Emerging issues in water and health research

Tim Ford

ABSTRACT

In the less developed nations, hygiene and sanitation remain overriding factors in population health and the burden of waterborne disease. Both morbidity and mortality from diseases, such as cholera, remain high, but the overwhelming burden of diarrhoeal diseases inevitably goes undiagnosed. Enterotoxic *E. coli*, shigellosis and campylobacteriosis are prevalent amongst bacterial diseases and giardiasis is often diagnosed among protozoan diseases. In terms of viral diseases, hepatitis A is frequently associated with water and rotavirus, and more recently norovirus, infections are suspected to be major causes of gastroenteritis, although they are seldom diagnosed. From the perspective of research and training, and despite the efforts of major international organizations, effective programs that teach basic hygiene and sanitation remain elusive.

Key words | emerging disease, gastroenteritis, health, hygiene, sanitation, water

Tim Ford
Department of Microbiology,
Montana State University,
109 Lewis Hall,
Bozeman MT, 59717,
USA
Tel: 406 994 2901
Fax: 406 994 4926
E-mail: *tford@montana.edu*

PRIORITY AREAS IN WATER AND HEALTH

Table 1 provides a summary of priority areas for water quality in developing countries, transition economies and developed countries. Although the order is very subjective, the highest priorities are listed first.

The following sections discuss some of these priority areas in more detail.

DEVELOPING ECONOMIES

The connection between hygiene, sanitation and disease is clearly demonstrated through the relationship between socioeconomic status and disease incidence. For example, a City like Hyderabad in India is divided into administrative zones which conveniently provide a "socioeconomic" index shown in Figure 1. The zone designated as "1" is primarily a slum area adjacent to the City's Musi River which carries predominantly wastewater for much of the year. In contrast, the zone designated 18, is a relatively wealthy area built on the higher points of the City.

Cholera (caused by *Vibrio cholerae*) remains the "best known" waterborne disease of the developing world. The disease remains both epidemic and pandemic due in part to its ability to survive and multiply in the environment in association with plankton and other aquatic organisms (Colwell 1996). The ecology of this infectious agent has attracted considerable attention over the past several decades, because of its environmental connections. The arrival of cholera in South America in 1991 has been attributed to a number of different events, including discharge of ship's bilge water, transport in imported foods or resurgence of endemic disease through breakdown in sanitation. It has also been suggested that its rapid spread may have been related to movement of "infected" plankton with coastal currents (Epstein *et al.* 1993). However the cholera resurgence occurred in South America, the human health and economic consequences were enormous (more than 1 million cases and 10,000 deaths, Tauxe *et al.* 1994). Hence, understanding the ecology and predicting the resurgence of diseases, like cholera, has major implications for public health.

There is also evidence that the nature of cholera epidemics is beginning to change. The causative agent of

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Table 1 | Priority areas

Developing	Transition	Developed
Source water quality & quantity	Source water quality	Deteriorating infrastructure
Absent or deteriorating infrastructure	Deteriorating infrastructure	Operator training
Education in hygiene and sanitation	Failing technologies	Surveillance
Wastewater collection and treatment	Selected opportunistic pathogens	Source water quality
Susceptible populations	Susceptible populations	Opportunistic pathogens (and the CCL)
Low cost, low maintenance, treatment technologies	Disinfection byproducts	Chemicals (pesticides, nitrates, metals, etc.)
Emerging pathogens	Chemicals (pesticides, nitrates, metals, etc.)	Disinfection byproducts
Operator training	Surveillance	Molecular techniques

the past seven pandemics has been *V. cholerae*, serogroup O1. However, in the 1990s, *V. cholerae,* serogroup O139 emerged in India in epidemic form. This new epidemic strain is thought to be derived from O1 strains through genetic modification (Faruque *et al.* 1998). The critical research question is which conditions promoted the emergence of the toxigenic O139 serogroups, pathogens which may be environmentally hardier than O1 strains (Islam *et al.* 1993)? Although, in the case of cholera, genetic modification is suspected, two scenarios may be possible, as illustrated in Figure 2.

