it is unlikely that these agents represent a serious threat to human health through drinking water. Of course, the absence of any information linking these agents to human disease does not mean that in future linkages will not emerge. For example, the Hepatitis Delta agent is essentially a viroid encapsulated in a hepatitis B coat.

In contrast, Prions, infectious proteinaceous material, have risen to prominence following the devastating economic and perceived human health threat from the BSE outbreak in the UK. Although prions have not been isolated from drinking waters, it is reasonable to at least consider the risks of contamination from, for example, rendering wastes, abattoirs and landfills. As previously mentioned, Paul Gale from the WRc-NSF Ltd., UK, conducted a provisional risk assessment on drinking water-related infections with BSE. The risk assessment was based on mice infectivity studies suggesting that the oral ID<sub>50</sub> is one gram of BSE infected bovine brain, equivalent to ~10<sup>13</sup> BSE prion protein molecules. Taking into account the rapid dispersion of contaminants in the aquatic environment, Gale's research group estimated that an individual would be exposed to only minute subfractions of an ID<sub>50</sub> from lifetime consumption of drinking water. In addition, the inherent stickiness of prions suggests that they would be rapidly sequestered to particles and easily removed in drinking water treatment. In fact, worst case assumptions suggested that "an individual would have to consume 2 liters per day of tap water for 45 million years to have a 50% chance of infection through drinking water drawn from the aquifer." Of course, there is still considerable uncertainty here, not least of which is the absence of dose-response information for BSE.



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### Biographical Sketch

**Timothy Edgcumbe Ford** has taken the position of Vice President for Research and Dean of Graduate Studies at the University of New England in Biddeford and Portland, Maine, USA. Prior to June 2008, Ford was department head of Microbiology at Montana State University (MSU), Bozeman, USA. He retains an adjunct appointment at the Harvard School of Public Health, Boston, Massachusetts, USA, where he was both a faculty member and Director of the Program in Water and Health from 1992 until 2002. Prior to 1992, he was a Research Fellow and Lecturer in the Division of Applied Sciences at Harvard University.

His research interests (resulting in over 140 publications, to date) have included source and drinking water microbiology, microbial cycling and transformation of pollutants, surface microbiology (biofilms), microbiologically influenced deterioration of materials, and microbial populations as biomarkers of environmental stress. He has both directed and participated in water quality related projects in the US, Canada, the UK, Honduras, Mexico, India and Russia, and is now developing relationships in China. Current research projects focus on the fate of opportunistic pathogens in drinking water biofilms, epidemiological studies on water and international health, microbial interactions with pollutants and environmental health on Montana's American Indian Reservations.

Relevant activities have included:

- Co-Chair, American Academy of Microbiology Scientific Colloquium, "Global Issues in Microbiological Water Quality for the Next Century," Guayaquil, Ecuador, April 1995.
- Chair, Congressional briefing on "Increased Flooding Events and Risks to Human Health" Washington, DC (1998).
- Chair, Congressional briefing on "Water, Population and Human Health" Washington, DC. (1999).
- Chair, Congressional briefing on "Genetically Modified Crops" with Sea Change, Washington, DC.
- Invited participant: American Academy of Microbiology Scientific Colloquium, "Re-evaluation of Microbial Water Quality: Powerful New Tools for Detection and Risk Assessment," Amelia Island, Florida, March 2000
- Plenary speaker and moderator: Water Environment Federation (WEF)/ITT Industries forum, "Water and the Next Generation: a discussion on countermeasures to the water crisis," held at the UN on World Water Day, 2001
- Steering Committee member: American Academy of Microbiology Scientific Colloquium on "Infections through the Gastrointestinal Tract," Galway, Ireland, 2002
- Invited participant for WHO/US-EPA Expert group on environmental mycobacteria, Guildford, UK, 2002
- Waksman Foundation for Microbiology Speaker, 2003/2004
- Chair, International Colloquium on Protecting Public Health in Small Water Systems, Bozeman, Montana, 2004
- Member, Institute for Public Health and Water Research Board, 2004
- Invited EPA CCL Microbial Expert Focused Workshop: Phase II, Arlington, VA, June 2006

- Invited Participant: American Academy of Microbiology Scientific Colloquium, “Clean Water: What is Acceptable Microbial Risk?” Tucson, Arizona, October 2006
- Gen-Probe Joseph Award for exemplary leadership and service in the field of public health, 2006
- Invited Participant: American Academy of Microbiology Scientific Colloquium, “The Uncharted Microbial World: Microbes and Their Activities in the Environment.” Seattle, Washington, February 2007
- Invited participant and discussion leader, National Summit on Coping with Climate Change, University of Michigan, Ann Arbor, MI, May 2007
- Chair, "Environmental Change and Infectious Disease," Division III Symposium, American Society for Microbiology Annual Meeting, Toronto, May 2007
- Member, editorial board of the Journal of Industrial Microbiology and Biotechnology
- Member, editorial board of the Journal of Environmental Science and Health
- Member, editorial board of Environmental Engineering Science
- Member, editorial board of Microbial Ecology