An area of research which currently receives little attention in developing countries is the emergence of new disease. It has been argued that any organisms which change in virulence or antibiotic resistance should be considered emerging pathogens (Ford 1999; Levin *et al.* 2002). The example given above is for *V. cholerae*, however it could equally apply to other pathogens such as the toxigenic *E. coli*. In the case of gene transfer, virulence factors could also be transferred between species. Both mutation and gene transfer would appear reasonable

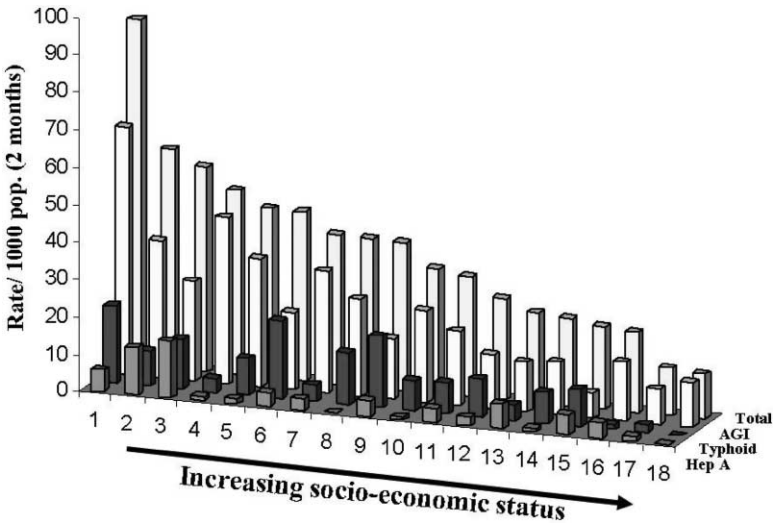

Figure 1 | Waterborne diseases in Hyderabad by zone (adapted from Mohanty *et al.* 2002).

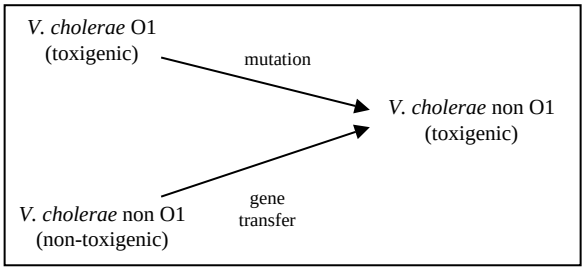

Figure 2 | Emergence of new epidemic serogroups of *Vibrio cholerae* (adapted from Ford 2004).

amongst organisms capable of growth within the drinking water distribution system, where organisms are likely to be exposed to a variety of stressors such as chlorine and metal ions (Ford 1993).

Today, on a global basis morbidity and mortality from *E. coli* infections are thought to far exceed those of cholera and other identified waterborne bacterial diseases. Collectively referred to as ETEC, *E. coli* can be enterotoxigenic, enteropathogenic, or enterohemorrhagic, as in the notorious *E. coli* O157-H7 outbreak in Walkerton. Estimates of morbidity and mortality from cholera are in the tens of thousands per year. In contrast, ETEC infections are estimated to cause approximately 400 million diarrhoeal episodes with 700,000 deaths among children less than 5 years of age each year (Chakraborty *et al.* 2001). Progress is being made in the isolation of both *V. cholerae* and ETEC from Ganges River water in the Varanasi region in order to begin to investigate both intra- and inter-species transfer of virulence factors.

In summary, key areas for research and training are:

- Hygiene and sanitation
- Emerging disease (and the ecology of infectious diseases)

TRANSITION ECONOMIES

Work in Russia has shown that failing infrastructures may represent one of the most important health risks for countries with weakened economies. Infrastructures for water and waste treatment, originally built for populations far smaller than they are today, is often woefully under capacity. Source water quality may be particularly poor due to the lack of resources for watershed protection and long histories of development which lack consideration for the environment.

In the example of the industrialized northern city of Cherepovets, recognized as a zone of environmental crisis due to production of industrial wastes, source water quality is poor and equipment is deteriorating. High organic loading in the source waters coupled with chlorination both prior to addition of alum and secondary to rapid filtration, results in extremely high concentrations of disinfection byproducts (Egorov *et al.* 2003a). Water is distributed through an aging system primarily to multi-apartment buildings. However, plant capacity is limited and water pressure is seldom sufficient to reach higher floors resulting in home storage of water (e.g. in the bathtub) and the risks of back siphonage. Figure 3 provides a simplified schematic of the Cherepovets' water treatment system.

A temporal examination of a water quality indicator (turbidity) and gastrointestinal disease, suggests a potential relationship between disease and exposure to water at times consistent with both viral (1–2 days) and protozoan diseases (6–7 days) (Figure 4).

The study of *Cryptosporidium parvum* in this city suggests that it is a common contaminant of the water system, a common cause of gastrointestinal disease and through seroprevalence studies, an extremely common cause of asymptomatic infections (Egorov *et al.* 2002; 2004).

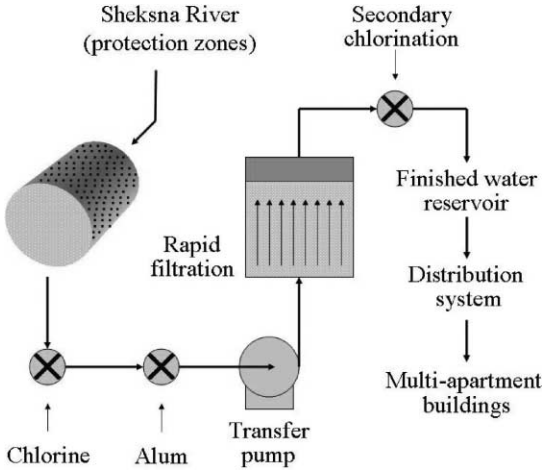

Figure 3 | Cherepovets' water treatment.

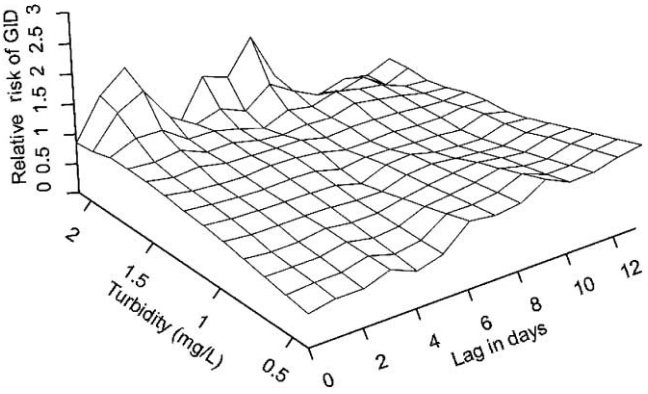

Figure 4 | TERS plot of associations between turbidity and self-reported GI diseases in Cherepovets (from Egorov *et al.* 2003b).

In summary, key areas for research and training are:

- Source water quality
- Failing infrastructure
- Failing technology
- Burden of opportunistic infections
- Health consequences from Disinfection by-products (DBPs)

MORE DEVELOPED NATIONS

In all countries, failing infrastructure, and, in particular, the condition of distribution system pipelines is of paramount importance. However, in the United States, the related health issue is partially moderated by the ability of at least the larger utilities to maintain sufficient pressure so that leakage tends to be out rather than into the pipes. The result, of course, is considerable wastage of water and frequent pipeline breakages.

Drinking water research in the United States has been driven for the past two decades by the Safe Drinking Water Act (SDWA) (see http://www.epa.gov/safewater/sdwa/index.html). In the SDWA, passed in 1974 and amended in 1986 and 1996, the US Congress mandated the US EPA to regulate contaminants in drinking water which might be a risk to human health. To achieve this mandate, the US EPA establishes maximum contaminant level goals, below which there is no known or expected risk to health, and maximum contaminant levels which are the legally enforceable standards for drinking water.

To date, the US-EPA has published National Primary Drinking Water Regulations (NPDWR) (see http://www.epa.gov/safewater/mcl.html) which include 53 organic compounds, 16 inorganic compounds, 4 classes of radionuclides, 4 types of disinfection byproducts, 3 disinfectants, *Cryptosporidium, Giardia lamblia, Legionella, viruses*, heterotrophic plate counts, turbidity, and total coliform (including fecal coliform and *E. coli*). Research in the US has been largely directed by the US EPA's need to update the NPDWR to meet the goal of the SDWA.

To this end, the US EPA publishes its Contaminant Candidate List (CCL). Now into its second iteration (CCL2), the list currently includes 42 chemical and 9 microbiological contaminants. These chemical and microbial contaminants have been identified as both likely to be present in drinking water and likely to pose human health risks. In terms of the chemicals, extensive toxicity assessments, and risks of exposure through drinking water are characterized to the degree that current methodologies allow. In terms of microbes, much of the focus is on detection methods. Microbial contaminants listed on the CCL2 list are:

- Viruses - Adenoviruses, Caliciviruses, Coxsackieviruses, Echoviruses
- Bacteria - *Aeromonas hydrophila*, *Helicobacter pylori*, *Mycobacterium avium intracellulare* (MAC), Cyanobacteria and their toxins
- Protozoa - *Microsporidia* (*Enterocytozoon* and *Septata*)
- Algae - freshwater algae and their toxins

With the possible exception of *A. hydrophila*, the US EPA is still a long way from regulating these organisms, primarily because accurate detection methods are not available.

The area of research which poses the most interesting questions is the survival and, in some cases, proliferation of pathogens in drinking water. To this end, work has focused on how biofilms provide a protective environment for pathogens such as *M. avium* Complex, *H. pylori*, *Pseudomonas aeruginosa* and *E. coli* O157-H7. Both proteomic and genomic methods are being used to examine gene expression in response to the biofilm mode of growth.

In reference to the CCL2, research focus over the past few years has been on the environmental mycobacteria, and in particular the *Mycobacterium avium* Complex group.

An extensive exposure assessment study was conducted in four different municipalities in Massachusetts (Boston, Cambridge, Lowell and Duxbury) (Prommasith *et al.* 2004). The data are still being analyzed, but to date, both cold water (e.g., drinking water, toilet flushing) and hot water (e.g., showering and bathing) appear to be major exposure routes with the predominance of *M. avium* subspecies *intracellulare* in cold water and *M. avium* subspecies *avium* in both hot and cold water.

From testing the efficacy of biocides to interspecies gene transfer, many in the drinking water field believe that the biofilm mode of growth is far more representative of the drinking water system than growth in suspension. A number of methods have been investigated to both simulate drinking water systems on the laboratory bench and to directly measure mycobacteria within a water system by inserting coupons into a bypass. Figure 5 is a schematic of the bypass system currently plumbed into the re-circulating hot water system of the Cooley Microbiological Laboratories at MSU (Karmacharya *et al.* 2004).

A number of different analyses are possible using a system like the one shown in Figure 5. Coupons can be removed from the system over a designated time course and analyzed in a number of different ways:

(1) Presence of MAC can be determined by a decontamination step followed by direct plating onto a selective media (reviewed in Stinear *et al.* 2004).
(2) Isolates of MAC, or even crude DNA extracts from the biofilm itself can be further typed by analysis for specific genetic markers such as the insertion sequence IS1245 or heat shock protein hsp 65. Restriction fragment patterns of these markers can then be used to identify specific species (Stinear *et al.* 2004).
(3) Biofilms can be imaged directly using confocal microscopy or other techniques such as cryosectioning and antibody staining (e.g., Figure 6). In the example shown in figure 6, it is interesting how different species may communicate to provide a biofilm structure which appears to select for a predominance of MAC at the substratum/biofilm interface. Recent work suggests that signal molecules may be important in MAC biofilm formation (Geier and Ford 2005).

In summary, key areas for research and training are:

- Methods for CCL organisms
- Proteomics and genomics approaches to better understand pathogen survival

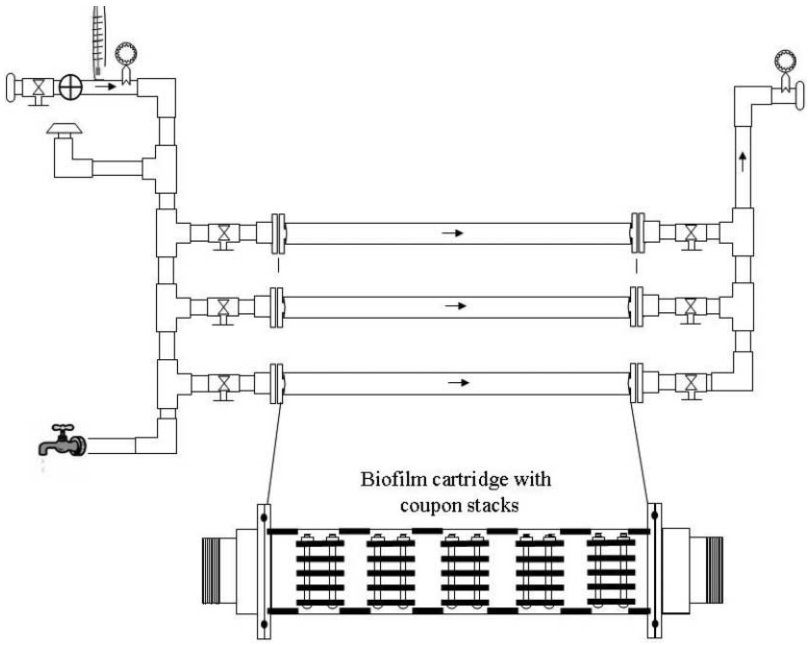

Figure 5 | Schematic of the by-pass system built in to the Microbiology Laboratories hot water system at MSU (picture courtesy of Anand Patel, USC and Patel *et al.* 2002).

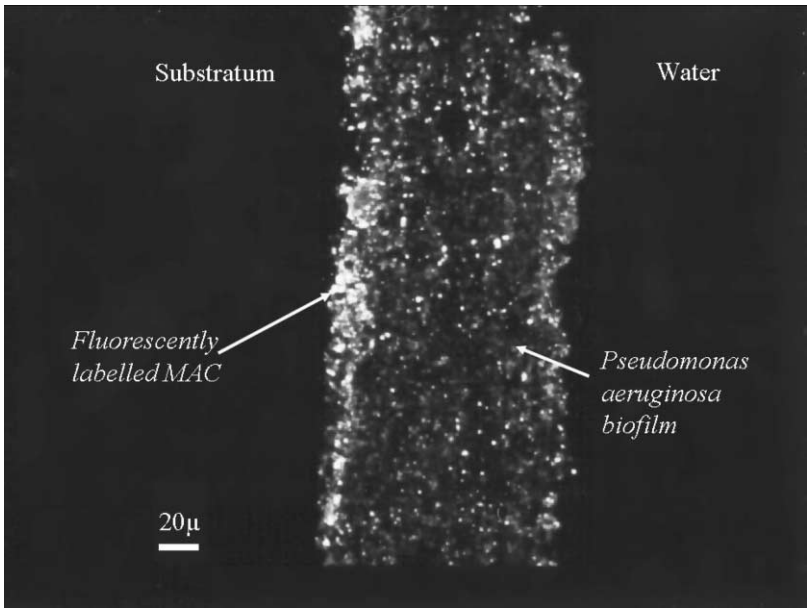

Figure 6 | Cryosection of a dual species biofilm of *Pseudomonas aeruginosa* and *Mycobacterium avium* grown in a laboratory recirculation system. *M. avium* is stained with a fluorescently labeled antibody to lipoarabinomannan. Reproduced with permission from *Enviromental Health Perspectives* (Ford 1999).

- Piping materials
- Health consequences from Disinfection by-products (DBPs)
- Disinfection alternatives
- Biofilm analyses (including cell to cell signaling)

CONCLUSION

A recent International Colloquium on Protecting Public Health in Small Water Systems (http://water.montana.edu/colloquium/)held in Bozeman, MT in May 2004 concluded the following priority lists:

- Training:

An opportunity may exist to develop and promote training modules for small water systems. Many waterborne disease outbreaks, including Walkerton, Ontario (where over a thousand people were sickened and seven people died) could be attributed to poor operator training (Hrudey & Hrudey 2004).

- Surveillance:

There is an enormous need and opportunity for physician and other health provider education. Although long recognized by the public health community, the medical community is still largely focused on individual rather than population health. The medical community provides, however, the critical first step of recognition in an effective surveillance system.

- Health linkage and data integration:

With multiple routes of exposure to most pathogens (and chemicals), more effective tools are needed to link a specific exposure pathway with disease. There is room for more integration between public utilities and health services. Computer-based tools which can rapidly link water quality parameters (or climate information) with health databases need to be developed.

- Risk communication and culture:

Training modules in risk communication could be developed which take into account cultural differences or are targeted at specific rural or ethnic groups.

- Development of corrosion and biofilm resistant piping materials, chlorine alternatives and sustainable chemical-free treatments:

There are clear opportunities for materials and chemicals research.

- Simple, fast, cheap detection methods:

Methods for a variety of parameters were discussed and include: biofilm monitors, TOC tests, and tests for algal toxins.

- Cheaper technologies:

Cheaper technologies were discussed and in particular membrane technologies with an emphasis on remote monitoring and control.

The full text of the report from this colloquium can be found at http://water.montana.edu/colloquium/products/colloquium_report_final.pdf

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